First Committee Meeting Summary

Application number: BLA STN 125742.0
Product name: COVID-19 mRNA Vaccine (COMIRNATY)
Proposed Indication: Active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals ≥16 years of age
Applicant: BioNTech Manufacturing GmbH
Meeting date & time: June 3, 2021; 4:00PM - 5:30PM EDT
Committee Chair: Ramachandra Naik, Ph.D.
Meeting Recorders: CAPT Michael Smith, Ph.D. and Laura Gottschalk, Ph.D.

Table 1: Review Committee (attendees are listed in bold font)

Review responsibility	Committee Member	Team Leader / Supervisor(s)	Division Director
Chairperson	**Ramachandra Naik,** PhD	TL: **Kirk Prutzman,** PhD BC: **Elizabeth Sutkowski**, PhD	DD: **Loris McVittie**, PhD SA: **Kirk Prutzman,** PhD (acting)
Regulatory Project Managers	**CAPT Mike Smith,** PhD **Laura Gottschalk,** PhD	TL: **Kirk Prutzman,** PhD BC: **Elizabeth Sutkowski,** PhD	DD: **Loris McVittie,** PhD SA: **Kirk Prutzman,** PhD (acting)
Clinical	**Susan Wollersheim,** MD **CAPT Ann Schwartz,** MD	TL: **Lucia Lee,** MD BC: **Maria Allende,** MD	DD: **Doran Fink,** MD, PhD
Product (CMC) DVP Regulatory coordinator, DVP Product Specialist	**Haruhiko Murata,** MD, PhD **Xiao Wang,** PhD **Anissa Cheung,** MSc	BC: **Keith Peden,** PhD BC: **Keith Peden,** PhD	DD: **Jerry Weir,** PhD DDD: **Robin Levis,** PhD
DS and DP release assays DS and DP release assays DS and DP release assays DS and DP release assays DS and DP release assays LRP and Testing Plan Dev.	**Hsiaoling Wang,** PhD **Emnet Yitbarek,** PhD **Karla Garcia,** MS **Anil Choudhary,** PhD, MBA **Esmeralda Alvarado,** PhD **Marie Anderson,** PhD	TL: **Tao Pan,** PhD TL: **Tao Pan,** PhD BC: **CDR James Kenney,** DSc BC: Muhammad Shahabuddin, PhD BC: Muhammad Shahabuddin, PhD **Maryna Eichelberger,** PhD	DD: **Maryna Eichelberger,** PhD DDD: N/A
Toxicology	Nabil Al-Humadi, PhD	BC: Martin Green, PhD	DD: **Doran Fink,** MD, PhD
Statistics, both Clinical data & assays	**Lei Huang,** PhD	BC: **Tsai-Lien Lin**, PhD	DD: **John Scott**, PhD DDD: Shiowjen Lee, PhD
Epidemiology/ Pharmacovigilance	**Deborah Thompson,** MD, MSPH	TL: LCDR Jane Baumblatt, MD BC: **Manette Niu,** MD	DD: Narayan Nair, MD DDD: Meghna Alimchandani, MD
DMPQ Reviewer/Inspector DMPQ Reviewer/Inspector DMPQ Reviewer DMPQ Inspector DMPQ Inspector DMPQ Inspector Lot Release DMPQ RPM	**Kathleen Jones,** PhD **Laura Fontan**, PhD **Gregory Price,** PhD **Zhongren Wu,** PhD **CDR Donald Ertel**, MS **Ekaterina Allen**, PhD **Cheryl Hulme** **Iryna Zubkova,** PhD	TL: **Nicole Li** BC: **Lori Peters,** MS TL: **CDR Donald Ertel**, MS BC: **Lori Peters**, MS BC: Anthony Lorenzo BC: **Joseph Quander** BC: James Crim	DD: **John Eltermann,** RPh, MS DDD: **Carolyn Renshaw**
BIMO	**Haecin Chun,** MT(ASCP)SBB, MS	BC: **Dennis Cato**	DD: **Carrie Mampilly,** MPH
APLB Labeling reviewer	**CDR Oluchi Elekwachi,** PharmD, MPH **Dana Jones**	BC: **Lisa Stockbridge,** PhD	DD: Robert Sausville
Container Labeling	**Daphne Stewart**	BC: Timothy Nelle, PhD	DD: **Loris McVittie**, PhD
Electronic integrity	CDR David Schwab, MSIS	**Loris McVittie**, PhD	DD: **Loris McVittie,** PhD
CDISC consult	**Brenda Baldwin,** PhD **Kirk Prutzman,** PhD	BC: **Elizabeth Sutkowski,** PhD	DD: **Loris McVittie,** PhD

Other attendees that were not listed in the review committee table: Maureen Hess, Leslie Taylor, Laura Montague, Konstantin Vernik, Cassandra Overking, David Cho, Varsha Garnepudi, Hector Izurieta, Jeff Roberts, Joseph Kulinski, Nicki DeVore, Douglas Pratt, Sara Gagneten, David Rouse, Sudhakar Agnihothram, Tatiana ClarodaSilva, Swati Verma and Nadine Kaelber

Review Timetable (PDUFA Milestones are in blue)

Review Milestone	**Target Due Date**
Submitted	
Roll 1 Submission:	06-MAY-2021
Roll 2 Submission (final):	18-MAY-2021
Received:	18-MAY-2021
Committee Assignment:	09-JUN-2021
First Committee Meeting:	03-JUN-2021
Proper name designation:	08-JUN-2021
Filing checklist/reviews complete:	23-JUN-2021
Filing Meeting:	29-JUN-2021
Filing Action:	16-JUL-2021
Deficiencies Identified:	31-JUL-2021
Initial proprietary name review:	16-AUG-2021
Primary Draft Reviews & Reviewer Reports Due (4 days prior to Mid-Cycle meeting):	25-AUG-2021
Mid-Cycle Meeting (Internal):	31-AUG-2021
Mid-Cycle Communication:	13-SEP-2021
Final draft primary reviews with supervisory Concurrence (upload not required):	01-SEP-2021
PLI Inspections completed:	30-JUL-2021
BiMO Inspections completed:	30-JUL-2021
PeRC briefing materials due to PeRC:	27-JUL-2021
PeRC Meeting:	10-AUG-2021
Final reviews & addenda signed & uploaded:	15-SEP-2021
Lot release protocol & testing plan finalized:	30-AUG-2021
Notify OCOD of pending approval:	30-AUG-2021
Draft SBRA	30-AUG-2021
Labeling Comments to Applicant:	30-AUG-2021
Notify Applicant of PMC/PMR:	30-AUG-2021
Targeted Action Due Date (ADD)	**30-SEP-2021**
PDUFA ADD:	**16-JAN-2022**

Table 2: Scheduled Meetings

PDUFA Meetings:
• **First Committee Meeting:** June 3, 2021, 4:00PM – 5:30PM
• **Filing Meeting:** June 29, 2021, 2:00PM – 3:30PM

• **Internal Mid-Cycle:** August 31, 2021, 2:00PM – 3:30PM
• **Mid-Cycle Communication:** September 13, 2021, 3:00PM – 4:00PM
Monthly Committee Meetings:
• July 15, 2021, 3:30PM – 5:00PM
• August 9, 2021, 1:30PM – 3:00PM
• September 10, 2021, 12:30PM – 2:00PM
Labeling Meetings:
• August 4, 2021, 3:00PM – 5:00PM
• August 6, 2021, 3:00PM – 5:00PM
• August 11, 2021, 3:00PM – 5:00PM
• August 16, 2021, 11:00AM – 12:30PM (Carton & Container)
• August 18, 2021, 3:30PM – 5:00PM (Carton & Container)
• September 2, 2021, 4:00PM – 5:30PM
• September 7, 2021, 2:00PM – 4:00PM
• September 21, 2021, 3:00PM – 5:00PM

Background and Purpose:
This meeting was to discuss the new original BLA (STN 125742/0) from BioNTech Manufacturing GmbH (in partnership with Pfizer, Inc.) for COVID-19 mRNA Vaccine (COMIRNATY, pronounced “koh-MER nah-tee”), for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals ≥16 years of age. This is a Rolling BLA submission, so it will be handled in RMS-BLA, not eMRP. The first roll containing eCTD sections 2, 4, and 5 was submitted and received on May 6, 2021. The second and final roll containing eCTD Section 3 (and the rest of Section 1 items) was submitted and received on May 18, 2021.

The purpose of this First Committee Meeting was to discuss the milestones, roles and responsibilities of each member of the review team.

Discussion Summary:

The Chair provided a brief overview of the submission and highlighted several important points for the review of the BLA.

- A table of the full review committee and their corresponding team leaders, managers and directors, was included in the agenda for the meeting. The review committee was asked to review it and let the regulatory review team know if anything needs to be corrected.

- The submission is an 8-month Priority Review BLA with a PDUFA Action Due Date (ADD) of January 16, 2022. However, the targeted ADD is September 30, 2021.

- The Chair summarized the review milestones (as shown on page 2).

- A Late Cycle Meeting (LCM) will likely not take place since the PDUFA deadline for the LCM is November 1, 2021, and this is after the Target Action Due Date of September 30, 2021.

- In an effort to reduce the burden for reviewers, the Chair questioned whether Filing Checklists should be completed for this submission. Management said that they will check with CBER IOD about the requirement for Filing Checklists and let the review team know.

- It was confirmed that an Advisory Committee Meeting will not be needed for the BLA since five Advisory Committee Meetings would have occurred from October 22, 2020 to June 10, 2021 to discuss the development, Emergency Use Authorization and licensure of COVID-19 vaccines.

- The Chair asked about the best method for the review team to provide regular status updates to Management. Management will discuss this internally and will provide an answer to the review team soon.

- The Chair announced that an internal meeting is scheduled for Friday, June 4, 2021, with the DVP and DBSQC teams to discuss tests that will be part of the lot release protocol and in-support testing.

Updates from Discipline Reviewers:

1. Chair (Ramachandra Naik):

    - See discussion summary above.

2. Clinical (Susan Wollersheim and Ann Schwartz):

    - The clinical reviewers have found the review to be more burdensome than expected since much of the clinical information is referenced from the prior IND and EUA, plus the clinical information was not well organized and a summary document would be helpful. They will discuss internally to see if there is something that can be requested from the Applicant that can aid them in their review, including potentially having a teleconference with the Applicant. The clinical team thought they will likely have a safety data information request, but they were going to discuss with the statistical team first.

3. CMC (Haruhiko Murata and Xiao Wang):

    - No issues have been identified.

4. DBSQC (Hsiaoling Wang, Emnet Yitbarek, Karla Garcia, Anil Choudhary, Esmeralda Alvarado and Marie Anderson):

    - No issues have been identified. However, the Lot Release Protocol appears to be missing and an information request will be sent to the Applicant to request this document.

5. Toxicology (Nabil Al-Humadi):

    - Dr. Green informed the regulatory team prior to the meeting that the toxicology team will not be able to attend the meeting, but no issues have been identified and there should be no problem making the deadlines.

6. Statistics (Lei Huang):

    - No issues have been identified.

7. Epidemiology/Pharmacovigilance (Deborah Thompson):

    - The reviewer noted that a pregnancy registry was mentioned in the submission, and it will need to be determined if it will be considered a PMC.

8. DMPQ (Kathleen Jones, Laura Fontan, Gregory Price, Zhongren Wu, Donald Ertel, Ekaterina Allen, Cheryl Hulme and Iryna Zubkova):

    - No issues have been identified and inspections for Wyeth BioPharma Division of Wyeth Pharmaceuticals LLC (FEI: 1222181, referred to as Pfizer, Andover) and Pfizer Manufacturing Belgium NV (FEI: 100654629, referred to as Pfizer, Puurs) sites are tentatively being planned for July 19th – 23rd and June 24th - July 2nd, respectively. They are waiting on the EIR from the Pharmacia & Upjohn Company (FEI: 1810189, referred to as Pfizer, Kalamazoo) site that was issued by TeamBio to see if the inspection can be waived since the site was recently inspected (May 11-20, 2021).

9. BiMO (Haecin Chun):

    - BiMO is not planning on issuing any more inspections since inspections of 10 study sites were already conducted under the IND and EUA, under 2 protocols. The BiMO team stated that the inspections that occurred under the IND and EUA did not inspect data integrity because there wasn't anything to inspect at the time. However, if the clinical and statistical reviewers encounter issues relevant to data integrity, BIMO should be made aware as soon as possible so that arrangements for inspections can be made. Lastly, the BiMO team noted that the agenda for this meeting included a BiMO inspections completed milestone of July 30, 2021, and

they mentioned that this is not feasible and too early in the review cycle if inspections were to be assigned.

10. APLB (Oluchi Elekwachi):

    - No issues have been identified and the propriety name review will be similar to what was submitted under the IND.

11. Container Labeling (Daphne Stewart):

    - The reviewer noted that she will have a few minor comments on the carton and container labels early next week.

12. CDISC (Brenda Baldwin and Kirk Prutzman):

    - Dataset validation will not be done for this BLA. The included datasets are the same as those in the EUA amendment for adolescents 12 through 15 years of age, which were validated during the review of the EUA amendment.

Action Items:

- Management
  - Find out if Filing Checklists will be required.
  - Determine the best method for the review team to keep management apprised of the review progress.
- Clinical
  - Determine, as soon as possible, if there are issues that will prevent the review from being completed on time and keep management informed on what is decided.

Post-meeting updates:

- CBER IOD informed the regulatory team that discipline reviewer checklists do not need to be completed for this BLA. The reviewers were informed of this decision on June 7, 2021 and encouraged to refer to the checklists for guidance during the review of the BLA. The RPM filing checklist will be completed and uploaded to RMS-BLA/EDR.

Explanation of Milestones

First Committee Meeting: Committee must meet by this date to discuss the review of the BLA.

Filing Meeting: Meeting at which the review committee determines whether the BLA can be filed. Reviewers must determine whether the information included in the BLA is sufficient to allow the reviewer to conduct an adequate review. The purpose is not

	to determine the acceptability of the data but rather to determine whether the appropriate information was submitted to allow the reviewer to conduct a meaningful review.
Filing Action:	Date by which a filing letter (either accepting or refusing to file the BLA) must be issued.
Deficiencies Identified:	Date by which a letter must be issued in which review issues identified to date are conveyed to the applicant.
Mid-cycle Meeting:	Meeting at which each reviewer is expected to document their review progress and discuss the relevant content of the submission and present an overview. A draft review memorandum identifying key issues should be completed by the time of the meeting. First line supervisors for each review discipline as well as the Director and Deputy Director for DVRPA and OVRR, or their representative, should attend the meeting.
Action Due Date:	Date by which final action regarding the BLA must be conveyed to the applicant (issue Approval or Complete Response letter, depending on review decision). All review memos, regardless of the Action being taken, must be signed and uploaded to the EDR prior to the date of Action.

Explanation of Roles and Responsibilities (See CBER SOPP 8401 for more detail)

- Chair – Manages the administrative processing of reviews and ensures the regulatory and scientific content of submissions and their reviews are appropriate.
- Director and/or Deputy Director – the Signatory Authority who signs action letters and is responsible for content of reviews.
- Regulatory Project Manager (RPM) – Manages the review of submissions, including reviewing assigned portions, performing quality control checks, capturing review committee communications, and ensures that the review and review file is administratively complete. The RPM(s) works in tandem with the Chair to ensure that amendments are disseminated to the appropriate reviewers and that a meaningful short summary is entered into eMRP. Throughout the review cycle, the RPM ensures that all FDA documents are uploaded into the EDR as they are generated, and the documentation review memo is maintained in real-time.
- Review Committee – Perform review of all assigned areas of submissions, participate in review meetings, and perform and document a review of the submission that is scientifically sound and follows Good Review Management Principles. Documentation of a discipline review may be in the form of a

primary review, discipline review letter, and a review addendum. It is imperative that the review committee endeavor to follow the review timetable and finish reviews in a timely manner to allow for adequate supervisory review. It is critical that the review committee keeps management, including senior management, abreast of any significant review issues.

- Supervisors – Ensure the overall content of reviews are appropriate, all administrative processing steps are being completed, including database data entry, and all deadlines are met. Reviews and approves employees' review memorandums and other submission documents per CBER policies and procedures. Supervisory review is considered the Secondary Review.

Documentation of Review

Each discipline reviewer is expected to prepare a written review documenting their review of the file. Timely submissions are imperative to allow time for adequate management review. The following is recommended:

- Identify all materials assigned for review and include an executive summary in each final or complete review memo.
- List and summarize all material reviewed. The summary should identify each amendment reviewed and include a list of the submission dates, sections and page numbers etc., as applicable.
- A list of questions communicated to the applicant, in letter-ready format, along with the responses received and reviewed should be clearly identified.
- A recommendation for action, approval or CR, based upon the review summary should be clearly stated.
- Draft reviews should be prepared and discussed with the reviewer's supervisor and a copy should be given to the Chair by the draft due date(s). Draft reviews should not be uploaded to the EDR.
- Reviewer's and supervisor's electronic signatures should be placed on the final PDF version of the review. A Word version should be attached, and the PDF should be certified and locked to prevent modification. The review should be entered into eMRP using the date of the Reviewer's approval stamp as the date of the memo and the certified PDF should be uploaded into the EDR.
- If a Complete Response (CR) Letter is issued, a complete written review is expected and should reflect all amendments that have been reviewed through the date of the CR decision. The final signed and certified PDF version of the review should be uploaded by the date of the CR action.

Communication Plan

We can communicate with the applicant via several methods such as telecon, secure e-mail, and letter. The following is recommended:

- All communication regarding requests for information or advice for the applicant will be coordinated by the RPMs and communicated either via telecon or secure email. Please contact **Ramachandra Naik** (Chair), **Mike Smith** and **Laura Gottschalk** (RPMs) if you need to communicate with the applicant.

- Although every effort should be made to include the RPMs and/or Chair when communicating with the applicant, in rare instances it may be appropriate, with permission from Ramachandra Naik and/or Laura Gottschalk and Mike Smith, to communicate some requests for information (e.g., something that is relatively simple) to the applicant via a telecon. Please ensure that all such communication is formally documented (i.e., write up a telecon memo and send it to the RPMs to include in the file).
- Formal telecons with the applicant can be scheduled to address issues for which a direct discussion is helpful. The RPMs will coordinate this if/when it is needed.
- Letters can also be used to communicate review issues to the applicant. Although both secure e-mail and letters provide the necessary documentation for the file, letters are a more formal process than secure e-mail (letters must go through more levels of supervisory review and concurrence) so typically letters are reserved for communication of policy or serious review issues.
- Please “cc” the Chair on significant e-mail communication and meetings (internal and external). It is helpful for the Chair to have a general overview of the review status and review issues in the various disciplines (allows for more effective communication with internal upper level management and the applicant when necessary).
- Supervisory concurrence will be sought, when appropriate, prior to sending communications to the applicant (e.g., memos with request for information, providing advice, etc.).

U.S. FOOD & DRUG ADMINISTRATION

Date: June 17, 2021

From: Christopher Joneckis, Associate Director For Review Management

Subject: Issuance of BLA License Number in Advance of Approval

To: STN 125742, COVID-19 mRNA Vaccine

I am authorizing release of the BLA license number for Pfizer/ BioNtech Covid vaccine in advance of the typical notification in the approval letter. A significant consideration in this decision is that this product has been authorized under an Emergency Use Authorization, and therefore CBER is familiar with and has reviewed much of the information provided in the BLA application. This deviation from our normal practice is done to facilitate product labeling and distribution and is consistent with other Center practices to facilitate vaccine delivery during the declared Public Health Emergency. When providing the license number, we should communicate that this license number does not constitute any determination by FDA on the application.

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20903
www.fda.gov

FILING MEETING SUMMARY

Application number: BLA STN 125742/0
Product name: COVID-19 mRNA Vaccine (COMIRNATY)
Proposed Indication: Active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older
Applicant: BioNTech Manufacturing GmbH
Meeting date & time: June 29, 2021; 2:00 - 3:30 PM EDT
Committee Chair: Ramachandra Naik, Ph.D.
Meeting Recorders: CAPT Michael Smith, Ph.D. and Laura Gottschalk, Ph.D.

Ramachandra Naik -S
Digitally signed by Ramachandra Naik -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2001232361, cn=Ramachandra Naik -S
Date: 2021.07.26 10:58:23 -04'00'

Background:
This meeting was to discuss the new original BLA (STN 125742/0) from BioNTech Manufacturing GmbH (in partnership with Pfizer, Inc.) for COVID-19 mRNA Vaccine, for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older. This is a Rolling BLA submission. The first roll containing eCTD sections 2, 4, and 5 was submitted and received on May 6, 2021. The second and final roll containing eCTD Section 3 (and the rest of Section 1 items) was submitted and received on May 18, 2021. As agreed during the Pre-BLA interaction, the COVID-19 case strain sequencing report was submitted on June 7, 2021.

The purpose of this meeting was to discuss 1) the completeness of the BLA submission and 2) whether it is acceptable to be filed.

Table 1: Review Committee and Discipline Filing Decision Summary

Discipline/Organization	Name	Attended meeting	Fileable	RTF	Deficiencies Identified
Regulatory Project Managers (RPM)	CAPT Michael Smith, PhD Laura Gottschalk, PhD	✓ ✓	✓		
Chair	Ramachandra Naik, PhD	✓	✓		
Division Director - Clinical	Doran Fink, MD, PhD	✓	✓		
Division Director/Deputy (Acting) – Regulatory	Loris McVittie, PhD/ Kirk Prutzman, PhD	✓	✓		
Office Director/Deputy	Marion Gruber, PhD/ Philip Krause, MD, PhD	✓ ✓	✓		
Clinical Reviewers	Susan Wollersheim, MD CAPT Ann Schwartz, MD	✓ ✓	✓		
Toxicology Reviewer	Nabil Al-Humadi, PhD	✓	✓		
CMC Reviewers	Xiao Wang, PhD Anissa Cheung, MSc	✓	✓		

Discipline/Organization	Name	Attended meeting	Fileable	RTF	Deficiencies Identified
OCBQ/DMPQ Reviewers	Kathleen Jones, PhD Laura Fontan, PhD Gregory Price, PhD Zhongren Wu, PhD CDR Donald Ertel, MS Ekaterina Allen, PhD Cheryl Hulme Iryna Zubkova, PhD	✓ ✓ ✓	✓		
OCBQ/APLB Reviewers	CDR Oluchi Elekwachi, PharmD, MPH Dana Jones (Back up)	✓	✓		
OCBQ/BIMO Reviewer	Haecin Chun, MT (ASCP) SSB, MS	✓	✓		
OCBQ/DBSQC Reviewers	Hsiaoling Wang, PhD Emnet Yitbarek, PhD Karla Garcia, MS Anil Choudhary, PhD, MBA Esmeralda Alvarado, PhD Marie Anderson, PhD	 ✓ ✓ ✓ ✓	✓		
Statistical Reviewer of clinical and nonclinical data	Lei Huang, PhD	✓	✓		
Postmarketing Safety Epidemiological/ Pharmacovigilance Reviewer	Deborah Thompson, MD, MSPH	✓	✓		
Labeling Reviewer	Daphne Stewart	✓	✓		
CDISC Consult	Brenda Baldwin, PhD Kirk Prutzman, PhD		✓		

Other Attendees:
Maria Allende, Nicolette Devore, Maryna Eichelberger, John Eltermann, Karen Farizo, Theresa Finn, Sara Gagneten, Varsha Garnepudi, Dave Green, Marion Gruber, Hector Izurieta, Philip Krause, Lucia Lee, Robin Levis, Nicole Li, Carrie Mampilly, Narayan Nair, Manette Niu, Tim Nelle, Cassandra Overking, Tao Pan, Keith Peden, Lori Peters, Douglas Pratt, Joseph Quander, Carolyn Renshaw, Jeff Roberts, David Rouse, Muhammad Shahabuddin, Lisa Stockbridge, Elizabeth Sutkowski, Swati Verma and Jerry Weir

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DISCUSSION SUMMARY

The Chair highlighted updates that had taken place since the First Committee Meeting:

1. **No Filing Checklists are required**
   - ADRM agreed that the discipline reviewers don't need to complete the filing checklists for this BLA. However, the discipline reviewers were reminded to refer to the filing checklists to initiate the process and look for special items that should be included in the submission.
   - This exception to policy, not requiring filing checklists, is intended to help facilitate the expedient review of the application, but in no way alleviates reviewers from performing their due diligence to ensure that the application is complete for the purposes of filing.
   - Normally, major issues or IRs being drafted will be listed in Filing Checklists. However, as this is the Priority Review BLA with the short review timeline, the reviewers have already started sending IRs and inspecting the vaccine manufacturing facilities (see below for additional details).

2. **BLA License Number generated in advance of approval**
   - The Applicant requested a US License Number for BioNTech Manufacturing GmbH with agreement that they will not use it until after the BLA is approved.
   - Dr. Joneckis wrote a memo to the file authorizing release of the BLA license number in advance of the typical notification in the approval letter.
   - RIMS generated the license number which will be provided to the Applicant, after filing, in an email message.

3. **PeRC meeting is scheduled for August 10, 2021**

UPDATES FROM REVIEW DISCIPLINES:

1. **Chair** (Ram Naik):
   - See discussion summary above.

2. **Regulatory Project Managers** (Mike Smith and Laura Gottschalk):
   - The RPMs summarized the IRs and Amendments to the BLA to date (please see details at end of document).

- The BLA is fileable.
- To ensure the regulatory items were covered in the submission, the RPM Checklist was completed and will be uploaded to the file.

3. **Clinical** (Susan Wollersheim and Ann Schwartz):
    - The BLA is fileable and the clinical reviewers agree with the Priority Review designation.

4. **CMC** (Xiao Wang):
    - The BLA is fileable and no major issues have been identified that warrant discussion.
    - The CMC reviewer noted that she used the Filing Checklist during her review and no major deficiencies were identified.
    - A list of clarification Information Requests is being generated for the Applicant.

5. **DBSQC** (Hsiaoling Wang, Emnet Yitbarek, Karla Garcia, Anil Choudhary, Esmeralda Alvarado and Marie Anderson):
    - The BLA is fileable.

6. **Toxicology** (Nabil Al-Humadi):
    - The BLA is fileable.

7. **Statistics** (Lei Huang):
    - The BLA is fileable.

8. **Epidemiology/Pharmacovigilance** (Deborah Thompson):
    - The BLA is fileable.

9. **DMPQ** (Kathleen Jones, Laura Fontan, Gregory Price, Zhongren Wu, Donald Ertel, Ekaterina Allen, Cheryl Hulme and Iryna Zubkova):
    - The BLA is fileable.
    - Laura Fontan is currently in Belgium carrying out inspections of the Pfizer, Puurs facilities.
    - There will most likely be a waiver for inspections of the Pfizer, Kalamazoo site.
    - Kathleen Jones will be leading the inspections of the Pfizer, Andover site scheduled for July 19-23, 2021.

10. **BiMO** (Haecin Chun):
    - The BLA is fileable.
    - At this time, they are not planning on issuing inspections in support of this BLA (inspections of 9 clinical sites were conducted for Protocol C4590001 under the IND/EUA).

11. **APLB** (Oluchi Elekwachi):
    - The BLA is fileable.

12. **Container Labeling** (Daphne Stewart):
    - The BLA is fileable.
    - The labeling reviewer is finalizing an IR.

13. **CDISC** (Brenda Baldwin and Kirk Prutzman):
    - The BLA is fileable.
    - As previously noted, the datasets submitted with this BLA will not be validated since they were already validated under an amendment to EUA 27034.

UPDATES FROM MANAGEMENT:

1. **Advisory Committee Meeting**
    - The Office Director confirmed that, unless a significant new safety concern or other important issue is discovered during the review of the submission that would necessitate convening the VRBPAC, an Advisory Committee Meeting will not be needed for this BLA.

2. **Regular Updates to Management on Review Progress**
    - The Office Director noted that at this time, review progress updates provided during the Monthly Review Committee Meetings would suffice. This plan can be revisited during August and September to determine if more frequent updates to Managers should be provided.

REGULATORY CONCLUSIONS / DEFICIENCIES:

1. **Does the application, on its face, appear to be suitable for filing or is the application unsuitable for filing and require an RTF letter?**
   The application appears to be suitable for filing.

2. **If fileable, list any substantive deficiencies or issues that have significant impact on the ability to complete the review or approve the application**:
   No substantive deficiencies or issues have been identified that would have a significant impact on the ability to complete the review or approve the application.

3. **If RTF, list any substantive deficiencies or issues that would make this application unsuitable for filing:**
   NA

FILING MEETING DISCUSSION, IF FILED:

4. **Indicate any comments on the status of the proprietary name review (PNR).**
   The IND PNR memo for COMIRNATY was completed on November 9, 2020 and the decision was communicated to the Sponsor on November 20, 2020. The BLA PNR review memo is being finalized.

5. **Indicate whether the product sh/would be subject to lot release, surveillance, or exempt from lot release. Verify sample availability.**
   The product is subject to lot release. DBSQC's request for Lot Release Protocol, samples and reagents, was sent to the Applicant on June 25, 2021.

6. **Confirm review schedule for the application. If priority review, include justification from clinical reviewer filing review checklist. [Standard Review, Priority Review, or Expedited Review]**
   The review schedule for this BLA submission is an 8-month Priority Review with a PDUFA Action Due Date (ADD) of January 16, 2022. However, the targeted expedited ADD is September 30, 2021. The review timeline may be revised to address public health needs and as feasible. (See Review Timetable above for dates)

7. **Indicate the decision regarding the need for an Advisory Committee.**
   At this time, an Advisory Committee Meeting will not be needed for the BLA. Five Advisory Committee Meetings have occurred from October 22, 2020 to June 10, 2021 to discuss the development, Emergency Use Authorization and licensure of COVID-19 vaccines.

8. **Indicate whether the submission triggers PREA. If yes, a PeRC meeting is needed. Verify whether the applicant has an initial pediatric study plan (iPSP) in place.**
   The submission triggers PREA because it contains a new active ingredient, and a meeting with PeRC has been scheduled for August 10, 2021. The Applicant has an iPSP in place.

9. **Indicate whether the submission contains a proposed REMS. If yes, or if a REMS may be needed as a condition of approval, schedule an internal REMS meeting between the Product Office and OBE/DE.**
   The submission does not contain a proposed REMS.

10. **Is a comprehensive and readily located list of all clinical sites included or referenced in the application?**
    A comprehensive and readily located list of all clinical sites is included in the application.

11. **Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application?**
    A comprehensive and readily located list of all manufacturing facilities is included in the application.

12. **Indicate any updates since the First Committee Meeting on pre-license inspection, pre-approval inspection, or BIMO sites requiring inspections (Is the establishment(s) ready for inspection?)**
    See updates from the DMPQ reviewers above.

BIMO is not issuing any inspections under this BLA; see updates from the BIMO reviewer above.

13. **If the application is affected by the Application Integrity Policy (AIP), has the division made a recommendation regarding whether an exception to the AIP should be granted to permit review based on medical necessity or public health significance?**
The application is not affected by the AIP.

14. **Is the product an Original Biological Product or a New Molecular Entity (NME) for an NDA?**
The product is an Original Biological Product.

FOR APPLICATIONS IN THE PDUFA PROGRAM (NME NDAs/Original BLAs), IF FILED:

15. **Confirm that any late submission components were submitted within 30 days. List any late submission components that arrived after 30 days.**
As agreed, a strain sequence analysis report for all COVID-19 cases was submitted in amendment 5 (sequence 0006) dated June 7, 2021. There were no late submission components that arrived after 30 days.

16. **Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components?**
The application was complete upon submission.

ADMINISTRATIVE DETAILS, IF FILED:

17. **Review the Milestone Schedule and indicate if there are any issues with the schedule. Note: This is a confirmation to capture any changes made since the First Committee Meeting.**
No changes have occurred in the Milestone Schedule since the First Committee Meeting. Please see Review Timetable above.

INFORMATION REQUESTS (IRs):

1. 05/18/2021: Three questions regarding datasets (Response in 125742/0.3)

2. 05/20/2021: Four facilities questions and a request for a telecon on 5/25/21 or 5/26/21 to discuss production schedule and the shutdown activities planned for the Puurs, Belgium site (Response in 125742/0.4)

3. 06/08/2021: Three clinical questions regarding datasets and the PI (Response in 125742/0.6)

4. 06/09/2021: Clinical IR requesting dates for PREA deferred studies (Response in 125742/0.7)

5. 06/25/2021: DBSQC IR regarding the lot release protocol (LRP) template and samples and reagents (Awaiting response)

6. 06/25/2021: Clinical IR regarding the document titled “bnt162-01-intrim3-report-body” (Awaiting response)

AMENDMENTS:

1. 05/18/2021: Second roll and final piece of the BLA, which started the review clock. This amendment was not submitted in response to an IR.

2. 05/19/2021: Request for Proprietary Name Review. This amendment was not submitted in response to an IR.

3. 05/19/2021: Response to May 18, 2021, IR RE three dataset questions.

4. 05/24/2021: Response to DMPQ’s May 20, 2021, IR RE four facilities questions and a request for a t-con on 5/25/21 or 5/26/21 to discuss production schedules and the shutdown activities planned for the Puurs, Belgium site.

5. 05/24/2021: COVID-19 case strain sequencing data. This amendment was not submitted in response to an IR.

6. 06/16/2021: Response to June 8, 2021, clinical IR on three clinical questions regarding datasets and the PI.

7. 06/17/2021: Response to June 9, 2021, clinical IR requesting dates for PREA deferred studies.

U.S. FOOD & DRUG ADMINISTRATION

Memorandum

Date: July 2, 2021

From: Oluchi Elekwachi, PharmD, MPH, Regulatory Review Officer
OCBQ/DCM/APLB

Through: Lisa Stockbridge, PhD, Branch Chief
OCBQ/DCM/APLB

Robert A. Sausville, Division Director
OCBQ/DCM

To: Michael Smith, RPM, OVRR\DVRPA\CMC3
Susan Wollersheim, Medical Officer, CBER/OVRR/DVRPA/CRB1

Subject: Review of Proposed Proprietary Name **COMIRNATY** (Pfizer-BioNTech COVID-19) Vaccine
STN: BLA 125742
Applicant: Pfizer, Inc.

Recommendation: **COMIRNATY – Acceptable**

Executive Summary

APLB has completed the proprietary name review (PNR) for the proposed proprietary name, **COMIRNATY**, for Pfizer-BioNTech's COVID-19 vaccine. We recommend that the proposed proprietary name, **COMIRNATY**, be found **Acceptable**.

According to SOPP 8001.4 Review of CBER Regulated Product Proprietary Names, the product office, Office of Vaccine Research and Review (OVRR), makes the final decision on the acceptability of a proposed proprietary name. To meet the PDUFA performance goal, OVRR must communicate this decision to the applicant within 90 days of the receipt of the proprietary name review (PNR) submission. The PDUFA goal date for this PNR is August 17, 2021.

If OVRR accepts our recommendation that the proposed primary proprietary name, **COMIRNATY**, be found **Acceptable**, we offer the following communication-ready language:

> *In consultation with CBER's Advertising and Promotional Labeling Branch, we conclude that under the Federal Food, Drug, and Cosmetic Act and applicable regulations your proposed proprietary name, **COMIRNATY**, is Acceptable.*

OVRR is responsible for communicating CBER's decision to the applicant and should enter the communication issuance date into the FDA electronic record before August 17, 2021, in order to meet the deadline and stop the performance clock. Please notify APLB when this action has been completed.

Background

On May 19, 2021, Pfizer, Inc. submitted a PNR request for its COVID-19 vaccine (BLA 125742). The proposed proprietary name is **COMIRNATY** (pronounced *koh-MER' nah-tee*). The proposed indication is for the active immunization against COVID-19.

According to the sponsor, **COMIRNATY** is an invented word with no inherent meaning. The sponsor did not propose an alternative name.

COMIRNATY will be supplied in 0.45 mL multiple dose vials containing a frozen, concentrated liquid suspension with no preservative. Each vial must be thawed and diluted prior to administration. Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)], then the concentrated liquid in the vial will require dilution with sterile 0.9% Sodium Chloride Injection, USP. After dilution, 0.3 mL doses of vaccine may be withdrawn from the vial, using commercially available disposable sterile syringes with appropriate graduations. Each vial contains sufficient volume to provide 6 individual doses, where each 0.3 mL dose contains 30 µg vaccine for intramuscular injection.

COMIRNATY will be administered intramuscularly as a series of two 30 µg doses (0.3 mL each) according to the following schedule: A single 0.3 mL dose followed by a second 0.3 mL dose 21 days later.

Cartons of **COMIRNATY** multiple dose vials will be shipped in thermal containers over dry ice. Once received, cartons should be removed immediately from the thermal container and stored in an ultra-low temperature freezer between -80ºC to -60ºC (-112ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks.

Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned one time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed two weeks.

If an ultra-low temperature freezer is not available, the thermal shipping may be used as temporary storage when consistently re-filled to the top of the container with dry ice. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage within this temperature range is not considered an excursion from the recommended storage condition.

The vaccine will be administered by a qualified healthcare professional.

Method

APLB utilized the FDA Phonetic and Orthographic Computer Analysis (POCA) and the following databases:

1. CBER list of Licensed Products ending June 24, 2021, at http://www.fda.gov/downloads/BiologicsBloodVaccines/UCM149970.pdf
2. DailyMed at http://dailymed.nlm.nih.gov/dailymed/about.cfm
3. Drugs@FDA current through June 24, 2021, at http://www.accessdata.fda.gov/scripts/cder/drugsatfda
4. Electronic Orange Book current through June 24, 2021, at http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm
5. Google Internet search at http://www.google.com
6. Micromedex at http://www.micromedexsolutions.com/micromedex2/librarian
7. United States Patent and Trademark Office (USPTO) at http://www.uspto.gov/trademarks/index.jsp
8. USAN Stem at http://www.ama-assn.org/ama1/pub/upload/mm/365/stem-list-cumulative.pdf

APLB also consulted the review team on the proprietary name.

Results

1. Prescreening for Objectionable Naming Practices

The proposed proprietary name, **COMIRNATY**, was screened against the following:

- Obvious similarities in spelling and pronunciation
- Manufacturing characteristics
- Medical and/or coined abbreviations
- Inert or inactive ingredients
- Combination of active ingredients
- United States Adopted Name (USAN) stems
- Same proprietary name for products containing different active ingredients
- Reuse of proprietary names
- Dosage form or route of administration
- Dosing interval
- Established or proper name
- Modifiers as components of a proprietary name
    - Use of numerals as modifiers
    - Device-related modifiers
    - Descriptive modifiers
- Brand name extensions (Umbrella branding)

- Dual proprietary names
- Foreign drug proprietary name
- Prescription-to-OTC switch
- Use of symbols
- Incorporation of the applicant's name

2. Evaluating for Promotional and Safety Concerns

a. Promotional Review [21 CFR 201.10 (c)(3), 202.1 (e)(5)(i), and (e)(6)(i)]

The proposed proprietary name, **COMIRNATY**, is not regarded to be false, misleading, or fanciful.

b. Look-alike Sound-alike Safety Review [21 CFR 201.10 (c)(5)]

Since drug products are prescribed through written, verbal, and/or electronic orders, such forms of communication may lead to medication errors, particularly if proprietary or established names sound or look alike. APLB conducted a search using POCA, with DPRF, Drugs@FDA, Cerner US Legend and OTC, CBER Biologic, Orange Book, and RxNorm as data sources, to identify existing names of concern with potential combined orthographic and phonetic similarity to **COMIRNATY**. There were 105 names found to be moderately phonetically or orthographically similar to **COMIRNATY**. Differences in dose, form, or strength can mitigate confusion with moderately similar names, and none of the names shared dose, form, or strength with **COMIRNATY**.

Recommendation

Given that the moderately similar names had differences in dosage form, dose, and/or strength to **COMIRNATY**, APLB recommends that **COMIRNATY** be found Acceptable at this time.

If you have any questions regarding this review please contact Oluchi Elekwachi, PharmD, MPH Regulatory Review Officer, at 240-402-8930.

BLA 125742

Firm name: Pfizer Ireland Pharmaceuticals

STN: BLA 125742

Letter type: PNR Memorandum

Bcc: OElekwachi
LStockbridge
RSausville
DCM Files

History:

Prepared:	OElekwachi	6/25/2021
Concur w/rev:	LStockbridge	7/1/2021
Finalized:	OElekwachi	7/2/2021

File name: PNR_COMIRNATY_BLA125742_FINAL

Concurrence box:

MailCode or Office	Name	Approval
APLB	OElekwachi	Oluchi Elekwachi -S3 Digitally signed by Oluchi Elekwachi -S3 DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300216724, cn=Oluchi Elekwachi -S3 Date: 2021.07.02 15:21:33 -04'00'
APLB	LStockbridge	Lisa L. Stockbridge -S Digitally signed by Lisa L. Stockbridge -S Date: 2021.07.02 15:18:18 -04'00'
DCM	RSausville	Robert A. Sausville -S Digitally signed by Robert A. Sausville -S DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300045570, cn=Robert A. Sausville -S Date: 2021.07.02 16:01:44 -04'00'

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use TRADENAME safely and effectively. See full prescribing information for TRADENAME.

TRADENAME (COVID-19 Vaccine, mRNA) suspension for r injection, for intramuscular use
Initial U.S. Approval: YYYY

----------INDICATIONS AND USAGE----------
TRADENAME is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
TRADENAME is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

----------CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of TRADENAME. (4)

---------- WARNINGS AND PRECAUTIONS ----------
Postmarketing reports of adverse events suggest increased risks of myocarditis and pericarditis, particularly following the second dose. (5.X)

Syncope (fainting) may occur in association with administration of injectable vaccines, including TRADENAME. Procedures should be in place to avoid injury from fainting. (5.X)

----------ADVERSE REACTIONS----------
In clinical studies of participants 16 years of age and older, the most commonly reported adverse reactions (>10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, fever, and injection site swelling. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

Summary of Comments on 36A_BLA 125742-0_07-28-2021_Telecon_Labeling Target Cl.pdf

Page: 1

Number: 1 Author: Author Date: Indeterminate
Pfizer: Please provide percentages for each adverse reaction—i e , “ were pain at the injection site (X%), fatigue (X%) broken out by age (16 through 55 yrs and 56 and older), “

Number: 2 Author: Author Date: Indeterminate
Pfizer: we have inserted a place holder W/P for myocarditis/pericarditis based on the fact sheet language We anticipate that this will be further revised

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

TRADENAME is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

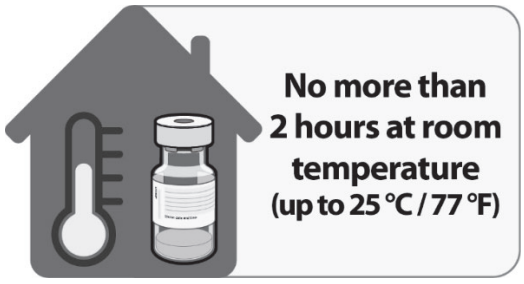
2.1 Preparation for Administration

Prior to Dilution

- TRADENAME Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

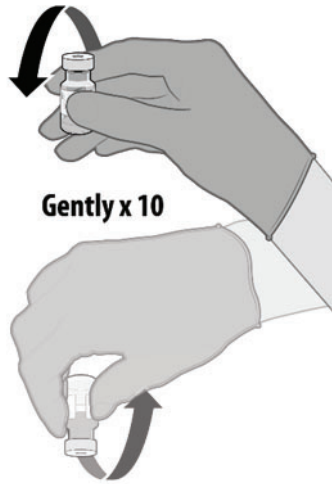
Dilution

- Dilute the vial contents using 1.8 mL of 0.9% Sodium Chloride Injection, USP (provided but shipped separately) to form TRADENAME. Do not add more than 1.8 mL of diluent.
- ONLY use the provided 0.9% Sodium Chloride Injection, USP as the diluent.
- After dilution, 1 vial contains 6 doses of 0.3 mL.
- Refer to dilution and dose preparation instructions in the panels below.

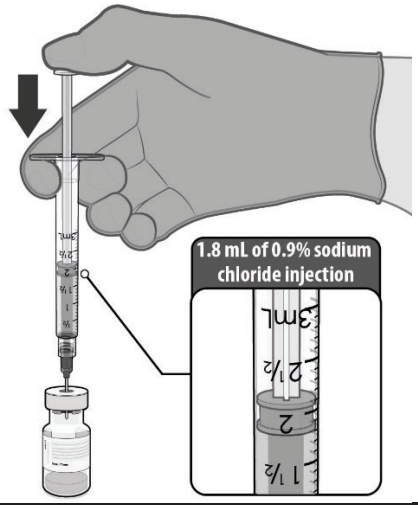
THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of TRADENAME before use either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 5 days (120 hours). o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.

Number: 1 Author: Author Date: Indeterminate
Pfizer: based on information in the BLA the saline diluent will be provided separately from the vials of vaccine We have revised the text since the diluent is provided separately

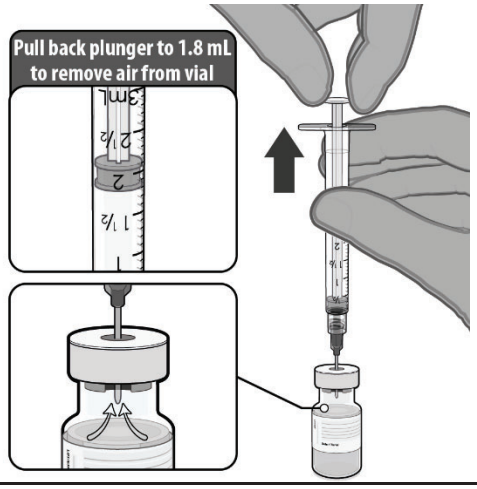
Number: 2 Author: Author Date: Indeterminate
Pfizer: the storage time in the fact sheets is one month Please explain why this is 5 days

<table>
<tr><td> 
</td><td>

- Before dilution invert vaccine vial gently 10 times.
- Do not shake.
- Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles.
- Do not use if liquid is discolored or if other particles are observed.

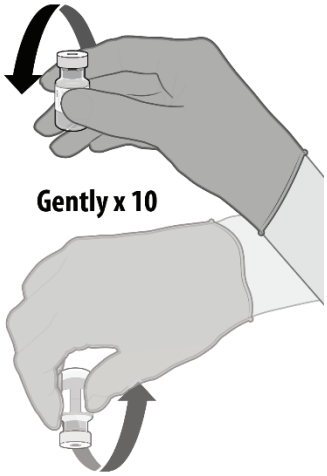
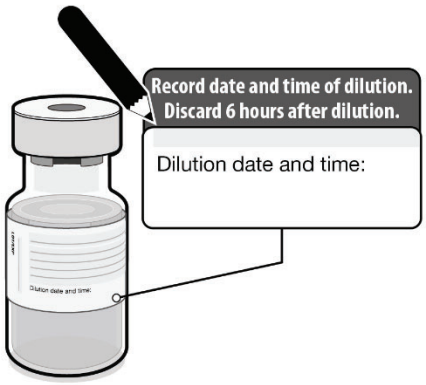
</td></tr>
<tr><td colspan="2">DILUTION</td></tr>
<tr><td> 
</td><td>

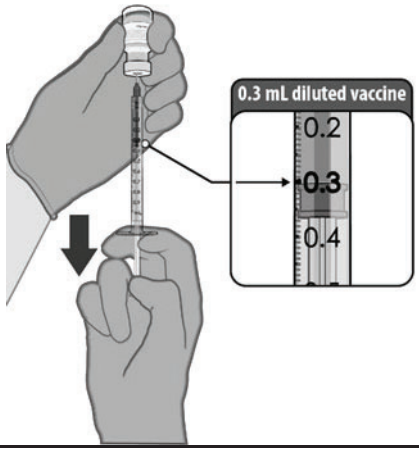
- Use the provided sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent.
- Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle).
- Cleanse the vaccine vial stopper with a single-use antiseptic swab.
- Add 1.8 mL of 0.9% Sodium Chloride Injection, USP into the vaccine vial.

</td></tr>
<tr><td> 
</td><td>

- Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.

</td></tr>
</table>

	• Gently invert the vial containing the TRADENAME 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the TRADENAME vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF TRADENAME	
	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of TRADENAME preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Visually inspect each dose in the dosing syringe prior to administration. The vaccine will be an off-white suspension. During the visual inspection,

- verify the final dosing volume of 0.3 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

Administer TRADENAME intramuscularly.

After dilution, vials of TRADENAME contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.3 Vaccination Schedule

TRADENAME is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of TRADENAME with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of TRADENAME should receive a second dose of TRADENAME to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

TRADENAME is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer TRADENAME to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the TRADENAME *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of TRADENAME.

5.2 Myocarditis and Pericarditis

Text based on FS (changed "Pfizer-BioNTech COVID-19 Vaccine" to "TRADENAME"
Reports of adverse events following use of TRADENAME under EUA suggest increased risks of myocarditis and pericarditis, particularly following the second dose. Typically, onset of symptoms has been within a few days following receipt of TRADENAME. Available data from short-term follow-up suggest that most

individuals have had resolution of symptoms, but information is not yet available about potential long-term sequelae. The decision to administer TRADENAME to an individual with a history of myocarditis or pericarditis should take into account the individual's clinical circumstances. The CDC has published clinical considerations relevant to myocarditis and pericarditis associated with administration of Tradename (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including TRADENAME. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the TRADENAME.

5.5 Limitation of Effectiveness

TRADENAME may not protect all vaccine recipients.

6 ADVERSE REACTIONS

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6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of TRADENAME was evaluated in participants 16 years of age and older in 2 clinical studies conducted in the United States, Europe, Turkey, South Africa, and South America. Study BNT162-01 (Study 1) was a Phase 1/2, 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3, multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection (Phase 1) and efficacy (Phase 2/3) study that has enrolled approximately 46,000 participants, 12 years of age or older. Of these, approximately 44,047 participants (22,026 TRADENAME; 22,021 placebo) in Phase 2/3 are 16 years of age or older (including 378 and 376 adolescents 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses.

At the time of the analysis of Study 2 for the Emergency Use Authorization (EUA) with a data cut-off of November 14, 2020, there were 37,586 participants (18,801 TRADENAME and 18,785 placebo) 16 years of age or older followed for a median of 2 months after the second dose of TRADENAME. At the time of the analysis of Study 2 for the EUA with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants

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(13,031 TRADENAME and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

The[1] safety evaluation in Study 2 is ongoing. The safety population includes participants enrolled by October 9, 2020, and includes safety data accrued through March 13, 2021. Participants 16 years and older in the reactogenicity subset are monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].[2]

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received TRADENAME and those who received placebo. Overall, among the total participants who received either TRADENAME or placebo, 50.9% were male and 49.1% were female, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of TRADENAME and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of TRADENAME and placebo for participants 56 years of age and older.

In participants 16 to 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the TRADENAME group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the TRADENAME group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	TRADENAME Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	TRADENAME Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)

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Pfizer: We have included a couple of very high level comments in this section of the PI Additional comments will be provided after review of this section

Number: 2 Author: Author Date: Indeterminate

Pfizer: Please revise text to clarify that Study 1 was conducted in Germany and that Study 2 was conducted in the United States, Argentina, Brazil, Turkey, South Africa, and Germany

	TRADENAME Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	TRADENAME Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	TRADENAME Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	TRADENAME Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)

	TRADENAME Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	TRADENAME Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	TRADENAME Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	TRADENAME Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	TRADENAME Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	TRADENAME Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0

	TRADENAME Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	TRADENAME Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.

f. Severity was not collected for use of antipyretic or pain medication.

Table 5 and Table 6 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of TRADENAME and placebo for participants 16 years of age and older with confirmed stable HIV infection.

Table 5: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – HIV-Positive Participants 16 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	TRADENAME Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	TRADENAME Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Redness[c]				
Any (>2.0 cm)	2 (3.7)	3 (5.4)	4 (6.7)	1 (1.6)
Mild	2 (3.7)	1 (1.8)	3 (5.0)	1 (1.6)
Moderate	0	0	1 (1.7)	0
Severe	0	2 (3.6)	0	0
Swelling[c]				
Any (>2.0 cm)	3 (5.6)	1 (1.8)	5 (8.3)	0
Mild	2 (3.7)	0	2 (3.3)	0
Moderate	1 (1.9)	0	3 (5.0)	0
Severe	0	1 (1.8)	0	0
Pain at the injection site[d]				
Any	34 (63.0)	9 (16.1)	32 (53.3)	5 (8.1)
Mild	26 (48.1)	8 (14.3)	22 (36.7)	5 (8.1)
Moderate	8 (14.8)	1 (1.8)	9 (15.0)	0
Severe	0	0	1 (1.7)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in HIV-positive participants 16 years of age and older.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 6: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – HIV-Positive Participants 16 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	TRADENAME Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	TRADENAME Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Fever				
≥38.0°C	1 (1.9)	4 (7.1)	9 (15.0)	5 (8.1)
≥38.0°C to 38.4°C	1 (1.9)	2 (3.6)	4 (6.7)	5 (8.1)
>38.4°C to 38.9°C	0	0	4 (6.7)	0
>38.9°C to 40.0°C	0	2 (3.6)	1 (1.7)	0
>40.0°C	0	0	0	0

	TRADENAME Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	TRADENAME Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Fatigue[c]				
Any	22 (40.7)	15 (26.8)	24 (40.0)	12 (19.4)
Mild	15 (27.8)	9 (16.1)	12 (20.0)	5 (8.1)
Moderate	7 (13.0)	5 (8.9)	9 (15.0)	7 (11.3)
Severe	0	1 (1.8)	3 (5.0)	0
Headache[c]				
Any	11 (20.4)	18 (32.1)	18 (30.0)	12 (19.4)
Mild	7 (13.0)	10 (17.9)	8 (13.3)	8 (12.9)
Moderate	4 (7.4)	7 (12.5)	8 (13.3)	4 (6.5)
Severe	0	1 (1.8)	2 (3.3)	0
Chills[c]				
Any	6 (11.1)	5 (8.9)	14 (23.3)	4 (6.5)
Mild	5 (9.3)	4 (7.1)	5 (8.3)	3 (4.8)
Moderate	1 (1.9)	1 (1.8)	8 (13.3)	1 (1.6)
Severe	0	0	1 (1.7)	0
Vomiting[d]				
Any	1 (1.9)	3 (5.4)	2 (3.3)	2 (3.2)
Mild	1 (1.9)	1 (1.8)	1 (1.7)	1 (1.6)
Moderate	0	0	1 (1.7)	1 (1.6)
Severe	0	2 (3.6)	0	0
Diarrhea[e]				
Any	5 (9.3)	8 (14.3)	4 (6.7)	9 (14.5)
Mild	5 (9.3)	6 (10.7)	1 (1.7)	6 (9.7)
Moderate	0	1 (1.8)	2 (3.3)	3 (4.8)
Severe	0	1 (1.8)	1 (1.7)	0
New or worsened muscle pain[c]				
Any	9 (16.7)	10 (17.9)	10 (16.7)	5 (8.1)
Mild	7 (13.0)	7 (12.5)	5 (8.3)	1 (1.6)
Moderate	2 (3.7)	3 (5.4)	5 (8.3)	4 (6.5)
Severe	0	0	0	0
New or worsened joint pain[c]				
Any	5 (9.3)	7 (12.5)	10 (16.7)	5 (8.1)
Mild	5 (9.3)	4 (7.1)	4 (6.7)	1 (1.6)
Moderate	0	3 (5.4)	6 (10.0)	4 (6.5)
Severe	0	0	0	0
Use of antipyretic or pain medication[f]	7 (13.0)	8 (14.3)	16 (26.7)	7 (11.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in HIV-positive participants 16 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each event or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

	TRADENAME Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	TRADENAME Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.
f. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

Upon issuance of the EUA for TRADENAME, participants were unblinded to offer placebo participants TRADENAME. Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began in a phased manner for participants in the study. Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (TRADENAME =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 2.1 per 100 person-years among TRADENAME recipients and 2.4 per 100 person-years among placebo recipients. In a similar analysis, in participants 56 years of age and older (TRADENAME =8931, placebo = 8895), serious adverse events were reported at an incidence rate of 4.9 per 100 person-years among TRADENAME recipients and 4.6 per 100 person-years among placebo recipients who received at least 1 dose of TRADENAME or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 6.6 per 100 person-years among TRADENAME recipients and 6.9 per 100 person-years among placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to TRADENAME.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received TRADENAME and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 88.4 per 100 person-years among participants who received TRADENAME and 43.5 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (TRADENAME = 8931, placebo = 8895), all events, which include non-serious adverse events were reported at an incidence rate of 75.7 per 100 person-years among participants who received TRADENAME and 43.3 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 95.8 per 100 person-years among participants who received

TRADENAME and 52.0 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among TRADENAME recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the TRADENAME group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to TRADENAME.

6.2 Post Marketing Experience

The following adverse reactions have been identified during post marketing useof TRADENAME, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Gastrointestinal Disorders: diarrhea, vomiting
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on TRADENAME administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of TRADENAME on four occasions, twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine [see *Animal Data below*.]

Data

Animal Data

In a reproductive and developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of TRADENAME was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether TRADENAME is excreted in human milk. Data are not available to assess the effects of TRADENAME on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TRADENAME and any potential adverse effects on the breastfed child from TRADENAME or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of TRADENAME in adolescents 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14)]*.

The safety and effectiveness of TRADENAME in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of TRADENAME recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

TRADENAME (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. TRADENAME is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of the provided sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of TRADENAME contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each dose of the TRADENAME also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

TRADENAME does not contain preservative. The vial stoppers are not made with natural rubber latex.

Number: 1 Author: Author Date: Indeterminate
Pfizer- Please re-order list of systems alphabetically

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in TRADENAME is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

TRADENAME has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In studies in rats with TRADENAME, there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

14.1 Efficacy in Participants 16 Years of Age and Older

Study 2 is a multicenter, multinational, Phase 1/2/3, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In the Phase 2/3 portion of Study 2, based on data accrued through November 14, 2020, approximately 44,000 participants 12 years of age and older were randomized equally and received 2 doses of TRADENAME or placebo. The efficacy analyses included participants that received their second vaccination within 19 to 42 days after their first vaccination. The majority (93.1%) of vaccine recipients received the second dose 19 days to 23 days after Dose 1. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the TRADENAME group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. Table 7 presents the specific demographic characteristics in the studied population.

Number: 1 Author: Author Date: Indeterminate
Pfizer: this was revised to be consistent with the NP name

Table 7: Demographics (Population For the Primary Efficacy Endpoint)[a]

	TRADENAME (N=18,242) n (%)	Placebo (N=18,379) n (%)
Sex		
Male	9318 (51.1)	9225 (50.2)
Female	8924 (48.9)	9154 (49.8)
Age (years)		
Mean (SD)	50.6 (15.70)	50.4 (15.81)
Median	52.0	52.0
Min, max	(12, 89)	(12, 91)
Age group		
≥12 through 15 years	46 (0.3)	42 (0.2)
≥16 through 64 years	14,216 (77.9)	14,299 (77.8)
≥65 through 74 years	3176 (17.4)	3226 (17.6)
≥75 years	804 (4.4)	812 (4.4)
Race		
White	15,110 (82.8)	15,301 (83.3)
Black or African American	1617 (8.9)	1617 (8.8)
American Indian or Alaska Native	118 (0.6)	106 (0.6)
Asian	815 (4.5)	810 (4.4)
Native Hawaiian or other Pacific Islander	48 (0.3)	29 (0.2)
Other[b]	534 (2.9)	516 (2.8)
Ethnicity		
Hispanic or Latino	4886 (26.8)	4857 (26.4)
Not Hispanic or Latino	13,253 (72.7)	13,412 (73.0)
Not reported	103 (0.6)	110 (0.6)
Comorbidities[c]		
Yes	8432 (46.2)	8450 (46.0)
No	9810 (53.8)	9929 (54.0)

a. All eligible randomized participants who receive all vaccination(s) as randomized within the predefined window, have no other important protocol deviations as determined by the clinician, and have no evidence of SARS-CoV-2 infection prior to 7 days after Dose 2.
b. Includes multiracial and not reported.
c. Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease:
   - Chronic lung disease (e.g., emphysema and chronic bronchitis, idiopathic pulmonary fibrosis, and cystic fibrosis) or moderate to severe asthma
   - Significant cardiac disease (e.g., heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and pulmonary hypertension)
   - Obesity (body mass index ≥30 kg/m^2)
   - Diabetes (Type 1, Type 2, or gestational)
   - Liver disease
   - Human Immunodeficiency Virus (HIV) infection (not included in the efficacy evaluation)

Efficacy Against COVID-19

The population in the primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

Number: 1 Author: Author Date: Indeterminate
Pfizer: Subsection 8 1 refers to a single study Please clarify if “studies” should be revised to “a study “

Number: 2 Author: Author Date: Indeterminate
Pfizer: We have not reviewed this section Comments will be provided after review

The vaccine efficacy information is presented in Table 8.

Table 8: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**TRADENAME N[a]=18,198 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.3, 97.6)[f]
16 to 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)[g]
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)[g]
65 to 74 years	1 0.406 (3074)	14 0.406 (3095)	92.9 (53.1, 99.8)[g]
75 years and older	0 0.102 (774)	5 0.106 (785)	100.0 (-13.1, 100.0)[g]
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**TRADENAME N[a]=19,965 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,172 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	9 2.332 (18,559)	169 2.345 (18,708)	94.6 (89.9, 97.3)[f]
16 to 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1 0.530 (4044)	19 0.532 (4067)	94.7 (66.8, 99.9)[g]
65 to 74 years	1 0.424 (3239)	14 0.423 (3255)	92.9 (53.2, 99.8)[g]
75 years and older	0 0.106 (805)	5 0.109 (812)	100.0 (-12.1, 100.0)[g]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. No confirmed cases were identified in participants 12 to 15 years of age.
f. Two-sided credible interval for vaccine efficacy was calculated using a beta-binomial model with a beta (0.700102, 1) prior for θ=r(1-VE)/(1+r(1-VE)), where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.
g. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Updated efficacy analyses were performed with additional confirmed COVID-19 cases accrued during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2 for participants in the efficacy population.

The updated vaccine efficacy information is presented in Table 9.

Table 9: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**TRADENAME N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
16 through 64 years	70 4.859 (15,519)	710 4.654 (15,515)	90.6 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
65 through 74 years	6 0.994 (3350)	98 0.966 (3379)	94.1 (86.6, 97.9)
75 years and older	1 0.239 (842)	26 0.237 (847)	96.2 (76.9, 99.9)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**TRADENAME N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
16 through 64 years	74 5.073 (16,218)	727 4.879 (16,269)	90.2 (87.6, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)
65 through 74 years	6 1.021 (3450)	102 0.992 (3468)	94.3 (87.1, 98.0)
75 years and older	1 0.246 (865)	26 0.240 (858)	96.2 (77.2, 99.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

f. Included confirmed cases in participants 12 through 15 years of age: 0 in the TRADENAME group (both without and with or without evidence of prior SARS-CoV-2 infection); 16 and 18 in the placebo group (without and with or without evidence of prior SARS-CoV-2 infection, respectively).

The updated subgroup analyses of vaccine efficacy by demographic characteristics are presented in Table 10 and Table 11.

Table 10: Vaccine Efficacy– First COVID-19 Occurrence From 7 Days After Dose 2 – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 by Demographic Characteristics – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	TRADENAME N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Sex			
Male	42 3.246 (10,637)	399 3.047 (10,433)	90.1 (86.4, 93.0)
Female	35 3.001 (10,075)	451 2.956 (10,280)	92.4 (89.2, 94.7)
Ethnicity			
Hispanic or Latino	29 1.786 (5161)	241 1.711 (5120)	88.5 (83.0, 92.4)
Not Hispanic or Latino	47 4.429 (15,449)	609 4.259 (15,484)	92.6 (90.0, 94.6)
Race			
Black or African American	4 0.545 (1737)	48 0.527 (1737)	91.9 (78.0, 97.9)
White	67 5.208 (17,186)	747 5.026 (17,256)	91.3 (88.9, 93.4)
All others[f]	6 0.494 (1789)	55 0.451 (1720)	90.0 (76.9, 96.5)

Subgroup	TRADENAME N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Country			
Argentina	15 1.012 (2600)	108 0.986 (2586)	86.5 (76.7, 92.7)
Brazil	12 0.406 (1311)	80 0.374 (1293)	86.2 (74.5, 93.1)
Germany	0 0.047 (236)	1 0.048 (242)	100.0 (-3874.2, 100.0)
South Africa	0 0.080 (291)	9 0.074 (276)	100.0 (53.5, 100.0)
Turkey	0 0.027 (228)	5 0.025 (222)	100.0 (-0.1, 100.0)
United States	50 4.674 (16,046)	647 4.497 (16,094)	92.6 (90.1, 94.5)

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).
Included confirmed cases in participants 12 through 15 years of age: 0 in the TRADENAME group; 16 in the placebo group.

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
f. All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

Table 11: Vaccine Efficacy– First COVID-19 Occurrence From 7 Days After Dose 2 – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 by Demographic Characteristics – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	TRADENAME N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Sex			
Male	44 3.376 (11,103)	411 3.181 (10,920)	89.9 (86.2, 92.8)
Female	37 3.133 (10,539)	462 3.093 (10,769)	92.1 (88.9, 94.5)

Subgroup	TRADENAME N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Ethnicity			
Hispanic or Latino	32 1.862 (5408)	245 1.794 (5391)	87.4 (81.8, 91.6)
Not Hispanic or Latino	48 4.615 (16,128)	628 4.445 (16,186)	92.6 (90.1, 94.6)
Race			
Black or African American	4 0.611 (1958)	49 0.601 (1985)	92.0 (78.1, 97.9)
White	69 5.379 (17,801)	768 5.191 (17,880)	91.3 (88.9, 93.3)
All others[f]	8 0.519 (1883)	56 0.481 (1824)	86.8 (72.1, 94.5)
Country			
Argentina	16 1.033 (2655)	110 1.017 (2670)	85.7 (75.7, 92.1)
Brazil	14 0.441 (1419)	82 0.408 (1401)	84.2 (71.9, 91.7)
Germany	0 0.047 (237)	1 0.048 (243)	100.0 (-3868.6, 100.0)
South Africa	0 0.099 (358)	10 0.096 (358)	100.0 (56.6, 100.0)
Turkey	0 0.029 (238)	6 0.026 (232)	100.0 (22.2, 100.0)
United States	51 4.861 (16,735)	664 4.678 (16,785)	92.6 (90.2, 94.6)

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

Included confirmed cases in participants 12 through 15 years of age: 0 in the TRADENAME group; 18 in the placebo group.

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

f. All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

The updated subgroup analyses of vaccine efficacy by risk status in participants are presented in Table 12 and Table 13.

Table 12: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	TRADENAME N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First COVID-19 occurrence from 7 days after Dose 2[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
At risk[g]			
Yes	35 2.797 (9167)	401 2.681 (9136)	91.6 (88.2, 94.3)
No	42 3.450 (11,545)	449 3.322 (11,577)	91.0 (87.6, 93.6)
Age group (years) and risk status			
16 through 64 and not at risk	41 2.776 (8887)	385 2.661 (8886)	89.8 (85.9, 92.8)
16 through 64 and at risk	29 2.083 (6632)	325 1.993 (6629)	91.5 (87.5, 94.4)
65 and older and not at risk	1 0.553 (1870)	53 0.546 (1922)	98.1 (89.2, 100.0)
65 and older and at risk	6 0.680 (2322)	71 0.656 (2304)	91.8 (81.4, 97.1)
Obese[h]			
Yes	27 2.103 (6796)	314 2.050 (6875)	91.6 (87.6, 94.6)
No	50 4.143 (13,911)	536 3.952 (13,833)	91.1 (88.1, 93.5)
Age group (years) and obesity status			
16 through 64 and not obese	46 3.178 (10,212)	444 3.028 (10,166)	90.1 (86.6, 92.9)
16 through 64 and obese	24 1.680 (5303)	266 1.624 (5344)	91.3 (86.7, 94.5)
65 and older and not obese	4 0.829 (2821)	79 0.793 (2800)	95.2 (87.1, 98.7)
65 and older and obese	3 0.404 (1370)	45 0.410 (1426)	93.2 (78.9, 98.7)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

f. Included confirmed cases in participants 12 through 15 years of age: 0 in the TRADENAME group; 16 in the placebo group.

Subgroup	TRADENAME N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]

g. At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age]).
h. Obese is defined as BMI ≥30 kg/m^2. For 12 through 15 years age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	TRADENAME N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First COVID-19 occurrence from 7 days after Dose 2[f]	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
At risk[g]			
Yes	36 2.925 (9601)	410 2.807 (9570)	91.6 (88.1, 94.2)
No	45 3.584 (12,041)	463 3.466 (12,119)	90.6 (87.2, 93.2)
Age group (years) and risk status			
16 through 64 and not at risk	44 2.887 (9254)	397 2.779 (9289)	89.3 (85.4, 92.4)
16 through 64 and at risk	30 2.186 (6964)	330 2.100 (6980)	91.3 (87.3, 94.2)
65 and older and not at risk	1 0.566 (1920)	55 0.559 (1966)	98.2 (89.6, 100.0)
65 and older and at risk	6 0.701 (2395)	73 0.672 (2360)	92.1 (82.0, 97.2)
Obese[h]			
Yes	28 2.207 (7139)	319 2.158 (7235)	91.4 (87.4, 94.4)
No	53 4.301 (14,497)	554 4.114 (14,448)	90.8 (87.9, 93.2)
Age group (years) and obesity status			
16 through 64 and not obese	49 3.303 (10,629)	458 3.158 (10,614)	89.8 (86.2, 92.5)
16 through 64 and obese	25 1.768 (5584)	269 1.719 (5649)	91.0 (86.4, 94.3)
65 and older and not obese	4 0.850 (2899)	82 0.811 (2864)	95.3 (87.6, 98.8)
65 and older and obese	3 0.417 (1415)	46 0.420 (1462)	93.4 (79.5, 98.7)

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	TRADENAME N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.
f. Included confirmed cases in participants 12 through 15 years of age: 0 in the TRADENAME group; 18 in the placebo group.
g. At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age]).
h. Obese is defined as BMI ≥30 kg/m^2. For the 12 through 15 years of age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Efficacy Against Severe COVID-19

Updated efficacy analyses of secondary efficacy endpoints supported benefit of TRADENAME in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 14) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the TRADENAME and placebo groups.

Table 14: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants With or Without* Prior SARS-CoV-2 Infection Based on FDA† or Centers for Disease Control and Prevention (CDC)‡ Definition After Dose 1 or From 7 Days After Dose 2 in the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence Based on FDA Definition			
	TRADENAME Cases n1[a] Surveillance Time (n2[b])	Placebo Cases n1[a] Surveillance Time (n2[b])	Vaccine Efficacy % (95% CI[c])
After Dose 1[d]	1 8.439[e] (22,505)	30 8.288[e] (22,435)	96.7 (80.3, 99.9)
7 days after Dose 2[f]	1 6.522[g] (21,649)	21 6.404[g] (21,730)	95.3 (70.9, 99.9)

Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	TRADENAME Cases n1[a] Surveillance Time (n2[b])	**Placebo Cases n1[a] Surveillance Time (n2[b])**	**Vaccine Efficacy % (95% CI[c])**
After Dose 1[d]	1 8.427[e] (22,473)	45 8.269[e] (22,394)	97.8 (87.2, 99.9)
7 days after Dose 2[f]	0 6.514[g] (21,620)	32 6.391[g] (21,693)	100 (88.0, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 as defined by FDA is confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. n2 = Number of participants at risk for the endpoint.
c. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
d. Efficacy assessed based on the Dose 1 all available efficacy (modified intention-to-treat) population that included all randomized participants who received at least 1 dose of study intervention.
e. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.
f. Efficacy assessed based on the evaluable efficacy (7 Days) population that included all eligible randomized participants who receive all dose(s) of study intervention as randomized within the predefined window, have no other important protocol deviations as determined by the clinician.
g. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

16 HOW SUPPLIED/STORAGE AND HANDLING

TRADENAME Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately. After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of TRADENAME Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -80ºC to -60ºC (-112ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which TRADENAME arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage within this temperature range is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 5 days (120 hours). A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours. Any hours used for transport at 2°C to 8°C (35°F to 46°F) count against the 120-hour limit for storage at 2°C to 8°C (35°F to 46°F).

Number: 1 Author: Author Date: Indeterminate
Pfizer: Please include instructions on how to store the provided saline diluent

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with TRADENAME

Inform vaccine recipient of the importance of completing the two dose vaccination series

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov

[1]

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This product's labeling may have been updated. For the most recent prescribing information, please visit www.pfizer.com.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer

[2]

Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.1

US Govt. License No. x

[3]

Number: 1 Author: Author Date: Indeterminate
Pfizer: This is not consistent with the FS which states "Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition " Please revise if necessary

Number: 2 Author: Author Date: Indeterminate
Pfizer: the storage time in the FS is "1 month" Please explain why this is 5 days

Number: 3 Author: Author Date: Indeterminate
Pfizer: This statement is not in the FS See comments above regarding whether storage of undiluted vials at 2-8C is for 5days or one month

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

----------INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

----------CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

----------ADVERSE REACTIONS----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

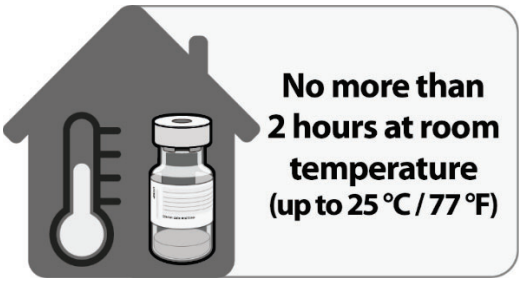
2.1 Preparation for Administration

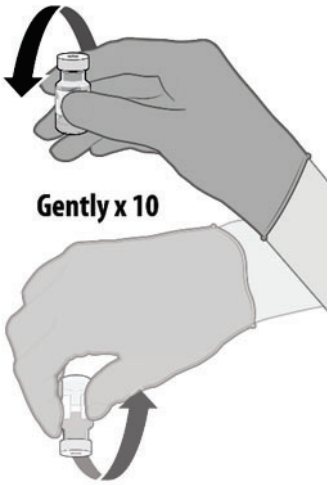
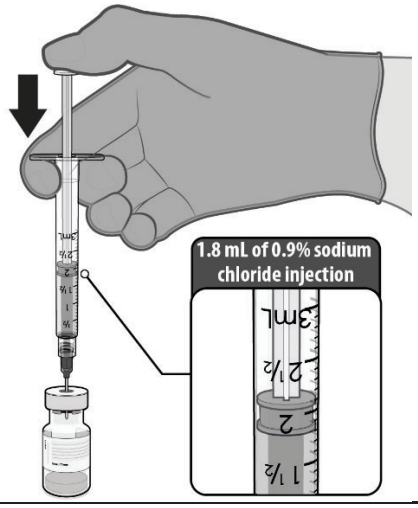
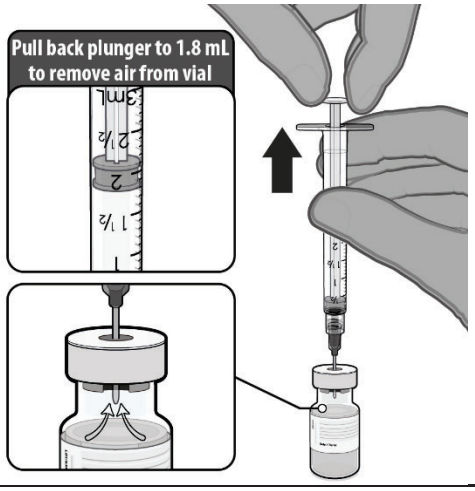
Prior to Dilution

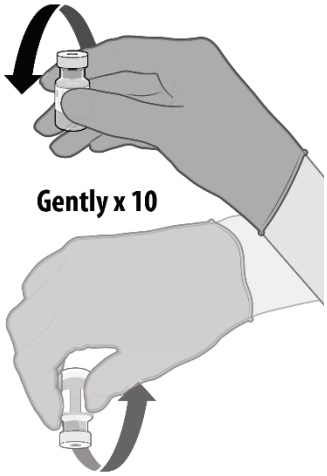
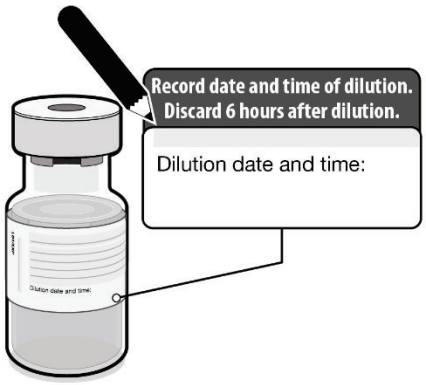
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

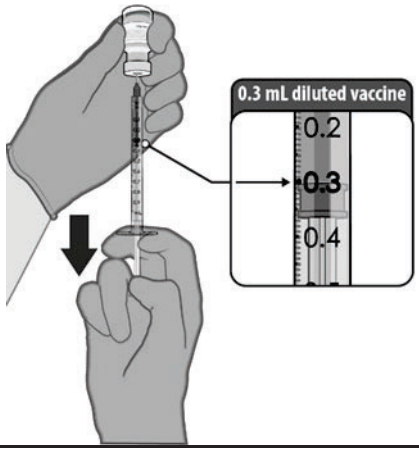
Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not use diluent vials to dilute multiple vials of COMIRNATY.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes.

	• Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.
	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.

	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.

- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk has been highest in adolescent and young adult males under 40 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of symptoms. Information is not yet available about potential long-term sequelae. The CDC has published considerations for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

Number: 1 Author: Author Date: Indeterminate
Pfizer,
Please note, we intend to communicate additional comments regarding Section 5 to you next week

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Number: 1 Author: Author Date: Indeterminate
Pfizer,
Please delete Our intent is to convey the most commonly reported adverse reactions in this section

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	**Placebo Dose 1 N[a]=2908 n[b] (%)**	**COMIRNATY Dose 2 N[a]=2682 n[b] (%)**	**Placebo Dose 2 N[a]=2684 n[b] (%)**
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Upon issuance of the EUA for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began in a phased manner for participants in the study. Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 2.1 per 100 person-years among COMIRNATY recipients and 2.4 per 100 person-years among placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported at an incidence rate of 4.9 per 100 person-years among COMIRNATY recipients and 4.6 per 100 person-years among placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 6.6 per 100 person-years among COMIRNATY recipients and 6.9 per 100 person-years among placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 88.4 per 100 person-years among participants who received COMIRNATY and 43.5 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include non-serious adverse events were reported at an incidence rate of 75.7 per 100 person-years among participants

Number: 1 Author: Author Date: Indeterminate

Pfizer,

This description is redundant from the overall safety description provided above, so it has been deleted

To clarify our request: please add a subsection to describe the frequencies of unsolicited non-serious and serious adverse events that occurred from Dose 1 through the March 2021 data cutoff, in the original vaccine recipients that have follow-up for at least 6 months after Dose 2 (n 12,006)

Number: 2 Author: Author Date: Indeterminate

Pfizer,

We do not think that the presentation of these data using incidence rates is helpful for the healthcare provider

Additionally, we do not agree with the method by which the incidence rates are calculated It appears that the incidence rate for each event type is based on the number of subjects who reported at least one event divided by the total person-years contributed by all subjects from Dose 1 to unblinding but does not account for the number of events a subject may report, or the timing of these events in deriving the total length of period "at risk " This may be misleading as it under-reports the true incidence rate In addition, we note that the total lengths of follow-up between arms are within 2% in both age groups (18 through 55, 56 and above), thus differences in follow-up appear to be minor Therefore, we continue to request the use of proportions to present safety data

who received COMIRNATY and 43.3 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 95.8 per 100 person-years among participants who received COMIRNATY and 52.0 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg

Number: 1 Author: Author Date: Indeterminate

Pfizer,

We do not concur because it appears that OTIS is recruiting from a wide variety of sites We request that you include contact information for the registry in the PI as follows:

"There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting www "

cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.5% were male and 48.6% or 49.5% were female, 75.1% or 75.1% were 16 through 64 years of age, 20.1% or 20.3% were 65 years of age and older, 16.1% or 16.3% were 65 through 74 years of age, 4.0% or 4.0% 75 years of age and older, 82.9% or 83.1% were White, 8.5% or 8.6% were Black or African American, 0.9% or 0.9% were American Indian or Alaska Native, 4.6% or 4.5% were Asian, 0.3% or 0.1% Native Hawaiian or other Pacific Islander, 24.9% or 24.6% were Hispanic/Latino, 74.6% or 74.8% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 44.6% or 44.4% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index

category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 48.3 or 48.2 years and median age was 50.0 or 50.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

The vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=18,198 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.3, 97.6)[f]
16 to 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)[g]
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)[g]
65 to 74 years	1 0.406 (3074)	14 0.406 (3095)	92.9 (53.1, 99.8)[g]
75 years and older	0 0.102 (774)	5 0.106 (785)	100.0 (-13.1, 100.0)[g]
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=19,965 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,172 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	9 2.332 (18,559)	169 2.345 (18,708)	94.6 (89.9, 97.3)[f]
16 to 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1 0.530 (4044)	19 0.532 (4067)	94.7 (66.8, 99.9)[g]
65 to 74 years	1	14	92.9

Number: 1 Author: Author Date: Indeterminate

Pfizer,

Please revise the demographics to describe the efficacy population used for the updated VE analyses in participants 16 years of age and older (please exclude participants 12-15 years of age) Results should be the same as those provided in Shell Table F with STN 126472/0 32

	0.424 (3239)	0.423 (3255)	(53.2, 99.8)[g]
75 years and older	0 0.106 (805)	5 0.109 (812)	100.0 (-12.1, 100.0)[g]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. No confirmed cases were identified in participants 12 to 15 years of age.
f. Two-sided credible interval for vaccine efficacy was calculated using a beta-binomial model with a beta (0.700102, 1) prior for $\theta=r(1-VE)/(1+r(1-VE))$, where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.
g. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were XX (X%) participants (XX COMIRNATY and XX placebo) followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

The updated vaccine efficacy information is presented in Table 6.

Table 6: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	COMIRNATY Na=21,047 Cases n1b Surveillance Timec (n2d)	Placebo Na=21,210 Cases n1b Surveillance Timec (n2d)	Vaccine Efficacy % (95% CIe)
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 7) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 7: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1a Surveillance Timeb (n2c)	Placebo Cases n1a Surveillance Timeb (n2c)	Vaccine Efficacy % (95% CId)
7 days after Dose 2d	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)

Number: 1 Author: Author Date: Indeterminate

Pfizer:
We continue to request deletion of this Table because the information is redundant with the updated VE analysis that follows with additional confirmed cases Please insert the text requested below:

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95 0% The case split was 8 COVID-19 cases in the BNT162b2 group compared to 162 COVID-19 cases in the placebo group The 95% credible interval for the vaccine efficacy was 90 3% to 97 6%, indicating that the true VE is at least 90 3% with a 97 5% probability, which met the pre-specified success criterion

Number: 2 Author: Author Date: Indeterminate

Pfizer,
Revised the language to mirror description of the Safety population

We note that these numbers were derived from follow-up times, based on the safety population Please update the information, based on the follow up time after Dose 2 for the efficacy population

Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
[1] 7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Number: 1 Author: Author Date: Indeterminate

Pfizer,

This general statement is misleading because some of the subgroup analyses were limited by the size of the subgroup and low number of confirmed cases, which limits the interpretation of those analyses We disagree with this addition and request deletion

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -80ºC to -60ºC (-112ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Number: 1 Author: Author Date: Indeterminate
Pfizer,
Please update this section to include information on the diluent manufactured at the Pfizer Healthcare India site

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by calling ….. Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit www.comirnatyglobal.com.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.3

US Govt. License No. x

CPT® Code x

Number: 1 Author: Author Date: Indeterminate
Pfizer,
Please see comment in Section 8 1

August 17, 2021

Please Note,

The lots below are associated with this Supplement.

STN	Supp. #	License Number	Company	Product	Lot Type	Lot Number	Sample Received Date
125742	0	2229	BioNTech Manufacturing GmbH	COVID-19	FC	FD7220	17 Aug 2021
125742	0	2229	BioNTech Manufacturing GmbH	COVID-19	FC	FE3592	17 Aug 2021
125742	0	2229	BioNTech Manufacturing GmbH	COVID-19	FC	FF2587	17 Aug 2021
125742	0	2229	BioNTech Manufacturing GmbH	COVID-19	FC	FF2588	17 Aug 2021
125742	0	2229	BioNTech Manufacturing GmbH	COVID-19	FC	FF2590	17 Aug 2021
125742	0	2229	BioNTech Manufacturing GmbH	COVID-19	FC	FF2593	17 Aug 2021
125742	0	2229	BioNTech Manufacturing GmbH	COVID-19	FC	FF8841	17 Aug 2021

The lot(s) associated with this BLA/supplement will be released upon completion of protocol review, any requested sample testing and approval of the BLA/supplement.

Since lots are associated with this BLA/supplement please be sure to provide a copy of the signed approval to the Product Release Branch by fax to 301.594.6924 or e-mail the letter to CBER Lot Clearance.

Biologist, Product Release Branch
CBER/OCBQ/DMPQ
WO, Building 71, Room G6062
240-402-9165 (main)/ 240-402-5839 (office)/301-595-1253 (fax)
Lot Release Information

From: Gottschalk, Laura <Laura.Gottschalk@fda.hhs.gov>
Sent: Tuesday, August 17, 2021 10:49 AM
To: CBER Lot Clearance <cberlotclearance@fda.gov>; Beshir, Leyla <Leyla.Beshir@fda.hhs.gov>
Cc: Smith, Michael (CBER) <Michael.Smith2@fda.hhs.gov>; Naik, Ramachandra <Ramachandra.Naik@fda.hhs.gov>; Eichelberger, Maryna <Maryna.Eichelberger@fda.hhs.gov>; Quander III, Joseph <Joseph.Quander@fda.hhs.gov>; Hulme, Cheryl <Cheryl.Hulme@fda.hhs.gov>
Subject: OVRR: Lot Clearance Request for STN 125742/0 - Please Respond by COB Thursday
Importance: High

Dear Lot Clearance,

Please confirm that there are no lots associated with this Submission. Please note, although the official action due date is January 16, 2022, we are aiming to approve within the week. Therefore, please provide a response by **COB Thursday, Aug 19.**

The lots are supposed to be received today. I have cc'ed some of the DBSQC team here in case they would like to provide any clarification or answer any questions that you may have.

- **Applicant Name:** BioNTech Manufacture GmbH (in partnership with Pfizer, Inc.)
- **License Number:** 2229
- **Company Address:** An der Goldgrube 12
  Mainz, Germany 55131
- **Application STN:** 125742/0
- **Product Name:** COVID-19 Vaccine, mRNA (COMIRNATY)
- **Submission Type:** Original Application (Priority 8 Month)
- **Action Due Date:** January 16, 2022 (please see note above)
- **Short Summary:** For active immunization to prevent COVID-19 disease caused by SARS-CoV-2 in individuals 16 years of age and older.

Thanks in advance and please let us know if you have any questions.

Best,
Laura

Laura Gottschalk, PhD
Regulatory Project Manager/Primary Reviewer

Center for Biologics Evaluation and Research
Office of Vaccines Research and Review
U.S. Food and Drug Administration
Tel: 301-796-0798

U.S. FOOD & DRUG ADMINISTRATION

From: Marion Gruber, PhD, Director, Office of Vaccines Research and Review, Center for Biologics Evaluation and Research

To: BLA STN 125742/0

Date: August 17, 2021

Subject: Rationale for designation of a nonproprietary name for COVID-19 Vaccine, mRNA (Comirnaty) that does not include a distinguishing suffix

Introduction: BioNTech Manufacturing GmbH has submitted a Biologics License Application for a COVID-19 vaccine (STN 125742, Action Due Date January 16, 2022). The proposed indication and usage statement from the draft package insert is as follows: "COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older."

This memorandum documents the justification for and my supervisory concurrence with the decision to depart from the recommendations in the Guidance for Industry: Nonproprietary Naming of Biological Products (January 2017) ("Naming Guidance") in approving a non-proprietary name without a suffix for this product.[1]

Summary:

I have concluded that the existing mechanisms to track this product are sufficient to ensure safety and pharmacovigilance and a suffix on the nonproprietary name is not necessary for the safe use of this vaccine.

The issue of whether to designate the nonproprietary names of vaccines without a distinguishing suffix was discussed with the FDA Biosimilar Policy Council on April 10, 2019.[2] The Council, including Dr. Marks and Dr. Woodcock, agreed with OVRR that a distinguishing suffix was not needed for vaccines and further recommended that if we designate a proper name without a distinguishing suffix for a vaccine, we should document this departure from the Naming Guidance. As Director of OVRR, I am the supervisor to OVRR staff who reviewed this BLA. This memo documents my concurrence with the decision to depart from the Naming Guidance.

[1] See 21 C.F.R. § 10.115(d)(3) ("Although guidance documents do not legally bind FDA, they represent the agency's current thinking. Therefore, FDA employees may depart from guidance documents only with appropriate justification and supervisory concurrence.")

[2] The FDA Biosimilar Policy Council is a cross-center workgroup within FDA that discusses issues regarding the implementation of the BPCI Act.

The fundamental question for this memo is whether the inclusion of the suffix in the proper name for Comirnaty is necessary for safe use, or whether other measures are in place to that are sufficient to ensure safe use and pharmacovigilance.

This memo describes unique vaccine administration recording requirements and safety monitoring programs for U.S.-licensed vaccines, including requirements for vaccines subject to the National Vaccine Compensation Injury Program. The totality of circumstances associated with the administration of vaccines, including the unique recordkeeping requirements, monitoring systems, and public health considerations, supports the review team recommendation and my decision to depart from the Naming Guidance and to designate a proper name without a distinguishing suffix for this vaccine.

1. Vaccination Records

Unique recordkeeping requirements associated with the administration of vaccines in the U.S., including those associated with the National Childhood Vaccine Injury Act and Immunization Information Systems, provide for the identification of most vaccines by their manufacturer (and potentially by lot number), without the need for a distinguishable suffix.

National Childhood Vaccine Injury Act: Most US-licensed vaccines are subject to The National Childhood Vaccine Injury Act of 1986. Covered vaccines are those recommended for routine administration to children or pregnant women by the CDC, subject to an excise tax by federal law and added to the Vaccine Injury Compensation Table by the Secretary for HHS. [3]

For vaccines included in the "Vaccine Injury Table" (which include most of the US-licensed vaccines) there are additional recordkeeping requirements that permit the identification of the vaccine administered without a suffix. For those vaccines included in the "Vaccine Injury Table" the National Childhood Vaccine Injury Act of 1986 requires each healthcare provider (HCP) who administers a vaccine included in the "Vaccine Injury Table" to record in the vaccinee's permanent medical record 1) the date of administration of the vaccine, 2) the vaccine manufacturer and lot number, and 3) the name and address and, if appropriate the title of the HCP administering the vaccine.[4] This requirement is unique for vaccines. This Act applies to any vaccine for which there is a routine recommendation to children or pregnant women, even if many or most doses of the vaccine are administered to adults in general (e.g., influenza vaccine).

For those vaccines that are not included on the Vaccine Injury Table, the Advisory Committee on Immunization Practices recommends that "This information should be kept for all vaccines, not just for those required by the Act."(https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/records.html).

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[3] Covered vaccines: Diphtheria, Tetanus, Pertussis, *Haemophilus influenzae* type b, Hepatitis A, Hepatitis B, Human papillomavirus, Seasonal Influenza, Measles, Mumps, and Rubella, Meningococcal, Pneumococcal conjugate, Polio, Rotavirus, and Varicella, in any combination.

[4] https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/vaccine-injury-table.pdf

Immunization Information Systems: Unlike records associated with other drugs or biologics, vaccination records are required for childcare, school, summer camps and international travel. These records are retained by the clinic or HCP office in a patient's chart. To facilitate retrieval of records, all states have an Immunization Information System (IIS). IIS are centralized population-based repositories of immunization related information. They receive and share data on individual clients/patients with a number of other systems, including Electronic Health Record systems (EHR-S). One of the goals of the IIS is to promote vaccine safety in public and private provider settings and enable the identification of vaccine recipients by vaccine lot, manufacturer, provider, and/or time frame – consistent with the NCVIA of 1986 but not limited to vaccines subject to the Act.

Participation in IIS is widespread and supported by the federal government. One of the national Healthy People objectives for 2020 was 95% participation of children aged <6 years in a fully operational population-based IIS (participating in an IIS means having two or more vaccinations recorded in the IIS). IIS data from 2012 indicate that approximately 86% of children aged <6 years with two or more vaccinations were participating in IISs (CDC. Progress in immunization information systems – United States, 2012. *MMWR Morb Mortal Wkly Rep.* 2013;62(49):1005-1008. Mangione-Smith R, DeCristofaro AH, Setodji CM, et al. The quality of ambulatory care delivered to children in the United States. *N Engl J Med.* 2007;357(15):1515-1523. DOI: 10.1056/NEJMsa064637). From 2013 to 2016 the percentage of children with ≥2 immunizations recorded in IISs increased from 90% to 94%, approaching the *Healthy People 2020* objective of ≥95%. (CDC. Progress in childhood vaccination data in immunization information systems – United States, 2013-2016. *MMWR Morb Mortal Wkly Rep.* 2017;66(43):1178-1181).

Nationally, 57.8 million U.S. adults aged 19 years or older participated in an IIS in 2012 (CDC. Progress in immunization information systems – United States, 2012. *MMWR Morb Mortal Wkly Rep.* 2013;62(49):1005-1008.). This number reflects adults who may have had childhood vaccines entered during childhood and now have aged to adults. In 2013, 32% of U.S. adults had a record in the IIS and at least one vaccination administered during adulthood.

The National Vaccine Advisory Committee (established to comply with Section 2105 of the Public Health Service Act) recommends that public health departments work toward including adults in all state IISs, reduce barriers to including adult vaccination records in IISs, and ensure that IISs meet new standards of EHR interoperability to track and maintain adult vaccination records.

For vaccines administered to the military each branch records and tracks immunizations (https://www.health.mil/Military-Health-Topics/Health-Readiness/Immunization-Healthcare/Immunization-Tracking-Systems).

2. **Vaccine Safety Monitoring Systems**

The Vaccine Adverse Reporting System:
VAERS is a national program managed by the FDA and CDC to monitor the safety of all vaccines licensed for use in the US. FDA and CDC conduct safety surveillance for vaccine-associated safety concerns utilizing VAERS. This system is valuable for signal detection, and it has unique characteristics that differentiate it from other adverse event surveillance systems. As a preliminary matter, in addition to

mandatory reporting of adverse events by manufacturers that is common to all drugs and biologics, for vaccines covered by the National Childhood Vaccine Injury Act, there is mandatory reporting for healthcare providers for any event listed by the vaccine manufacturer as a contraindication to subsequent doses of the vaccine and any adverse event found in the "Reportable Events table" that occurs within the specified time after vaccination.

The form that is used for VAERS, which mirrors the information required to be collected under the NCVIA, further permits the accurate identification of the event and the vaccine administered. VAERS requires the vaccine name ("type and brand name"), manufacturer, and lot number. The form permits the user to enter the vaccine type/brand name manually or to select a specific vaccine identified by abbreviation/disease and proprietary name from a "pick list." (https://vaers.hhs.gov/pdf/VAERSForm_Mar2021.pdf). While it may be possible for the FAERS system that covers other biologics and drugs to adopt a similar format, at this time, this format is unique to VAERS and is permitted, in part, because of the limited scope of products covered by the reporting system.

The Vaccine Safety Datalink: The Vaccine Safety Datalink (VSD) project is a collaboration between the National Immunization Program of the CDC and several HMOs. The project began in 1990 with the purpose of rigorously evaluating concerns about the safety of vaccines. According to the CDC, the VSD generates rapid, important safety assessments for both routine vaccinations and emergency vaccination campaigns.[5] To accomplish this, the VSD uses electronic health data from each participating site that includes information on vaccine type, vaccine manufacturer, vaccine lot number, date of vaccination, and other vaccinations given on the same day. Participating healthcare organizations cover more than 9.1 million people nationwide (over 3% of the US population).

3. Additional considerations for vaccines:

The four-letter suffix will likely be interpreted by some individuals to refer to an unintended and non-specific attribute to the product. Some individuals may believe this refers to an unidentified ingredient, a new adjuvant or an abbreviation for a chemical. This may cause confusion and concern regarding the safety of the vaccine. This confusion is particularly concerning given increased public concerns about the safety of vaccination and rising levels of refusals to vaccinate. Decreased confidence in vaccine safety does not just affect the health of patients who refuse to vaccinate, as is the case with decreased confidence in therapeutic biologic products. Confusion surrounding vaccine safety could undermine the effectiveness of the vaccine program overall and, ultimately, lead to negative public health effects, including outbreaks of preventable diseases.

[5] Vaccine 32 (2014) 5390–5398

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

----------INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL (3)

----------CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

----------ADVERSE REACTIONS----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, fever, and injection site swelling. (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, injection site swelling, fever, and injection site redness. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

Summary of Comments on 82A_BLA 125742-0_08-17-2021_Telecon_Labeling via FAX_e.pdf

Page: 1

Number: 1 Author: Author Date: Indeterminate
Pfizer,
Please add the percentages as we previously requested Without the percentages, stating the frequencies ≥10% is misleading

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

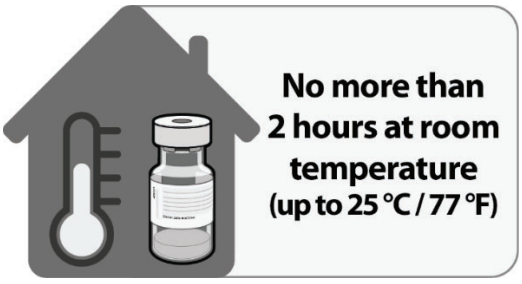
2.1 Preparation for Administration

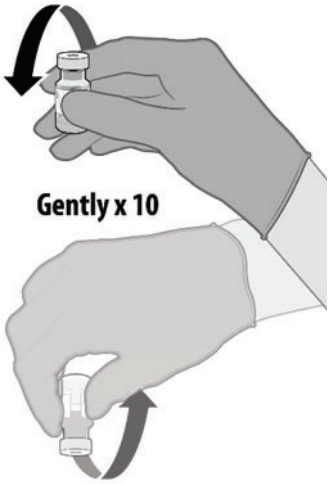
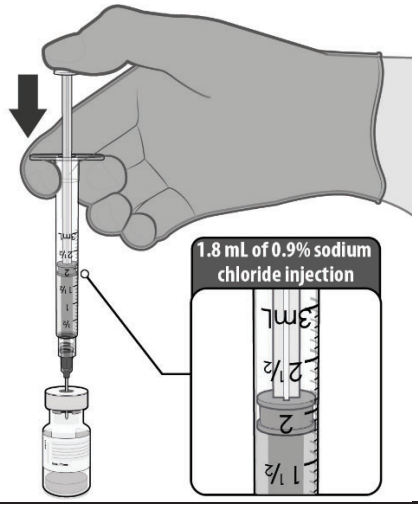
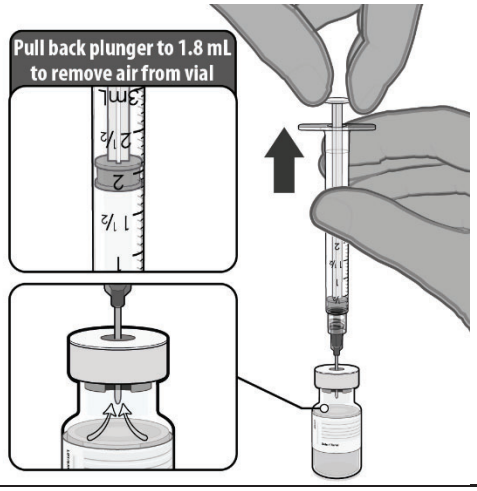
Prior to Dilution

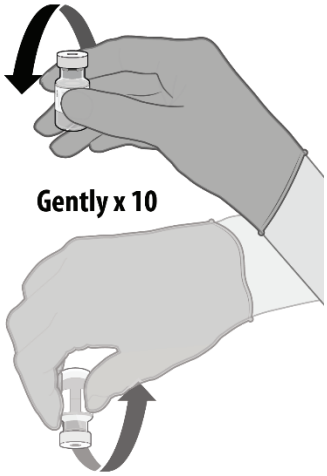
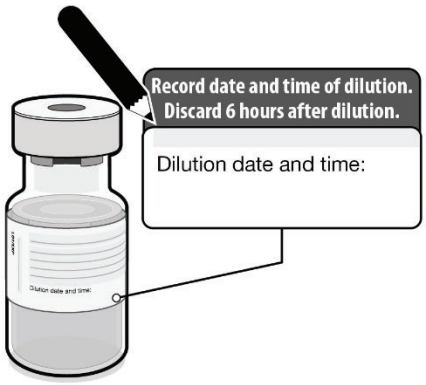
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

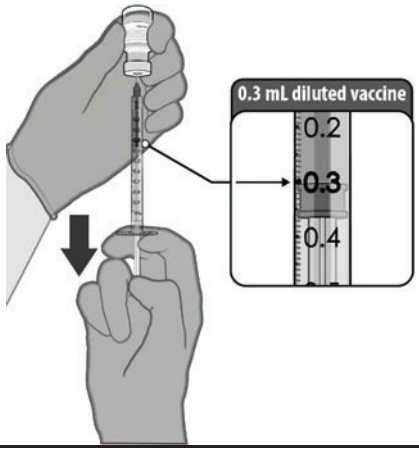
Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than one vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes.

	• Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.
	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.

	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination,

including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the EUA (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events[1]

Overall, xx,xxx (51.1%) participants in the COMIRNATY group and xx,xxx (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional xx (8.1%) and xx (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

Unsolicited Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

A total of xx,xxx (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8,931, placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis[2] of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

Number: 1 Author: Author Date: Indeterminate

Pfizer,

This is a mixture of list of solicited and unsolicited adverse reactions Some of these are captured in the tables above and others that we consider adverse reactions are presented below

Number: 2 Author: Author Date: Indeterminate

Pfizer,

We agree that presentation of the number of participants who originally received vaccine and had total follow up time for at least 6 months should be displayed

We disagree with the addition of follow up time for placebo recipients who received vaccine as safety data from the unblinded follow up time is not being displayed

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4396 (33.8%) participants who received COMIRNATY and 2136 (16.4%) participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include nonserious adverse events were reported by 2551 (28.6%) participants who received COMIRNATY and 1432 (16.1%) participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 29 (29%) participants who received COMIRNATY and 15 (15%) participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see*

Clinical Studies (14.1)]. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials ; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine--related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or

hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% Credible Interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group. .

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine vs. placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	COMIRNATY Na=19,993 Cases n1b Surveillance Timec (n2d)	Placebo Na=20,118 Cases n1b Surveillance Timec (n2d)	Vaccine Efficacy % (95% CIe)
All participantsf	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	COMIRNATY Na=21,047 Cases n1b Surveillance Timec (n2d)	Placebo Na=21,210 Cases n1b Surveillance Timec (n2d)	Vaccine Efficacy % (95% CIe)
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2

infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium

Number: 1 Author: Author Date: Indeterminate

Pfizer,

We reiterate that this general statement is misleading because some of the subgroup analyses were limited by the size of the subgroup and low number of confirmed cases, which limits the interpretation of those analyses We disagree with this addition and again request deletion

Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit www.comirnatyglobal.com.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.4

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

----------INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL (3)

----------CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

----------ADVERSE REACTIONS----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 08/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FDA-CBER-2021-5683-0652290

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

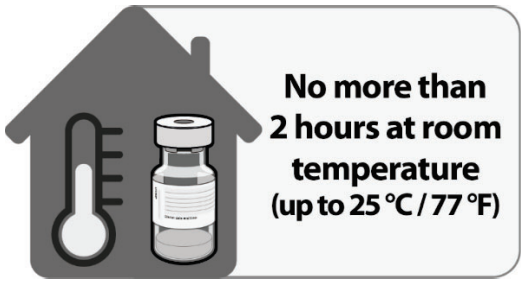
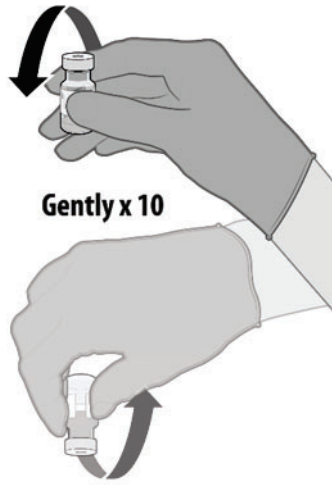
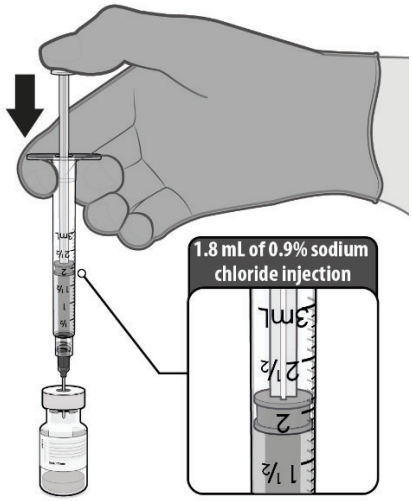
2.1 Preparation for Administration

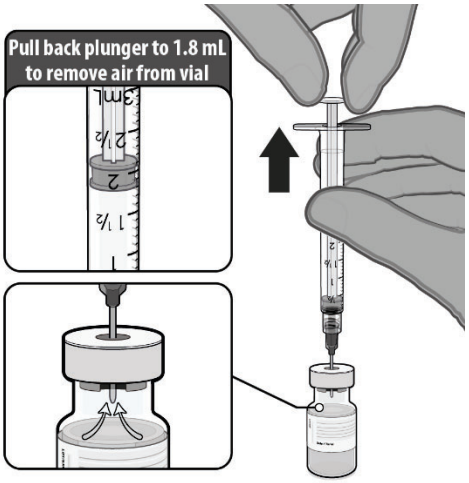
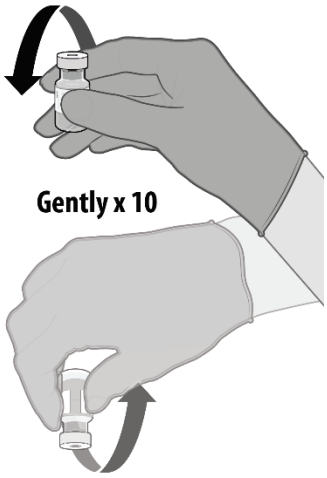
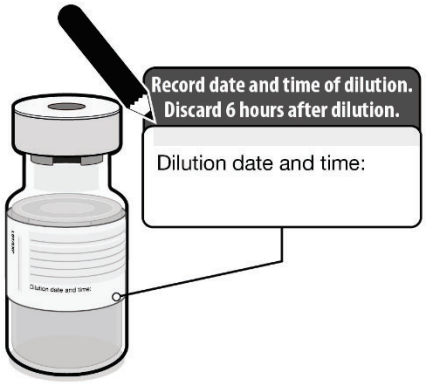
Prior to Dilution

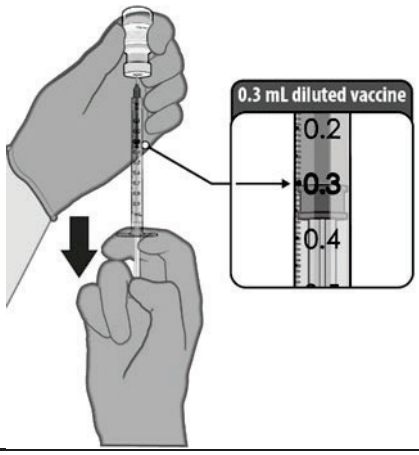
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

In clinical studies, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were nausea (1.4%), malaise (0.7%),, asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%),, lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

Unsolicited adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded

Number: 1 Author: Author Date: Indeterminate

Pfizer,
The events not contained in the Tables 1-4 above were not solicited, thus they should be categorized correctly and moved into the discussion of Non-Serious Unsolicited Adverse Events, below, using a format consistent with presentation of those events, by treatment arm and follow-up time period
Events discussed elsewhere should not be included (lymphadenopathy, injection site redness)

follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4,396 (33.8%) participants who received COMIRNATY and 2,136 (16.4%) participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), all events, which include nonserious adverse events were reported by 2,551 (28.6%) participants who received COMIRNATY and 1,432 (16.1%) participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 29 (29%) participants who received COMIRNATY and 15 (15%) participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were

immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, and participants with obesity and medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Number: 1 Author: Author Date: Indeterminate
Pfizer,
Please see our revised statement regarding subgroup analyses off vaccine efficacy

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/ or www.comirnatyglobal.com.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.5

US Govt. License No. x

Number: 1 Author: Author Date: Indeterminate

Pfizer,

We continue to request to only provide a link to DailyMed as this is sufficient Furthermore, the other site may contain elements that are promotional and have not been reviewed by FDA

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

----------INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

----------CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

----------ADVERSE REACTIONS----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FDA-CBER-2021-5683-0652314

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

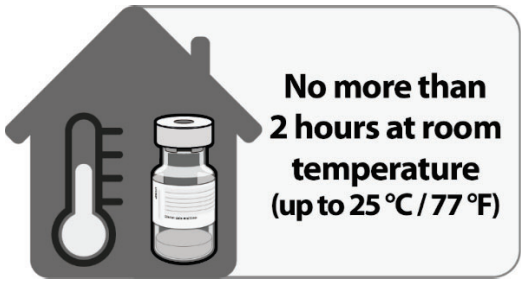
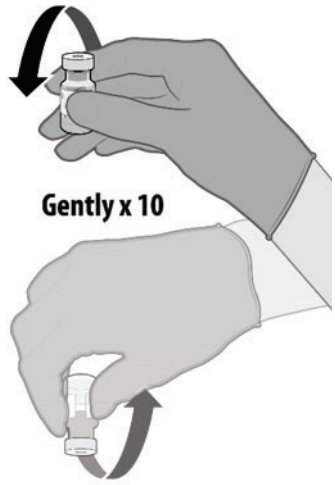
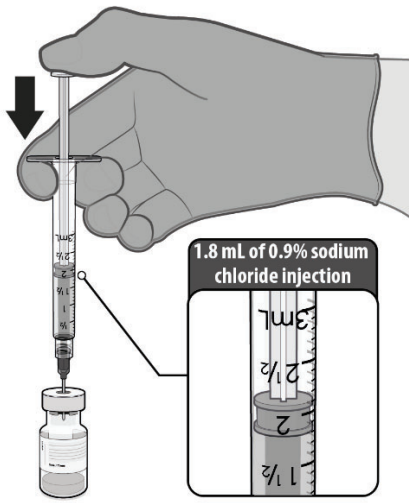
2.1 Preparation for Administration

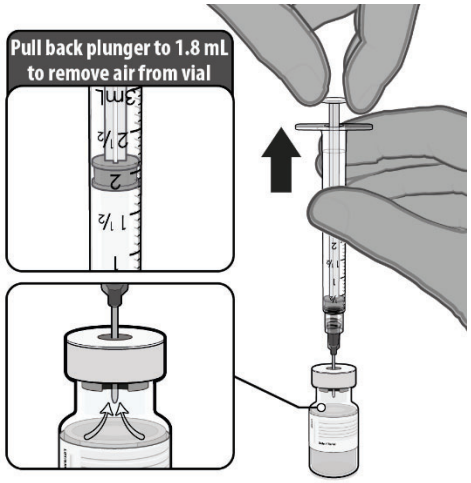
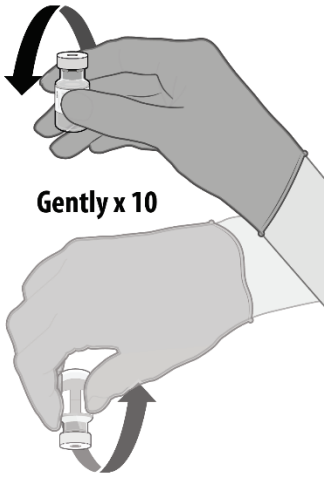
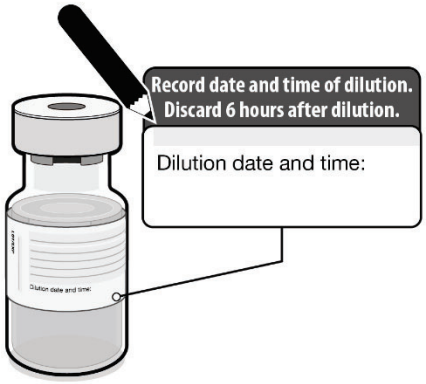
Prior to Dilution

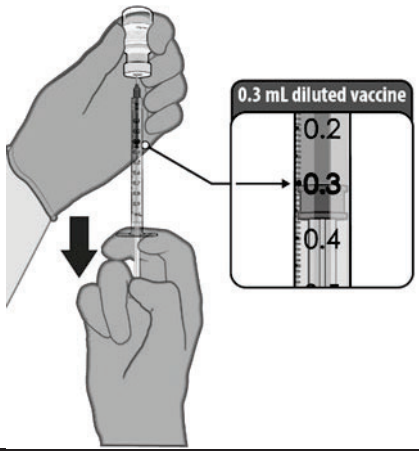
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of serious and non-serious unsolicited adverse events reported through 1 month after Dose 2 in participants 16 through 55 years of age following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.4% vs. 0.5%), malaise (0.7% vs. 0.1%), asthenia (0.4% vs. 0.1%), decreased appetite (0.2% vs. <0.1%), hyperhidrosis (0.1% vs. <0.1%), lethargy (0.1% vs. <0.1%), and night sweats (0.1% vs. <0.1%).

In an analysis of serious and non-serious unsolicited adverse events reported through 1 month after Dose 2 in participants 56 years of age and older following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.0% vs. 0.3%), malaise (0.5% vs. 0.1%), asthenia (0.3% vs. 0.1%), lethargy (0.2% vs. <0.1%), decreased appetite (0.1% vs. <0.1%), hyperhidrosis (0.1% vs. <0.1%), and night sweats (0.1% vs. <0.1%).

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed

stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

In analyses of non-serious unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, non-serious unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, non-serious unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection, non-serious unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87, one of which was serious) versus the placebo group (8). Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Number: 1 Author: Author Date: Indeterminate
Pfizer,
Please ensure that the numbers in this paragraph only include the non-serious adverse events

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.

b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.6

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

----------INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

----------CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

----------ADVERSE REACTIONS----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FDA-CBER-2021-5683-0652336

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

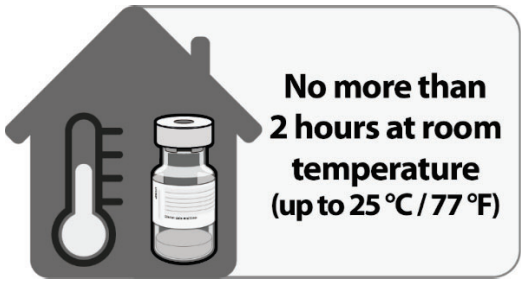
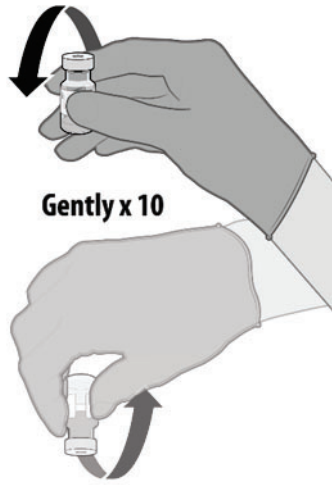
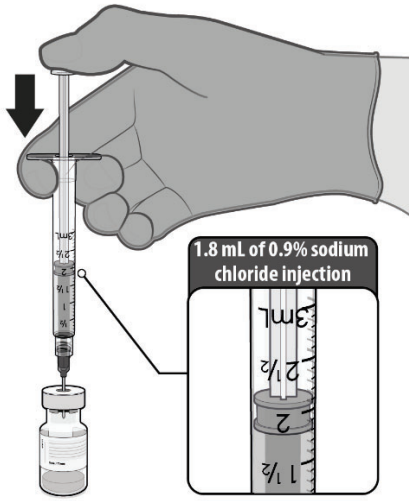
2.1 Preparation for Administration

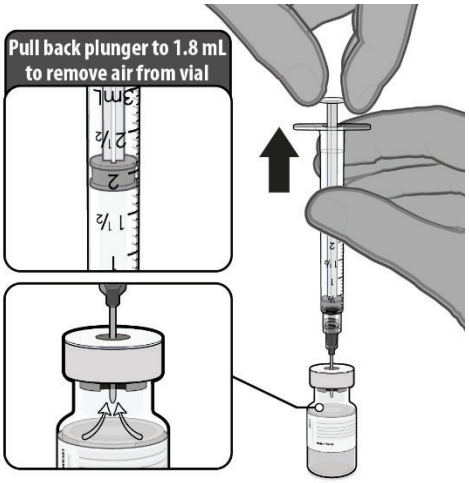
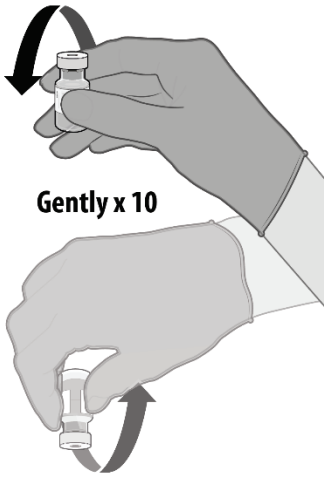
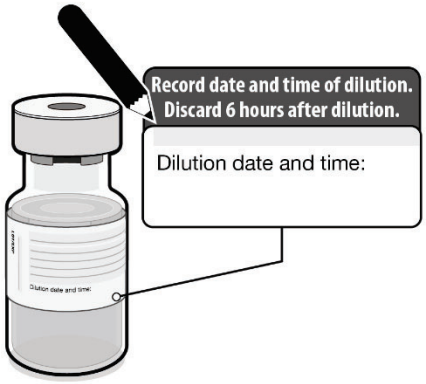
Prior to Dilution

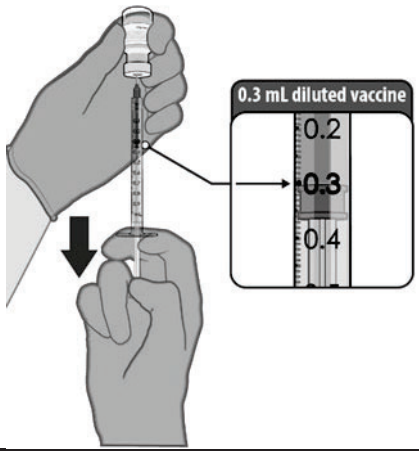
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of all unsolicited adverse events reported through 1 month after Dose 2 in participants 16 through 55 years of age following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.4% vs. 0.5%), malaise (0.7% vs. 0.1%), asthenia (0.4% vs. 0.1%), decreased appetite (0.2% vs. <0.0%), hyperhidrosis (0.1% vs. <0.0%), lethargy (0.1% vs. <0.0%), and night sweats (0.1% vs. <0.0%).

In an analysis of all unsolicited adverse events reported through 1 month after Dose 2 in participants 56 years of age and older following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.0% vs. 0.3%), malaise (0.5% vs. 0.1%), asthenia (0.3% vs. 0.1%), lethargy (0.2% vs. <0.0%), decreased appetite (0.1% vs. <0.0%), hyperhidrosis (0.1% vs. <0.0%), and night sweats (0.1% vs. <0.0%).

In analyses of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, non-serious unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, non-serious unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection, non-serious unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients compared to placebo recipients was

Summary of Comments on 106A_2_BLA 125742-0_08-20-2021_Telecon_Labeling via FAX_e.pdf

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Pfizer,
Instead of presenting percentages for the two age groups separately, report the number of subjects (16 years of age and older) in the vaccine group and the placebo group reporting each event Please also include lymphadenopathy and delete the sentence pertaining to lymphadenopathy below

primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI[e])
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI[e])
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior

SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium

Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.7

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

----------INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

----------CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

----------ADVERSE REACTIONS----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FDA-CBER-2021-5683-0652357

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

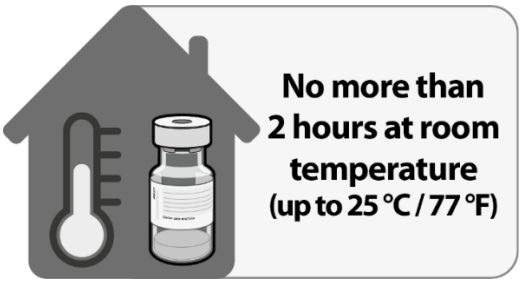
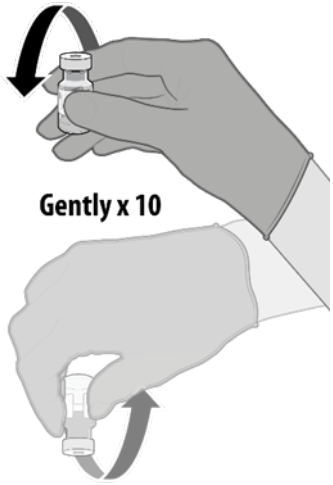
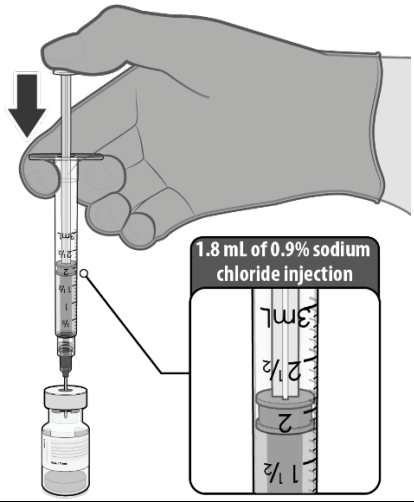
2.1 Preparation for Administration

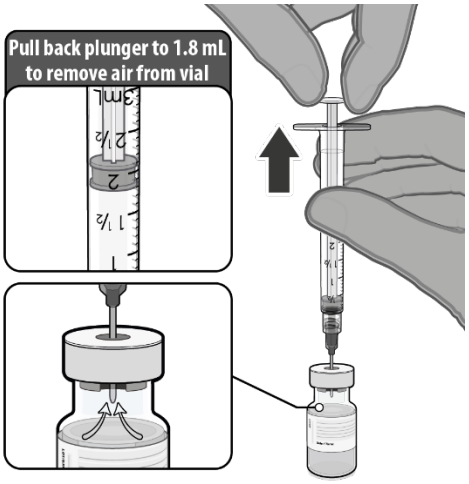
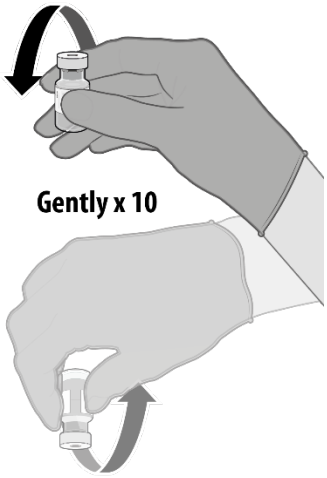
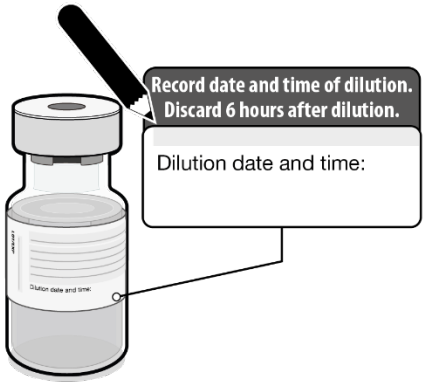
Prior to Dilution

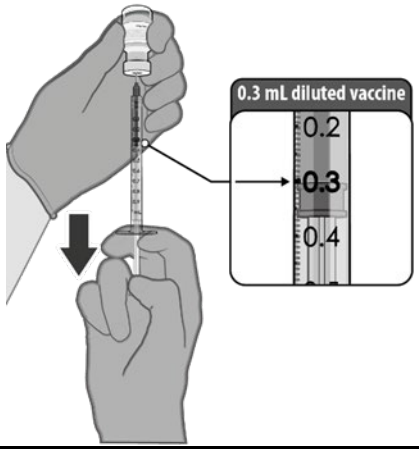
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of all unsolicited adverse events reported following any dose, through 1 month after Dose 2, in participants 16 years of age and older (N=43,847; 21,926 COMIRNATY group vs. 21,921 placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (274 vs. 87), malaise (130 vs. 22), lymphadenopathy (83 vs. 7), asthenia (76 vs. 25), decreased appetite (39 vs. 9), hyperhidrosis (31 vs. 9), lethargy (25 vs. 6), and night sweats (17 vs. 3).

In analyses of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection that included 100 COMIRNATY recipients and 100 placebo recipients, unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there

were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to

4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Specific Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more

comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by

Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.8

US Govt. License No. x

Transmittal Memo

TO: Lorrie McNeill
Director
Office of Communication, Outreach and Development

FROM: Marion F. Gruber, Ph.D.
Director
Office of Vaccines Research and Review

Marion F. Gruber -S

Digitally signed by Marion F. Gruber -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300077111, cn=Marion F. Gruber -S
Date: 2021.08.23 08:22:53 -04'00'

RE: Action Package for: STN 125742/0, COVID-19 Vaccine, mRNA (COMIRNATY)

DATE: August 23, 2021

Office Point of Contact: Laura Gottschalk, Ph.D.

Please include the following information for posting on Web pages:

Proper Name: COVID-19 Vaccine, mRNA
Tradename: COMIRNATY
Manufacturer: BioNTech Manufacturing GmbH
Indication: COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

Please review and redact the documents indicated in the options below and post on CBER's Approval Web page. Additional WORD documents (including labeling) are provided via e-mail to '*CBER-OCOD-Action Packages'* on the date of approval.

The documents identified as "Post to Web" in CBER regulatory systems comprise the official Action Package for Posting under Section 916 of FDAAA for original BLAs/NDAs.

Please add the following information to CBER's Approval Web page:
Demographic Subgroup Information – COVID-19 Vaccine, mRNA (COMIRNATY)

Refer to Section 1.1 of the Clinical Review Memo for information about participation in the clinical trials and any analysis of demographic subgroup outcomes that is notable.

In addition, please post appropriate documents on the Web pages indicated in the following table.

Web page	**Post?** (Add "X" if Yes)
FDA's PREA Web page https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/biologics-prea-reviews-and-labeling-changes	X
Vaccines Licensed for Use in the United States (https://www.fda.gov/vaccines-blood-biologics/vaccines/vaccines-licensed-use-united-states)	X
Approved Cellular and Gene Therapy Products (https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products)	

Web page	**Post?** (Add "X" if Yes)
Complete List of Donor Screening Assays for Infectious Agents and HIV Diagnostic Assays (https://www.fda.gov/vaccines-blood-biologics/complete-list-donor-screening-assays-infectious-agents-and-hiv-diagnostic-assays) [IF SELECTED, PROVIDE THE APPLICABLE ASSAY TABLE AND DATA TO BE INCLUDED IN TABLE]	
Infectious Disease Testing (http://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/BloodDonorScreening/InfectiousDisease/default.htm)	
Testing Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) Donors for Relevant Communicable Disease Agents and Diseases (https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/testing-human-cells-tissues-and-cellular-and-tissue-based-product-hctp-donors-relevant-communicable)	

U.S. FOOD & DRUG ADMINISTRATION

LABELING REVIEW MEMORANDUM

To: The File

Date: September 1, 2021

STN: 125742/0

Applicant: BioNTech Manufacturing GmbH (in partnership with Pfizer, Inc.)

Product: COVID-19 Vaccine, mRNA (COMIRNATY)

From: Laura Gottschalk, Ph.D.
OVRR/DVRPA/RRB3

Through: Elizabeth M. Sutkowski, Ph.D.
OVRR/DVRPA/RRB3

Summary:
This memorandum outlines the labeling review of the original BLA (STN 125742/0) from BioNTech Manufacturing GmbH (in partnership with Pfizer, Inc.) for COVID-19 Vaccine, mRNA (COMIRNATY) for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. This BLA was a Rolling Submission and the labeling information was included in the second (last) roll (STN 125742/0.1) submitted and received on May 18, 2021.

The product labeling submitted in this original BLA included carton and container labels and a proposed Package Insert (PI) incorporating safety and efficacy data that support the licensure of COMIRNATY for use in individuals 16 years of age and older. Additionally, a Dear Health Care Provider (HCP) Letter was submitted as part of the labeling to be included with the packaging of lots considered by CBER to be BLA-compliant.

COMIRNATY is packaged at two sites: Pfizer Manufacturing Belgium NV (Puurs) and Pharmacia and Upjohn Company LLC (Kalamazoo). Separate carton and container labels for both Kalamazoo and Puurs were included in the submission. Labels for the following COMIRNATY cartons and containers were submitted:

- COMIRNATY Multiple Dose Vial Labels (Kalamazoo)
- COMIRNATY Multiple Dose Vial Labels (Puurs)
- COMIRNATY 25 Vial Carton Labels (Kalamazoo)
- COMIRNATY 25 Vial Carton Labels (Puurs)
- COMIRNATY 195 Vial Carton Labels (Kalamazoo)
- COMIRNATY 195 Vial Carton Labels (Puurs)

Vials of sterile 0.9% Sodium Chloride Injection, USP will also be provided but shipped separately for use as a diluent for COMIRNATY. The diluent is supplied by two manufacturers: Fresenius Kabi USA, LLC and Hospira, Inc. Separate carton and container labels for both Fresenius Kabi and Hospira were included in the submission. Labels for the following diluent cartons and containers were submitted:

- Diluent Vial Label (Fresenius Kabi) – 2 mL single dose vial
- Diluent Vial Label (Hospira) – 10 mL single dose vial
- Diluent Carton Labels (Fresenius Kabi) – 25 single-dose vials
- Diluent Carton Labels (Hospira) – 25 single-dose vials
- Diluent Supplemental Carton Stamp (Fresenius Kabi)
- Diluent Supplemental Carton Sticker (Hospira)

Revisions to the proposed labels for the cartons and containers, PI and Dear HCP Letter were communicated to Pfizer/BioNTech, as indicated below in Table 1, and the corresponding amendments that were received are described in Table 2. The principal reviewers of the PI were the Clinical Reviewers, the Pharmacovigilance Reviewer, the Biostatistics Reviewers, the Advertising and Promotional Labeling Branch Reviewer, the Committee Chair, the RPMs, and supervisors, with additional advice from DVP, DVRPA and OVRR Immediate Office of the Director.

Table 1. Labeling Review History

Date	Action	Labels		
		PI	Cartons & Containers	Dear HCP Letter
07/28/2021	First set of labeling comments regarding the PI were sent.	✓		
08/04/2021	Internal labeling meeting	✓		
08/05/2021	Internal labeling meeting	✓		
08/05/2021	Second set of labeling comments regarding the PI were sent.	✓		
08/05/2021	Four questions regarding the diluent were sent.	✓		
08/09/2021	Internal labeling meeting		✓	
08/09/2021	First set of labeling comments regarding the cartons and containers were sent.		✓	
08/11/2021	Internal labeling meeting	✓		
08/13/2021	Internal labeling meeting	✓		
08/13/2021	Third set of labeling comments regarding the PI were sent.	✓		
08/16/2021	Two internal labeling meetings: one carton and container discussion and one PI discussion	✓	✓	
08/16/2021	Second set of labeling comments regarding the cartons and containers were sent.		✓	
08/16/2021	Teleconference with Pfizer to discuss identification of BLA-compliant lots and a draft Dear HCP Letter			✓
08/17/2021	Two internal labeling meetings: one carton and container discussion and one PI discussion	✓	✓	

Date	Action	Labels		
		PI	Cartons & Containers	Dear HCP Letter
08/17/2021	Two separate set of comments were sent: Third set of carton and container comments and fourth set of PI comments.	✓	✓	
08/18/2021	A request was sent to submit to the BLA the information that was emailed to Mary Malarkey on 08/16/2021 regarding identification of BLA-compliant lots and a draft Dear HCP Letter.			✓
08/18/2021	Internal labeling meeting	✓		
08/18/2021	Fifth set of PI comments sent and a request to submit specific carton and container label versions together in a new amendment for ease of refencing in the Approval Letter was sent.	✓	✓	
08/19/2021	Internal labeling meeting	✓		
08/19/2021	Sixth set of labeling comments regarding the PI were sent.	✓		
08/20/2021	Two internal labeling meetings: one PI discussion and one Dear HCP Letter discussion	✓		✓
08/20/2021	Seventh set of labeling comments regarding the PI were sent.	✓		
08/20/201	First set of comments regarding identification of BLA lots/Dear HCP Letter were sent.			✓
08/21/2021	Internal meeting to discuss the PI, carton and container labels and Dear HCP Letter	✓	✓	✓
08/21/2021	The Applicant was notified that the carton and container labels submitted in Amendment 63 on August 19, 2021 are considered the Final Draft Labels.		✓	
08/21/2021	Eighth set of labeling comments regarding the PI sent	✓		
08/21/2021	Second set of comments regarding the Dear HCP Letter were sent.			✓
08/21/2021	The Applicant was notified that there are no additional comments on their Dear HCP Letter.			✓
08/22/2021	The Applicant was notified that the PI submitted in Amendment 74, dated August 21, 2021 is considered the Final Draft Label.	✓		

Table 2. Labeling Amendments

Date	Amendment	Summary	Labels		
			PI	Cartons & Containers	Dear HCP Letter
08/02/2021	125742/0.27	Response to July 28, 2021, first set of labeling comments regarding the PI.	✓		
08/09/2021	125742/0.36	Response to four questions regarding the diluent from dated August 5, 2021.	✓		

Date	Amendment	Summary	Labels		
			PI	Cartons & Containers	Dear HCP Letter
08/09/2021	125742/0.38	Response to August 5, 2021, second set of comments on the PI.	✓		
08/13/2021	125742/0.46	Response to August 9, 2021 first set of comments on the carton and container labels.		✓	
08/16/2021	125742/0.49	Response to August 13, 2021, third set of comments on the PI.	✓		
08/17/2021	125742/0.53	Response to August 16, 2021 second set of comments on the carton and container labels. This amendment also contains the full diluent carton labels and diluent vial labels that were not included in the original BLA submission.		✓	
08/18/2021	125742/0.58	Response to August 17, 2021, fourth set of comments on the PI.	✓		
08/19/2021	125742/0.63	Responses to August 18, 2021, third set of comment on the carton and container labels.		✓	
08/18/2021	125742/0.64	Response to August 18, 2021, comments regarding identification of BLA-compliant lots/Letter to HCP.			✓
08/19/2021	125742/0.66	Response to August 18, 2021, fifth set of comments on the PI.	✓		
08/20/2021	125742/0.68	Response to August 19, 2021, sixth set of comments on the PI.	✓		
08/20/2021	125742/0.71	Response to August 20, 2021, seventh set of comments on the PI.	✓		
08/20/2021	125742/0.73	Response to August 20, 2021, first set of comments regarding identification of BLA lots/Dear HCP Letter.			✓
08/21/2021	125742/0.74	Response to August 21, 2021, eighth set of comments on the PI.	✓		
08/21/2021	125742/0.76	Response to August 21, 2021, second set of comments regarding identification of BLA lots/Dear HCP Letter.			✓
08/23/2021	125742/0.77	Final PI	✓		
08/24/2021	125742/0.78	Final PI with license number included.	✓		

Regarding Pfizer/BioNTech's amendments containing revisions to the PI:
Pfizer/BioNTech submitted to CBER eight versions of the PI (as amendments to the BLA) in response to CBER's comments in the following amendments: 125742/0.27, 125742/0.38,

125742/0.49, 125742/0.58, 125742/0.66, 125742/0.68, 125742/0.71 and 125742/0.74. The clean copy Word version of the PI submitted on August 21, 2021 (Amendment 74) was considered the Final Draft PI for approval. Pfizer/BioNTech was notified on August 23, 2021, that CBER considered the clean version of the PI included in Amendment 74 as the Final Draft PI for approval.

Two additional versions of the PI were submitted to the BLA after the date of approval. A Final Version of the PI with an updated version number was submitted in Amendment 77 on August 23, 2021. Pfizer/BioNTech then submitted a revised Final Version of the PI in Amendment 78 on August 24, 2021 which included the license number that was inadvertently left off previous versions. Pfizer/BioNTech submitted each of these final versions of the PI in amendments to the BLA without being requested to do so by CBER.

Regarding Pfizer/BioNTech's amendments containing revisions to the carton and container labels:
Pfizer/BioNTech submitted to CBER three versions of the revised carton and container labels in response to CBER's comments in the following amendments: 125742/0.46, 125742/0.53 and 125742/0.63. Pfizer/BioNTech was notified on August 21, 2021, that the carton and container labels submitted in Amendment 63 on August 19, 2021 were considered the Final Draft Labels.

Regarding Pfizer/BioNTech's amendments containing revisions to the Dear HCP Letter:
In response to CBER's inquiry about BLA-compliant EUA-labeled lots that may be available for use upon licensure of COMIRNATY, Pfizer submitted information listing which lots they considered to be manufactured according to the BLA. To address the issue of these lots not bearing the vial label associated with BLA-approval, CBER worked with Pfizer to develop a Dear HCP letter to be included with lots considered by CBER to be BLA-compliant. This letter explained that some lots labeled for EUA use were also considered BLA-compliant and refers HCP to a website for additional information. CBER requested and Pfizer agreed that only EUA-labeled lots that had also undergone CBER lot release according to the BLA would be considered BLA-compliant and listed at the website included in the Dear HCP letter.

Pfizer/BioNTech submitted to CBER two versions of the revised Dear HCP Letter in response to CBER's comments in the following amendments: 125742/0.73 and 125742/0.76. Pfizer/BioNTech was notified on August 21, 2021, that CBER has no additional comments on the Dear HCP Letter provided in Amendment 76 on
August 21, 2021.

Review of National Drug Codes (NDCs):
A review of the NDCs on the COMIRNATY and diluent carton and container labels was conducted according to the Job Aid JA 900.08.

Table 3. NDC assignments for COMIRNATY and diluent carton and container labels

Label	NDC#
COMIRNATY Vial Label (Kalamazoo and Puurs)	0069-1000-01
COMIRNATY 25 Vial Carton Label (Kalamazoo and Puurs)	0069-1000-03
COMIRNATY 195 Vial Carton Label (Kalamazoo and Puurs)	0069-1000-02

Diluent Vial Label (Fresenius Kabi) – 2 mL single dose vial	63323-186-04
Diluent Carton Label (Fresenius Kabi) – 25 single-dose vials	63323-186-02
Diluent Vial Label (Hospira) – 10 mL single dose vial	0409-4888-02
Diluent Carton Label (Hospira) – 25 single-dose vials	0409-4888-10

The first segments (NDC labeler code) were verified using the NDC/NHRIC Labeler Code site. The first segments are correct and appropriately assigned.

Table 4. Search Results for NDC Labeler Codes

NDC Labeler Code	Firm Name
0069	Pfizer Laboratories Div Pfizer Inc
63323	Fresenius Kabi USA, LLC
0409	Hospira, Inc.

The second segments (the product code that identifies a specific strength, dosage form, and formulation) are different (unique) for COMIRNATY labels (-1000-) and diluent labels (-186- [Fresenius Kabi] and -4888- [Hospira]).

The third segments (the package code that identifies package sizes and types) are different (unique) for labels of cartons containing 25 (-03) and 195 (-02) vials of COMIRNATY and for the individual vials (-01) of COMIRNATY. Additionally, the third segments are also distinct for the two diluent cartons (-02 [Fresenius Kabi] and -10 [Hospira]) and the two diluent vials (-04 [Fresenius Kabi] and -02 [Hospira]).

2D Bar Code Review Under the Drug Supply Chain Security Act (DSCSA):
During the COVID-19 public health emergency, FDA interprets the exemption and exclusion from certain requirements of the DSCSA to cover the distribution of prescription drug products either (a) issued an emergency use authorization under section 564 of the FD&C Act (21 U.S.C. 360bbb-3) to combat COVID-1917 or (b) approved by FDA to diagnose, cure, mitigate, treat, or prevent COVID-19. Therefore, COMIRNATY is exempt from the product identifier requirements, including serialization.

Additional information can be found in the Guidance for Industry: *Exemption and Exclusion from Certain Requirements of the Drug Supply Chain Security Act During the COVID-19 Public Health Emergency* (April 2020).

Recommendation:
The discipline reviewers mentioned above have reviewed the relevant labeling documents and found them to be acceptable as Final Draft Labeling for approval. As the Regulatory Project Manager, I concur with their recommendation. The Final Draft PI will be provided to the Office of Communication, Outreach and Development as part of the approval package for web posting.

16.1.3.1 LIST OF INDEPENDENT ETHICS COMMITTEE (IEC) OR INSTITUTIONAL REVIEW BOARD (IRB)

ARGENTINA

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1231	Comité Institucional de Revisión de Ensayos Clínicos (C.I.R.E.C.) del Hospital Militar Central "Cirujano Mayor Dr Cosme Argerich" Av. Luis María Campos 726, Edificio PACE Piso 5 CABA, 1426 ARGENTINA

BRAZIL

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1226	CONEP (Comissao Nacional de Etica em Pesquisa) SRTV 701, Via W 5 Norte, lote D, Edificio PO 700, 3º andar - Asa Norte Brasilia, DF 70719-040 BRAZIL Comite de Etica em Pesquisa da Faculdade de Medicina do ABC\Fundacao do ABC-- FMABC Avenida Lauro Gomes, 2000 - Vila Sacadura Cabral Santo Andre/SP, 09060-870 BRAZIL
1241	Comite de Etica em Pesquisa do Hospital Santo Antonio /Obras Sociais Irma Dulce Avenida Luiz Tarquínio, snº, portao 9, 1º andar, sala 1, Roma Salvador, BA 40414-120 BRAZIL CONEP (Comissão Nacional de Ética em Pesquisa) SRTV 701, Via W 5 Norte, lote D, Edifício PO 700, 3° andar -Asa Norte Brasília/DF, 70719-040 BRAZIL

GERMANY

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1185	Landesaerztekammer Baden-Wuerttemberg Liebknechtstr. 33 Stuttgart, 70565 GERMANY
1194	Landesaerztekammer Baden-Wuerttemberg Liebknechtstr. 33 Stuttgart, 70565 GERMANY
1195	Landesaerztekammer Baden-Wuerttemberg Liebknechtstr. 33 Stuttgart, 70565 GERMANY
1197	Landesaerztekammer Baden-Wuerttemberg Liebknechtstr. 33 Stuttgart, 70565 GERMANY
1202	Landesaerztekammer Baden-Wuerttemberg Liebknechtstr. 33 Stuttgart, 70565 GERMANY
1203	Landesaerztekammer Baden-Wuerttemberg Liebknechtstr. 33 Stuttgart, 70565 GERMANY

SOUTH AFRICA

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1229	Pharma Ethics Independent Research Ethics committee 123 Amcor Road, Lyttelton Manor Centurion, 0157 SOUTH AFRICA
1230	Pharma-Ethics (Pty) Ltd 123 Amkor Road, Lyttelton Manor Centurion, 0157 SOUTH AFRICA
1246	Pharma-Ethics (Pty) Ltd 123 Amkor Road, Lyttelton Manor Centurion, 0157 SOUTH AFRICA
1247	Pharma-Ethics (Pty) Ltd 123 Amkor Road, Lyttelton Manor Centurion, 0157 SOUTH AFRICA

TURKEY

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1205	Kocaeli Üniversitesi Klinik Arastirmalar Etik Kurulu Kocaeli Üniversitesi Tip Fakültesi Klinik, Arastirmalar Birimi Umuttepe Yerleskesi Kocaeli TURKEY
1207	Kocaeli Üniversitesi Klinik Arastirmalar Etik Kurulu Kocaeli Üniversitesi Tip Fakültesi Klinik, Arastirmalar Birimi Umuttepe Yerleskesi Kocaeli TURKEY
1208	Kocaeli Üniversitesi Klinik Arastirmalar Etik Kurulu Kocaeli Üniversitesi Tip Fakültesi Klinik, Arastirmalar Birimi Umuttepe Yerleskesi Kocaeli TURKEY
1209	Kocaeli Üniversitesi Klinik Arastirmalar Etik Kurulu Kocaeli Üniversitesi Tip Fakültesi Klinik, Arastirmalar Birimi Umuttepe Yerleskesi Kocaeli TURKEY
1210	Kocaeli Üniversitesi Klinik Arastirmalar Etik Kurulu Kocaeli Üniversitesi Tip Fakültesi Klinik, Arastirmalar Birimi Umuttepe Yerleskesi Kocaeli TURKEY
1212	Kocaeli Üniversitesi Klinik Arastirmalar Etik Kurulu Kocaeli Üniversitesi Tip Fakültesi Klinik, Arastirmalar Birimi Umuttepe Yerleskesi Kocaeli TURKEY
1213	Kocaeli Üniversitesi Klinik Arastirmalar Etik Kurulu Kocaeli Üniversitesi Tip Fakültesi Klinik, Arastirmalar Birimi Umuttepe Yerleskesi Kocaeli TURKEY

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1214	Kocaeli Üniversitesi Klinik Arastirmalar Etik Kurulu Kocaeli Üniversitesi Tip Fakültesi Klinik, Arastirmalar Birimi Umuttepe Yerleskesi Kocaeli TURKEY
1217	Kocaeli Üniversitesi Klinik Arastirmalar Etik Kurulu Kocaeli Üniversitesi Tip Fakültesi Klinik, Arastirmalar Birimi Umuttepe Yerleskesi Kocaeli TURKEY

UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1001	NYU Langone Grossman School of Medicine IRB One Park Ave, 6th Fl New York, NY 10016 UNITED STATES
1002	Western Institutional Review Board 1019 39th Ave., SE, Ste 120 Puyallup, WA 98374 UNITED STATES
1003	Western Institutional Review Board 1019 39th Ave SE, Ste 120 Puyallup, WA 98374 UNITED STATES
1005	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1006	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1007	Cincinnati Children's Hospital Medical Center IRB 3333 Burnet Ave, MLC 5020 Cincinnati, OH 45229 UNITED STATES
1008	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1009	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1011	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1012	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1013	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1015	WCG IRB 1019 39th Ave Se, Ste 120 Puyallup, WASHINGTON 98374 UNITED STATES
1016	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1018	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1019	Copernicus Group IRB 5000 CentreGreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1021	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1022	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1024	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1027	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1028	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1030	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1036	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1037	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1038	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1039	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1042	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1044	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1046	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1047	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1048	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1052	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1054	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1055	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1056	Copernicus Group Institutional Review Board 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1057	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1066	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1068	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1071	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1072	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1073	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1077	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1079	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1080	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1081	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1082	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1083	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1084	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1085	Copernicus Group IRB 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1087	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1088	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1089	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1090	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1091	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1092	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1093	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1094	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1095	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1096	Copernicus Group IRB 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1097	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1098	Copernicus Group Institutional Review Board 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1101	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1107	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1109	Copernicus Group IRB 5000 CentreGreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1110	WCG IRB 1019 39th Ave Se, Ste 120 Puyallup, WASHINGTON 98374 UNITED STATES
1111	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1112	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1114	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1116	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1117	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1118	Copernicus Group Institutional Review Board 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1120	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1121	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1122	WESTERN INSTITUTIONAL REVIEW BOARD 1019 39th Ave S.E, Ste 120 Puyallup, WA 98374 UNITED STATES
1123	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1124	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1125	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1126	Kaiser Permanente Northern California Institutional Review Board 1800 Harrison St, 10th Fl Oakland, CA 94612 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1127	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1128	Copernicus Group IRB 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1129	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1130	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1131	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1133	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1134	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1135	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1136	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1139	WESTERN INSTITUTIONAL REVIEW BOARD 1019 39th Ave SE, Ste 120 Puyallup, WASHINGTON 98374-2115 UNITED STATES
1140	WESTERN INSTITUTIONAL REVIEW BOARD 1019 39th Ave S.E, Ste 120 Puyallup, WA 98374 UNITED STATES
1141	Western Institutional Review Board 1019 39th Ave SE, Ste 120 Puyallup, WASHINGTON 98374 UNITED STATES
1142	Copernicus Group IRB 5000 CentreGreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1145	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1146	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1147	WCG IRB 1019 39th Ave Se, Ste 120 Puyallup, WASHINGTON 98374 UNITED STATES
1149	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1150	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1152	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1156	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1157	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1161	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1162	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1163	Copernicus Group IRB 5000 CentreGreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1166	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1167	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1168	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1169	Lehigh Valley Health Network/Institutional Review Board/Research Participant Office 1255 S Cedar Crest Blvd, Ste 3200 Allentown, PA 18103 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1170	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1171	Copernicus Group Institutional Review Board 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1174	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1177	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1178	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1179	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1204	Western Institutional Review Board 1019 39th Ave SE, Ste 200 Puyallup, WA 98374-2115 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1218	Indian Health Service National IRB 5600 Fishers Ln, MS 09E10D Rockville, MARYLAND 20857 UNITED STATES
	Johns Hopkins Bloomberg School of Public Health 615 N. Wolfe St, Rm E1100 Baltimore, MARYLAND 21205 UNITED STATES
1219	Navajo Nation Human Research Review Board Window Rock Blvd, Administration Bldg #2, Division of Health, P.O. Box 1390 Window Rock, ARIZONA 86515 UNITED STATES
	Johns Hopkins Bloomberg School of Public Health 615 N. Wolfe St, Rm E1100 Baltimore, MARYLAND 21205 UNITED STATES
1220	Navajo Nation Human Research Review Board Window Rock Blvd, Administration Bldg #2, Division of Health, P.O. Box 1390 Window Rock, ARIZONA 86515 UNITED STATES
	Johns Hopkins Bloomberg School of Public Health 615 N. Wolfe St, Rm E1100 Baltimore, MARYLAND 21205 UNITED STATES
1221	Johns Hopkins Bloomberg School of Public Health 615 N. Wolfe St, Rm E1100 Baltimore, MARYLAND 21205 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
	Navajo Nation Human Research Review Board Window Rock Blvd, Administration Bldg #2, Division of Health, P.O. Box 1390 Window Rock, ARIZONA 86515 UNITED STATES
1223	Yale University Human Research Protection Program (Human Investigation Committee) 25 Science Park, 3rd Fl, 150 Munson St New Haven, CT 06520 UNITED STATES
1224	Copernicus Group IRB 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1232	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1235	Western Institutional Review Board 1019 39th Ave. SE, Ste 120 Puyallup, WA 98374 UNITED STATES
1248	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1251	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1252	Copernicus Group Institutional Review Board 5000 Centregreen Way, Ste 200 Cary, NORTH CAROLINA 27513 UNITED STATES
1254	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1258	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1260	Western Institutional Review Board 1019 39th Ave SE, Ste 120 Puyallup, WA 98374 UNITED STATES
1261	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1264	Western Institutional Review Board 1019 39th Ave SE, Ste 120 Puyallup, WA 98374 UNITED STATES
1265	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES

Study Site Number	Independent Ethics Committee or Institutional Review Board Address(es)
1269	Copernicus Group Institutional Review Board 5000 CentreGreen Way, Ste 200 Cary, NC 27513 UNITED STATES
1270	Kaiser Permanente Northern California Institutional Review Board 1800 Harrison St, 10th Fl Oakland, CA 94612 UNITED STATES

Protocol Number: C4591001		**Assent Version Date: Phase 2/3, 03Feb2021**	
☑ **Study** ☐ **Country** ☐ **Site**	**Language: English**	**Center ID:** Not Applicable	**Country:** Not Applicable
Assent Derived From: Older Children Assent, Phase 2/3, 07Dec2020			

- This template is used by informed consent document authors to develop the assent document for 11-year-olds through legal age of adulthood.
- Do not delete the header at the top of this page until the assent is customized at the country/site-level.
- Before sending the assent to the institutional review board (IRB)/independent ethics committee (IEC), remove the header at the top of this page, remove all inapplicable text, remove all instructional green text, and replace all blue text with appropriate language.
- The assent must be filed in the Pfizer Trial Master File.

Protocol Number: C4591001		**Assent Version Date: Phase 2/3, 03Feb2021**	
☑ Study ☐ Country ☐ Site	**Language: English**	**Center ID:** Not Applicable	**Country:** Not Applicable
Assent Derived From: Older Children Assent, Phase 2/3, 07Dec2020			

A RESEARCH STUDY TO SEE IF A VACCINE AGAINST COVID-19 IS SAFE AND WORKS

We are asking if you would like to be in a research study to see if a vaccine to prevent COVID-19 is safe and if it can help prevent children and adults from getting COVID-19. Research studies are the way we find out if test medicines or vaccines are safe and if they work.

The study is being done with healthy children and adults and that is why the study doctor wants to know if you want to take part in the research study.

WHY ARE WE DOING THIS STUDY?

We are doing this study to collect information in children and adults to see if the vaccine is safe and if it can help prevent people from getting COVID-19.

The study doctor and nurses will explain the study and answer any questions that you have. You can circle or highlight things on this paper you want to know more about. If you don't understand something, just ask us. It is okay to ask questions now and anytime later that you think of them.

If you decide to be in this study, you will be asked to sign this form. Your parent(s) or your guardian(s) will sign another form. You can talk to your parent(s) or your guardian(s) and ask to read the information the study doctor gives them.

WHAT WILL HAPPEN TO ME IF I GO INTO THE STUDY?

The study starts with an appointment with the study doctor and some tests to see if you can be in the study. If you decide to take part in the study you will be given an injection in your arm at your first and second visit and will need to give at least 5 blood samples. There will be at least 6 visits to the study clinic over roughly the next 2 years.

If you get ill with COVID-19 like symptoms you will need to visit the study clinic and give another blood sample. This blood sample is 20 mL if you are 16 years of age or above, and it is 10 mL if you are between 12 to 15 years of age. If you would like to know what 10 mL or 20 mL looks like please ask the study team and they will be able to show you the tubes they will collect the blood in.

Protocol Number: C4591001		**Assent Version Date: Phase 2/3, 03Feb2021**	
☑ **Study** ☐ **Country** ☐ **Site**	**Language: English**	**Center ID:** Not Applicable	**Country:** Not Applicable
Assent Derived From: Older Children Assent, Phase 2/3, 07Dec2020			

At your first visit, the study doctor or nurse will give you or your parent(s)/ guardian(s) a device (a bit like a mobile phone) or ask to download an application ('app') to smart phone if you or your parent(s)/ guardian(s) have one. The device/app is secure and your information will be maintained in confidence. The study doctor will show you or your parent(s)/ guardian(s) on how to fill in the electronic diary (also called e-Diary).

There are 2 parts to the electronic diary. Everyone will need to complete the COVID-19 illness part of the e-Diary on the device or app on their smartphone. The COVID-19 illness e-Diary will prompt you or your parent(s)/ guardian(s) to record any COVID-19 symptoms every 7 days or at any time you have COVID-19 symptoms. You or your parent(s)/ guardian(s) may also receive text messages to your/ their device or your/ their own smartphone, or emails (if you or your parent(s)/ guardian(s) provide an email address) to remind you or your parent(s)/ guardian(s) to complete the COVID-19 illness part of the e-Diary.

If you are part of a selected group of participants, you or your parent(s)/ guardian(s) will also be asked to fill in an e-Diary about how you are feeling for 7 days afer your vaccine injections.

If you decide the take part the following will happen:

At your first visit:

- Before you are given your injection, the study doctor or nurse will take your temperature, measure your height and weight, do a physical exam and ask you some questions about your health.
- The study doctor or nurse will take a blood sample from your arm using a needle (this will be either 20mL or 10 mL depending on your age group) and take a sample from your nose using a swab (like a Q-tip).
- You will then be given an injection into the muscle at the top of your arm.
- If you are part of the selected group of participants, you or your parent(s)/ guardian(s) will be asked to complete an electronic diary about how you are feeling for 7 days after the visit.

At your second visit:

- You will be given your second injection, the study doctor or nurse will take your temperature and ask you some questions about your health before they give your injection in your arm.

- If you are part of the selected group of participants, you or your parent(s)/ guardian(s) will be asked to complete an electronic diary about how you are feeling for 7 days after the visit.

It is very important that you or your parent(s)/ guardian(s), as appropriate, complete the e-Diary regularly as instructed. If this was not completed, your study doctor or nurse will contact you or your parent(s)/ guardian(s) to check how you are doing.

At the other 4 visits the study doctor or nurse will ask you some questions about your health and will take a blood sample from your arm using a needle. Each blood sample will be either about 20mL (4 teaspoons) or 10 mL (2 teaspoons) depending on your age group.

When you visit the study doctor, the study doctor will write down information about you. Only people who are working on this study will see your information. They are required to keep your information private.

What are the Study Injections?

There are 2 types of injections in the study. The active study injection and a dummy placebo injection. A dummy placebo is a pretend vaccine that looks just like the test vaccine but has no active ingredients in it.

Once the study doctor has checked that it is OK for you to be in the study a computer will decide if you will get the active study injection or the dummy placebo. **You and your parent(s)/guardian(s) will not be told which injection you will get.**

For every 1 child/young person who receives the study vaccine, 1 child/young person will receive the placebo. No one (including you, your parents, your personal doctor or the study team) can choose which injection you will get.

WHAT ARE THE POSSIBLE BENEFITS TO ME IF I AGREE TO BE IN THIS STUDY?

Vaccination with BNT162b2 (which is active study injection) has been shown to be effective in preventing COVID-19 in the groups of people already studied, but not yet in children/young people like you. Because of this, and the fact that you may receive the placebo vaccination, you still need to follow local recommendations about how to avoid COVID-19 (for example, social distancing and mask use).

WHAT ARE THE POSSIBLE UNCOMFORTABLE OR HARMFUL THINGS THAT COULD HAPPEN TO ME IF I AGREE TO BE IN THIS STUDY?

There is a chance that during the study you could feel pain or feel bad or uncomfortable. Please let the study doctor know if you experience any of these things. The study team will monitor you for risks or discomforts during the study. However, the study team does not know all the effects that the vaccine, or your participation in this study, may have on you.

The injection could cause pain, swelling, and redness where it is given.

Other side effects could include fatigue (tiredness), increased body temperature (fever), chills, headache, joint aches, muscle aches, feeling sick (nausea), enlarged lymph glands, allergic reaction (symptoms may include rash, itching, hives, and swelling of the face or lips), pain in arm, feeling weak or unwell, and severe allergic reaction (anaphylaxis).

In addition,

- Taking a blood sample may:
  - hurt when the needle goes into your arm.
  - cause a red spot or bruise on your arm or your arm might feel sore.
  - make you feel dizzy.
  - cause an infection at the place where the needle went into your arm.
- Taking a swab from your nose may:
  - hurt when the sample is taken.
  - Cause your nose to bleed.
- You may feel embarrassed by the questions the study doctor or nurse asks you.

You might also feel other things. Remember to tell your parent(s) or your guardian(s) and the study doctor everything you are feeling while you are in the study including if you feel unwell.

Pregnancy, Contraceptives and Babies (do I need to use birth control?)

If you are a girl:

If you are pregnant, planning to become pregnant or breast feeding a baby, you cannot be in the study.

If you think you are pregnant during the study, you must tell the study doctor immediately. The study doctor may ask for information about the pregnancy and the birth of the baby. The study doctor may share this information with others who are working on this study.

If you have started to have periods, the study doctor or nurse will test your urine to make sure you are not pregnant before you are given your injections. The doctor or nurse will tell you if the test results show you are pregnant. Depending on the laws of your area, the study doctor or nurse may also tell your parent(s) or your guardian(s) about the results of the pregnancy test.

If you are sexually active, you must use birth control consistently and correctly during the study and for at least 28 days after your second injection. Your study doctor or nurse will discuss this with you if it is appropriate to do so.

If you are a boy:

If you are sexually active, you must use birth control (eg a condom) consistently and correctly during the study and for at least 28 days after your second injection. Your study doctor or nurse will discuss this with you if it is appropriate to do so.

If you think that you may have gotten a girl pregnant, you must tell your study doctor immediately. The study doctor may ask for information about the pregnancy and the birth of the baby. The study doctor may share this information with others who are working on this study.

WHAT OTHER OPTIONS ARE THERE?

This study is for research purposes only. Your alternative is to not take part in this study.

Taking part is voluntary and **you do not have to be in the study if you don't want to.**

It is your choice if you want to be in this study or not. No one will be mad if you choose not to take part.

Your doctors or your parent(s) or your guardian(s) cannot make you be in the study if you don't want to be in it. If you say okay now to being in the study and you change your mind about it later, you can stop being in the study. Just tell the study doctor or your parent(s) or your guardian(s) if you want to stop at any time. If you quit the study, you will be asked to come in for one last visit.

WHAT IF I HAVE QUESTIONS?

You can ask questions about the study at any time.

You can call the study doctor any time.

If you want to ask questions about what it means to be in a research study, you or your parent(s) or your guardian(s) can call [insert IRB/IEC name] (a group of people who review the study to protect your rights) at [insert IRB/IEC number].

For you to be in this study, you and your parent(s) or your guardian(s) must agree to you being in it. But it is still up to you if you *want* to do it.

Protocol Number: C4591001		**Assent Version Date: Phase 2/3, 03Feb2021**	
☑ **Study** ☐ **Country** ☐ **Site**	**Language: English**	**Center ID:** Not Applicable	**Country:** Not Applicable
Assent Derived From: Older Children Assent, Phase 2/3, 07Dec2020			

Please check one box below to show whether or not you want to be in this study.

☐ Yes, I want to be in this study.

☐ No, I do not want to be in this study.

_____
Printed Name of Child/Young Person

_____ _____ _____
Child/Young Person Signature Date Time

Statement of person conducting assent discussion:

1. I have explained all aspects of the research to the participant to the best of his or her ability to understand.
2. I have answered all questions of the participant relating to this research.
3. I believe the participant's decision to enroll or not enroll is voluntary.
4. If the participant decides to enroll, the study doctor and study staff agree to respect the participant's physical or emotional dissent at any time during this research when that dissent pertains to anything being done solely for the purpose of this research.

Printed Name of Person Obtaining Assent: _____

Signature of Person Obtaining Assent: _____ Date: _____ Time: _____

Protocol Number: C4591001		**ICD Version Date: Phase 2/3, 03Feb2021**	
☑ **Study** ☐ **Country** ☐ **Site**	**Language: English**	**Center ID:** Not Applicable	**Country:** Not Applicable
ICD Derived From: Study level, Phase 2/3, 08Dec2020			

Table of Contents

This Table of Contents describes the different sections of this consent document. Be sure to read through all sections of this consent document before making your decision about whether or not to participate in this study.

1. Key Study Information and Contact Information

The study team will address any questions, concerns or complaints you may have before, during and after you complete the study. The study team includes the study doctor, nurses, and others who work with the study doctor.

Phone numbers for the study team are listed below under "Study Site Contact Information." **You also will be given a card with important emergency contact information, including a 24-hour number.** Show this card to any doctor, nurse or other health care provider if you seek emergency care while you are taking part in this study. This card includes information about the study that will help them treat you.

If you have any general questions about your rights as a study participant, or would like to obtain information from, offer suggestions to, or speak with someone not directly involved in the study, you may contact **[**For the site-level ICD, include as appropriate: the Institutional Review Board ***or*** the Independent Ethics Committee, patient rights advocate, and/or bioethicist**]** listed below.

Name of Study: **A PHASE 1/2/3, PLACEBO-CONTROLLED, RANDOMIZED, OBSERVER-BLIND, DOSE-FINDING STUDY TO EVALUATE THE SAFETY, TOLERABILITY, IMMUNOGENICITY, AND EFFICACY OF SARS-COV-2 RNA VACCINE CANDIDATES AGAINST COVID-19 IN HEALTHY INDIVIDUALS**

[Institution] Study Number:

Sponsor Study Number: **C4591001**

Name of Company Sponsoring the Study: **BioNTech. Pfizer is conducting the study for BioNTech**

Name of Principal Investigator (Study Doctor):

Study Site Contact Information:

Contact Person:

Address:

Phone Number (Normal Business Hours):

Phone Number (Off-Hours or Emergency):

[Complete the following entries for the site-level ICD as appropriate.**]**

[Institutional Review Board *or* Independent Ethics Committee] Contact Information:

Contact Person:

Address:

Phone Number:

Patient Rights Advocate:

Contact Person:

Address:

Phone Number:

Bioethicist:

Contact Person:

Address:

Phone Number:

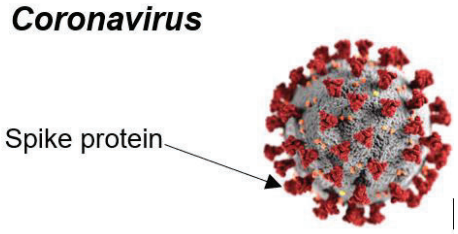
2. Brief Summary of this Study

This is a research study involving both Pfizer and BioNTech. Pfizer and BioNTech are separate companies who are cooperating to perform this study. Pfizer is responsible for conducting this study. BioNTech is the regulatory sponsor of this study. Funding for this study is provided by BioNTech and Pfizer and [the study doctor/institution] will be paid to conduct this study.

A new respiratory disease appeared in Wuhan, China in December 2019 and has since rapidly spread to many other countries around the world. In January 2020, the cause of this disease was found to be a new Coronavirus; and the disease it causes was named COVID-19 (Coronavirus disease 2019). Since then, many companies around the World have quickly started to look for treatments and ways to prevent COVID-19.

Vaccines help your body to produce antibodies to help you to fight off a disease. This research study involves 2 investigational vaccines to prevent COVID-19, that will be given to healthy volunteers. The vaccines are given by injection. The vaccines are slightly different but work in the same way. The study will also test each of these vaccines at different dose levels (amounts of vaccine).

These vaccines do not contain the whole virus, or the parts of the virus that can make you ill, instead the vaccines are made up of part of the virus's genetic code, surrounded by fatty particles called lipids. They use your own cells' protein making machinery to produce some, or all, of the spike protein seen on the outside of the virus. This spike protein, made by your own body, may help your body to produce antibodies to fight against COVID-19. We will check how many antibodies you make by taking blood samples and testing them.



This study is different from your regular medical care. The purpose of regular medical care is to improve or otherwise manage your health, but the purpose of research is to gather information to advance science and medicine and does not replace your regular medical care. If you need medical care during your time in the study, you should contact your regular provider and inform the study team, as described later in this document.

Taking part in this study is voluntary (your choice). There is no penalty or change to your regular medical care if you decide not to participate. You can choose to take part in the study now, and then change your mind later at any time without losing any benefits or medical care to which you are entitled. We encourage you to have conversations with your family, caregivers, doctors, and study team about taking part in this study and whether it is right for you. The study team will work with you to answer any questions that you may have about the study.

You will receive a signed copy of this consent document for your records. Please keep this consent document for your reference.

3. What is the purpose of this study?

The World Health Organization (WHO) has declared COVID-19 to be a pandemic (a disease that has spread all over the world and is affecting lots of people); finding a vaccine to prevent COVID-19 is an urgent need. To test this investigational vaccine as quickly as possible, this study has been separated into 2 phases. In both the phases we will try to see if the vaccine works to prevent COVID-19, as well as:

- **Phase 1** where we choose which vaccines at which dose levels are safest and make the most antibodies.
- **Phase 2/3** where we look at one vaccine at one dose level in lots of people to collect even more information about the safety of the vaccines and the amounts of antibodies they produce.

You are being asked to take part in **Phase 2/3.**

The study will compare the results of the people who receive the study vaccine (BNT162b2) with those who receive a placebo (a placebo does not contain any active ingredients). In this study the placebo will be salt-water, also known as normal saline. Everyone in Phase 2/3 of the study will receive 2 injections of either:

- Study vaccine followed by study vaccine
- Placebo followed by placebo

In Phase 2/3 everyone who receives the study vaccine will receive the same vaccine at the same dose, that was chosen based on the results from Phase 1.

The study doctor will determine whether you are eligible for the study. This study will require you to visit the study doctor to undergo study procedures and to provide information about your health. You will also be required to contact the study doctor if you experience any of the COVID-19 symptoms (explained later in this document).

4. How long will I participate in this study?

You could be in this study for up to about 26 months. You will need to visit the study site 6 to 7 planned times during the study, and any time after you have experienced COVID-19 symptoms and are feeling better in about a month's time.

5. How many people will take part in this study?

Approximately 44,193 healthy people could take part in the 2 phases of this study. In Phase 2/3 of the study up to 43,998 people will take part.

It is expected that about [number] people will participate in Phase 2/3 of the study at this location.

6. What will happen during this study?

Before any study procedures begin, or before you begin preparing for the study, you will be asked to read and sign this consent document.

After signing this consent document, the study doctor will check if you meet all of the requirements to take part in this study. If you do not meet the requirements, you will not be able to take part in the study and the study doctor will explain why this is the case.

Study Vaccines

Once the study doctor has confirmed you meet the study requirements, you will be randomly assigned (like flipping a coin) to receive the study vaccine or placebo. For every 1 person who receive the study vaccine, 1 person will receive the placebo. No one (including you, your personal doctor and the study team) can choose this assignment.

This is an 'observer-blind study', which means that you and the study doctor will not know whether you are receiving the study vaccine or placebo, but the person who gives you the vaccine will know because the vaccine and placebo do not look the same. However, the syringe will be covered with a label so the contents are not visible and the person that gives you the vaccine will not be able to talk about it with you. In case of

urgent need, the study doctor can learn quickly whether you have received study vaccine or placebo.

The study vaccine or placebo will be given to you through an injection into the muscle in your upper arm. Everyone will receive 2 injections, approximately 3 weeks apart. On the days you receive the study vaccine or placebo, you will be asked to wait at the study site for at least 30 minutes for observation after receiving the study vaccine or placebo.

Overview of Study Procedures and Assessments

The table below lists the tests and procedures or assessments that you will have done in this research study. In addition to the visits listed, your study doctor may ask you to come in for extra visit(s) if necessary, to protect your well-being.

For people taking part in Phase 2/3, the study doctor or nurse will:

Visit Number	1	2	3	4	5	6
Visit Description	**Study Vaccine 1**	**Study Vaccine 2**	**1-Month Visit**	**6-Month Visit**	**12-Month Visit**	**24-Month Visit**
Ask about Medical history as well as date of birth, sex, race and ethnicity	X					
Ask about medicines you are currently taking	X	X	X	X	X	X
Perform clinical assessment	X					
Record latest CD4 count and viral load (for HIV positive participants only)	X		X	X	X	X
Measure body temperature	X	X				
Measure height and weight	X					
Urine pregnancy test (if appropriate)	X	X				
Ask about other vaccinations you have had	X	X	X	X		
Check you meet all the study requirements	X	X				
Check contraceptives (if appropriate)	X	X	X			
Collect blood sample to test antibody levels	~20 mL		~20 mL	~20 mL	~20 mL	~20 mL
Take a nasal swab	X	X				
Get the study injection, followed by a 30mins observation period	X	X				
Give you an e-diary or help you download one	X					
Vaccination e-diary completion for 7 days (if you are part of chosen group to self-report potential side effects daily for 7 days following each vaccination)	X	X				
COVID-19 illness e-diary completion	X	X	X	X	X	X
Ask how you are feeling generally	X	X	X	X	X	X

Blood samples for antibody testing

You will have blood taken 5 times during the planned visits of the study. This will be used to test if you already had antibodies against the coronavirus that causes COVID-19 when you enrolled in the study and may be used to test your antibody levels after vaccination. About 20mL of blood (about 4 teaspoons) will be collected from your arm using a needle at these visits.

E-Diary

At Visit 1, the study team will show you how to fill in an electronic diary (or e-Diary). We will either give you a device (a bit like a mobile phone) or ask you to download an application ('app') to your smart phone if you have one. The device/app is secure and your confidentiality will be maintained.

There are 2 parts to the e-Diary. Everyone will need to complete the COVID-19 illness part of the e-Diary on the device or app on your smartphone. The COVID-19 illness e-Diary will prompt you to record any COVID-19 symptoms (see below) every 7 days or at any time you have COVID-19 symptoms. You may also receive text messages to the device or your own smartphone, or emails (if you provide your email address) to remind you to complete the COVID-19 illness part of the e-Diary.

If you are part of a subset of participants, you will also be instructed by the study team to complete the vaccination part of the e-Diary for 7 days after each vaccination, once a day in the evening with the first day being the day of the vaccination.

You will be given a thermometer and a measuring device to take home. You will use the thermometer to measure your temperature under your tongue and you will use the measuring device to measure any redness or swelling where the injection was given. You will need to record these measurements in the vaccination part of the e-Diary.

The vaccination part of the e-Diary will also ask other questions about potential side effects you may have after the injection. If you have any severe symptoms after your vaccination, you should contact your study doctor and the study doctor or nurse may schedule an extra visit.

It is very important that you complete the e-Diary regularly as instructed. If you do not, your study doctor or nurse will contact you to check how you are.

Urine pregnancy test

If you're a woman who is able to have children, you will have a urine pregnancy test to check you are not pregnant before you get the study injection.

What happens if I have positive nasal swab test result?

Nasal swabs obtained during the study (at Visits 1 and 2, and at the time of a potential COVID-19 illness – see below) will be tested in a research laboratory. Positive results from the Visit 1 and 2 swabs, and all results from the illness visit swabs, will be provided to your study doctor, but this will take some time so you should not rely on these for medical treatment. If you has a positive nasal swab test result for the coronavirus that causes COVID-19, either at Visit 1 or any time between Visit 1 and Visit 2, but with no potential COVID-19 related symptoms, you will continue to receive the second study vaccine as normal. However, if the positive COVID-19 test result is accompanied by potential COVID-19 related symptoms, you will not be given the second study vaccine but will be requested to remain in the study.

If You Get COVID-19 Symptoms

If you get any of the following you must contact the study doctor straight away. Note that this is not instead of your routine medical care. If you feel unwell enough that you would normally see a healthcare professional, please contact your usual provider, as well as the study doctor.

- **A diagnosis of COVID-19;**
- **Fever;**
- **New or increased cough;**
- **New or increased shortness of breath;**
- **Chills;**
- **New or increased muscle pain;**
- **New loss of taste/smell;**
- **Sore throat;**
- **Diarrhea;**
- **Vomiting.**

The study doctor may ask you to have a telephone conversation, video call or to visit the site to talk about how you are feeling and if you have needed any other medical care. They will also ask you to take a nose swab or take one from you to check for the coronavirus. We will give you separate instructions about how to take a nose swab yourself and how to ship the swab to the laboratory if needed. The result from this swab will be provided to the study doctor once it is available, but this will take some time, and cannot be used to diagnose you with COVID-19. This is why it is important that you contact your usual provider if you have COVID-19 symptoms and think you need medical care.

If you are diagnosed with COVID-19, for the purposes of the study, the study doctor will contact your usual provider, and any facility where you are treated, to obtain details and collect medical records: by signing this informed consent document, you agree to this.

The study doctor will arrange an extra visit to the study site about a month after you became unwell and you will give another 20 mL (about 4 teaspoons) blood sample to test your antibody levels.

After the study

The study vaccine is available only during this study and not after the study is over. If you leave the study before receiving the study vaccine, it may be available to you through an authorized healthcare professional.

7. Are there any special instructions to follow for this study?

It is important you follow all the instructions given to you by the study nurse or doctor and tell them if:

- You don't understand anything about the study
- You are not able to comply with the study requirements
- There are changes in your health
- You take any new medications or receive any other vaccines
- You are going away for a long period
- You wish to take part in another research study

8. What are the possible risks and discomforts of this study?

Any research has some risks, which may include negative effects that could make you unwell or uncomfortable and even potentially be serious or life-threatening. All research participants taking part in the study will be watched carefully for any negative effects; however, the study team does not know all the effects that the study vaccine may have on you.

If you take part in this study, the most likely risks or discomforts to happen to you are discussed below.

It is important that you report to the study team all symptoms and side effects as soon as they occur. Phone numbers for the study team are listed in [Section 1] of this consent document.

Study Vaccine Risks

Up until the end of 2020, the safety of BNT162b2 has been studied in clinical trials that have included 21,744 people 16 yrs of age and older who have received at least one dose of the vaccine. In addition, since the vaccine has been approved for emergency use in many countries, about 26 million doses have been distributed.

Based on the clinical study results, and information gathered during general use, the following risks have been determined to be caused by BNT162b2 vaccine:

Very common (occurring in more than 1 in 10 people): injection site pain, injection site swelling, fatigue (tiredness), increased body temperature (fever, more common after the second dose), chills, headache, joint aches, and muscle aches.

Common (between 1 in 10 and 1 in 100 people): feeling sick (nausea), and injection site redness.

Uncommon (between 1 in 100 and 1 in 1,000 people): enlarged lymph glands, allergic reactions (symptoms may include rash, itching, hives, and swelling of the face or lips), pain in arm, and feeling weak or unwell.

Frequency cannot be estimated from available data: severe allergic reaction (anaphylaxis).

As in all research studies, the COVID-19 vaccine may involve risks that might be expected based on results from studies of similar vaccines, as well as risks that are currently unknown.

Therefore, it is important that you report all symptoms and side effects that you experience as soon as they occur, whether or not you think they are caused by the study vaccine.

Due to the way in which the study vaccines are made, they cannot cause COVID-19 disease.

If I catch COVID-19 disease, could the vaccine make it worse?

For some other vaccines tested in animals against similar viruses (but not the coronavirus that causes COVID-19), there have been reports of the illness being more severe in the animals that received the vaccine than in those that did not. So far this has not been seen with BNT162b2. It remains important for you to contact your study doctor if you develop symptoms that might be caused by COVID-19 (for example, fever, cough, shortness of breath).

Placebo Risks

As the placebo injection contains salt-water and no active ingredients, the chances of having the side effects mentioned above are less likely. In other studies using the same placebo, some people who received the placebo injection reported pain, bruising, swelling and redness at the site of injection.

Risks from Study Procedures

Risks and possible discomforts you might have from the study procedures include:

- **Blood samples:** The risks and possible discomforts involved in taking blood include pain from inserting the needle, or less often, swelling, bruising, or infection around the vein where the blood is collected. You may feel dizzy or may faint. If you have a previous history of feeling dizzy or fainting during blood sample collection, you should talk to the study doctor.
- **Nasal Swabs:** The risks and possible discomforts involved in taking nasal swabs may include pain or general discomfort. Sometimes it may cause the nose to bleed.

Pregnancy-Related Risks; Use of Birth Control

If you are currently pregnant, plan to become pregnant, or are breastfeeding a child, you should not join this study.

If you are able to have children and you are sexually active, you must use birth control consistently and correctly for at least 28 days after you receive your last injection. This applies to men as well as women who take part in the research study. The study doctor will discuss with you the methods of birth control that you should use while you are in this research study and will help you select the method(s) that is appropriate for you. The study doctor will also check that you understand how to use the birth control method and may review this with you at each of your research study visits.

Birth control methods, even when used properly are not perfect. If you or your partner becomes pregnant during the research study, or you want to stop your required birth control during the research study, you should tell the study doctor immediately. You may be withdrawn from the research study if you stop using birth control or you become pregnant.

Pregnancy Follow-up

If you or your partner become pregnant during the study, up until 6 months after you last study injection, please tell the study doctor **immediately**. Please also tell the doctor who will be taking care of you/your partner during the pregnancy that you took part in this study. The study doctor will ask if you/your partner or your pregnancy doctor is willing to provide updates on the progress of the pregnancy and its outcome. If you/your partner agree, this information will be provided to BioNTech/Pfizer for safety follow-up.

9. What are possible benefits of this study?

Vaccination with BNT162b2 has been shown to be effective in preventing COVID-19 in the groups of people already studied, but not yet in people like you. Because of this, and the fact that you may receive the placebo vaccination, you still need to follow local recommendations about how to avoid COVID-19 (for example, social distancing and mask use).

10. What will happen to my blood and nasal swab samples?

Your blood and nasal swab samples will be used only for scientific research. Each sample will be labeled with a code so that the laboratory workers testing the samples will not know who you are. Some of the samples may be stored for future testing and may be kept for up to 15 years after the study ends, at which time they will be destroyed. In addition to testing for this study, any samples left over after the study is complete may be used for additional research related to the development of products. No testing of your DNA will be performed.

You may request that your samples, if they can be identified, be destroyed at any time. Any data already collected from those samples will still be used for the study. The samples will remain the property of BioNTech/Pfizer and may be shared with other researchers as long as confidentiality is maintained and no testing of your DNA will be performed. You will not be told of additional tests, nor will you receive results of any of these tests.

11. What other choices do I have if I do not join this study?

This study is for research purposes only. Your alternative is to not take part in this study.

12. What happens if I am injured during this study?

For mandatory research injury language, <**click here**> (retain this link in the study-level ICD). The country-specific research injury language must be included verbatim in the country-level ICD.

13. What if I join this study and then change my mind?

If you agree to participate and then change your mind for any reason, you are free to stop participating at any time. Your decision will not affect your regular medical care or any benefits to which you are entitled. Tell the study doctor if you are thinking about stopping or decide to stop so that you can end participation in the study in the safest way.

While you are participating, the study team will tell you in a timely manner if new information is learned during the course of the study that could change your mind about continuing in this study. If you decide to withdraw from the study, you may be asked to

continue to participate in the study procedures even though you would no longer receive the study vaccine.

If you agree to continue with the study, information about your health will continue to be collected as described in [Section 6].

If you decide to stop participating in this study, you must notify the study doctor. The study team will explain what other procedures or discussions would occur.

Sometimes the study doctor or BioNTech/Pfizer may decide to take you out of the study (even if you do not agree) if:

- You are unable or unwilling to follow the instructions of the study team;
- The study doctor decides that the study is not in your best interest or that you are no longer eligible to participate; or
- The study is stopped by BioNTech/Pfizer, the institutional review board (IRB) or independent ethics committee (IEC) (a group of people who review the study to protect your rights), or by a government or regulatory agency.

The study team will give you a Privacy Supplement, which is considered part of this consent document. It describes what happens to your personal information (including your biological samples) and how it may be used if you withdraw from the study.

14. What will I have to pay for if I take part in this study?

You will not need to pay for any of the study vaccines (COVID-19 Vaccine or placebo), study-related procedures, or study visits.

15. Will I be paid for taking part in this study?

You will not receive any payment for taking part in this study. However, for each visit you complete, you will be reimbursed by the study site to cover reasonable expenses (for example, parking, meals, travel) that you have as a result of taking part in this study. You will be reimbursed by [enter, as applicable, method of reimbursement; amounts; and reimbursement schedule; note whether receipts are required].

BioNTech/Pfizer may use information resulting from the study to develop products or processes from which they may make a profit. There are no plans to pay you or provide you with any products developed from this research. BioNTech/Pfizer will own all products or processes that are developed using information from the study.

16. What will happen to my personal information?

<click here> for language to be inserted into this section. This text must be inserted verbatim. Any requested changes must be approved by Clinical Development Legal. Note that the Privacy Supplement follows this consent document, after the signature section.

17. Where can I find additional information about this study or the study results?

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

The study results, when available, may also be found on www.pfizer.com and https://www.clinicaltrialsregister.eu/.

In addition, a plain summary of the study results will be made available in the EU database at [insert link to the database]. This information will be provided no matter what the study's outcome. To the extent possible, you will be able to access these summaries in the EU database soon after they become available using the following EU trial number for the study: [insert trial number].

These Web sites are in English only. If you need assistance understanding these Web sites, please ask a member of the study team.

BioNTech/Pfizer will provide the study doctor with information about the study results when all participants have completed the study. At that time, certain of your individual study results may be given to you or your doctor (if different from the study doctor) in accordance with applicable law, but will not be given to your family, your employer or any insurance company.

If any exploratory research is done, it may not be possible to link any results from that exploratory research to specific individuals, including you. BioNTech/Pfizer does not plan to return information from any exploratory research to you, the study doctor, or your doctor (if different from the study doctor).

18. Signatures

Agreement to Participate and to Process Data
1. I confirm I have read (or, if I cannot read, a study team member has read to me) and understand this consent document for the study described above and have

had the opportunity to ask questions. I have had enough time to review this consent document. I also have had an opportunity to ask about the details of the study and to decide whether or not to participate.
2. I have read and understand the Privacy Supplement. I understand that taking part in the study will require the processing (including collection, use, transfer, storage, analysis and reporting) of my personal information, as explained in the Privacy Supplement. I understand and agree to the processing of my personal information within and outside my country of residence for health care, medical research and/or regulatory purposes.
3. I understand that taking part is voluntary and that I am free to stop taking part in this study or to withdraw my consent to the processing of my personal information at any time. I do not need to give any reason and my regular medical care and legal rights will not be affected. However, even if I withdraw my consent to processing, my personal information held at that time may be kept to comply with laws and regulations and to maintain the integrity of the study. I also understand that my biological samples may not be able to be destroyed because they may no longer be traceable to me, may have already been used, or may have been given to a third party.
4. I agree to the study team accessing my medical history, including information from medical records and test results and any medical treatment I receive during the course of the study, and if necessary, contacting my doctor or any other health care providers treating me for access to such information.
5. I understand that BioNTech/Pfizer and/or others working with or on behalf of BioNTech/Pfizer, institutional review boards (IRBs) or independent ethics committees (IECs), and regulatory agencies may need access to personal information about me generated at the study site or collected by the study team for the study and any other research. I agree that they may have access to my personal information.
6. I do not give up any of my legal rights by signing this consent document. I have been told that I will receive a signed and dated copy of this document.
7. I agree to take part in the study described in this document.

_____

Printed name of participant

_____ _____

Signature of participant Date of signature§

(If no legally acceptable representative is used)

§Participant must personally date their signature.

Person Obtaining Consent:

_____
Printed Name of the Person Conducting the Consent Discussion

_____ _____
Signature of the Person Conducting the Consent Discussion † Date of signature

†The investigator, or an appropriately qualified and trained person designated by the investigator to conduct the informed consent process, must sign and date the consent document during the same discussion when the participant signs the consent document.

PRIVACY SUPPLEMENT

For mandatory country-specific data privacy language to be inserted in this Privacy Supplement, <**click here**> (retain this link in the study-level ICD). The country-specific data privacy language must be included verbatim in the country-level ICD. Any requested changes must be approved by Clinical Development Legal.

Who will use my personal information, how will they use it, and where will it be stored?

[Mandatory study language – retain the below paragraph and delete this green text before finalisation]

Any personal information collected about you during this study will be entered into records, including health records, maintained by the study team at your study site. Your records that include information that directly identifies you may be uploaded to secure systems maintained by a third party engaged by BioNTech/Pfizer so that BioNTech/Pfizer and/or BioNTech/Pfizer representatives can review and verify study data. Some of the uploaded records will be kept for XX years. The remaining records that are uploaded will be temporary and removed from the secure system after the study is over.

Protocol Number: C4591001		**ICD Version Date: Parent ICD, Phase 2/3, 03Feb2021**	
☑ **Study** ☐ **Country** ☐ **Site**	**Language: English**	**Center ID:** Not Applicable	**Country:** Not Applicable
ICD Derived From: Parent ICD, Phase 2/3, 08Dec2020			

Table of Contents

This Table of Contents describes the different sections of this consent document. Be sure to read through all sections of this consent document before making your decision about whether or not to participate in this study.

1. Key Study Information and Contact Information

The study team will address any questions, concerns or complaints you or your child may have before, during and after your child complete the study. The study team includes the study doctor, nurses, and others who work with the study doctor.

Phone numbers for the study team are listed below under "Study Site Contact Information." **You also will be given a card with important emergency contact information, including a 24-hour number.** Show this card to any doctor, nurse or other health care provider if your child seeks emergency care while taking part in this study. This card includes information about the study that will help them treat your child.

If you have any general questions about your child's rights as a study participant, or would like to obtain information from, offer suggestions to, or speak with someone not directly involved in the study, you may contact **[**For the site-level ICD, include as appropriate: the Institutional Review Board ***or*** the Independent Ethics Committee, patient rights advocate, and/or bioethicist**]** listed below.

Name of Study: **A PHASE 1/2/3, PLACEBO-CONTROLLED, RANDOMIZED, OBSERVER-BLIND, DOSE-FINDING STUDY TO EVALUATE THE SAFETY, TOLERABILITY, IMMUNOGENICITY, AND EFFICACY OF SARS-COV-2 RNA VACCINE CANDIDATES AGAINST COVID-19 IN HEALTHY INDIVIDUALS**

[Institution] Study Number:

Sponsor Study Number: **C4591001**

Name of Company Sponsoring the Study: **BioNTech. Pfizer is conducting the study for BioNTech**

Name of Principal Investigator (Study Doctor):

Study Site Contact Information:

Contact Person:

Address:

Phone Number (Normal Business Hours):

Phone Number (Off-Hours or Emergency):

[Complete the following entries for the site-level ICD as appropriate.**]**

[Institutional Review Board *or* Independent Ethics Committee] Contact Information:

Contact Person:

Address:

Phone Number:

Patient Rights Advocate:

Contact Person:

Address:

Phone Number:

Bioethicist:

Contact Person:

Address:

Phone Number:

2. Brief Summary of this Study

You are being asked to allow your child to take part in a research study that involves comparing an investigational (study) vaccine against a placebo (injection with no active ingredient) to see if the vaccine can prevent COVID-19. The vaccine is given by injection.

Depending on your child's age, mental status and local laws, the study team **may need to verify your child's agreement (called "assent") to take part in this study**. Your child may give assent verbally, or they may be asked to print or sign their name on an assent document similar to this consent document. They may have an opportunity to meet privately with a member of the study team to ask confidential questions. Your child will also be able to decide not to take part for confidential reasons, which, if they request, would not be shared with you unless required by local law. Also, if your child reaches the legally recognized age of majority (adulthood) during the study, they must separately provide their consent to continue taking part in the study.

You are being asked to allow your child to be in this research study because your child is healthy and over the age of 12.

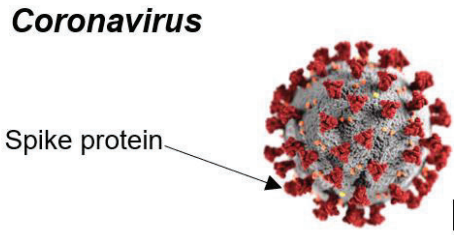
This is a research study involving both Pfizer and BioNTech. Pfizer and BioNTech are separate companies who are cooperating to perform this study. Pfizer is responsible for conducting this study. BioNTech is the regulatory sponsor of this study. Funding for this study is provided by BioNTech and Pfizer and [the study doctor/institution] will be paid to conduct this study.

A new respiratory disease appeared in Wuhan, China in December 2019 and has since rapidly spread to many other countries around the world. In January 2020, the cause of this disease was found to be a new Coronavirus; and the disease it causes was named COVID-19 (Coronavirus disease 2019). Since then, many companies around the World have quickly started to look for treatments and ways to prevent COVID-19.

Vaccines help your body to produce antibodies to help you to fight off a disease. This research study involves 2 investigational vaccines to prevent COVID-19, that will be

given to volunteers. The vaccines are given by injection. The vaccines are slightly different but work in the same way. The study will also test each of these vaccines at different dose levels (amounts of vaccine).

These vaccines do not contain the whole virus, or the parts of the virus that can make your child ill, instead the vaccines are made up of part of the virus's genetic code, surrounded by fatty particles called lipids. They use a persons cells' protein making machinery to produce some, or all, of the spike protein seen on the outside of the virus. This spike protein, made by your child's body, may help your child's body to produce antibodies to fight against COVID-19. We will check how many antibodies your child makes by taking blood samples and testing them.



This study is different from your child's regular medical care. The purpose of regular medical care is to improve or otherwise manage your child's health, but the purpose of research is to gather information to advance science and medicine and does not replace your child's regular medical care. If your child needs medical care during their time in the study, you should contact your regular provider and inform the study team, as described later in this document.

Allowing your child to taking part in this study is voluntary (your choice). There is no penalty or change to you or your child's regular medical care if you decide not to allow your child to participate. You can choose to let your child take part in the study now, and then change your mind later at any time without losing any benefits or medical care to which you or your child are entitled. We encourage you to have conversations with your family, friends, doctors, and study team about this study and whether it is right for your child. The study team will work with you to answer any questions that you may have about the study.

You will receive a signed copy of this consent document for your records. Please keep this consent document for your reference.

3. What is the purpose of this study?

The World Health Organization (WHO) has declared COVID-19 to be a pandemic (a disease that has spread all over the world and is affecting lots of people); finding a vaccine to prevent COVID-19 is an urgent need. To test this investigational vaccine as

quickly as possible, this study has been separated into 2 phases. In both the phases we will try to see if the vaccine works to prevent COVID-19, as well as:

- **Phase 1** where we choose which vaccines at which dose levels are safest and make the most antibodies.
- **Phase 2/3** where we look at one vaccine at one dose level in lots of people to collect even more information about the safety of the vaccines and the amounts of antibodies they produce.

Your child is being asked to take part in **Phase 2/3.**

The study will compare the results of the people who receive the study vaccine (BNT162b2) with those who receive a placebo (a placebo does not contain any active ingredients). In this study the placebo will be salt-water, also known as normal saline. Everyone in Phase 2/3 of the study will receive 2 injections of either:

- Study vaccine followed by study vaccine
- Placebo followed by placebo

In Phase 2/3 everyone who receives the study vaccine will receive the same vaccine at the same dose, that was chosen based on the results from Phase 1.

The study doctor will determine whether your child is eligible for the study. This study will require your child to visit the study doctor to undergo study procedures and to provide information about their health. You/your child will also be required to contact the study doctor if your child experience any of the COVID-19 symptoms (explained later in this document).

4. How long will my child participate in this study?

Your child could be in this study for up to about 26 months and will need to visit the study site 6 or 7 planned times during the study. Your child will also need to visit the study site if they experience COVID-19 symptoms and again after they have recovered from those symptoms approximately in a month's time.

5. How many adults and children will take part in this study?

Approximately 44,193 volunteers could take part in the 2 phases of this study.

In Phase 2/3 of the study up to 43,998 volunteers will take part, in which approximately 2000 will be of 12 to 15 years of age and the remaining will be above the age of 16 years.

6. What will happen during this study?

Before any study procedures begin, or before your child begins preparing for the study, you will be asked to read and sign this consent document. We may also ask your child to read and sign a similar document.

After signing this consent document, the study doctor will check if your child meets all of the requirements to take part in this study. If your child does not meet the requirements, they will not be able to take part in the study and the study doctor will explain why this is the case.

Study Vaccines

Once the study doctor has confirmed your child meets the study requirements, your child will be randomly assigned (like flipping a coin) to receive the study vaccine or placebo. For every 1 volunteer who receives the study vaccine, 1 volunteer will receive the placebo. No one (including you, your child, your child's personal doctor or the study team) can choose this assignment.

This is an 'observer-blind study', which means that you, your child and the study doctor will not know whether your child will receive the study vaccine or placebo. The person who gives your child the vaccine will know because the vaccine and placebo do not look the same. The syringe will be covered with a label so the contents are not visible and the person that gives your child the vaccine will not be able to talk about it. In case of urgent need, the study doctor can learn quickly whether your child received study vaccine or placebo.

The study vaccine or placebo will be given to your child through an injection into the muscle of the upper arm. All volunteers will receive 2 injections, approximately 3 weeks apart. On the days your child receives the study vaccine or placebo, you and your child will be asked to wait at the study site for at least 30 minutes for observation.

Overview of Study Procedures and Assessments

The table below lists the tests and procedures or assessments that will be done in this research study. In addition to the visits listed, the study doctor may ask your child to come in for extra visit(s) if necessary, to protect their well-being.

For people taking part in Phase 2/3, the study doctor or nurse will:

Visit Number	1	2	3	4	5	6
Visit Description	**Study Vaccine 1**	**Study Vaccine 2**	**1-Month Visit**	**6-Month Visit**	**12-Month Visit**	**24-Month Visit**
Ask about Medical history as well as date of birth, sex, race and ethnicity	X					
Ask about medicines your child is currently taking	X	X	X	X	X	X
Perform clinical assessment	X					
Record latest CD4 count and viral load (for HIV positive volunteers only)	X		X	X	X	X
Measure body temperature	X	X				
Measure height and weight	X					
If your child is female and started her periods, she will be asked to provide a urine sample for a pregnancy test.	X	X				
Ask about other vaccinations your child has had	X	X	X	X		
Check your child meets all the study requirements	X	X				
If needed, we will discuss with your child about appropriate birth control	X	X	X			
Collect blood sample to test antibody levels[a]	~20 mL/ ~10 mL		~20 mL/ ~10 mL	~20mL/ ~10 mL	~20 mL/ ~10 mL	~20 mL/ ~10 mL
Take a nasal swab	X	X				
Get the study injection, followed by a 30mins observations period	X	X				
Give you/your child an e-diary or help you/your child download one	X					
Vaccination e-diary completion for 7 days (if your child is part of a chosen group to report potential side effects daily for 7 days following vaccination)	X	X				

For people taking part in Phase 2/3, the study doctor or nurse will:

Visit Number	1	2	3	4	5	6
Visit Description	Study Vaccine 1	Study Vaccine 2	1-Month Visit	6-Month Visit	12-Month Visit	24-Month Visit
COVID-19 illness e-diary completion	X	X	X	X	X	X
Ask how your child is feeling generally	X	X	X	X	X	X

Abbreviations: HIV = human immunodeficiency virus; e-diary = electronic diary.

a. 20 mL is to be collected from participants ≥16 years of age; 10 mL is to be collected from participants 12 to 15 years of age.

Blood samples for antibody testing

Your child will have blood taken 5 times during the planned visits of the study. This will be used to test if they already had antibodies against the coronavirus that causes COVID-19 when they enrolled in the study and may be used to test their antibody levels after vaccination. If your child is 16 years of age or above, about 20 mL of blood (about 4 teaspoons) will be collected from their arm using a needle at these visits. Alternatively, if your child is between 12 to 15 years of age, about 10 mL of blood (about 2 teaspoons) will be collected from their arm using a needle at the above specified visits.

E-Diary

At Visit 1, the study team will show you or your child how to fill in an electronic diary (or e-Diary). Parent(s)/ legal guardian(s), as appropriate, will be required to complete the e-diary on behalf of younger age group children, whilst children in older age group might not require similar level of support from their parent(s)/ legal guardian(s). Therefore, older age group children (e.g. 16 years or above) are expected to complete the e-diary themselves.

We will either give you/ your child a device (a bit like a mobile phone) or ask to download an application ('app') to smart phone if you or your child has one. The device/app is secure, and your child's confidentiality will be maintained.

There are 2 parts to the e-Diary. Everyone will need to complete the COVID-19 illness part of the e-Diary on the device or app on their smartphone. The COVID-19 illness e-Diary will prompt you/ your child to record any COVID-19 symptoms (see below) every 7 days or at any time your child has COVID-19 symptoms. You or your child may also receive text messages to the device or your/your child's own smartphone, or emails (if you/they provide your/their email address) to remind you/your child to complete the COVID-19 illness part of the e-Diary.

If your child is part of a subset of participants, you/ your child will also be instructed by the study team to complete the vaccination part of the e-Diary for 7 days after each vaccination, once a day in the evening with the first day being the day of the vaccination.

You/ your child will be given a thermometer and a measuring device to take home. You/ your child will use the thermometer to measure temperature under the tongue and will use the measuring device to measure any redness or swelling where the injection was given. You/ your child will need to record these measurements in the vaccination part of the e-Diary.

The vaccination part of the e-Diary will also ask other questions about potential side effects your child may have after the injection. If your child has any severe symptoms

after vaccination, you/ your child should contact your study doctor and the study doctor or nurse may schedule an extra visit.

It is very important that you/ your child, as appropriate, complete the e-Diary regularly as instructed. If this was not completed, your study doctor or nurse will contact you/ your child to check how your child is doing.

Urine pregnancy test

If your child is female and has started her periods, she will be asked to provide a urine sample to check she is not pregnant before given the study injection.

What happens if my child has positive nasal swab test result?

Nasal swabs obtained during the study (at Visits 1 and 2, and at the time of a potential COVID-19 illness – see below) will be tested in a research laboratory. Positive results from the Visit 1 and 2 swabs, and all results from the illness visit swabs, will be provided to your study doctor, but this will take some time so you should not rely on these for your child's medical treatment. If your child has a positive nasal swab test result for the coronavirus that causes COVID-19, either at Visit 1 or any time between Visit 1 and Visit 2, but with no potential COVID-19 related symptoms, they will continue to receive the second study vaccine as normal. However, if the positive COVID-19 test result is accompanied by potential COVID-19 related symptoms, they will not be given the second study vaccine but will be requested to remain in the study.

<u>If Your Child Gets COVID-19 Symptoms</u>

If your child gets any of the following you must contact the study doctor straight away. Note that this is not instead of routine medical care. If your child feels unwell enough that you would normally see a healthcare professional, please contact your usual provider, as well as the study doctor.

- **A diagnosis of COVID-19;**
- **Fever;**
- **New or increased cough;**
- **New or increased shortness of breath;**
- **Chills;**
- **New or increased muscle pain;**
- **New loss of taste/smell;**
- **Sore throat;**
- **Diarrhea;**
- **Vomiting.**

The study doctor may ask you/your child to have a telephone conversation, video call or to visit the site to talk about how they are feeling and if they have needed any other medical care. The study team will also ask you to help your child to take a nose swab, or the study team may take a swab to check for the coronavirus. We will give you/your child separate instructions about how to take a nose swab and how to ship the swab to the laboratory if needed. The result from this swab will be provided to the study doctor once it is available, but this will take some time, and cannot be used to diagnose COVID-19. This is why it is important that you contact your usual provider if your child has COVID-19 symptoms and think your child needs medical care.

If your child is diagnosed with COVID-19, for the purposes of the study, the study doctor will contact your child's usual provider, and any facility where you child is treated, to obtain details and collect medical records: by signing this informed consent document, you agree to this.

The study team will arrange an extra visit to the study site about a month after your child became unwell and your child will need to give another 20 mL (about 4 teaspoons) or 10 mL (about 2 teaspoons) of blood sample, as appropriate, to test their antibody levels.

After the study

The study vaccine is available only during this study and not after the study is over. If you leave the study before receiving the study vaccine, it may be available to you through an authorized healthcare professional.

7. Are there any special instructions to follow for this study?

It is important you and your child follow all the instructions given by the study nurse or doctor and tell them if:

- You don't understand anything about the study
- You /your child are not able to comply with the study requirements
- There are changes in your child's health
- Your child takes any new medications or receive any other vaccines
- You or your child are going away for a long period
- Your child wishes to take part in another research study

8. What are the possible risks and discomforts of this study?

Any research has some risks, which may include negative effects that could make your child unwell or uncomfortable and even potentially be serious or life-threatening. All research participants taking part in the study will be watched carefully for any negative

effects; however, the study team does not know all the effects that the study vaccine may have on your child.

If your child takes part in this study, the most likely risks or discomforts are discussed below.

It is important that you/ your child report to the study team all symptoms and side effects as soon as they occur. Phone numbers for the study team are listed in [Section 1] of this consent document.

Study Vaccine Risks

Up until the end of 2020, the safety of BNT162b2 has been studied in clinical trials that have included 21,744 people 16 yrs of age and older who have received at least one dose of the vaccine. In addition, since the vaccine has been approved for emergency use in many countries, about 26 million doses have been distributed.

Based on the clinical study results, and information gathered during general use, the following risks have been determined to be caused by BNT162b2 vaccine:

Very common (occurring in more than 1 in 10 people): injection site pain, injection site swelling, fatigue (tiredness), increased body temperature (fever, more common after the second dose), chills, headache, joint aches, and muscle aches.

Common (between 1 in 10 and 1 in 100 people): feeling sick (nausea), and injection site redness.

Uncommon (between 1 in 100 and 1 in 1,000 people): enlarged lymph glands, allergic reactions (symptoms may include rash, itching, hives, and swelling of the face or lips), pain in arm, and feeling weak or unwell.

Frequency cannot be estimated from available data: severe allergic reaction (anaphylaxis).

As in all research studies, the COVID-19 vaccine may involve risks that might be expected based on results from studies of similar vaccines, as well as risks that are currently unknown.

Therefore, it is important that you/ your child report all symptoms and side effects that your child experiences as soon as they occur, whether or not you think they are caused by the study vaccine.

Due to the way in which the study vaccines are made, they cannot cause COVID-19 disease.

If my child catches COVID-19 disease, could the vaccine make it worse?

For some other vaccines tested in animals against similar viruses (but not the coronavirus that causes COVID-19), there have been reports of the illness being more severe in the animals that

received the vaccine than in those that did not. So far this has not been seen with BNT162b2. It remains important for you/ your child to contact your child's study doctor if your child develop symptoms that might be caused by COVID-19 (for example, fever, cough, shortness of breath).

Placebo Risks

As the placebo injection contains salt-water and no active ingredients, the chances of having the side effects mentioned above are less likely. In other studies, using the same placebo, some volunteers who received the placebo injection reported pain, bruising, swelling and redness at the site of injection.

Risks from Study Procedures

Risks and possible discomforts from the study procedures include:

- **Blood samples:** The risks and possible discomforts involved in taking blood include pain from inserting the needle, or less often, swelling, bruising, or infection around the vein where the blood is collected. Your child may feel dizzy or may faint. If your child has a previous history of feeling dizzy or fainting during blood sample collection, you should talk to the study doctor.
- **Nasal Swabs:** The risks and possible discomforts involved in taking nasal swabs may include pain or general discomfort. Sometimes it may cause the nose to bleed.

Pregnancy-Related Risks; Use of Birth Control

If your child is currently pregnant, plans to become pregnant, or is breastfeeding a child, they should not join this study.

If your child is able to have children and is sexually active, they must use birth control consistently and correctly for at least 28 days after they receive their last injection. This applies to males as well as females who take part in the research study. The study doctor will discuss with your child the methods of birth control that they should use while in this research study. The study doctor will help your child select the method that is appropriate for them. The study doctor will also check that your child understands how to use the birth control method and may review this with them at each of their research study visits.

Birth control methods, even when used properly are not perfect. If your child or their partner becomes pregnant during the research study, or if they want to stop their required birth control during the research study, they should tell the study doctor immediately. Your child may be withdrawn from the research study if they stop using birth control or they become pregnant.

Pregnancy Follow-up

If your child or their your partner become pregnant during the study, up until 6 months after their last study injection, please tell the study doctor **immediately**. Please also tell the doctor who will be taking care of your child/their partner during the pregnancy that your child took part in this study. The study doctor will ask if your child/their partner or their pregnancy doctor is willing to provide updates on the progress of the pregnancy and its outcome. If your child/their partner agree, this information will be provided to BioNTech/Pfizer for safety follow-up.

9. What are possible benefits of this study?

Vaccination with BNT162b2 has been shown to be effective in preventing COVID-19 in the groups of people already studied, but not yet in the case of your child. Because of this, and the fact that your child may receive the placebo vaccination, they still need to follow local recommendations about how to avoid COVID-19 (for example, social distancing and mask use).

10. What will happen to my child's blood and nasal swab samples?

Your child's blood and nasal swab samples will be used only for scientific research. Each sample will be labeled with a code so that the laboratory workers testing the samples will not know who your child is. Some of the samples may be stored for future testing and may be kept for up to 15 years after the study ends, at which time they will be destroyed. In addition to testing for this study, any samples left over after the study is complete may be used for additional research related to the development of products. No testing of your child's DNA will be performed.

You may request that your child's samples, if they can be identified, be destroyed at any time. Any data already collected from those samples will still be used for the study. The samples will remain the property of BioNTech/Pfizer and may be shared with other researchers as long as confidentiality is maintained, and no testing of your child's DNA will be performed. You and your child will not be told of additional tests, nor will you or your child receive results of any of these tests.

11. What other choices do I have if I do not want my child to join this study?

This study is for research purposes only. The only alternative is to not take part in this study.

12. What happens if my child is injured during this study?

For mandatory research injury language, <**click here**> (retain this link in the study-level ICD). The country-specific research injury language must be included verbatim in the country-level ICD.

13. Can I withdraw my child from the study?

Yes. You are free to withdraw your consent for your child and discontinue their participation in the research study at any time. Your decision will not affect your or your child's regular medical care or any benefits to which you/your child is are entitled. Tell the study doctor if you are thinking about stopping or decide to stop so that your child can end participation in the study in the safest way.

While your child is participating, the study team will tell you in a timely manner if new information is learned during the course of the study that could change your mind about your child continuing in this study. If you decide to withdraw your child from the study, your child may be asked to continue to participate in the study procedures even though they would no longer receive the study vaccine.

If your child continues with the study, information about their health will continue to be collected as described in [Section 6].

If you decide to stop your child participating in this study, you must notify the study doctor. The study team will explain what other procedures or discussions would occur.

Sometimes the study doctor or BioNTech/Pfizer may decide to take your child out of the study (even if you do not agree) if:

- You/your child are unable or unwilling to follow the instructions of the study team;
- The study doctor decides that the study is not in your child's best interest or that they are no longer eligible to participate; or
- The study is stopped by BioNTech/Pfizer, the institutional review board (IRB) or independent ethics committee (IEC) (a group of people who review the study to protect your rights), or by a government or regulatory agency.

The study team will give you a Privacy Supplement, which is considered part of this consent document. It describes what happens to your child's personal information (including biological samples) and how it may be used if you withdraw your child from the study.

14. What will I have to pay for if my child takes part in this study?

You will not need to pay for any of the study vaccines (COVID-19 Vaccine or placebo), study-related procedures, or study visits.

15. Will my child be paid for taking part in this study?

You will not receive any payment for your child taking part in this study. However, for each visit you/your child completes, you will be reimbursed by the study site to cover reasonable expenses (for example, parking, meals, travel) that you have as a result of taking part in this study. You will be reimbursed by [enter, as applicable, method of reimbursement; amounts; and reimbursement schedule; note whether receipts are required].

BioNTech/Pfizer may use information resulting from the study to develop products or processes from which they may make a profit. There are no plans to pay you/your child or provide you/your child with any products developed from this research. BioNTech/Pfizer will own all products or processes that are developed using information from the study.

16. What will happen to my child' personal information?

<**click here**> for language to be inserted into this section. This text must be inserted verbatim. Any requested changes must be approved by Clinical Development Legal. Note that the Privacy Supplement follows this consent document, after the signature section.

17. Where can I find additional information about this study or the study results?

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify your child. At most, the Web site will include a summary of the results. You can search this Web site at any time.

The study results, when available, may also be found on www.pfizer.com and https://www.clinicaltrialsregister.eu/.

In addition, a plain summary of the study results will be made available in the EU database at [insert link to the database]. This information will be provided no matter what the study's outcome. To the extent possible, you will be able to access these summaries in the EU database soon after they become available using the following EU trial number for the study: [insert trial number].

These Web sites are in English only. If you need assistance understanding these Web sites, please ask a member of the study team.

BioNTech/Pfizer will provide the study doctor with information about the study results when all participants have completed the study. At that time, certain of your child's individual study results may be given to you or your child's doctor (if different from the study doctor) in accordance with applicable law, but will not be given to your family, your employer or any insurance company.

If any exploratory research is done, it may not be possible to link any results from that exploratory research to specific individuals, including your child. BioNTech/Pfizer does not plan to return information from any exploratory research to you/your child, the study doctor, or your doctor (if different from the study doctor).

18. Signatures

Agreement to Participate and to Process Data
1. I confirm I have read (or, if I cannot read, a study team member has read to me) and understand this consent document for the study described above and have had the opportunity to ask questions. I have had enough time to review this consent document. I also have had an opportunity to ask about the details of the study and to decide whether or not to participate.
2. I have read and understand the Privacy Supplement. I understand that taking part in the study will require the processing (including collection, use, transfer, storage, analysis and reporting) of my child's personal information, as explained in the Privacy Supplement. I understand and agree to the processing of my child's personal information within and outside my country of residence for health care, medical research and/or regulatory purposes.
3. I understand that taking part is voluntary and that I am free to stop my child taking part in this study or to withdraw my consent to the processing of my child's personal information at any time. I do not need to give any reason and my child's regular medical care and legal rights will not be affected. However, even if I withdraw my consent to processing, my child's personal information held at that time may be kept to comply with laws and regulations and to maintain the integrity of the study. I also understand that my child's biological samples may not be able to be destroyed because they may no longer be traceable to my child, may have already been used, or may have been given to a third party.
4. I agree to the study team accessing my child's medical history, including information from medical records and test results and any medical treatment my child receive during the course of the study, and if necessary, contacting my child's doctor or any other health care providers treating my child for access to such information.
5. I understand that BioNTech/Pfizer and/or others working with or on behalf of BioNTech/Pfizer, institutional review boards (IRBs) or independent ethics committees (IECs), and regulatory agencies may need access to personal

information about my child generated at the study site or collected by the study team for the study and any other research. I agree that they may have access to my child's personal information.
6. I do not give up any of my child's legal rights by signing this consent document. I have been told that I will receive a signed and dated copy of this document.
7. I agree for my child to take part in the study described in this document.

In the section below, the term "legally acceptable representative" should be replaced with the term required per local regulation (country-level).

As the consenting adult providing permission for this child to participate in the study, I acknowledge that (Please check one of the following):

☐ I am the biological or adoptive parent of the child.

☐ I am the legal guardian or legally acceptable representative of the child.

[If neither option below is checked, then the consent of the second parent/guardian/legally acceptable representative must be obtained. If there are two parents/guardians/legally acceptable representatives available to give permission, and they disagree about allowing the child to participate in the study, the child should not be enrolled unless that disagreement can be resolved.**]**

I also acknowledge that (Please check one of the following):

☐ I have sole legal responsibility for the care and custody of the child.

☐ The other adult(s) with whom I share legal responsibility for the care and custody of the child (for example, biological parent, adoptive parent, or legal guardian or representative) is (1) aware of and agrees with my granting permission for this child to participate in the study OR (2) deceased, unknown, incompetent, or not reasonably available (someone is "not reasonably available" when he/she cannot be reached by phone/mail/email because, for example, he/she is on active military duty or is incarcerated).

_____

Printed name of parent/guardian/legally acceptable representative

_____ _____

Signature of parent/guardian/legally acceptable representative Date of signature§

[Include the statements and signature lines below for a second parent/guardian/legally acceptable representative if (1) required by the IRB/IEC; (2) required by local law (*e.g.*, parents are divorced and have shared custody of the child); or (3) the second parent/guardian/legally acceptable representative is (or would like to be) involved in the consent process and there is reason to believe that he/she may disagree with the decision of the first parent/guardian/legally acceptable representative.

Consent of Second Parent/Guardian/Legally Acceptable Representative:

As the consenting adult providing permission for this child to participate in the study, I acknowledge that (Please check one of the following):

☐ I am the biological or adoptive parent of the child.

☐ I am the legal guardian or legally acceptable representative of the child.

_____

Printed name of parent/guardian/legally acceptable representative

_____ _____

Signature of parent/guardian/legally acceptable representative Date of signature[§]]

Person Obtaining Consent:

_____

Printed name of person conducting the consent discussion

_____ _____

Signature of person conducting the consent discussion[†] Date of signature

§ Participant/parent/guardian/legally acceptable representative must personally date their respective signatures.

† The investigator, or an appropriately qualified and trained person designated by the investigator to conduct the informed consent process, must sign and date the consent document during the same discussion when the participant's parent/guardian/legally acceptable representative signs the consent document.

PRIVACY SUPPLEMENT

For mandatory country-specific data privacy language to be inserted in this Privacy Supplement, <**click here**> (retain this link in the study-level ICD). The country-specific data privacy language must be included verbatim in the country-level ICD. Any requested changes must be approved by Clinical Development Legal.

Who will use my child's personal information, how will they use it, and where will it be stored?

[Mandatory study language – retain the below paragraph and delete this green text before finalisation]

Any personal information collected about you/your child during this study will be entered into records, including health records, maintained by the study team at your study site. You/your child's records that include information that directly identifies you/your child may be uploaded to secure systems maintained by a third party engaged by BioNTech/Pfizer so that BioNTech/Pfizer and/or BioNTech/Pfizer representatives can review and verify study data. Some of the uploaded records will be kept for XX years. The remaining records that are uploaded will be temporary and removed from the secure system after the study is over.

INFORMED CONSENT ADDENDUM FOR A PHASE 1/2/3, PLACEBO-CONTROLLED, RANDOMIZED, OBSERVER-BLIND, DOSE-FINDING STUDY TO EVALUATE THE SAFETY, TOLERABILITY, IMMUNOGENICITY, AND EFFICACY OF SARS-COV-2 RNA VACCINE CANDIDATES AGAINST COVID-19 IN HEALTHY INDIVIDUALS

Protocol Number: C4591001

In this informed consent addendum, "you" always refers to the study participant. If you are a parent/guardian/legally acceptable representative, please remember that "you" refers to the study participant.

You have already signed a consent form to participate in the research study mentioned above. This addendum is part of the consent procedure. It has been written to provide you with additional information on your new schedule of study visits, tests, and procedures and the recent update to vaccine study risks section that you will want to know. All other information in the main consent form not addressed in this addendum still applies.

Administration of BNT162b2 to Participants Originally Assigned to Placebo

You were asked by the study site whether you would consider receiving BNT162b2 vaccine (active study vaccine) if you received placebo during the earlier part of the study. Since it is confirmed that you received placebo, and you have expressed willingness to receive the BNT162b2 vaccine, you are now being asked to read and sign this consent document before commencing any new set of study-related procedures.

After signing this consent document, the study doctor will check if you meet all the requirements to receive BNT162b2 vaccine. If you do not meet the requirements, you will not be able to receive the vaccine and the study doctor will explain why this is the case.

Once the study doctor has confirmed you meet the study requirements to receive BNT162b2 vaccine, you will receive 2 injections, approximately 3 weeks apart. The injection will be given into the muscle in your upper arm and will be asked to wait at the study site for at least 30 minutes for observation after receiving the vaccine.

Overview of Study Procedures and Assessments:

The table below lists the tests and procedures or assessments that you will have done for the remaining duration of the study. In addition to the visits listed, your study doctor may ask you to come in for extra visit(s) if necessary, to protect your well-being.

You may have blood taken once and this will be used to test if you already had antibodies against coronavirus that causes COVID-19. About 20mL of blood (about 4 teaspoons) will be collected from your arm using a needle at Visit-1.

For placebo participants receiving BNT162b2, the study doctor or nurse will:

Visit Number	1	2	3	4	5
Visit Description	BNT162b2 Vaccine 1	BNT162b2 Vaccine 2	1-Month Telephone Visit	6-Month Telephone Visit	18-Month Telephone Visit
Obtain urine pregnancy test (if appropriate)	X	X			
Check contraceptives (if appropriate)	X	X			
Ask about medicines you are currently taking	X	X	X	X	X
Record latest CD4 count and viral load (for HIV positive participants only)	X		X	X	X
Check you meet all the study requirements	X	X			
Collect blood sample to test antibody levels[a]	~20 mL				
Take a nasal swab	X	X			
Get the study injection, followed by a 30mins observation period	X	X			
COVID-19 illness e-diary completion	X	X	X	X	X
Ask how you are feeling generally	X	X	X	X	
Request to return the e-diary or assist to delete the app					X

a. Only if the sample was not taken as part of the study in last 7days

Key Reminders

- Vaccination with BNT162b2 has been shown to be effective in preventing COVID-19 but you still need to follow local recommendations about how to avoid COVID-19 (for example, social distancing and mask use).
- It is also very important that you continue to complete the COVID-19 Illness e-Diary regularly as instructed. If you do not, your study doctor or nurse will contact you to check how you are.

Study Vaccine Risks

Up until the end of 2020, the safety of BNT162b2 has been studied in clinical trials that have included 21,744 people 16 yrs of age and older who have received at least one dose of the vaccine. In addition, since the vaccine has been approved for emergency use in many countries, about 26 million doses have been distributed.

Based on the clinical study results, and information gathered during general use, the following risks have been determined to be caused by BNT162b2 vaccine:

Very common (occurring in more than 1 in 10 people): injection site pain, injection site swelling, fatigue (tiredness), increased body temperature (fever, more common after the second dose), chills, headache, joint aches, and muscle aches.

Common (between 1 in 10 and 1 in 100 people): feeling sick (nausea), and injection site redness.

Uncommon (between 1 in 100 and 1 in 1,000 people): enlarged lymph glands, allergic reactions (symptoms may include rash, itching, hives, and swelling of the face or lips), pain in arm, and feeling weak or unwell.

Frequency cannot be estimated from available data: severe allergic reaction (anaphylaxis).

As in all research studies, the COVID-19 vaccine may involve risks that might be expected based on results from studies of similar vaccines, as well as risks that are currently unknown.

Therefore, it is important that you report all symptoms and side effects that you experience as soon as they occur, whether or not you think they are caused by the study vaccine.

Due to the way in which the study vaccines are made, they cannot cause COVID-19 disease.

If I catch COVID-19 disease, could the vaccine make it worse?
For some other vaccines tested in animals against similar viruses (but not the coronavirus that causes COVID-19), there have been reports of the illness being more severe in the animals that received the vaccine than in those that did not. So far this has not been seen with BNT162b2. It remains important for you to contact your study doctor if you develop symptoms that might be caused by COVID-19 (for example, fever, cough, shortness of breath).

Please take as much time as you need to ask questions from the research study team before agreeing to continue. If after receiving this information you agree to continue taking part in this research study, please sign below.

SIGNATURES:

- I have read the information in this addendum to the informed consent document.
- I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction.
- I have been given enough time to decide whether or not I want to continue in the study.
- I voluntarily agree to continue taking part in this study.
- I do not give up any of my legal rights by signing this consent document.
- I have been told that I will receive a signed and dated copy of this document.

_____

Printed name of participant

SIGNATURE LINE TO BE COMPLETED FOR AN ADULT PARTICIPANT:

_____ _____

Signature of participant Date of signature§

SIGNATURE LINE(S) TO BE COMPLETED FOR A CHILD PARTICIPANT:

As the consenting adult providing permission for this child to participate in the study, I acknowledge that (Please check one of the following):

☐ I am the biological or adoptive parent of the child.

☐ I am the legal guardian or legally acceptable representative of the child.

I also acknowledge that (Please check one of the following):

☐ I have sole legal responsibility for the care and custody of the child.

☐ The other adult(s) with whom I share legal responsibility for the care and custody of the child (for example, biological parent, adoptive parent, or legal guardian or representative) is (1) aware of and agrees with my granting permission for this child to participate in the study OR (2) deceased, unknown, incompetent, or not reasonably available (someone is "not reasonably available" when he/she cannot be reached by phone/mail/email because, for example, he/she is on active military duty or is incarcerated).

_____

Printed Name of Parent / Guardian / Legally Acceptable Representative

_____ _____

Signature of Parent / Guardian / Legally Acceptable Representative Date of signature§

Consent of Second Parent/Guardian/Legally Acceptable Representative:

As the consenting adult providing permission for this child to participate in the study, I acknowledge that (Please check one of the following):

☐ I am the biological or adoptive parent of the child.

☐ I am the legal guardian or legally acceptable representative of the child.

_____ _____

Printed Name of Parent / Guardian / Legally Acceptable Representative

Relationship to study participant

_____ _____

Signature of Parent / Guardian / Legally Acceptable Representative

Date of signature§

If local IRB/IEC permits assent of older children to be obtained by the co-signature, include appropriate signature line.

_____ _____

Signature of Child Date of signature§

_____

Printed name of legally acceptable representative and relationship

_____ _____

Signature of legally acceptable representative Date of signature§

PERSON OBTAINING CONSENT

_____

Printed Name of the Person Conducting the Consent Discussion

_____ _____

Signature of the Person Conducting the Consent Discussion † Date of signature

§Participant/parent/guardian/legally acceptable representative must personally date their signature

†The investigator, or an appropriately qualified and trained person designated by the investigator to conduct the informed consent process, must sign and date the consent document during the same interview when the participant/parent/guardian/legally acceptable representative signs the addendum.

C4591001-Post-12-July-2020

TrialMax App™, TrialManager®
Site User Guide

Document index: A-1426-0086-5150UG
Document version: 5
Template version: 12
02NOV2020

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Trademark Notice

IMPORTANT POINTS

- Keep devices charged at all times – when stored at site, please ensure the device(s) are charged at least once per week, even if not in use. If the device battery runs flat, it might have an incorrect date and time when it is turned back on again. If this happens, send data from the device and it will sync to your current time zone.
- Data will send automatically each time the participant logs into the App as long as the device is charged, in an area where there is mobile phone service or Wi-Fi is available.
- Participants should bring their assigned device with the App to each clinic visit.
- Participant setup should occur on the day of vaccination, whilst the participant is at the study clinic.
- Each participant will be able to set their own PIN code when they first log in to the TrialMax device. Please recommend to them to select the same code for each device as it will be easier for them to remember.
- When setting up a participant for the study, make sure this is done on a computer with a printer, as you will need to print the activation information for the participant. You will only have the opportunity to print this once; however, it will also be emailed to the participant if their email address is provided during setup or sent via a text message if a mobile phone number is provided during setup.
- To receive SMS notifications in the US, please refer to 'Setting up SMS notifications' section for more details.
- Use the TrialManager web portal to regularly monitor participant data for the study.

- It is recommended to leave 0.5GB of free storage space on the participant's personal device to allow the TrialMax app to function properly. Please provide a provisioned device to the participant in the event the participant does not have the free space or does not want to make that space available. The participant may check their available storage below:
    - iPhone: Select 'Settings'->'General'->'iPhone Storage'
    - Android: Select 'Settings' ->'Device Care'->'Storage'
- If you cannot find help in this guide, then please call the Helpdesk.

Role	PIN Code
Default Participant	1234
Logistics Access PIN Code	7777
Logistics PIN Code	3311

TrialManager Website URL
http://trialmax.crfhealth.net/c4591001-Post-12-July-2020
TrialManager login details will be sent to you via email

Table of Contents

1 Signant Health Overview

Signant Health is the provider of the eCOA (electronic Clinical Outcome Assessment) system for this study. The eCOA system comprises the components as displayed below, along with 24/7 Helpdesk support. TrialMax App is the brand name, but we will refer to it simply as the “App”.

Data entered by Participant into the App

Data sent from App to Signant Health servers

Data available for sites, monitors and study team in web portal and TrialManager

TRIALMAX app

TRIALMANAGER®

2 Helpdesk

You may call the Helpdesk for any issue related to the TrialMax App, or TrialManager website.

Please have the following information ready when you call:

- The study protocol number: **C4591001-Post-12-July-2020**
- Helpdesk Priority PIN: **19**
- Signant Health project code: **A-1426-0086**
- Your site number
- The participant number (if applicable)
- The specific problem

2.1 Helpdesk Operating Hours

The Helpdesk is available 24 hours a day, 365 days a year.

If you are unable to reach an agent when you call, you can also leave a voicemail or send an email giving your contact information. The Helpdesk will contact you as soon as possible, at the latest by next business day.

2.2 Helpdesk Telephone Numbers

Country	Number
USA	(1) 866 402 1154
Helpdesk Priority Code	19

Note: Toll Free numbers are free from a landline; however local operator charges might be applied if calling from a mobile phone.

2.3 Helpdesk Email Address

For non-urgent issues, you can contact the Helpdesk by email:

C4591001-Post-12-July-2020_TM@support.signanthealth.com

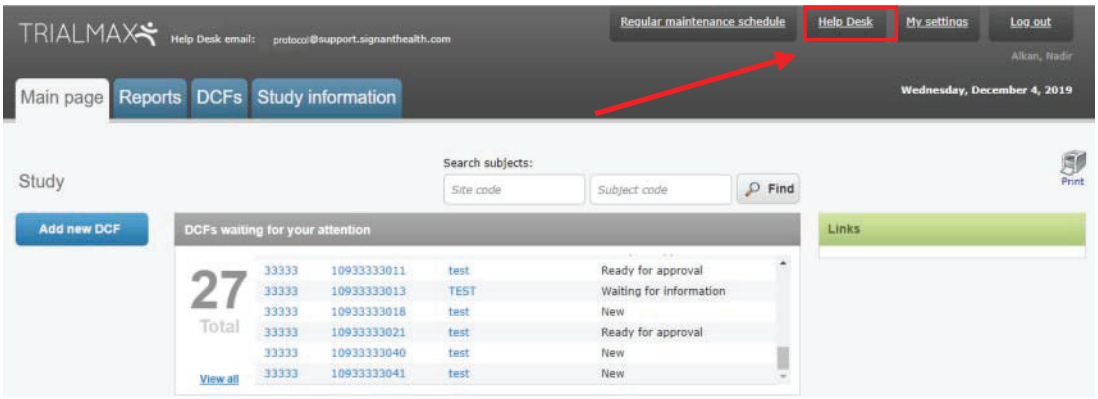
Note: Do not share this email address with participant. The participant's identity might be unintentionally revealed during communication via email.

Helpdesk Web Chat via TrialManager

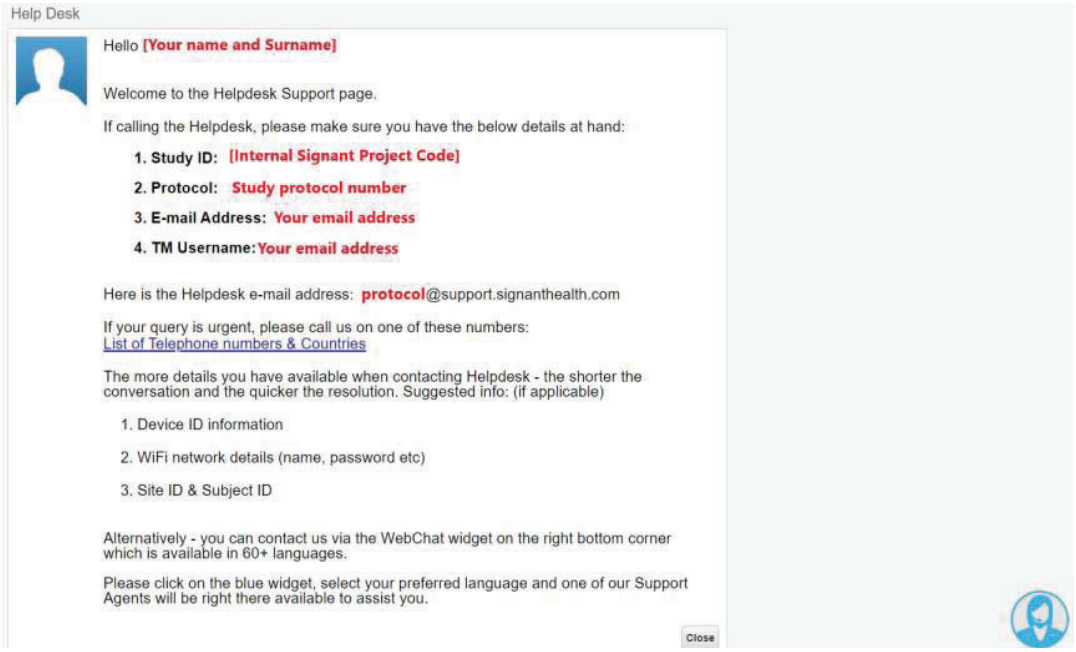
The Helpdesk Web-chat is available via the TrialManager Portal.

Helpdesk Web-chat can be accessed via the steps below:

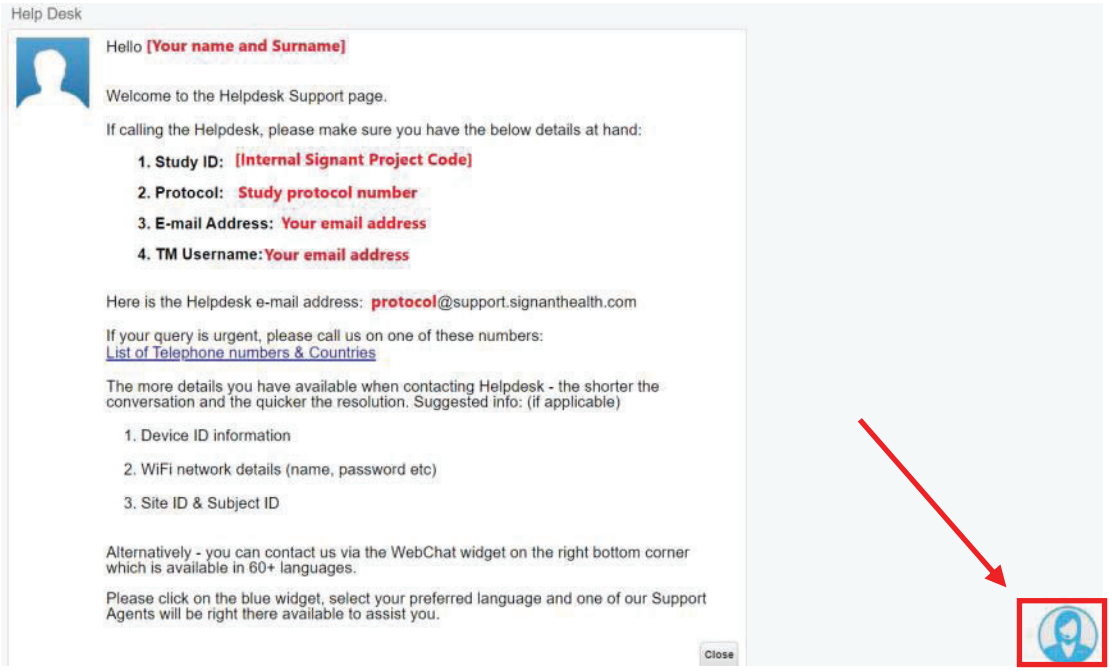
1) Please click the Help Desk button in the upper right corner of your screen.



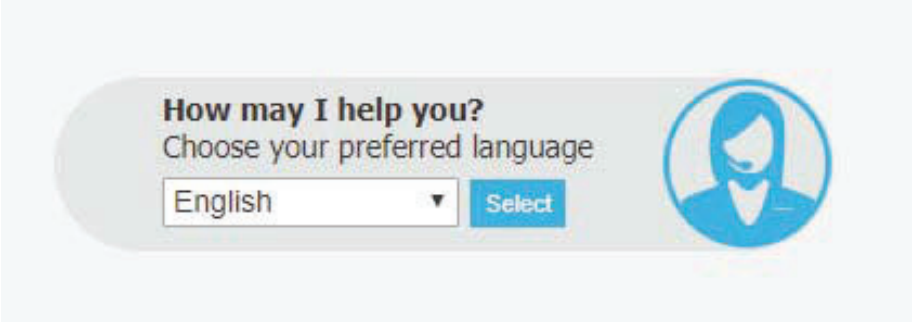
2) You will see a welcome page where all the texts highlighted in red will be pre-filled.

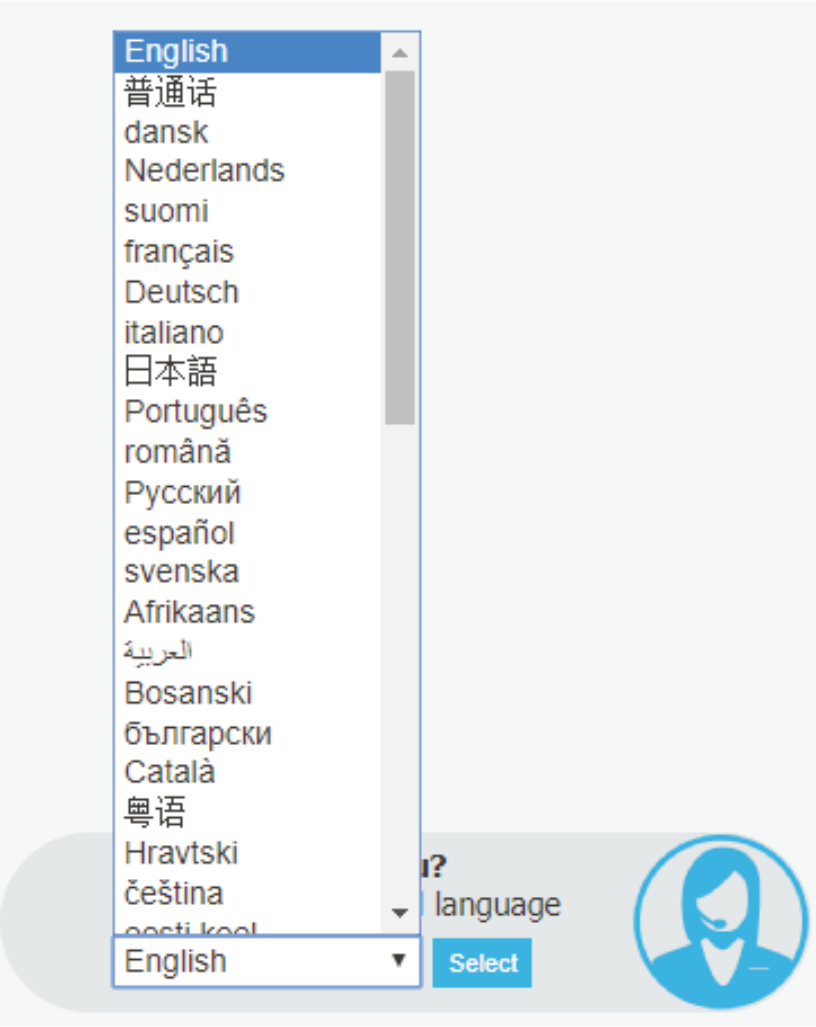


3) You can open the web-chat, available in 60+ languages, by clicking the blue widget in the lower left corner of the screen to start your live chat with one of our Support Agents.

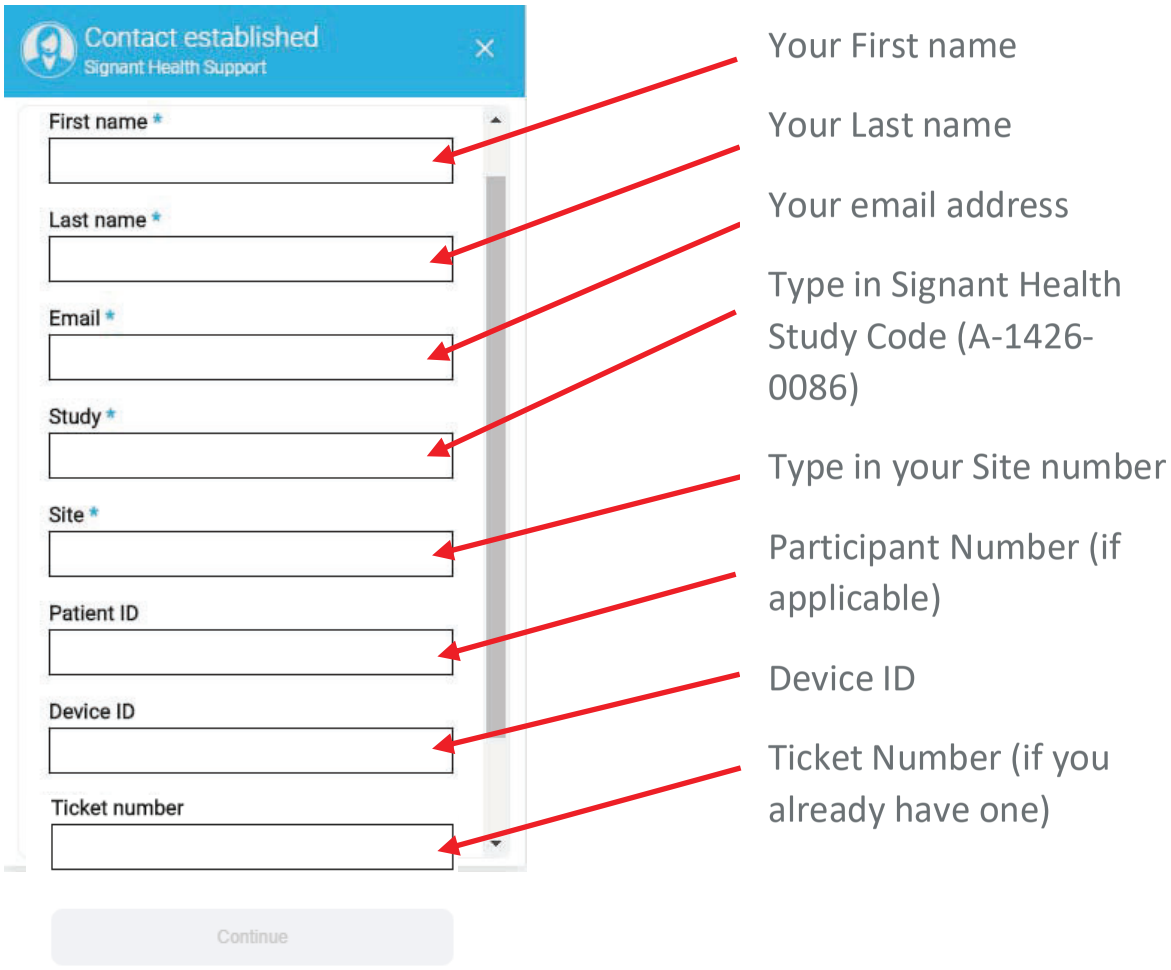


4) Once you click on this widget, you will be able to select your preferred language from the drop-down menu.





5) After selecting your language, you will need to complete the necessary information in the below screen and click the Continue button, then you will be connected to the next available support agent.



Fields with an asterisk (*) are required.

Once you click on "Continue", you will be connected to the Signant Health Helpdesk specialist, who will discuss your issue with you.

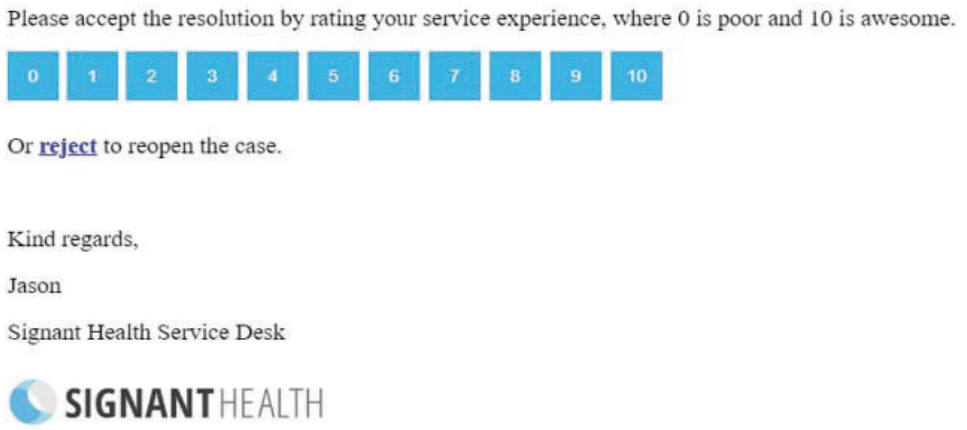
Please note that if a telephone call has already been placed make sure that you enter the Ticket Number you received from your telephone call into the web chat to ensure the background information is linked. If the ticket number is not entered, it will be counted as 2 separate calls.

Providing feedback about Helpdesk performance

Each time you request support from the Helpdesk, you can rate the level of your satisfaction from the provided service. This is important, as it helps us continuously improve to exceed your expectations.

You can provide the feedback in 2 ways:

- Each time you have spoken to the Helpdesk on the phone you can remain on the line and rate your experience on the scale 0 to 5, where 5 is awesome and 0 poor.
- When your request has been completed, you will receive an email, enabling you to evaluate the service or reject the resolution of the incident.


Please accept the resolution by rating your service experience, where 0 is poor and 10 is awesome.

0 1 2 3 4 5 6 7 8 9 10

Or reject to reopen the case.

Kind regards,

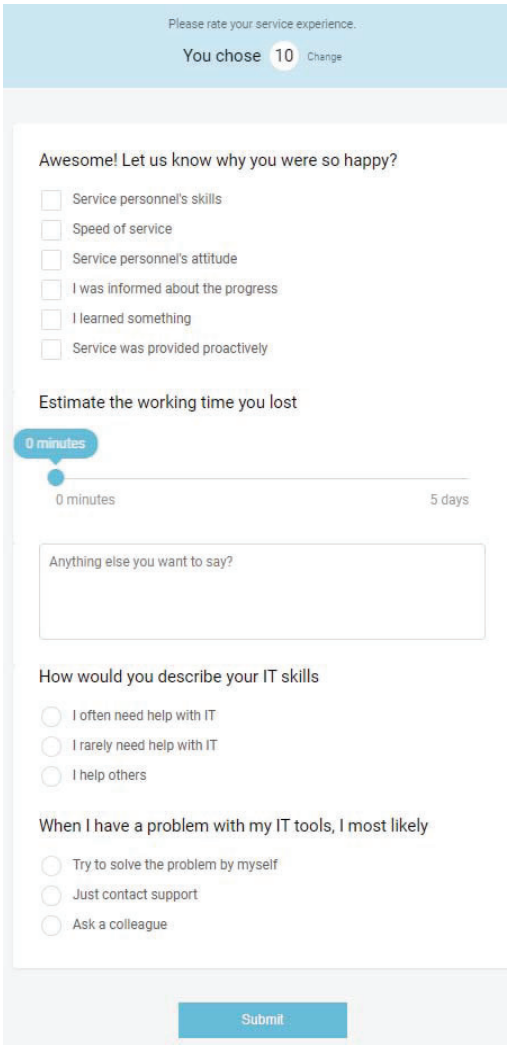
Jason

Signant Health Service Desk

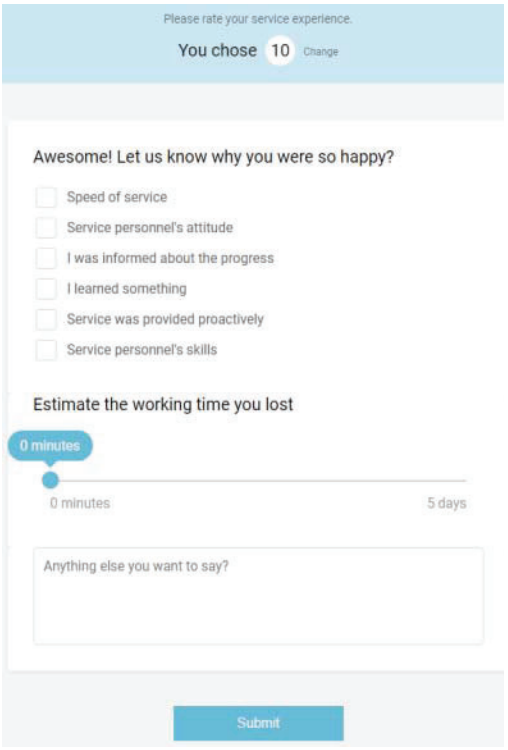
SIGNANTHEALTH

To provide feedback, you would click one of the numbered boxes (0-10), where 0 means poor and 10 awesome. Selecting any rating will take you to a form, where additional information can be provided. The form is a bit longer when you use it the first time and will be shorter with every further use (IT profile information needs only to be provided once).

Evaluation form 1st use

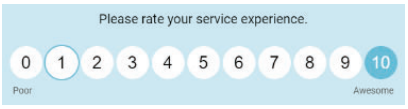


Evaluation form consecutive uses



Please remember that only 9 and 10 mean positive feedback, 7-8 average, 6 and below means negative feedback.

You can change your rating on the top of the form any time before submitting it.



3 Equipment

3.1 Supplies for participant

Provisioned device supplies -

- Motorola device with TrialMax App installed (if not using personal iOS or Android device), accompanied by an incorporated SD memory card (this backs up the data for recovery if needed) and a SIM card installed for mobile data sending.
- A device charger (power-cord and charging brick)
- TrialMax App sticker with country specific Helpdesk number
- Quick Reference Guide in the participant's language
- App Activation Guide in the participant's language
  Participant card with App activation details to be sent via email or SMS

Bring Your Own Device supplies -

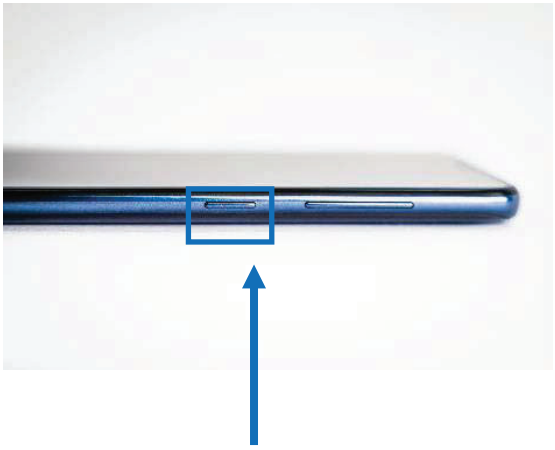
- TrialMax App sticker with country specific Helpdesk number
- Quick Reference Guide in the participant's language
- App Activation Guide in the participant's language
- Participant card with App activation details to be sent via email or SMS

3.2 Provisioned Device Basics

Each TrialMax App device has a sticker applied to it that contains the country specific Helpdesk phone number.

Please contact the Signant Health Helpdesk if a device is not working properly. The Helpdesk agents will assist you or the participant with technical questions.

3.3 How to turn on the Provisioned device



Press the power button on the side

The Motorola device is the provisioned device for this study.

Turn the Device on by pressing the power button on the right side of the device.

If the Device is left on for ten (10) minutes without use, it will hibernate and perform automatic log out.

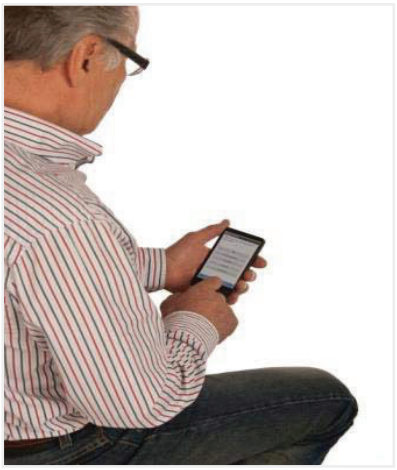
3.4 How to charge the Provisioned Device

The device has a rechargeable battery. Please remember to instruct the participant to **charge the battery <u>every day</u>.** If the device prompts the participant with a message that the battery is low, they should charge the device immediately. When the device is powered on it will display a battery status symbol on the top right side of the screen that indicates the amount of charge remaining in the device.

The participant can use the device while it is being charged but if discharged fully, it may take a little time to charge before use.

Connect the power charger cable to the provisioned device.
The device will usually fully charge in approximately 2 hours.

3.5 Device Navigation



Use your finger to navigate through the device.

Please do not use a stylus or sharp points as these will not function on the device and will damage the screen.

3.6 Additional Site Supplies

- Quick Reference Guide for the participant and TrialMax App device sticker
- App Activation Guide

4 TrialManager

TrialManager is an online, internet-based application used by investigators, coordinators, monitors and study personnel to view and monitor study progress. TrialManager enables the users to follow overall participant compliance and view the participant's Diary data.

TrialManager supports the following Internet browsers:

- Firefox 33 and up
- Internet Explorer 11 and up
- Chrome 32 and up
- Apple Safari v9 and up

4.1 Functions of TrialManager

After answering the questions on the electronic device, the participant will need to send their answers to the study database (TrialManager). Within minutes of sending data, you can view the data (and reports of the data) sent.

By using TrialManager, you can:

- View the participant's Diary answers
- Monitor participant compliance and other reports
- Monitor the number of days since the participant has last completed their Diary
- Raise Data Clarification Forms (DCFs) and monitor their progression through to closure
- View data audit trails for questionnaire entries (including changes to forms)
- Deactivate the participant

Note: You should be logging in to TrialManager only with your own login details (which will be sent to your email). Do not share your

password with your colleagues. It is also important to note that while the term "Participant" is used to describe the patient in this study, you will see the terms "Subjects" and "Participants" used interchangeably throughout the App and TrialManager platforms.

4.2 Accessing the TrialManager website

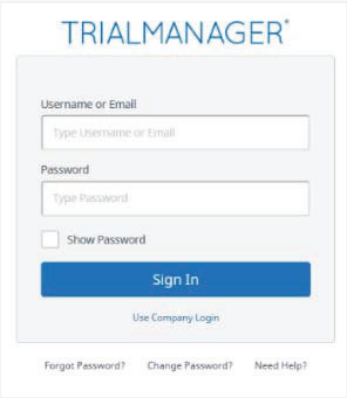
All people will have separate access based on their role within the study.

Your TrialManager username and initial password will be emailed to you. You will be prompted to change this password at your first login (see How to change your TrialManager password for more information). Your TrialManager password has no relation to the Site personnel PIN codes on the TrialMax App.

Note: If you have access to TrialManager for another Clinical Study, then you will be able to use the same Username and Password for each TrialManager. Please note that this feature is only available for the studies that started after September 1st, 2019. If you have a TrialManager account for older studies, you will not be able to use the same Username and Password for each TrialManager unless you change them manually to match with the rest of your credentials.

Type the following address into your web browser:

http://trialmax.crfhealth.net/c4591001-Post-12-July-2020



A login window will open. Bookmark this address for easy future access. Next, enter the username and password that was emailed to you.

4.2.1 How to change your TrialManager password

If you need to change your password, select 'My settings' in the top right-hand corner of the screen or "Change Password" from the Login Screen. There you will find an option to change your password.

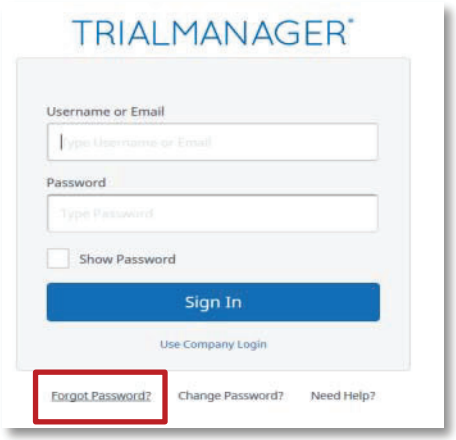
When you decide to change your password, you will be asked to type in your current password, your new password, and verify your new password by typing it in again. Click the 'Change' button to activate your new password.

Rules for creating new password:

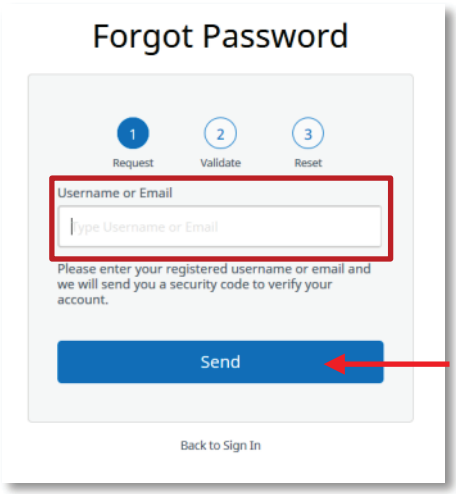
- Must be at least 8 characters.
- Must contain at least one lower case character.
- Must contain at least one upper case character.
- Must contain at least one number.
- Must not contain Unicode characters.
- Special characters in password are not necessary.
- Must not contain spaces, line breaks or new lines.

4.2.2 How to Reset your TrialManager Password

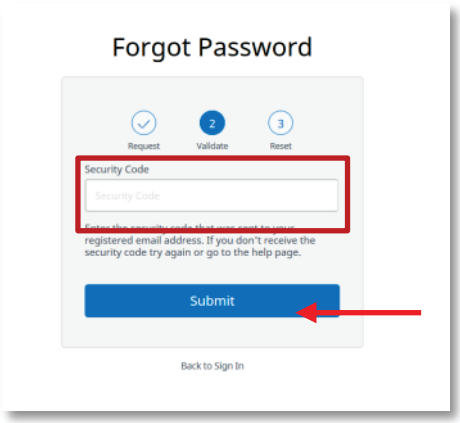
If you have forgotten your password to your TrialManager Account, you are able to reset the password directly within the TrialManager Portal.



From the log in page, select "Forgot Password"



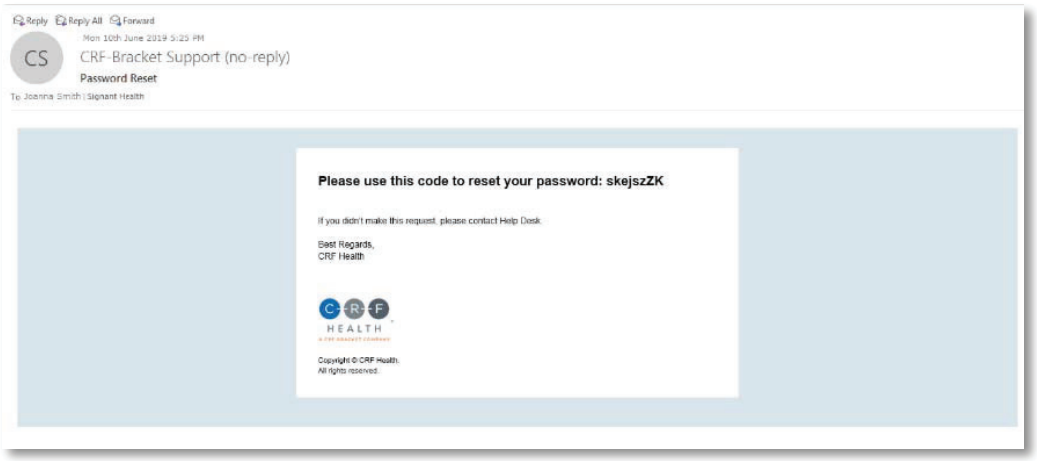
You will be asked to enter your email address so that the system can send you a security code for the password reset

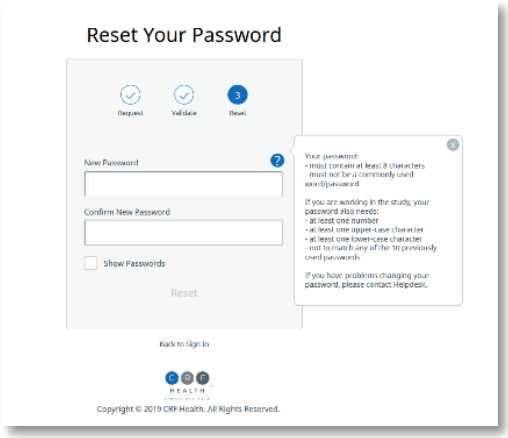


You will be taken to this screen

Check your email inbox and enter the security code, which has been sent to you

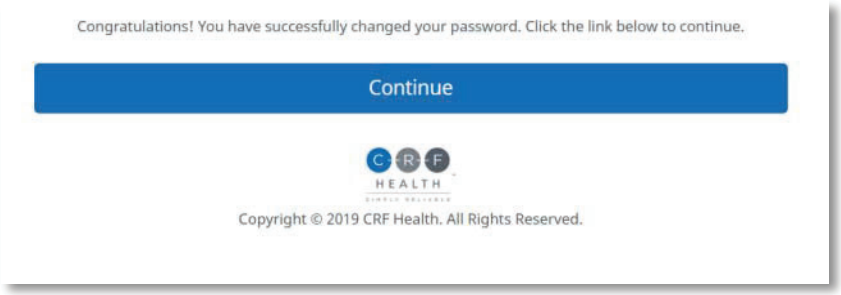
This is an example of the email which will be sent to you:





Enter a new password following the guidance on the screen

Once your reset has been successful, then you should see this screen:



4.2.3 How to request TrialManager access for new team members

In order to request TrialManager accounts for new team members you should add their information into the 'TrialManager User Order Form' and send the updated form to the Signant Health 'TM accounts' team, collating requests into 1 email per week.

Allow 5 business days to create new TrialManager accounts/make updates.

Urgent TrialManager requests can be requested via Helpdesk or directly contacting the Pfizer Study Team via your CRA/Monitor.

4.3 How to navigate the TrialManager website

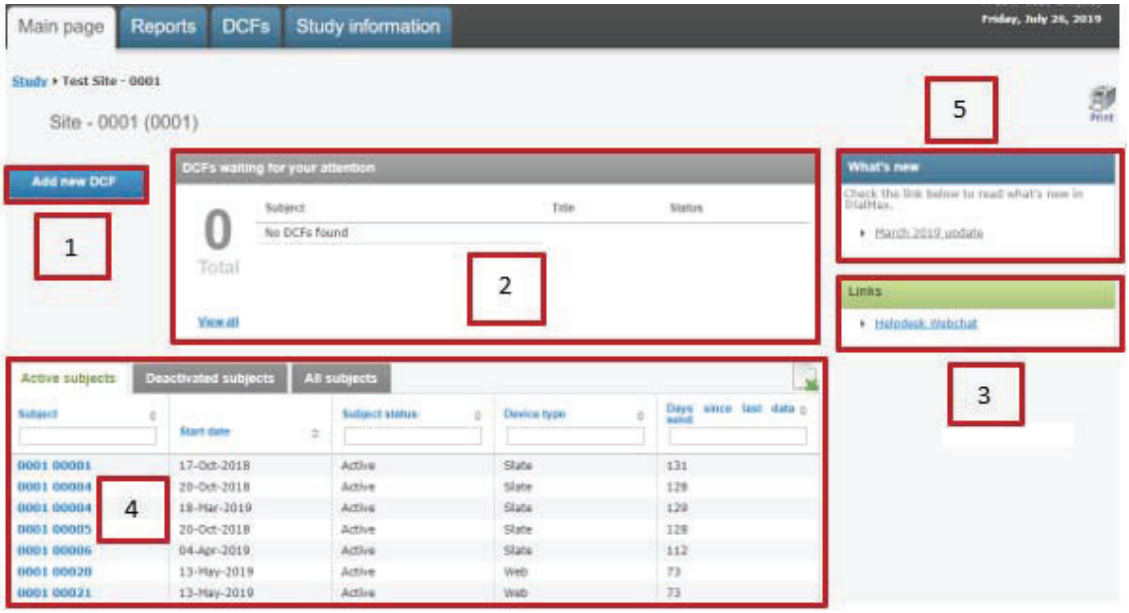
Investigators and Study Coordinators will see several tabs at the top of the screen. They are the 'Main Page', 'Reports', 'DCFs', and 'Study Information' tabs. These are selected by clicking on them.

The points below highlight the main functions and features of the tabs:

- **Main Page:** View a list of all your participants, navigate to individual participant pages, view open DCFs and navigate to the DCF tool, view the latest TrialMax updates
- **Reports:** Review, filter, and print information associated with your site and participants, such as compliance, DCFs, and administrative data
- **DCFs:** Create, approve, and monitor all requested data changes for your participants
- **Study Information:** Access supplemental reference content, such as electronic versions of the Site User Manual and DCF Guide

4.3.1 Main Page Tab

When you select “Main page” the following screen appears:



1. With this button, you are able to add DCFs (see Where to create DCFs in TrialManager).
2. This section is called the DCF Notice Board and will display all DCFs for your site that require your action. Simply click on the title of a particular DCF to see further details displayed. All DCFs created by you or anyone else will also need to be approved by a site user with DCF approval rights. Signant Health will be the one to implement the corrections requested in the DCFs.
3. Some useful web links for the study are displayed on the right-hand side of the screen, including the Helpdesk web chat.
4. The participant list section at the bottom of the screen will display all participants at your site.
    a. By default, this will display Active participants at the site. Click on the ‘Deactivated subjects’ or ‘All subjects’ to also

view participants that have already been deactivated from the TrialMax App.

b. You are able to sort and filter by any of the column headings by typing into the text boxes below the column headings.

c. Clicking on a subject number will take you to more detailed information regarding that participant (see Participant Details Card).

5. You can see the latest updates regarding any TrialManager system updates.

4.4 Add a new participant

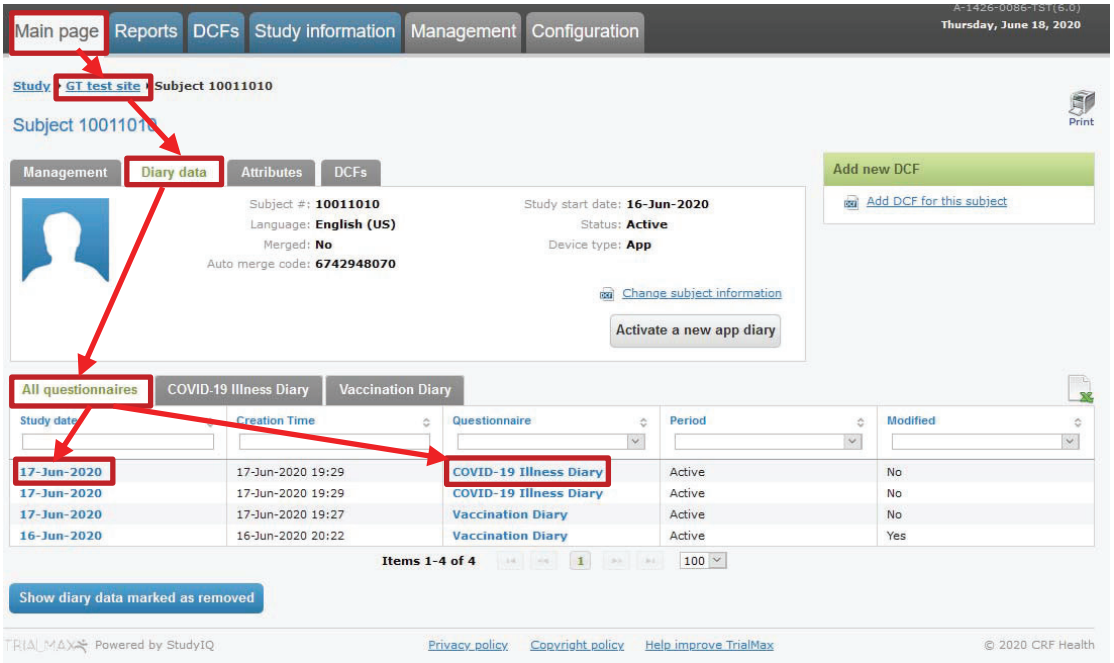
Please see **'How to set up a participant in TrialManager'**.

4.4.1 Participant Details Card

Upon clicking on a participant from the main page, the participant/subject's information card will display:

This will show details for the participant including: language, participant status, study start date, device type, and the participant's auto merge code, which is necessary for replacement devices.

Below the participant details card, you will be able to review the Diary forms submitted by the participant on the TrialMax App.

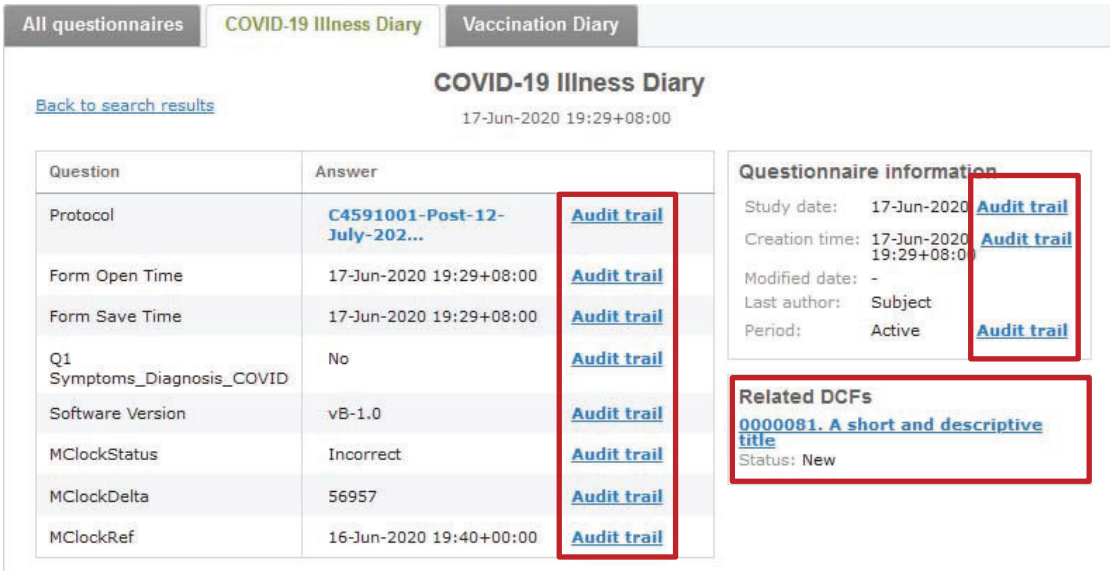


'All questionnaires' tab which contains 'Study date' and 'Questionnaire' links to each completed form. Each column can be filtered and sorted. Upon selecting a form link the form will open,

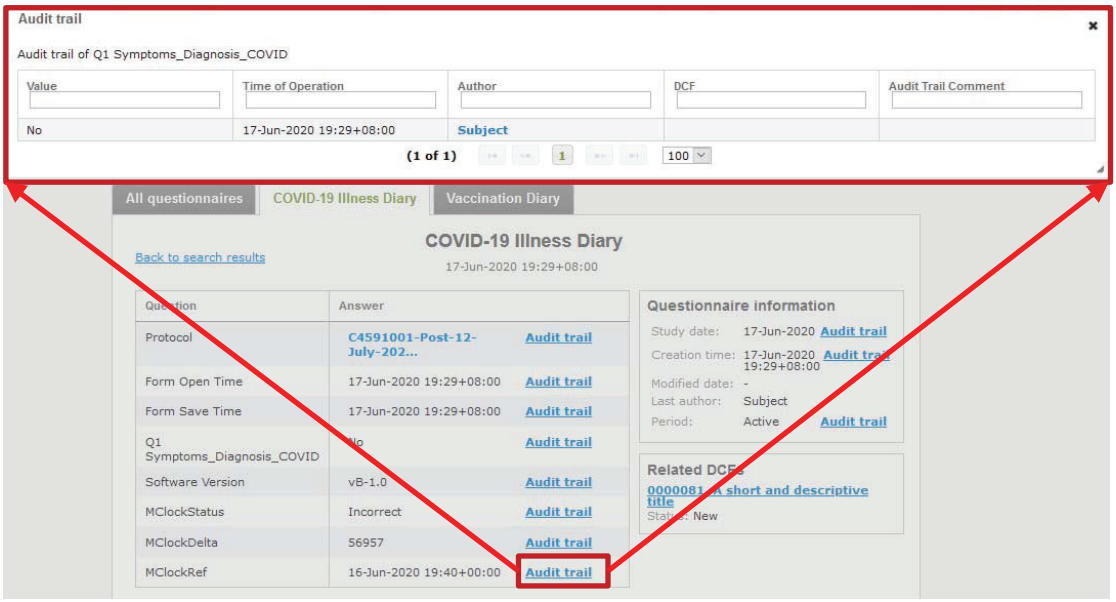
displaying a list of all form data items, including the questionnaire items and responses completed by the participant, and administrative items such as the date and time a completed form was saved.

4.4.2 Data Item Audit Trails

You will also be able to view the audit trails for each questionnaire data item from within these form pages. You can use the audit trails to review the original values and a full change history of any data item if changes were made via the TrialManager DCF tool. If there was a DCF associated with a questionnaire form, this will be displayed to the right of the form with a direct link to the DCF itself and the current DCF status.



To view the full audit trail of any available form item, including the original value and any changes, click the 'Audit trail' link to the right of the desired item. An audit trail of the item will open displaying a list of the data item elements, sorted newest to oldest from top to bottom. If only 1 row is displayed, this indicates that this is the original value of the data item, and that it has not been modified.



The Audit trail column headers are defined as follows:

- **Value:** the value of the data item itself
- **Time of Operation:** the date and time associated with the data item entry or modification
- **Author:** the user that committed the associated operation (participant, site, or Signant Health Data Management)
- **DCF:** the DCF ID number if a DCF was used to execute a change to the form
- **Audit Trail Comment:** free text field where the Signant Health data change implementer may post the DCF number, an external DCR number (if DCF was not used), or other useful reference information

Note: if a data item was modified via DCF within TrialManager, it will display a small clipboard icon to its right. Hovering with the mouse over the clipboard icon will trigger a pop-up with a brief summary of the change.

4.5 Reports Tab

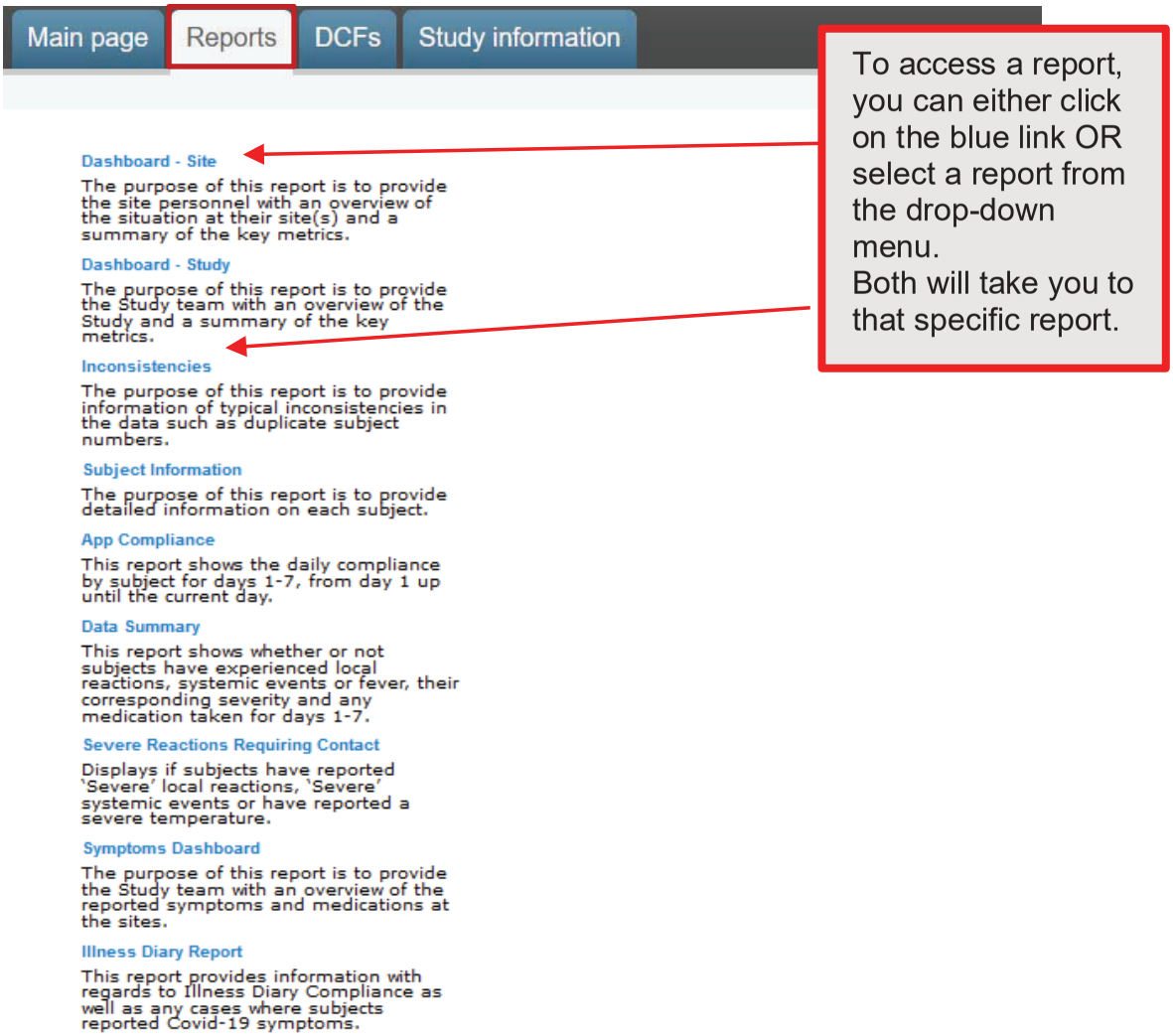
The ‘Reports’ tab will contain reports for you to view. These reports should be reviewed on a regular basis to ensure the participants are completing the questionnaires correctly with good compliance.

Note: TrialManager reports accessibility may not be available on the initial login of the user. The user may have to logout and log back in to view these reports.

The following reports will be available for this study:

- **Dashboard - Site:** The purpose of this report is to provide the site personnel with an overview of the situation at their site(s) and a summary of the key metrics.
- **Dashboard – Study:** The purpose of this report is to provide the Study team with an overview of the Study and a summary of the key metrics.
- **Inconsistencies:** The purpose of this report is to provide information of typical inconsistencies in the data such as duplicate participant numbers.
- **Subject Information:** The purpose of this report is to provide detailed information on each participant.
- **App Compliance**: This report shows the daily compliance by participant for days 1-7, from day 1 up until the current day.
- **Data Summary**: This report shows whether or not participants have experienced local reactions, systemic events or fever, their corresponding severity and any medication taken for days 1-7 following each vaccination.
- **Severe Reactions Requiring Contact**: Displays if participants have reported ‘Severe’ local reactions, ‘Severe’ systemic events or have reported a severe temperature.

- **Symptoms Dashboard**: The purpose of this report is to provide the Study team with an overview of the reported symptoms and medications at the sites.
- **Illness Diary Report**: This report provides information with regards to Illness Diary Compliance as well as any cases where subjects reported Covid-19 symptoms.

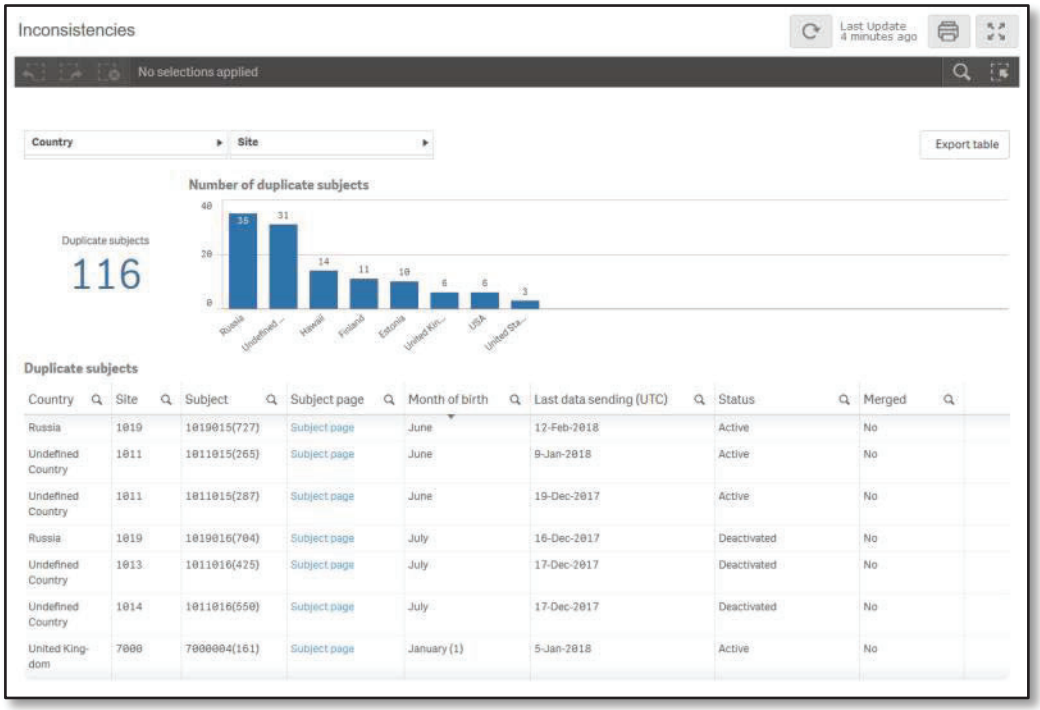


4.6 How To Review Reports

For monitoring purposes, you can view near real-time, graphical reports about the state of the study right inside TrialManager. Graphical visualizations allow you to identify quickly any deviations from the study protocol and take corrective action. For example, you can verify which study participants are still compliant (if they are completing their questionnaires on schedule) or verify the progress on resolving DCFs.

4.6.1 Reports User Guide

The Signant Health Reporting Solution supports a variety of visualizations, including bar charts and data tables. Below is an example of the Inconsistencies Report.



These report visualizations are interactive. When you select parts of the displayed data in report, all other sections update to filter for the selection automatically. This even works between reports in the same drop-down list and allows the user to ask questions about the data. Depending on your user role, you can select your site and/or participant number from the drop-down options at the top of the page. The report will automatically repopulate using the criteria

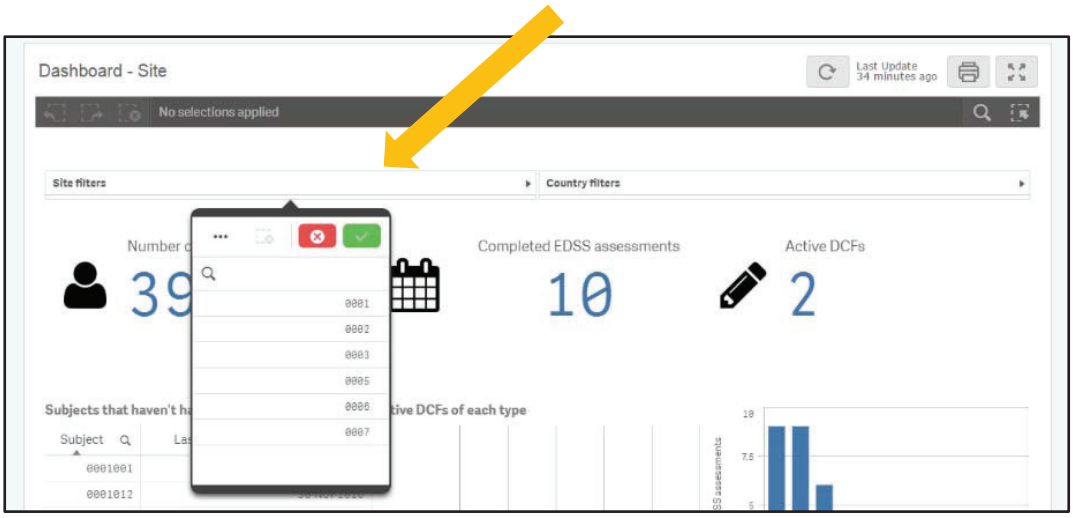
selected. Clicking on the drop-down options will automatically filter the whole report.

4.6.2 Hints and Tips for Viewing Reports

The reports used in this study are designed to give you easy access to key study details. Below are some hints and tips on how to get the best from the reports available in the study:

Filtering

Reports can be filtered in several ways. One way is by selecting from the drop-down filters appearing at the top of the reports, as shown below.



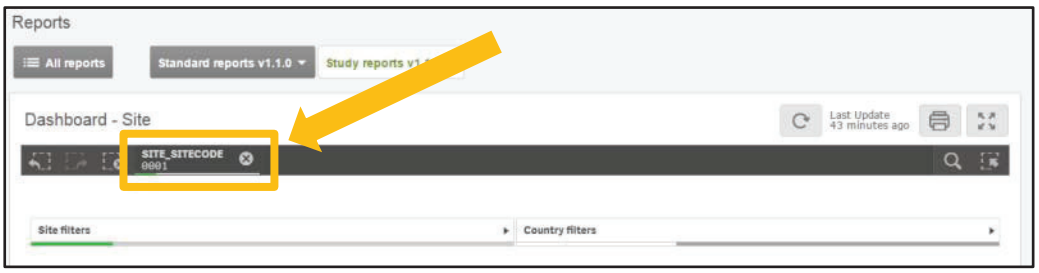
To use the drop-down filters, select an item or items, from the list and select the green tick to apply the filter. Select the red cross to close the filter list without applying the change.

Reports can also be filtered by selecting part of a table or chart, for example selecting a participant from a list, or selecting a bar in a chart.

Selecting the icon in column headings can also be used to filter reports.

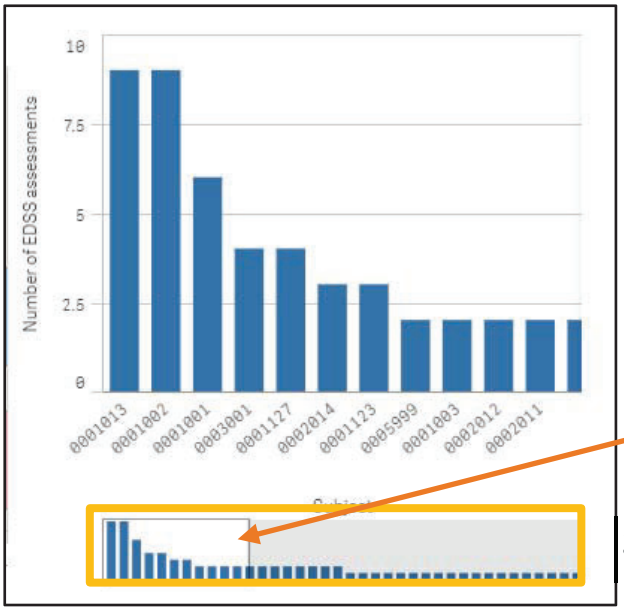
Once a filter selection has been made, all parts of the report and other reports viewed, will have this filter applied. All filters that are applied can be seen in the banner at the top of the report.

To remove a filter, select the “X” next to the filter in the banner at the top of the screen, as per the image below:



Viewing Bar Charts

Some reports contain bar charts to display specific data information. For bar charts with many data bars, it may not be possible to view all bars at the same time. When this is the case, a smaller ‘scroll bar’ version of the report can be seen. Move the white ‘viewing area’ box to the left or right on the scroll bar view to change the data shown in the main part of the report.



Hovering over a bar within a bar chart will display additional information.

Viewing Reports with Tables

For reports with large tables, you may wish to resize columns to ensure the best view in your browser. To do this, simply select the line between columns, and resize as required to fit all the columns in the view. If a column name is too wide to be displayed fully, hover over the column name with the mouse to view the full name.

You can rearrange the order that the columns will appear in by clicking on and dragging a column header into a different position, allowing you to focus on the columns you require.

You can select column headings to sort the report by that item. One click will sort the report in ascending order, a second click will sort the report in descending order. An arrow will appear on the column header to indicate the sorting applied.

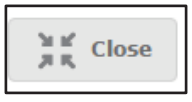
Select the 

button, where seen, to export information in a table to excel.

Standard Report Icons

The icons seen below can be found at the top left corner of all reports in the study.


This icon can be used to expand the viewing area for any report to full screen.



This icon will be seen to exit the full screen view.

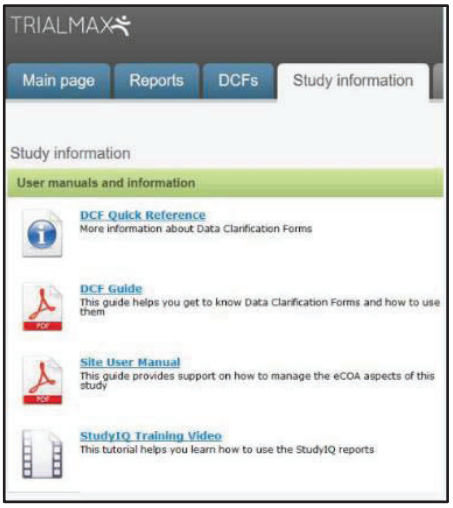
This icon can be used to print to pdf the report being viewed. This pdf copy of the report can be printed or saved, as required.

This icon can be used to reload of the data within the report.

To switch between reports, you can either return to the full list of reports by selecting the 'All Reports' option, or you can switch between reports using the drop-down options 'Standard reports' and 'Study reports'.

Note: Any filters applied to one report will also remain active on other reports viewed in the same drop-down list, unless specifically removed.

Further information and video training on how to use the reports can be found in the 'Study information' tab in Trial Manager.

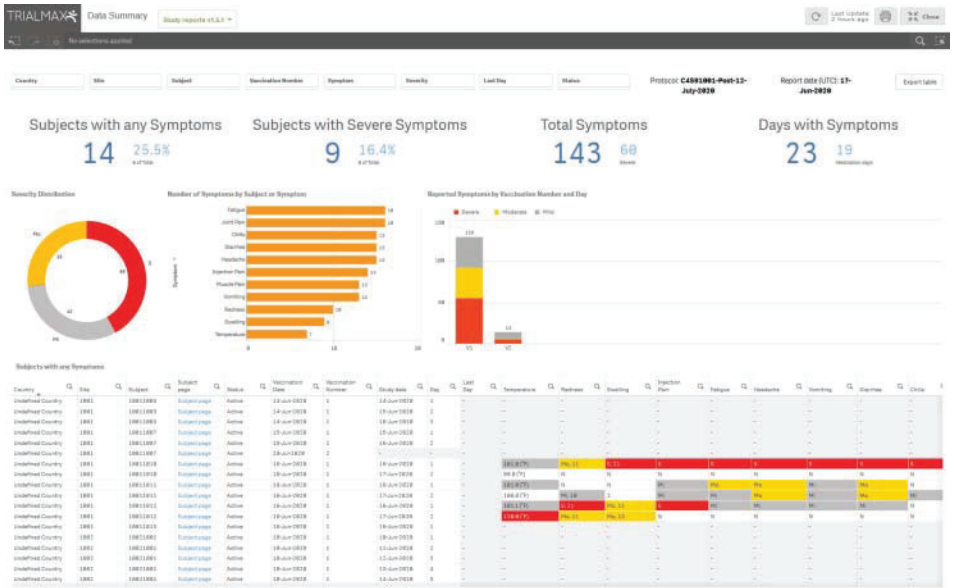


4.7 C4591001-Post-12-July-2020 Custom reports

4.7.1 Data Summary Report

This report shows whether or not participants have experienced local reactions, systemic events or fever, their corresponding severity and any medication taken for days 1-7.

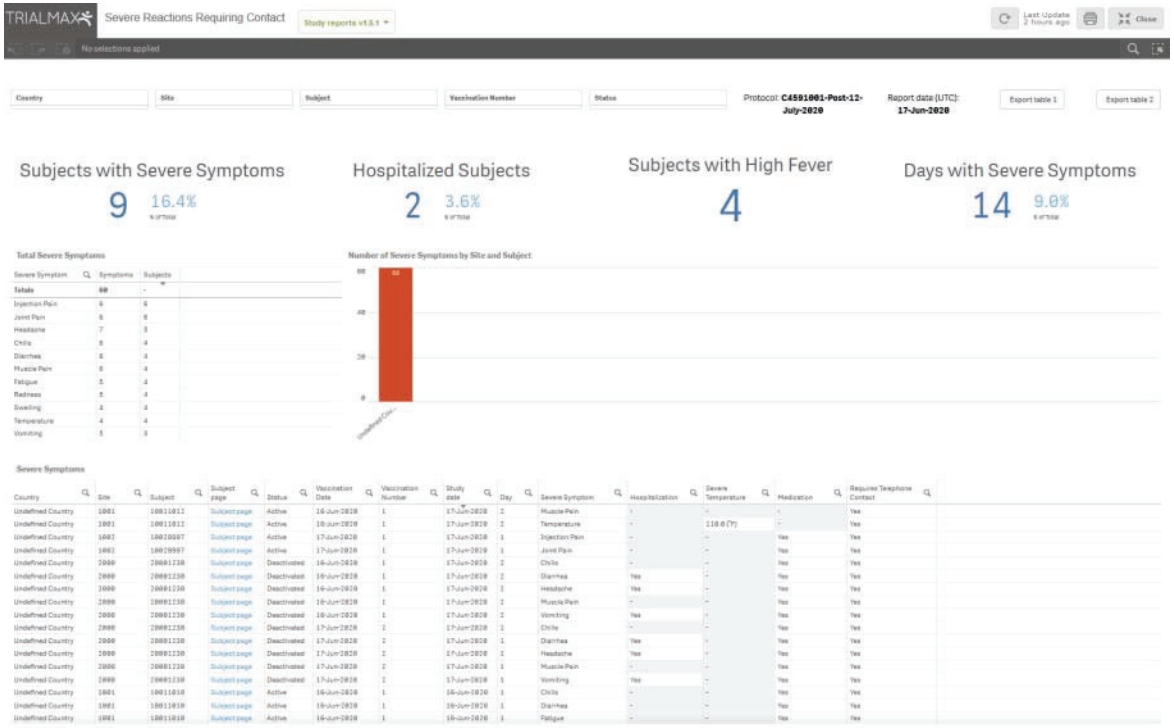
Columns will include: ”Country”, “Site”, “Participant”, “Participant page” (hyperlink which takes you to the participant page in TrialManager), “Status”, “Vaccination Date”, “Vaccination Number” (displays the vaccination number entered in the TrialManager), “Study Date” (displays date when diary form was opened. Future/ uncompleted diary dates will appear as [blank]), “Study Day” (fixed column listing ‘1’ – ‘7’ representing each of the study days for each participant), “Temperature”, “Injection Site Pain”, “Swelling”, “Redness”, “Fatigue”, “Chills”, “Diarrhea”, “Vomiting”, “Headache”, “Joint Pain”, “Muscle Pain”, and “Medication”.



4.7.2 Severe Reactions Requiring Contact Report

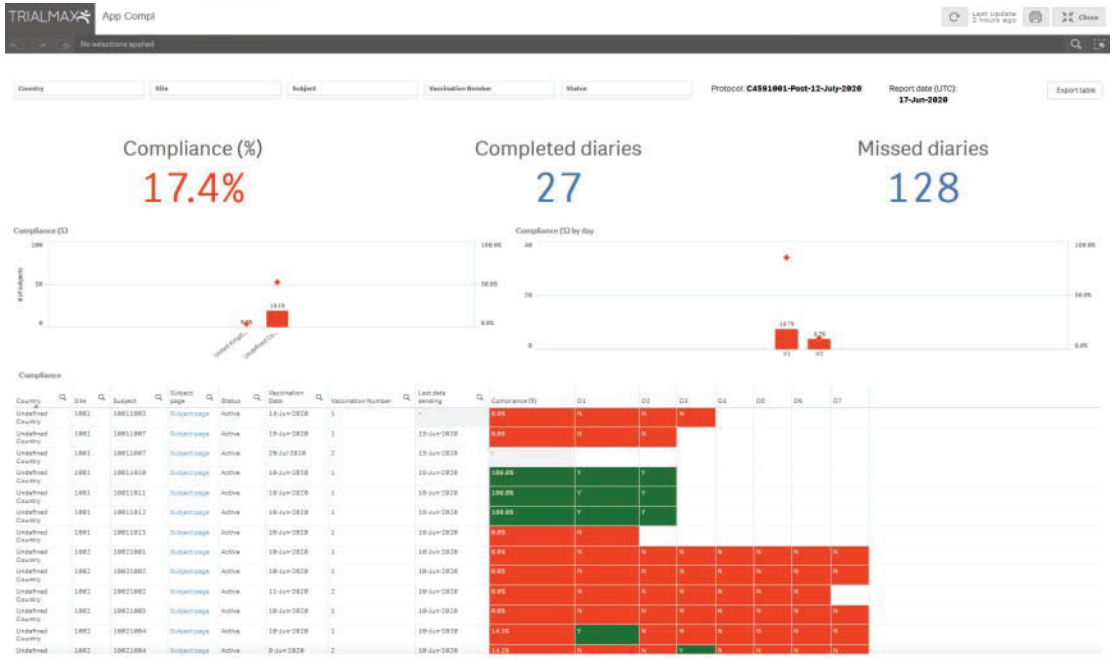
Displays if participant have reported 'Severe' local reactions, 'Severe' systemic events or has reported a severe temperature.

Columns will include: "Country", "Site", "Participant", "Participant page" (hyperlink which takes you to the participant page in TrialManager), "status", "Vaccination date", "Vaccination number" (displays the vaccination number entered in the TrialManager), "Study date", (displays date when diary form was opened. Future/ uncompleted diary dates will appear as [blank]) "Study Day" (fixed column listing '1' – '7' representing each of the study days for each participant), "Severe Symptoms", "Hospitalization", "Severe Temperature" (Any Temperature higher than 102°F), "Medication", and "Require Telephone Contact" .



4.7.3 Vaccination Diary Compliance Report

This report shows the daily compliance by participant for days 1-7, from day 1 up until the current day.



Columns will include: “Country”, “Site”, “Participant”, ”Participant page”, “Status”, “Vaccination date”, “Vaccination number”, “Last data sending” , & “% Compliance”.

Compliance (%): Displays the compliance rate.

D1-D7: represent the study days and will display the status of the participant’s diary completion for each day.

Color scheme display for the Compliance (%):

- Red: <40%
- Yellow: ≥ 40% - < 80%
- Green: ≥ 80%

Expected diary compliance will follow the standard color-coding scheme and thresholds. For active participants, diary completion expectations will be based on the current date. Once a participant is vaccinated, the participant will be expected to complete the diary every day for 7 days including on the day of the vaccination, for the participant. As each study day passes, the previous study days become expected and should have one diary completed. For deactivated participants, diary completion expectations will be based on the deactivation date. The participant will thus be expected to have completed one diary for each study day starting from the vaccination day and until the day before the Deactivation date. The exception here is that if the participant completed a diary on the day they were deactivated, that day will also be considered as expected.

4.7.4 Symptoms Dashboard Report

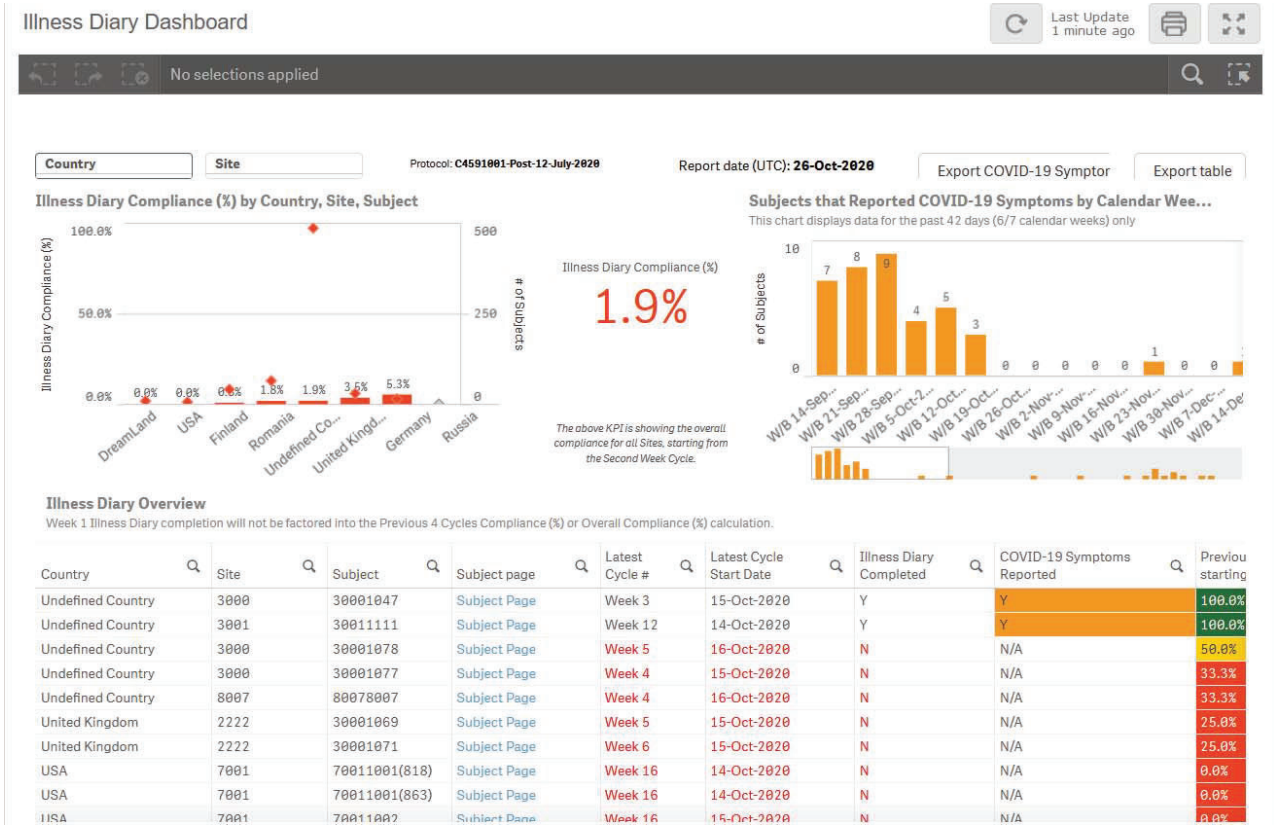
The purpose of this report is to provide the Study team with an overview of the reported symptoms and medications at the sites.

Symptom Distribution columns will include: “Symptom”, “S” (Severe), “Mo” (Moderate), “Mi” (Mild), & “Total”.

4.7.5 Illness Diary Report

This report provides information with regards to Illness Diary Compliance as well as any cases where subjects reported COVID-19 symptoms.

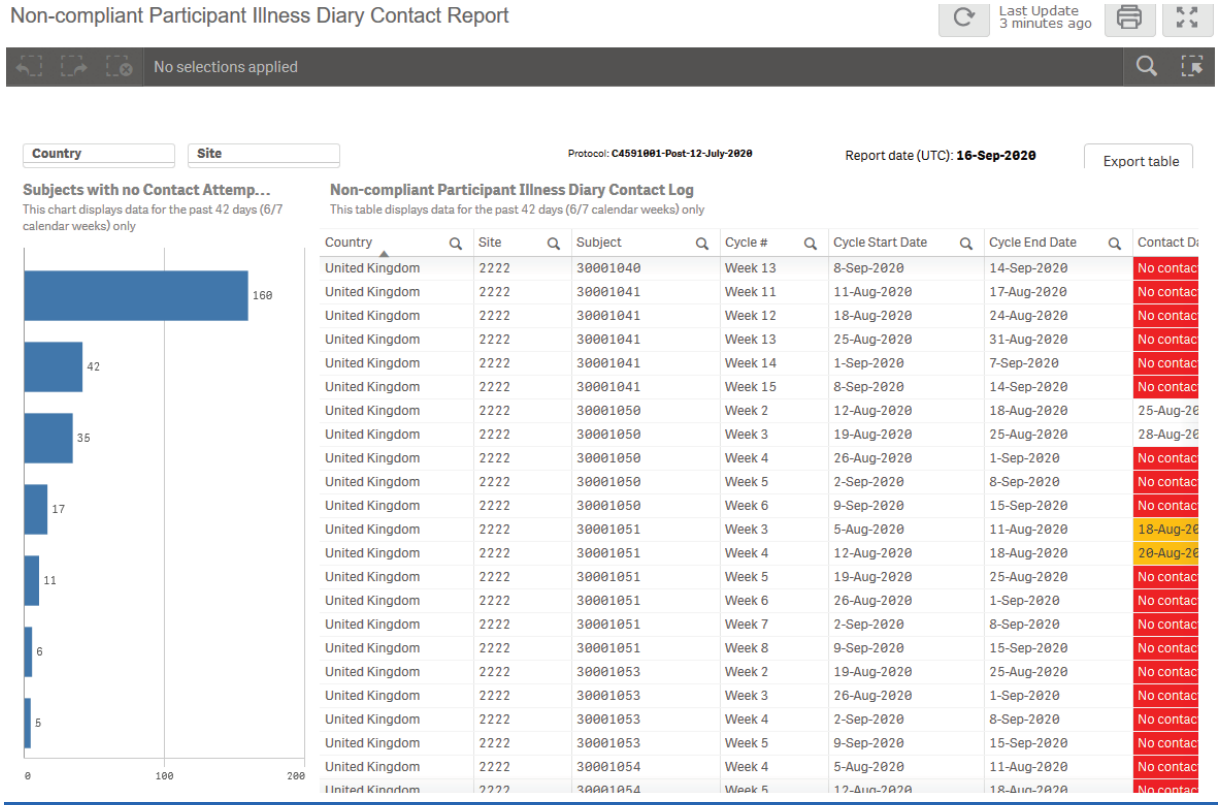
Columns will include: “Country”, “Site” “Subject”, “Subject page” (hyperlink which takes you to the participant page in TrialManager), “Latest Cycle #”, “Latest Cycle Start Date”, “Illness Diary Completed”, “COVID-19 Symptoms Reported”, “Previous 4 Cycles Compliance (%) starting from Cycle # 2”, “Overall Compliance (%)”



4.7.6 Non-compliant Participant Illness Diary Contact Report

This report provides information with regards to Non-Compliant Illness Diary subjects and attempts by the site to contact these subjects. The report will display each cycle (7 day period) where a subject has not completed an expected Illness Diary.

Columns will include: “Country”, “Site” “Subject”, “Cycle #”, “Cycle Start Date” “Cycle Start Date “Contact Date (latest)”, “Successful Contacts”, “Un-successful Contacts”



5 DATA CLARIFICATION FORM (DCF)

5.1 What is a DCF

TrialManager allows authorized personnel to request modifications to certain data items via the DCF process. The data reported by the sites and participant is considered to be the original electronic source data. This data is very rarely, if ever, changed, however, in some situations data changes are needed. The DCF is the audit trail for data changes. Each DCF and its full history are available for review during the study via TrialManager and will be provided to the sites and client at the end of the study via the site archive.

5.2 Types of data changes allowed:

The following data modifications are permitted for this study:

- Changes to data previously reported by the participant, i.e., increase or decrease in the severity of a local reaction or systemic event previously reported on a given day. It is the investigational sites responsibility to ensure such changes are only requested if supported by appropriate source documentation, e.g., telephone contact report detailing the initial data entered and the corrected data.

- Changes to device set-up information, i.e., corrections to the following when previously entered incorrectly:
    - Site number
    - Participant number
    - Vaccination number or date of vaccination

- Other administrative changes, i.e.:
    - Merging participant data and removal of duplicate data – allows cleaning of data issues that may result

from replacement or multiple devices being issued to participants.
    - Modifying timestamps - allow cleaning of data issues arising from when the diary device internal clock is inaccurate.
    - Changing participant status

When data is modified or duplicate data removed, no data is ever fully deleted, all data will remain in the data base audit trail.

The following data modifications are not permitted for this study:

- Addition of a form, e.g., addition of a diary that has previously been reported as missed, or if the device fails and the participant is unable to record their diary.

5.3 Where to create DCFs in TrialManager

You can add a new DCF for any participant where ever you see the 'Add new DCF' button in TrialManager.

It is also possible to add a DCF for a specific participant from the participant page (so the participant instance will be preselected), or from a participant's form view while reviewing data (so the participant instance and the specific form will be preselected).

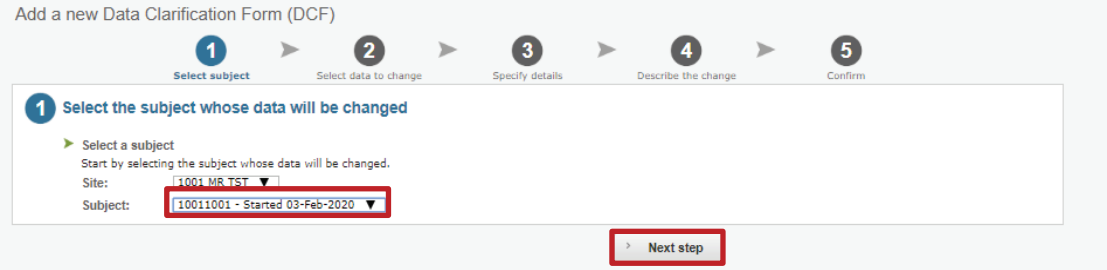
5.4 How to create a DCF

The steps required to complete a new DCF are detailed below. For certain DCFs, additional steps may be required to provide the necessary level of information. The system will guide you to select the necessary information, where this is required.

After initiating the DCF as outlined in Where to create DCFs in TrialManager:

1. **Select Site and Participant**

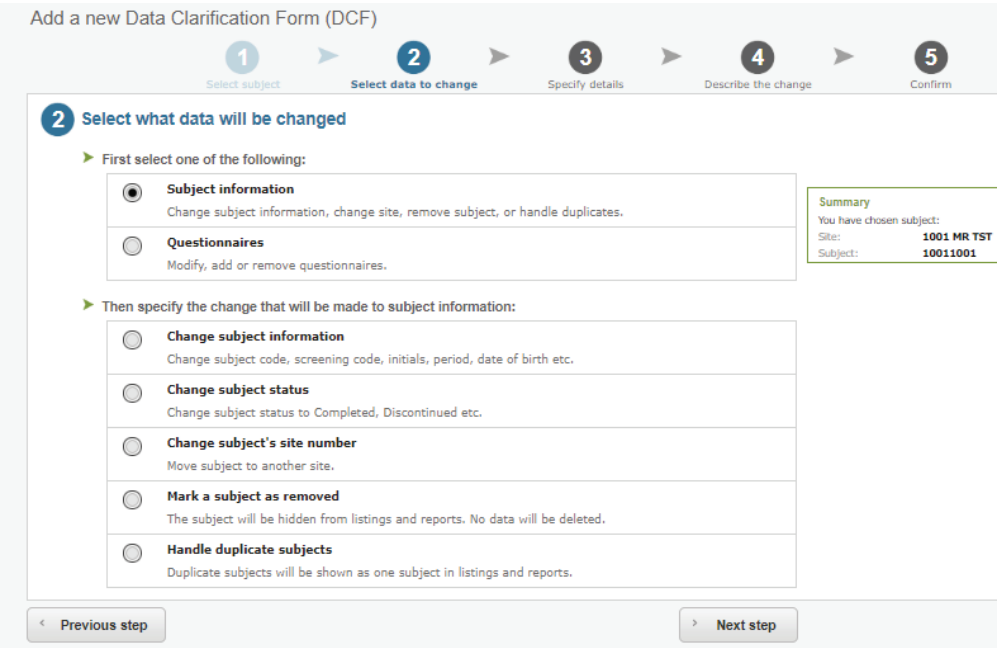
Note: If the DCF was raised at the participant or form level, entering the site and participant in the dropdown will not be necessary.



If there are multiple instances for the participant (i.e. multiple Diary instance) you must select the correct one based on the start date (found in the site index). Alternatively, raise the DCF from the participant level of the correct instance to pre-select the participant details.

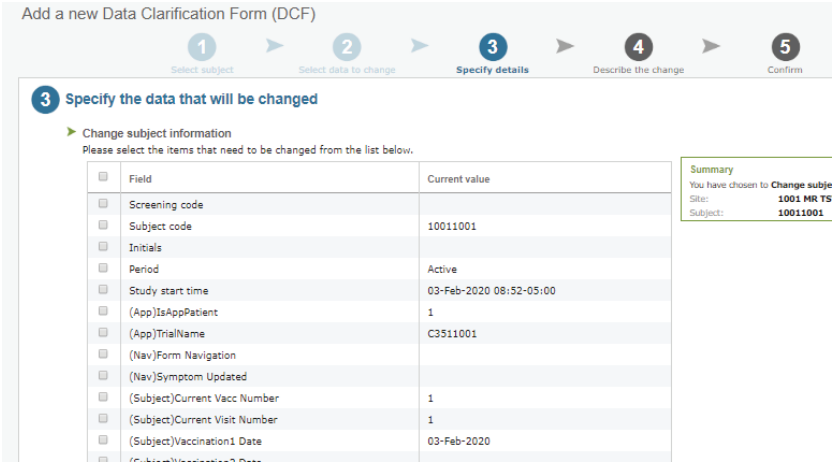
2. Select data to change

Select the data to be changed, either Participant Information or Questionnaires. Based on the selection a further list will appear, as per the example screenshots below. Select the option that best fits the change, then select 'Next step' to proceed to step 3.



3. Specify details (required for some DCF types)

Based on the options selected in the previous step, additional information may be required.



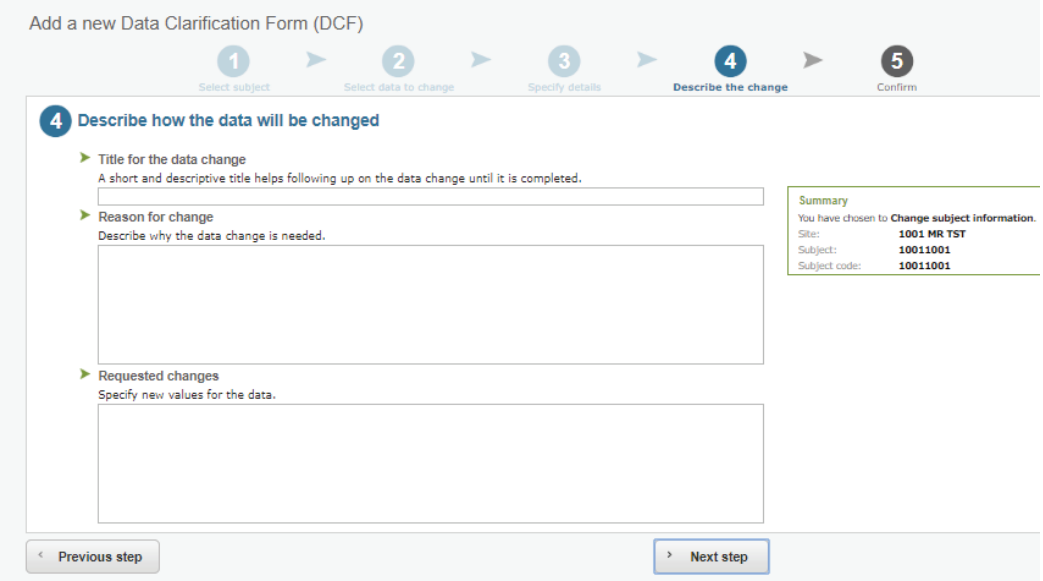
4. Describe the change

Fill in the 3 required free text boxes to describe the change, in as much detail as you can provide. When finished, click 'Next step':

a. **Title for the data change:** Give the DCF a brief title that describes the change (*e.g. 'Update participant number'*).

b. **Reason for change:** Describe the issue with as many details as possible. If this is not specific, processing may be delayed. This should not simply outline what change must be made but rather provide reason for the change explicitly, to act as the audit trail. (*e.g. 'Participant number was entered incorrectly on the device'*)

c. **Requested changes:** Detail the requested changes. Specify any values that need to be changed, including the original value and new value *(e.g. 'Please change X to Y.')*.



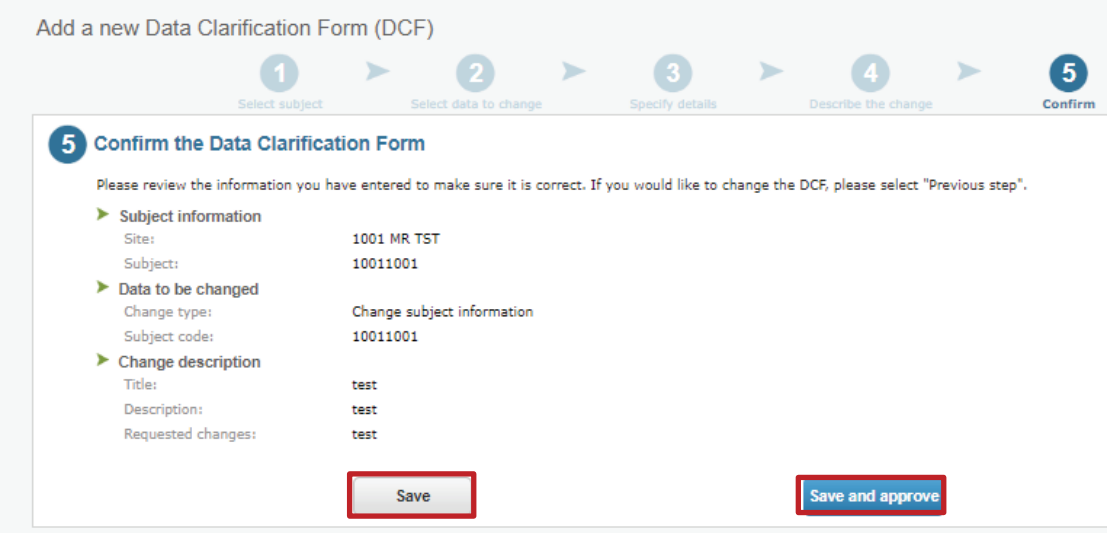
Additional information required for some DCF types:

- Requesting to change a participant's status: be sure to include the date of when the participant status has changed in Step 4 (Describe the change). This DCF type cannot be processed without a date when the new status started.

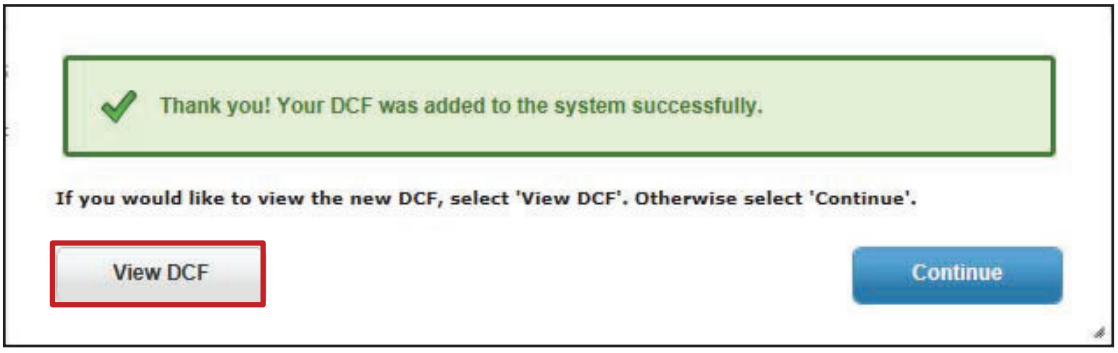
Marking a participant as removed: be sure to specify if forms saved under the participant should also be marked as 'removed' in Step 4 (Requested changes).

5. Confirm

When the DCF has been drafted, you will see a screen where you can review the information entered and click 'Save' to save the information required; or press 'Previous Step' to return to the last step and amend the information. The 'Save and approve' button can also be seen if your user role allows you to approve the DCF request. This button should only be used if you are sure the data entered in the DCF is correct and the request does not need to be reviewed by anyone else before sending to Signant Health Data Management.



You will receive a confirmation that the DCF was created successfully after pressing either 'Save' or 'Save and approve'. Select 'View DCF' to change the status of the DCF for processing by the Signant Health Data Management Team, if 'Save and approve' was not selected.



5.5 Approval of DCFs

When to approve DCFs

DCFs must be approved once they have been created and confirmed to have all the necessary and required information. This may be completed separately, once the DCF is created, or during the DCF creation process if the user has DCF approval rights. **Before Signant Health can implement a DCF, it must first be approved by the Site**.

How to Approve DCFs

DCFs pending site approval can be monitored in the weekly DCF notification emails, which will include links to each DCF, or by reviewing the DCF Dashboard on the study's TrialManager Main Page.

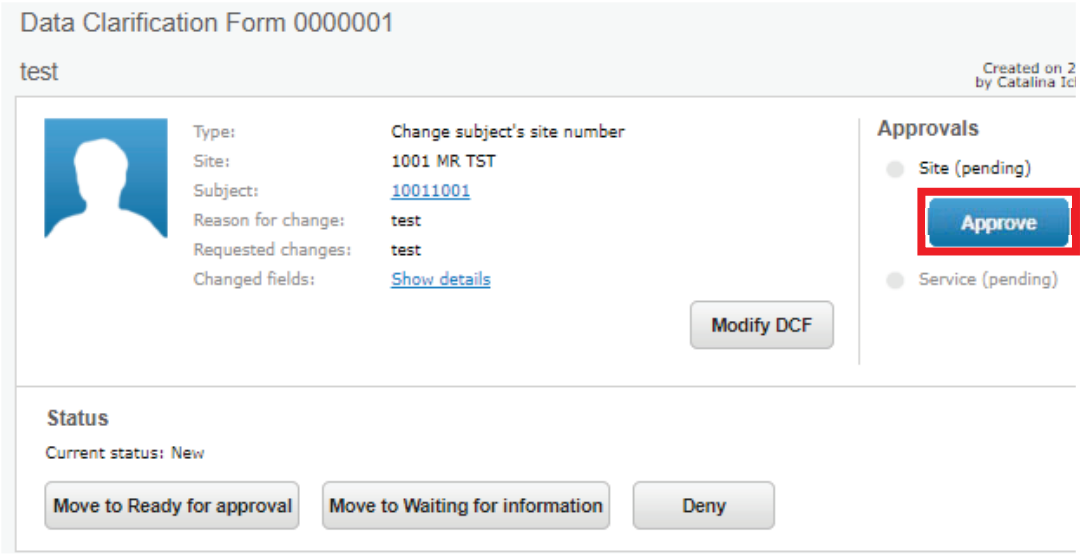
After clicking the DCF link from the email notification, the user will be taken directly to the page where the status of the DCF can be changed. User can also select the appropriate DCF from DCF Dashboard on TrialManager home page by clicking on the DCF title.

Before the change requested can be implemented, the DCF must be approved by the following levels:

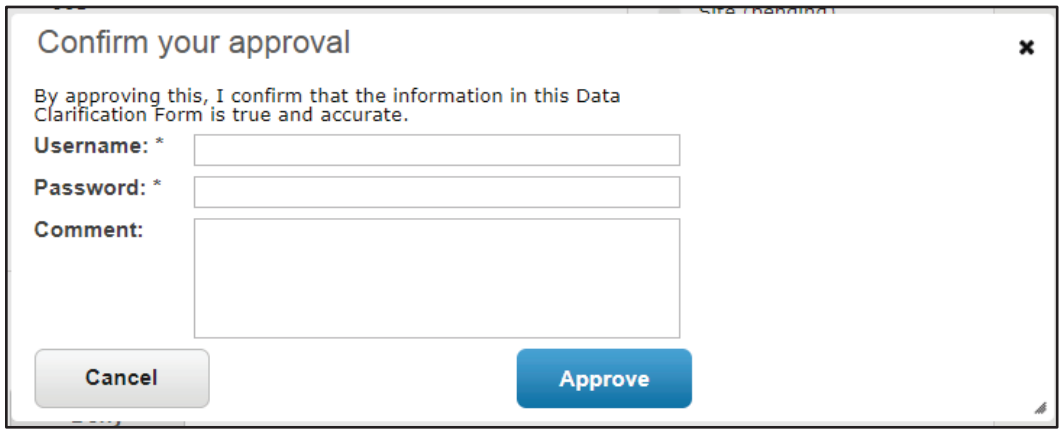
> **Level 1 (Site):** The first level of approval is the Site/Investigator approval. Steps below describe how site personnel can approve DCFs.
>
> **Level 2 (Service):** Finally, Signant Health Data Management Team approval is added once all approvals are received, and Signant Health have confirmed that the DCF includes all necessary information to implement the requested changes.

Follow the instructions below in order to ensure the DCF is approved for processing:

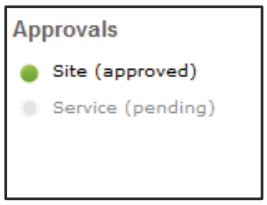
1. Navigate to the DCF and select the **'Approve'** button.



2. Next, a confirmation screen will appear which allows you to add a comment (*optional*) and approve the DCF. After entering your credentials, you can select approve. Please note only Investigator and Study Coordinator (DCF) roles can approve DCF.



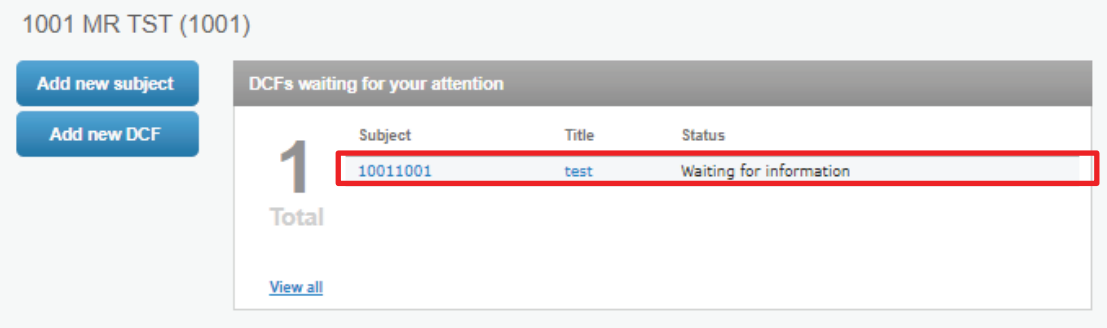
3. The DCF is now approved by the site; approval status is listed on the upper right corner of the DCF. Signant Health can now approve the DCF and implement the changes. **Note: Signant Health may change the status and request additional information see How to Answer Comments: Waiting for Information.)**



You can follow the progress by selecting the DCF and checking the status in the 'DCF' tab of TrialManager and the comments within the DCF.

5.6 Adding Additional Information to DCFs

How to Answer Comments: Waiting for Information



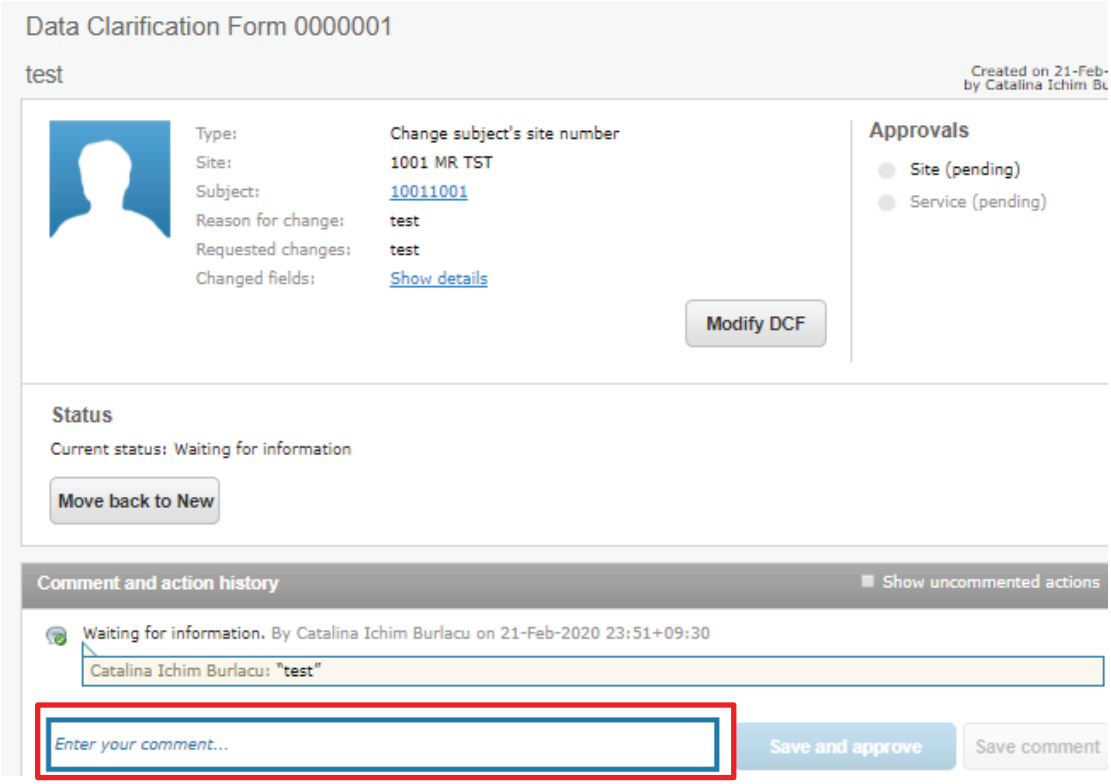
Sometimes, DCFs will need additional clarification and will be changed to the 'Waiting for information' status with questions that the site will need to answer. The DCFs waiting for information can be found on the 'Main page' tab of the TrialManager.

DCFs may be placed in a 'Waiting for information' status for the following reasons:

- DCF wording is unclear
- Wrong type of DCF was selected
- There is missing information that needs to be confirmed

The following steps will be required in order to add comments to DCFs in a 'Waiting for information' status:

1. Click on the Title link to review and read the comment history for the DCF in the 'Waiting for information' status.
2. Review the comments that details the information that needs to be clarified. Enter a clarifying comment in the 'Enter your comment…' text box. Try to respond to all questions raised with as much detail as possible**. If you are still unsure about what information is needed, please state this in your comment**. Press the 'Save comment' button when finished.



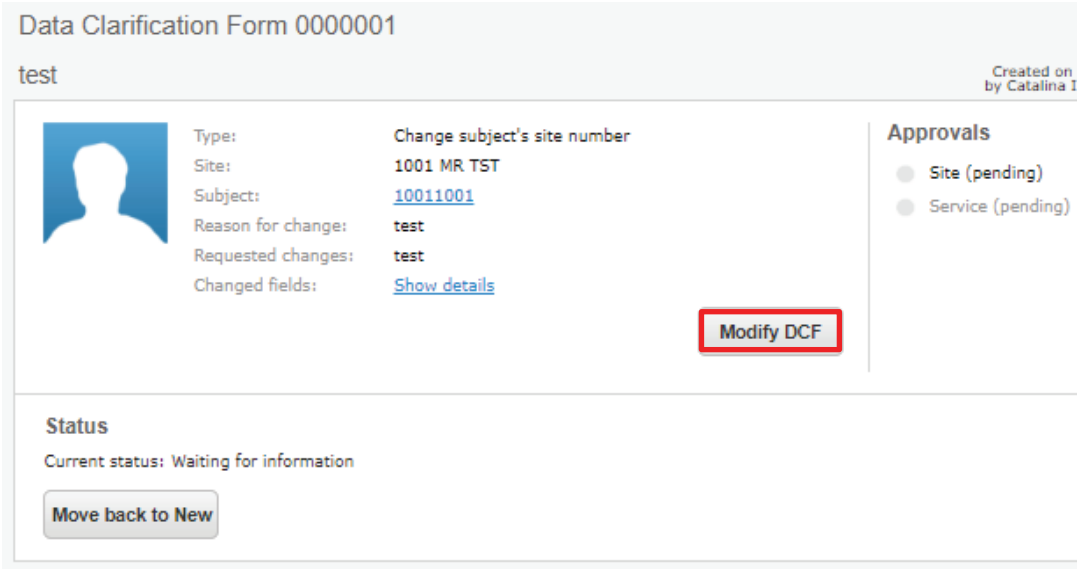
3. Once the necessary additional information has been added via a comment, **the DCF must be approved again**. Follow the steps outlined in How to Approve DCFs above.

You will notice that the DCF no longer appears on the DCF Notice Board on the Main page – this means that no further action is needed on that DCF. Continue the process with all remaining DCFs in your notice board until no DCFs appear in the DCF Notice Board. **Note: The DCF may be moved to a 'Waiting for information' status again if the comments in the DCF are not clear or do not clearly answer the questions from the Signant Health Data Management Team.**

How to Modify DCFs

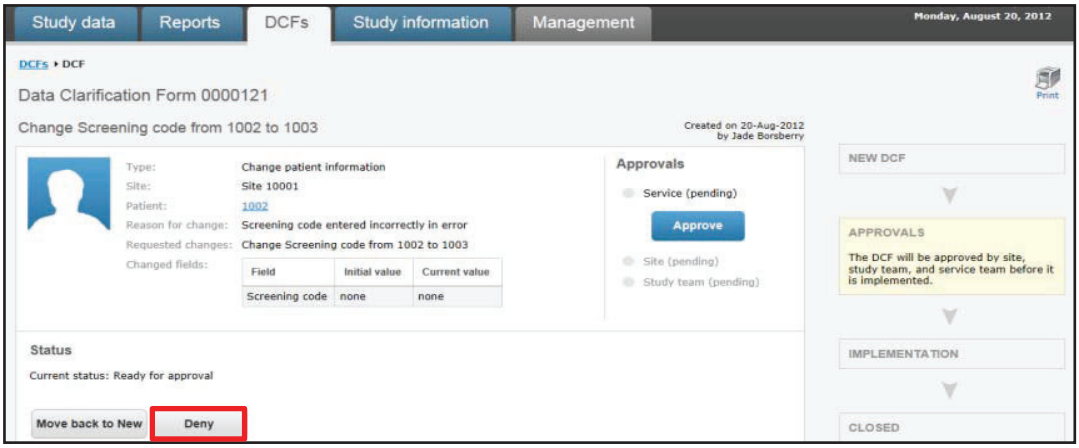
Until a DCF is either under 'Ready for approval' or any 'Approved' status, the site is able to modify the DCF. This can be accomplished by simply selecting the **'Modify DCF'** button on the DCF itself.

When making modifications, be sure to save all updates made to the DCF and move to 'Ready for approval' for processing.



How to Cancel/Deny DCFs

The site can cancel their entered DCF at any time prior to their first approval, by selecting the **'Deny'** button on the DCF page.

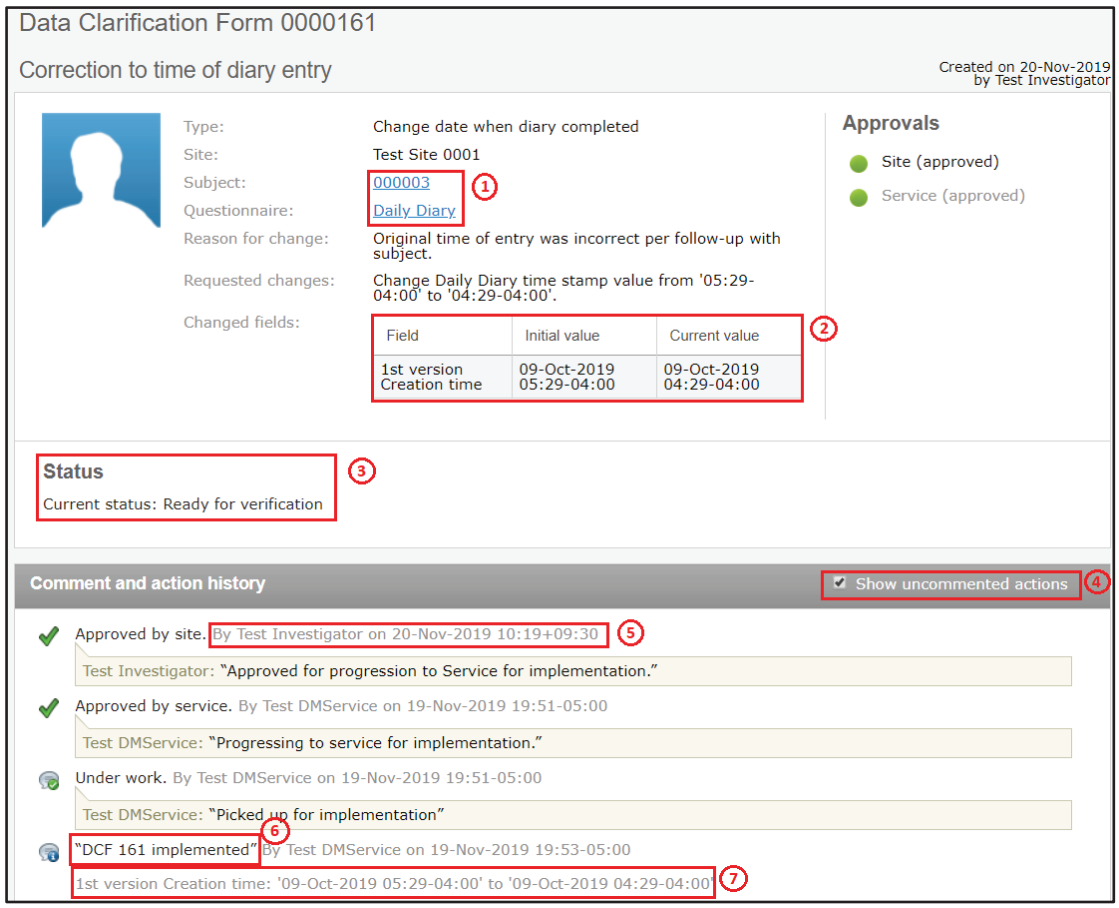


By selecting the 'Deny' button, this signals to the Signant Health Data Management Team that the change requested in the DCF should not be processed.

Note: The Signant Heath Data Management Team may deny DCFs that are not applicable for your protocol or are duplicate requests.

5.7 Viewing DCF Comment and Action History

A DCF will always retain the full history of all comments and actions committed. To view the latest activity for a DCF, navigate to the 'DCFs' tab, select the sub-tab, 'All', and then click the desired DCF link to view the DCF detail. Select the check box, 'Show uncommented actions', and the full history of actions committed in that DCF will be displayed in order of oldest to newest, top-to-bottom.



The elements of the DCF detail view pictured above are defined as follows:

1. Direct links to Participant card and the questionnaire under change, as applicable to the DCF
2. Changed fields will be displayed if specific fields were selected for change during DCF creation. 'Field' will display the data item, 'Initial value' will display the original data item value captured via the TrialMax device, and 'Current value' will display the data item's present value (this may match the 'Initial value' if the DCF has not been implemented yet)
3. The current status of the DCF will be displayed
4. Check box to show uncommented actions, such as a status change can be selected for a comprehensive view of the DCF's history or deselected for a reduced listing. The checkbox will default to unchecked when first opening the DCF
5. The name of the individual committing the action and the commit timestamp will display next to each committed comment or action
6. Comments entered will display within quotation marks
7. Committed changes directly associated with the DCF will display in grey text without quotations

Note: DCF comment and action history items comprise an audit trail of all comments and actions committed in the DCF and cannot be modified once committed.

5.8 DCF Timelines and Tips for Success

DCF Timelines

Once a DCF has been approved, Signant Health Data Management will review and implement the request within 5 working days. If a DCF must go to "Waiting for information" status, then the implementation time will restart on re-approval of the updated DCF.

Tips for Success

It is important that all the data that has been uploaded be reviewed and cleaned throughout the study. Please find below some important guidelines on best practices:

1. It is highly important that data is reviewed and DCFs are raised and approved on an ongoing basis to avoid high volumes of DCFs ahead of interim and final database locks.
   For example, you can use the **Inconsistencies report** to identify participants with potentially incorrect participant numbers, or who may need to be merged, and you should check the participant data to ensure visits are labelled correctly.
2. Sites should continuously review any DCFs waiting for more information to provide Signant Health with the information required to implement prior to lock dates. Regularly review the 'DCFs waiting for your attention' noticeboard on the TrialManager Main Page to find any DCFs that need action to be taken.
3. Sites should ensure that all devices at site have sent data so that all data is uploaded and visible in TrialManager.
4. Please be aware that Signant Health does not review data or raise DCFs.

6 Setting up SMS notifications

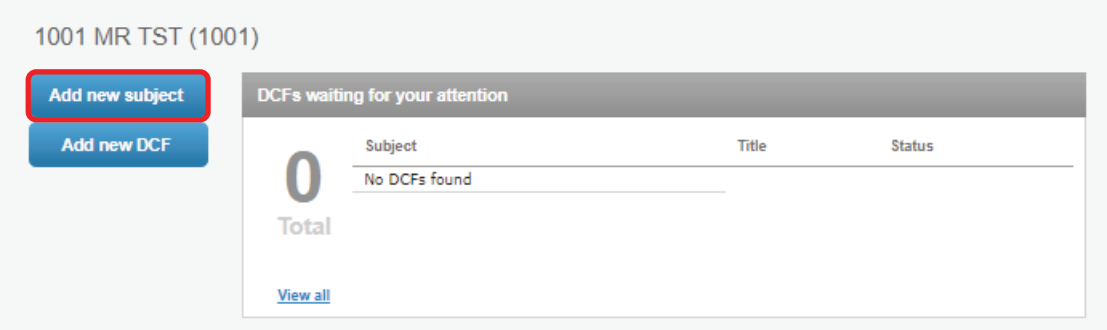
As part of participant setup, you can choose to enter a participant's personal mobile number to receive activation details via SMS. **US participants will need to** subscribe with the mobile phone number they wish to receive this message on. **This should be completed before setting up a participant.**

To opt-in to receive SMS activation code, send a text message with the word **SUBSCRIBE** to phone number **42526**. When you opt-in to the service, you will receive a reply confirming your signup. Once confirmation of subscription message is received, the participant will be able to receive SMS activation code.

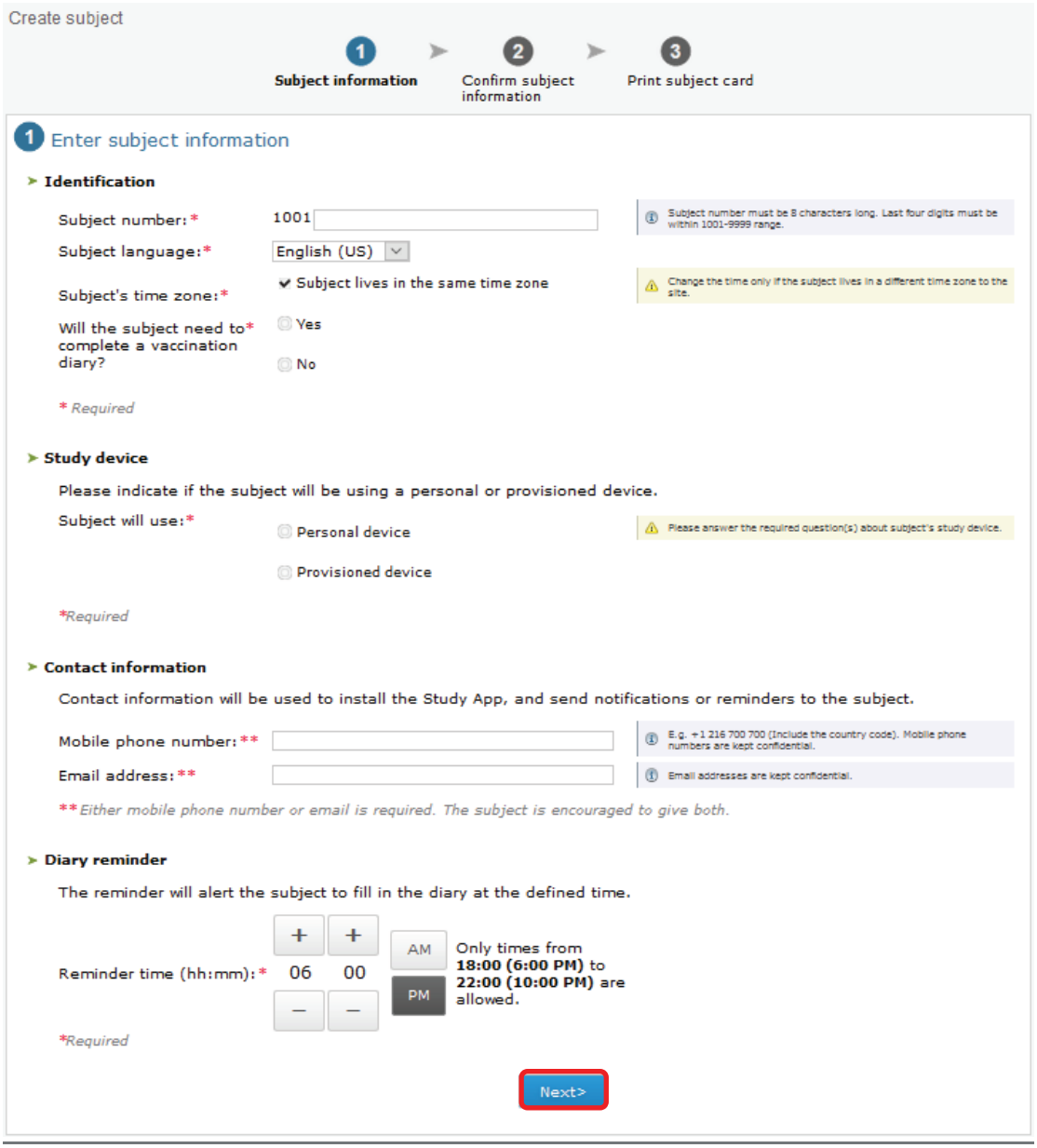
7 How to set up a participant in TrialManager

Participant setup must be performed by site staff through TrialManager for all participants. This must be done when the participant is at your site for their first study visit and not prior as it is a prerequisite for the participant to start entering data in the App. Login to TrialManager to begin.

Select 'Add new subject'



You will then be taken to a screen where you will need to enter the subject number and provide subject information; including their language, time zone, device type, contact information (for receiving activation details), and Diary reminder time.



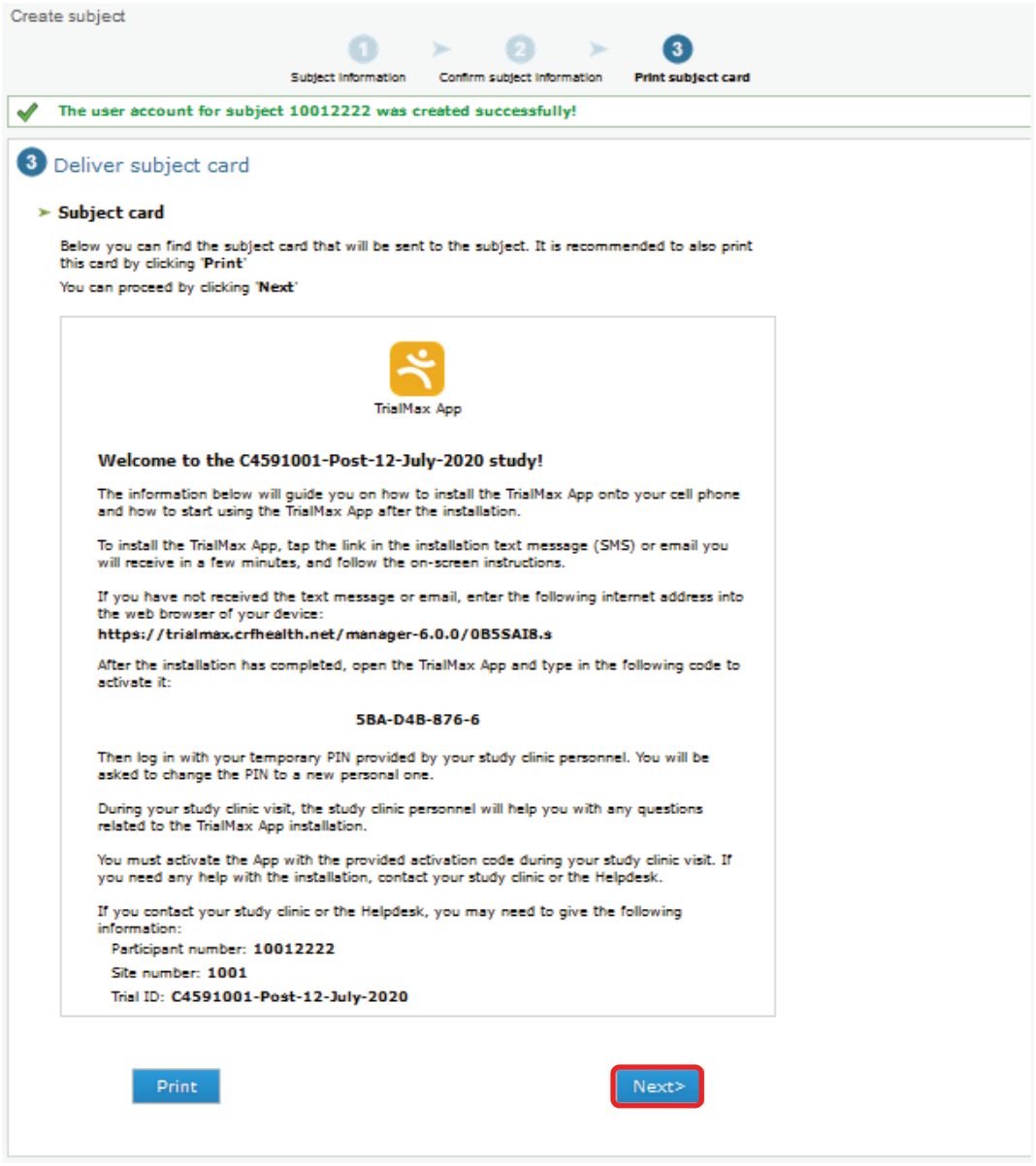
Select “Next” once all the required fields have been filled out.

Note: Mobile phone number and email address are used by the TrialMax system to send an activation code to participant. Therefore, it is important that this information is entered correctly. The participant should enter either their personal email address and/or mobile number to receive the activation code.

Next you will see a confirmation screen, where you will be able to review the participant contact information (mobile phone number and email address) you have entered. Carefully check the details and then select “Confirm”. This will lead you to another page confirming the other participant information that has been entered. Carefully check this information as well, then select “Confirm”.

You will then receive a message on screen that will confirm that the participant was created successfully. You will also see displayed a SubjectCard that is sent to the participant via email/SMS. This participant card contains their activation code and applicable instructions for getting set up with the App.

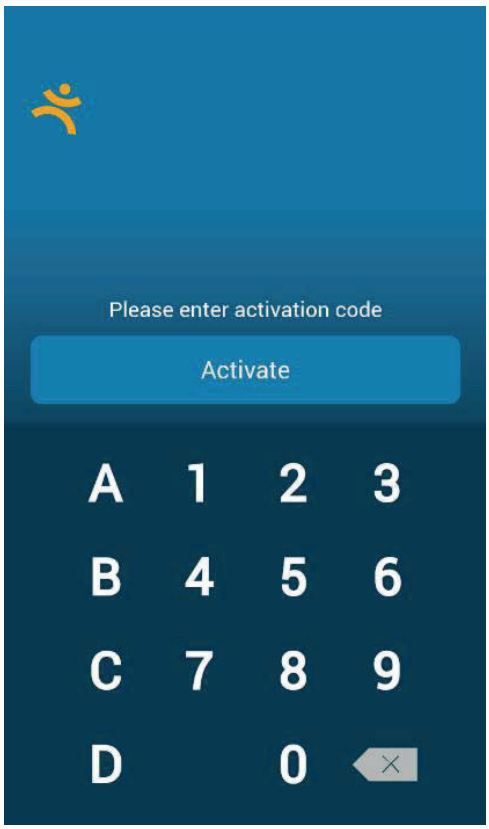
TrialManager will also display a copy of the participant’s card on screen and this should be printed if possible, to make it more convenient for the participant. **Be sure to write down the Activation Code displayed on screen and provide this to the participant.**



Press “Next” to conclude setup.

7.1 How to Activate the App

When the participant setup is complete and the participant receives their subjectt card with the welcome message and activation code, the participant should also be provided with a fully charged Motorola device (provisioned device) to use in the study.



The activation screen is the first screen presented when the provisioned device is turned on. Here, the participant will need to enter the activation code provided in the subject card/ SMS/email message.

Once the activation code has been entered appropriately, the participant will be taken to the login screen where they should enter the default PIN code '**1234**' to login for the first time.

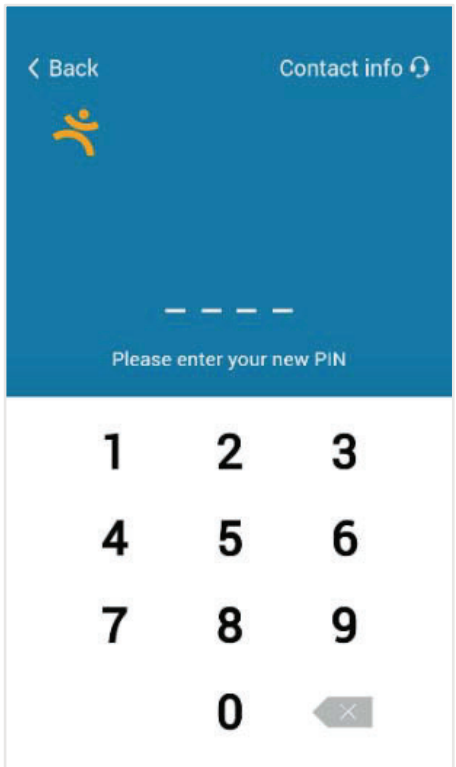
7.1.1 How to setup WiFi on the Provisioned Device

WiFi can be configured on the provisioned devices. To access the WiFi Settings on the provisioned device please follow these steps:

1. Press the 'home' button on the device.
2. Next, press the 'gear' symbol in the top right-hand corner of the screen.
3. Select 'WiFi settings' to display a list of available networks.
4. Select the appropriate network from the list and enter the password if required. *Once the connection is authenticated, the WiFi will connect.*
5. You can then return by clicking the 'home' button, and the App will automatically open.

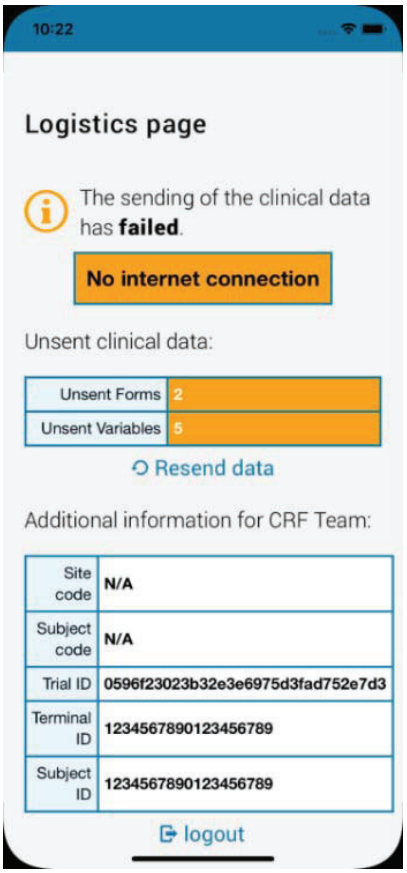
7.1.2 Instructions for reusing the Provisioned Device

The App supports the reuse of the Provisioned Devices, meaning that when one participant has finished using the device, it can be setup for a subsequent participant. To reuse the Provisioned Device for another participant, all unsent clinical data must first be sent to Signant Health.



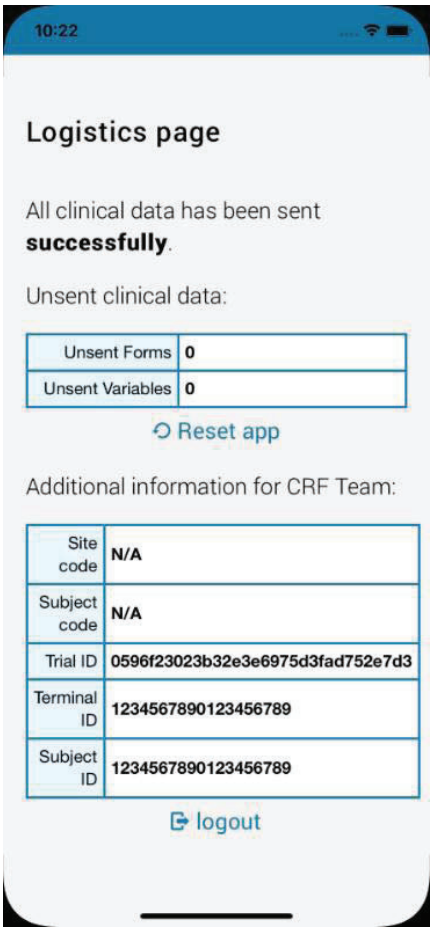
In order to do this, you will first need to login to the Logistics Page on the device.

- From the login screen, first enter the **'Special Code', 7777** to ready the device for the logistics pIN
- Then enter the **'Logistics PIN', 3311**
- Once both PINs have been entered in succession, you will be taken to the Logistics Page



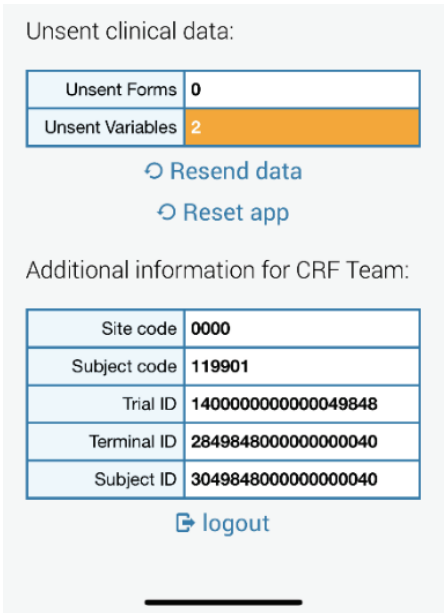
- From the Logistics Page, select 'Resend data' to send any unsent clinical data to Signant Health

The device cannot be reset until all clinical data has successfully been sent.

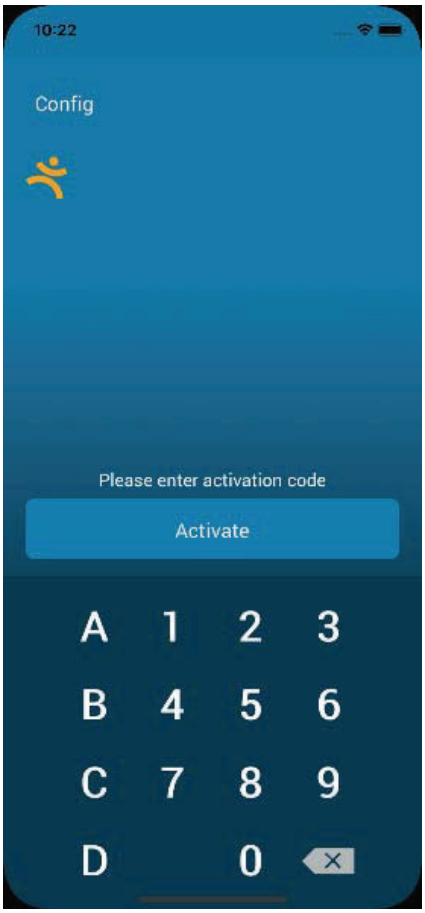


If there is no unsent data, or once all unsent data has successfully been sent, the 'Reset app' button will appear

Selecting 'Reset app Button will reset the App for the next participant



Note: if there are new unsent variables after the data send (due to protocol), but all Diary data has successfully been sent, then the App can still be reset



Selecting the 'Reset app' Button will reset the App; the App will do one more final data sync, then is reset and returns to pre-activated state, ready for another participant to be setup

7.2 Selecting a TrialMax App PIN

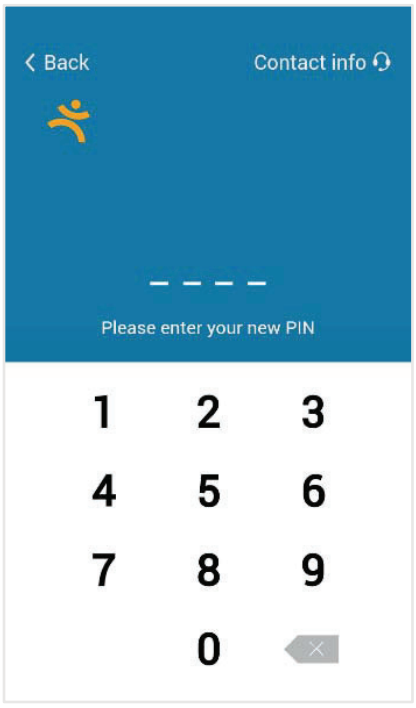
The TrialMax app has certain restrictions for PIN codes:

- Easily remembered by the user (ex: memorable date)
- It cannot be the same as the default PIN code
- It must be four digits
- It must not contain running numbers, e.g. 2345, 5678 will not be accepted
- It must not contain more than three consecutively repeated numbers, e.g. 1111, 2222 will not be accepted

The participant should not share their PIN code with anyone, not even with study staff. The new PIN code must remain confidential, with only the participant knowing the PIN code.

If a participant forgets their PIN code, they will need to contact the helpdesk who will be able to reset the PIN code.

7.3 Logging In & Setting Security Question



After the activation code is entered, the participant will be asked to log in to the App. The user will have to enter the default four-digit PIN code (**1234**) to access the App and will then be prompted to change their PIN to a unique 4-digit PIN.

The participant should not share his/her PIN code with anyone, not even with study staff. The new PIN code must remain confidential, with only the participant knowing the PIN code.

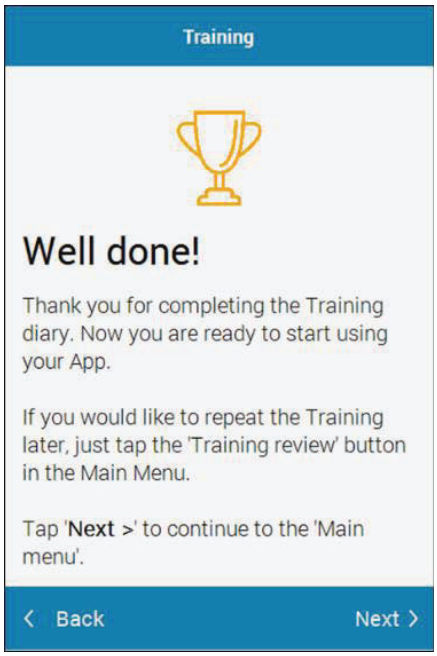
Once the participant has changed their PIN, they will be prompted to select and answer a security question which will assist the helpdesk in resetting their PIN code should they forget it during the study.

After PIN code change and security question selection is fully complete, the participant will be led straight into training on how to use the App.

7.4 Training on the TrialMax App

This initial, mandatory training is required to be completed before the participant can access any other portions of the App (including the Diary).

The training is brief and provides helpful information on App usage as well as a sampling of the types of questions they will encounter while using the App over the course of the study.



Once the participant has concluded the Training, they will receive this screen confirming their completion.

By tapping 'Next' the participant will then be directed to the main menu of the App where they will be able to complete their Diary and modify their settings.

***Please note** – any activities performed while logged into the App should be performed by the participant only. Site staff will not need to login to the App for any purposes.*

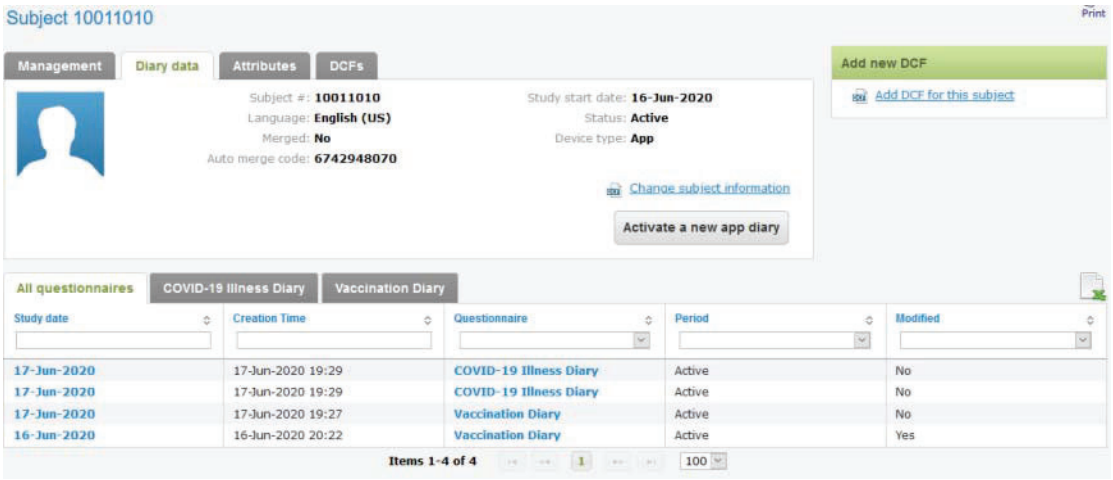
7.5 Software Updates

Site users/participants do not need to take any special action to perform a software update during the course of the study; any available update is automatically downloaded when the TrialMax App is opened and logged in. The login process may appear to take longer than usual when there is a software update, however a percentage will be displayed on the device indicating progress.

8 Managing Participants in TrialManager

8.1 Participant Card

Upon clicking on a participant number from the main page in TrialManager, the participant/subject's information card will display:



This will show details for the participant, including: language, participant status, study group, study start date, and the status of App installation.

Here is where you will activate a new App for a participant due to loss, theft, or change in provision device over the course of the study.

8.2 Activating a new App for an Existing Participant

This section will explain how the participant and site will handle activating new Apps for existing participants.

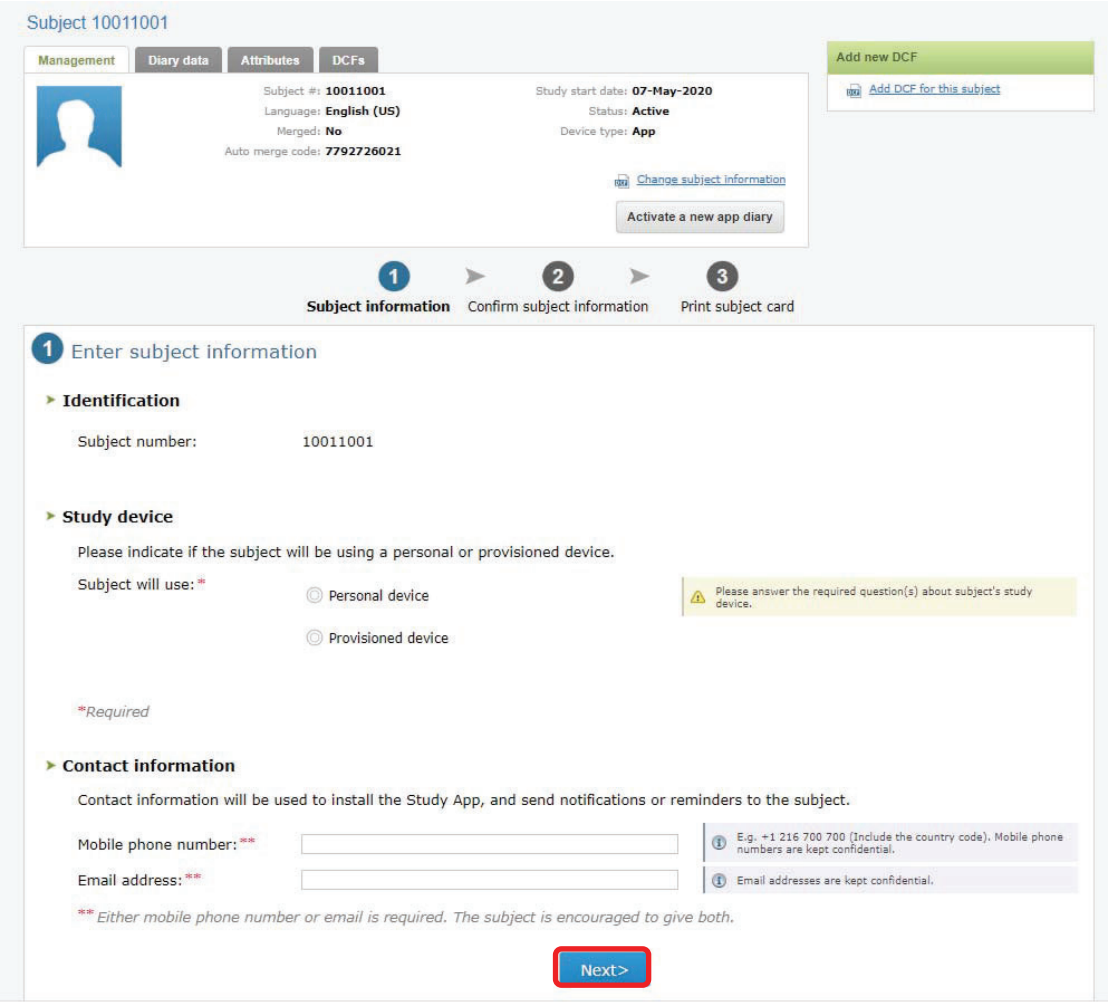
There are three instances in which a new App activation may be needed:

1) If the participant needs a new activation code due to broken device, loss or theft of device, changing device during the study, or
2) If the participant has not used their provided activation code within 72 hours which is the expiration limit. This should not occur since the participant is to activate the app as soon as possible at the visit, or
3) If the subject is switching between using their personal device and a provisioned device.

The steps to handle either of these situations are the same:

Login to TrialManager and select the appropriate participant. From the participant card screen, select the 'Activate a new app diary' button

You will be required to select the participant's mobile phone number and/or email address. Once entered, select 'Next'.



On the next page, make sure the entered information is correct, then select “Confirm”.

You will then receive a message on screen that will confirm that the participant was created successfully. You will also see displayed a Participant card that is sent to the participant via email/SMS (if provided). This Participant card contains their new activation code and applicable instructions for getting set up with the App. TrialManager will also display a copy of the card which can be printed to make it more convenient for the participant.

Press ‘Exit’ to return to your site in TrialManager.

TrialMax App

Welcome to the C4591001-Post-12-July-2020 study!

The information below will guide you on how to install the TrialMax App onto your cell phone and how to start using the TrialMax App after the installation.

To install the TrialMax App, tap the link in the installation text message (SMS) or email you will receive in a few minutes, and follow the on-screen instructions.

If you have not received the text message or email, enter the following internet address into the web browser of your device:
https://trialmax.crfhealth.net/manager-6.0.0/0B5SAI8.s

After the installation has completed, open the TrialMax App and type in the following code to activate it:

5BA-D4B-876-6

Then log in with your temporary PIN provided by your study clinic personnel. You will be asked to change the PIN to a new personal one.

During your study clinic visit, the study clinic personnel will help you with any questions related to the TrialMax App installation.

You must activate the App with the provided activation code during your study clinic visit. If you need any help with the installation, contact your study clinic or the Helpdesk.

If you contact your study clinic or the Helpdesk, you may need to give the following information:

Participant number: **10012222**

Site number: **1001**

Trial ID: **C4591001-Post-12-July-2020**

The participant should then follow the appropriate steps to install and/or activate their App as outlined in the **Participant Setup** section of this guide.

8.3 Management tab

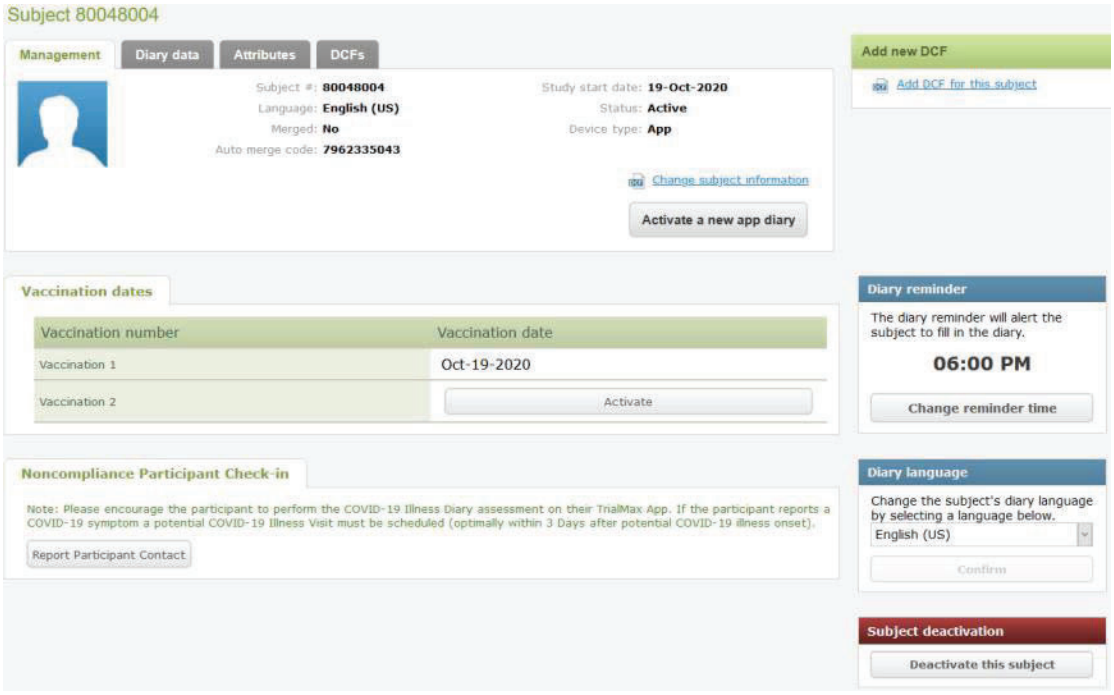
Upon clicking on a participant number from the main page in TrialManager, the participant's information card will display. Clicking on the button titled 'Management' will bring you to a page displaying several options/settings for that participant. Here you can log vaccination dates, update Diary reminder times, change participant language for the App, add or update participant information, and

deactivate a participant from the study. Details for each activity are provided in the following sections.

8.3.1 Activating a New Vaccination

When a participant comes in for the first vaccination the participant needs to be set up on TrialManager. The vaccination is automatically activated on the day of a new participant set up, for instance, in the example below, the participant was set up on TrialManager, and vaccinated on 02-Apr-2020.

****If their vaccination date is not set in TrialManager before they leave the site office, they will NOT be able to complete their Diary. Please be sure this is done before they leave.****

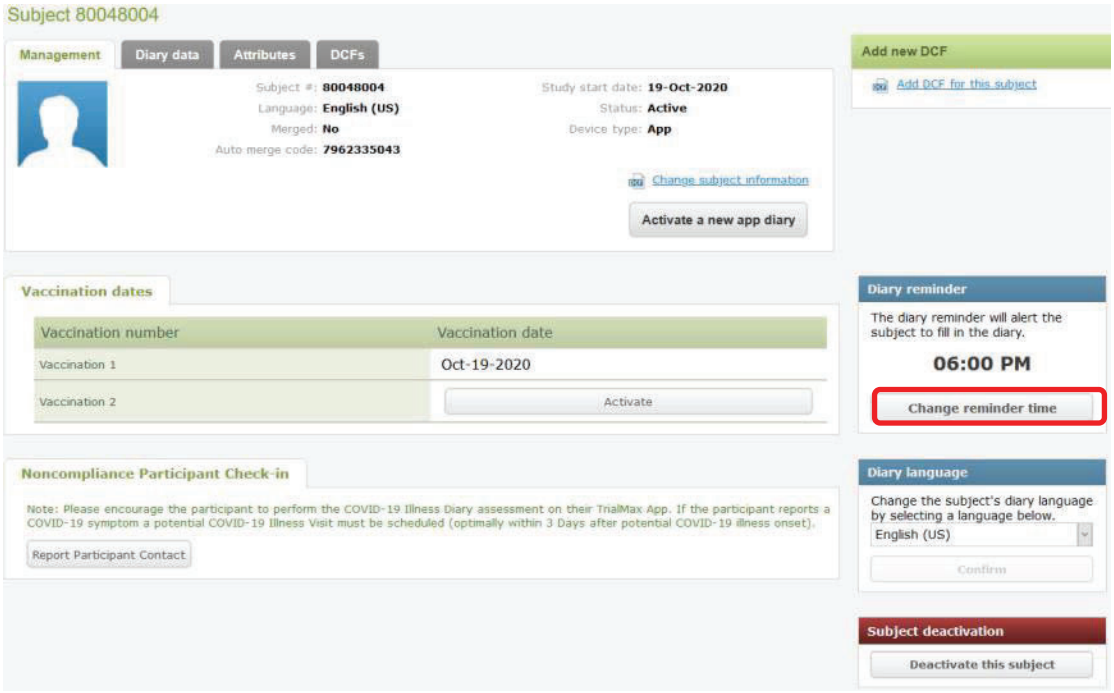


To activate subsequent diaries, click 'Activate' next to the appropriate visit. You will then be asked to select the date of the next vaccination. In the example above, Vaccination 2 still requires activation.

8.3.2 Changing Diary Reminder Time

Site staff have the ability to adjust the time that reminder notifications will be sent to participants to complete their Diary each day (during the post-vaccination periods). This can be modified by accessing the 'Management' tab in TrialManager for the particular participant.

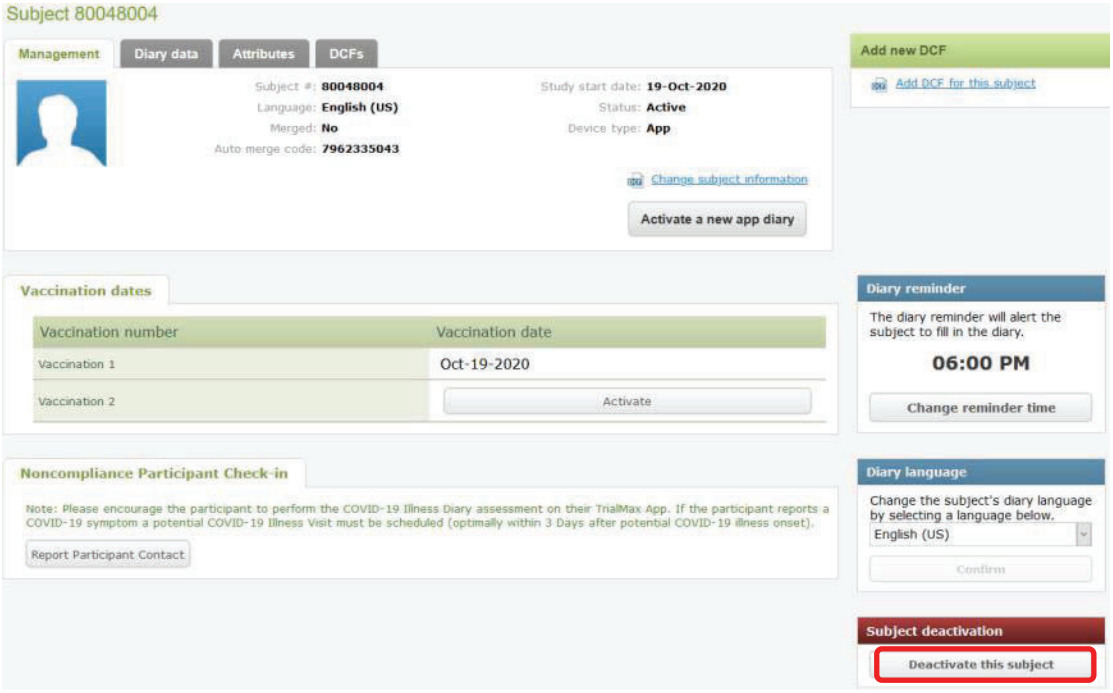
Additionally, participants may change this on their own by logging into the App and selecting 'Information and Settings' from the main menu screen. This will lead them to several options including 'Diary Reminder' which will allow them to adjust the time. The permitted window for reminders to be sent is between 6:00pm and 10:00pm in 15-minute increments.



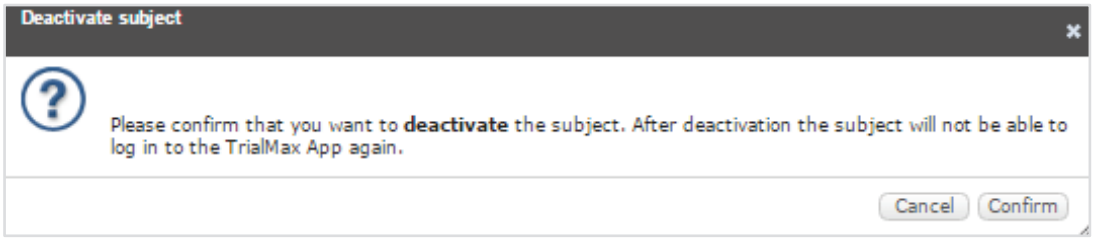
8.4 Deactivating a Participant from the Study

Whether the participant needs to be terminated early or has reached end of study, the participant must be deactivated by the site in TrialManager so that they can no longer login to the App and record study data.

This can be handled by accessing the 'Management' tab in TrialManager for the particular participant. Selecting 'Deactivate this participant' at the very bottom of the page (red header) will deactivate the participant and prevent further login to the App.



Upon clicking this button, you will be asked to confirm this is the desired action:

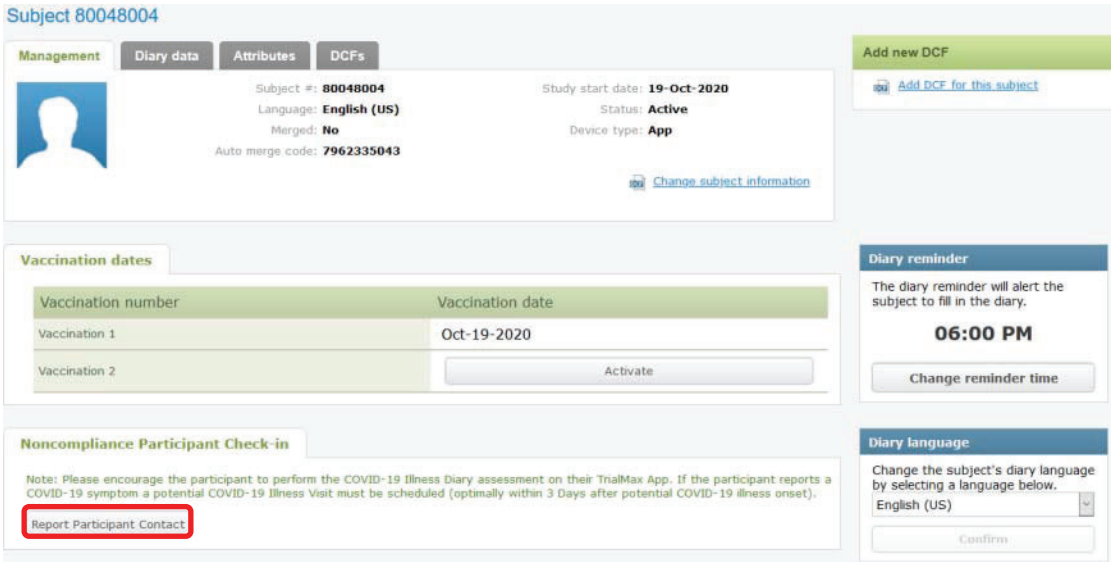


Selecting “Confirm” will successfully deactivate the participant while clicking “Cancel” will return you to the management tab for that participant.

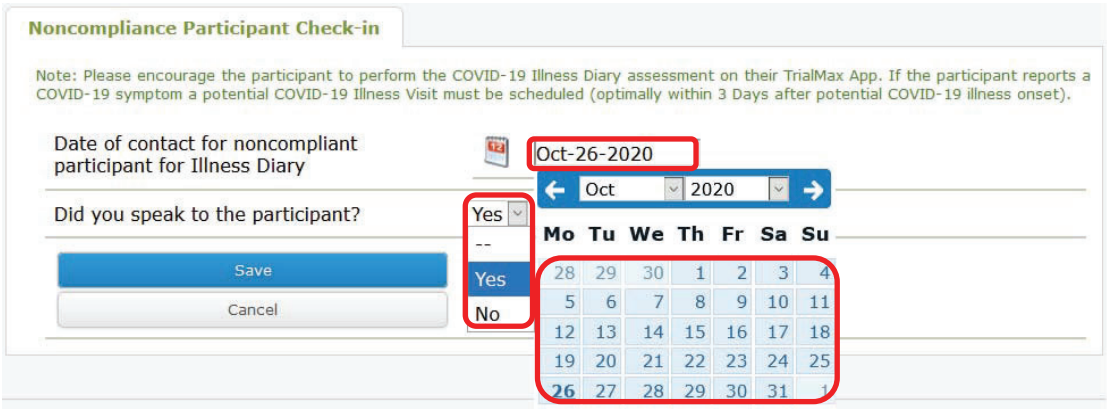
Once deactivated, participants will no longer display on the ‘Active Participants’ tab in your main page of TrialManager. There is a separate tab titled ‘Deactivated Subjects’ that will list any participants who have been deactivated.

8.5 Non-compliance Participant Check-in

Attempts to contact non-compliant participants can be logged in TrialManager. Access the ‘Management’ tab for the particular participant, and select ‘Report Participant Contact’.



Enter the date of contact by clicking into the empty box next to the icon and selecting a date from the calendar, pick from the dropdown whether you spoke with the participant (Yes/No), and then click ‘Save’.



The attempted contact will now be logged under the 'Report Participant Contact' tab of the 'Diary data' section of the subject page.

8.6 Participant Travel

All provisioned devices will update the time zone automatically if the participant travels between different time zones.

9 How to Request Additional Supplies

If a Site requires device re-supply (for example more provisioned devices than initially allocated in their first shipment), they can request it via the Helpdesk (see Helpdesk phone number in Helpdesk Operating Hours). The request must be approved by the Pfizer/ICON Study Team, as all initial site allocations are predetermined.

IMPORTANT NOTE: Remember that provisioned devices can be reused after one participant has finished using the device.

Once approved, it will take 5 business days to prepare any additional shipments. These will be shipped with standard delivery service.

Replacement device requests (for example for devices that are lost or broken during use) should be requested via the Helpdesk. A return shipment label will be provided, along with a Faulty Device Return form to indicate why a replacement is needed.

10 How to return the provisioned devices

At the end of the study ALL devices must be returned to Signant Health.

When returning devices to Signant Health, UPS will need to pick them up. If the site does not have a regular pickup, they will have to call their local UPS office for a pickup. The UPS number is different in each country. The UPS driver can bring a manual waybill to the site if they do not have one. Please see Appendix A for US Logistics device returns instructions.

If you need to return a faulty device to Signant Health, make sure to include a completed Faulty Device Return Form (refer to Signant Health Helpdesk for a form) with the return. Only devices with a Faulty Device Return Form included will be investigated for any unsent data.

11 Frequently Asked Questions

Q: Where can I get more help?

A: Please contact the Signant Health Helpdesk. The Helpdesk is available 24/7 via the phone number provided at the beginning of this guide or on the participant's Quick Reference Guide or Device Label. Please make sure to provide as much information as you can about the problem. For any protocol or health-related questions, please contact your study monitor.

Q: How often should the provisioned device be charged?

A: Please be sure to leave the provisioned device plugged into the charger when not in use to keep it fully charged.

Q: What do I do if my provisioned device does not switch on?

A: Charge the provisioned device for two (2) hours. After charging, turn the device on. If the home screen with message and App icons does not appear, call the Helpdesk.

Q: A participant forgot their PIN code and cannot use their provisioned device. How can the PIN code be retrieved?

A: The participant's PIN code can be retrieved. The participant should call the helpdesk who will retrieve their original PIN code.

Q: How will the participant know how to send data?

A: The App will do it automatically, as long as the device is online. The App will send data each time the participant logs in, and also when saving study answers.

Q: A participant forgot to complete their Diary on one day. Can that be added later on?

A: No. Data cannot be entered retrospectively. However, the participant can update their symptoms – both experience and severity within the same day.

Q: What should be done if the device is unable to send data?

A: As soon as the participant logs into the App, unsent data will be sent immediately once a connection is established. If the participant cannot seem to access a connection, please remind them that all data will be saved and automatically sent the next time they use the device online. If they continue to have issues with data sending, please contact helpdesk.

Q: Is the participant able to change the time and/or settings on a provisioned device?

A: The provisioned device is locked to only enable usage of the App and WiFi setup. The participant cannot change the time or make any other changes to the settings. Also, the device uses the network-provided date and time, so if the participant travels to a different time zone or there are changes in daylight savings, the time will automatically be updated.

Q: Can the participant send data while away on vacation in another country or region?

A: Yes, as long as they can connect to a network. Because of time zone differences, the time of entry may appear different.

Q: What happens if the participant forgets to log out of the App?

A: If the participant does not log out of the App, the App will automatically log the participant out. Please note that any unsaved answers will be deleted from the App at that time.

Q: Will the Helpdesk answer questions related to the Diary itself?

A: The Helpdesk can provide answers on how the Diary functions, but for any vaccine or study-related questions, the participant needs to contact the site.

Q: The participant does not understand the questions. What should I do?

A: If the participant does not understand the questions in the TrialMax App, you may have to explain what is being asked. The Helpdesk cannot answer any health-related questions. For further assistance with the questions, please contact your study monitor.

12 APPENDIX A: US LOGISTICS DEVICE RETURNS

US Logistics Device Returns

- When returning devices to Signant Health, UPS will need to pick them up.
- If the site does not have a regular pickup, they will have to call their local UPS office for a pickup. The number is different in each country.
- When calling for a pickup, the site will need to provide the **CRF Health (note CRF not Signant due to how account is set up with UPS) UPS account number 37V198 and postal code 19462** for the pickup charge to be billed on CRF Health(Signant Health)'s account. Sites with regular pickups will not have any issues with pickup charge.
- For returns from USA based sites can request their own return airway bill, quickly and easily. Using this portal sites will be able to choose a pick-up time which best suits their needs The site address is:

  https://row.ups.com/Ship/Ship/StandardShipGuest
- The UPS driver can bring a manual waybill to the site if they do not have one. Please complete the UPS Manual Waybill using the instructions below.
- For returns from outside of the USA or where a commercial invoice is required please email us-logistics@crfhealth.com please include all the information below and a UPS waybill will be emailed back to you.
  - Protocol Number/CRF Project code:
  - Name of sender:
  - Email address of person to be emailed the labels:
  - Contact number for sender:
  - Site Number:
  - Full Site Address:
  - How many electronic devices are being returned:
  - How many boxes will be used for the return of the devices:

13 APPENDIX B: UK LOGISTICS DEVICE RETURNS

UK Logistics Device Returns

- When returning devices to Signant Health, UPS will need to pick them up.
- If the site does not have a regular pickup, they will have to call their local UPS office for a pickup. The number is different in each country.
- When calling for a pickup, the site will need to provide the **CRF Inc Ltd (note CRF not Signant due to how account is set up with UPS) UPS account number 1F07X9 and postal code CT13 9FG** for the pickup charge to be billed on CRF Inc Ldt (Signant) account. Sites with regular pickups will not have any issues with pickup charge.
- For returns from Europe sites can request their own return airway bill, quickly and easily. Using this portal sites will be able to choose a pick-up time which best suits their needs The site address is:

  https://SignantHealth.com/RAWB
- For returns from outside of Europe or where a commercial invoice is required please email uklogistics@signanthealth.com please include all the information below and a UPS waybill will be emailed back to you.
  - Protocol Number/CRF Project code:
  - Name of sender:
  - Email address of person to be emailed the labels:
  - Contact number for sender:
  - Site Number:
  - Full Site Address:
  - How many electronic devices are being returned:
  - How many boxes will be used for the return of the devices:

C4591001

TrialMax App™, TrialManager®
Site User Guide

Document index: A-1426-0082-5150UG
Document version: 4
Template version: 12
01JUN2020

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IMPORTANT POINTS

- Keep devices charged at all times – when stored at site, please ensure the device(s) are charged at least once per week, even if not in use. If the device battery runs flat, it might have an incorrect date and time when it is turned back on again. If this happens, send data from the device and it will sync to your current time zone.
- Data will send automatically each time the participant logs into the App as long as the device is charged, in an area where there is mobile phone service or Wi-Fi is available.
- Participants should bring their assigned device with the App to each clinic visit.
- Participant setup should occur on the day of vaccination, whilst the participant is at the study clinic.
- Each participant will be able to set their own PIN code when they first log in to the TrialMax device. Please recommend to them to select the same code for each device as it will be easier for them to remember.
- When setting up a participant for the study, make sure this is done on a computer with a printer, as you will need to print the activation information for the participant. You will only have the opportunity to print this once; however, it will also be emailed to the participant if their email address is provided during setup or sent via a text message if a mobile phone number is provided during setup.
- To receive SMS notifications in the US, please refer to 'Setting up SMS notifications' section for more details.
- Use the TrialManager web portal to regularly monitor participant data for the study.

- It is recommended to leave 0.5GB of free storage space on the participant's personal device to allow the TrialMax app to function properly. Please provide a provisioned device to the participant in the event the participant does not have the free space or does not want to make that space available. The participant may check their available storage below:
    - iPhone: Select 'Settings'->'General'->'iPhone Storage'
    - Android: Select 'Settings' ->'Device Care'->'Storage'
- If you cannot find help in this guide, then please call the Helpdesk.

Role	PIN Code
Default Participant	1234
Logistics Access PIN Code	8888
Logistics PIN Code	4422

TrialManager Website URL
http://trialmax.crfhealth.net/c4591001
TrialManager login details will be sent to you via email

Table of Contents

1 Signant Health Overview

Signant Health is the provider of the eCOA (electronic Clinical Outcome Assessment) system for this study. The eCOA system comprises the components as displayed below, along with 24/7 Helpdesk support. TrialMax App is the brand name, but we will refer to it simply as the “App”.

Data entered by Participant into the App

Data sent from App to Signant Health servers

Data available for sites, monitors and study team in web portal and TrialManager

TRIALMAX app

TRIALMANAGER®

2 Helpdesk

You may call the Helpdesk for any issue related to the TrialMax App, or TrialManager website.

Please have the following information ready when you call:

- The study protocol number: **C4591001**
- Helpdesk Priority PIN: **19**
- Signant Health project code: **A-1426-0082**
- Your site number
- The participant number (if applicable)
- The specific problem

2.1 Helpdesk Operating Hours

The Helpdesk is available 24 hours a day, 365 days a year.

If you are unable to reach an agent when you call, you can also leave a voicemail or send an email giving your contact information. The Helpdesk will contact you as soon as possible, at the latest by next business day.

2.2 Helpdesk Telephone Numbers

Country	Number
USA	(1) 866 402 1154
Helpdesk Priority Code	19

Note: Toll Free numbers are free from a landline; however local operator charges might be applied if calling from a mobile phone.

2.3 Helpdesk Email Address

For non-urgent issues, you can contact the Helpdesk by email:

C4591001_TM@support.signanthealth.com

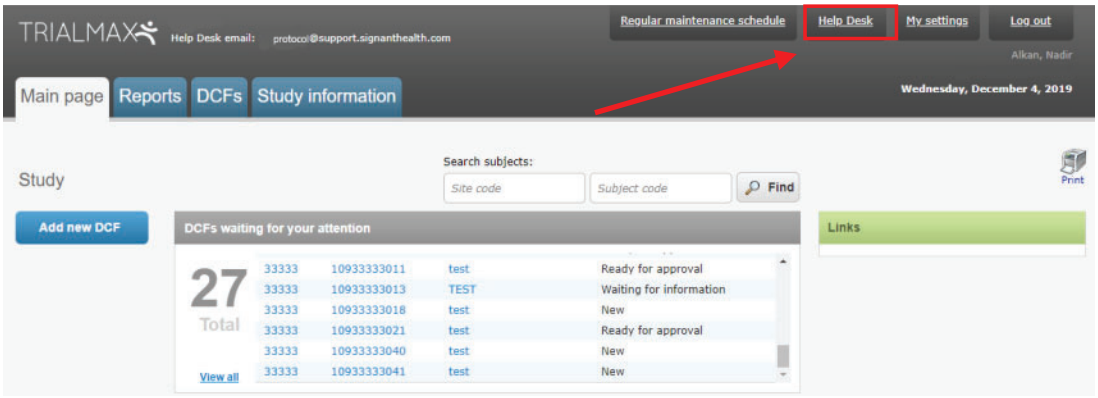
Note: Do not share this email address with participant. The participant's identity might be unintentionally revealed during communication via email.

Helpdesk Web Chat via TrialManager

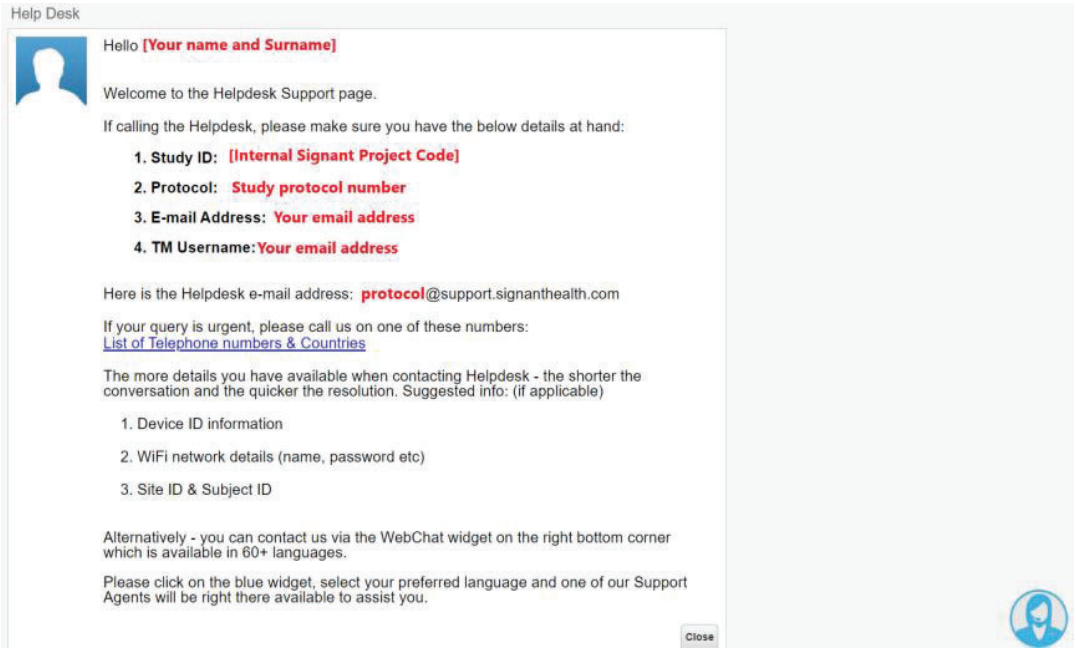
The Helpdesk Web-chat is available via the TrialManager Portal.

Helpdesk Web-chat can be accessed via the steps below:

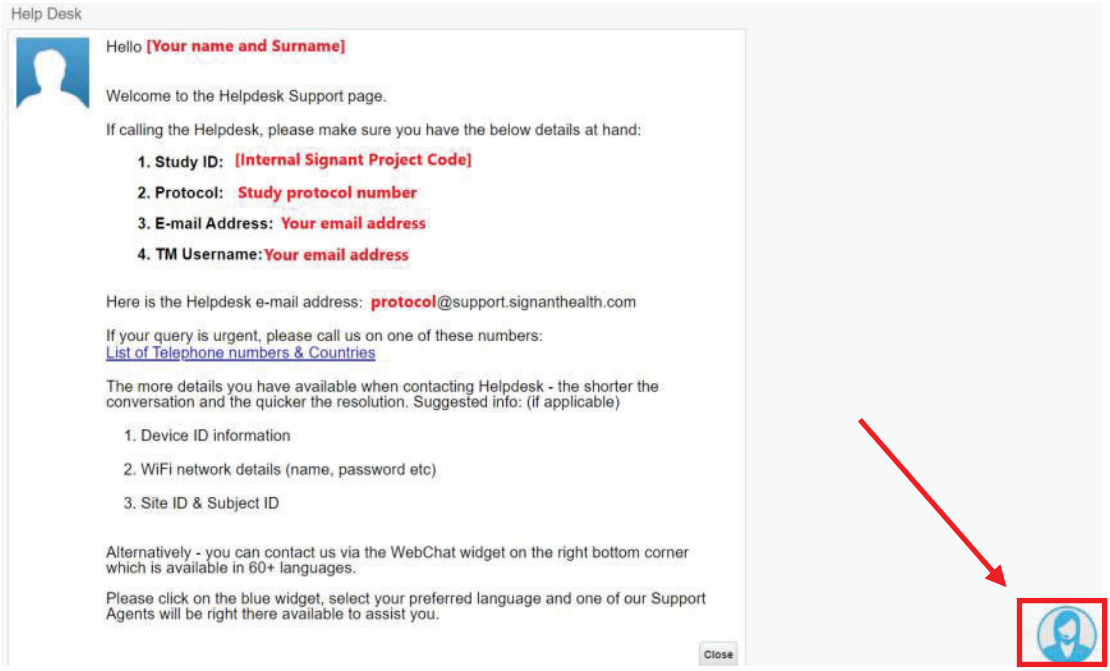
1) Please click the Help Desk button in the upper right corner of your screen.



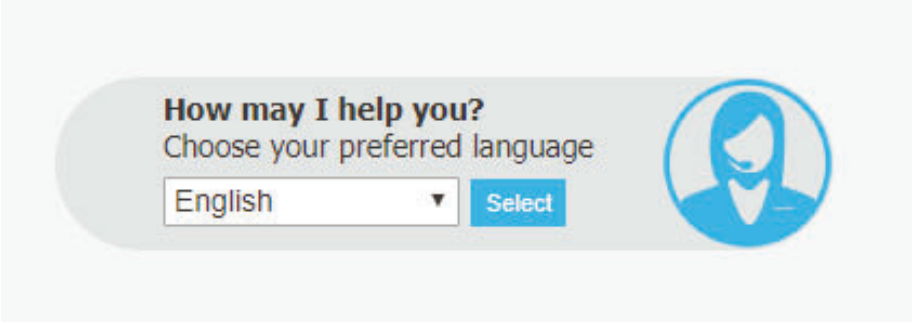
2) You will see a welcome page where all the texts highlighted in red will be pre-filled.

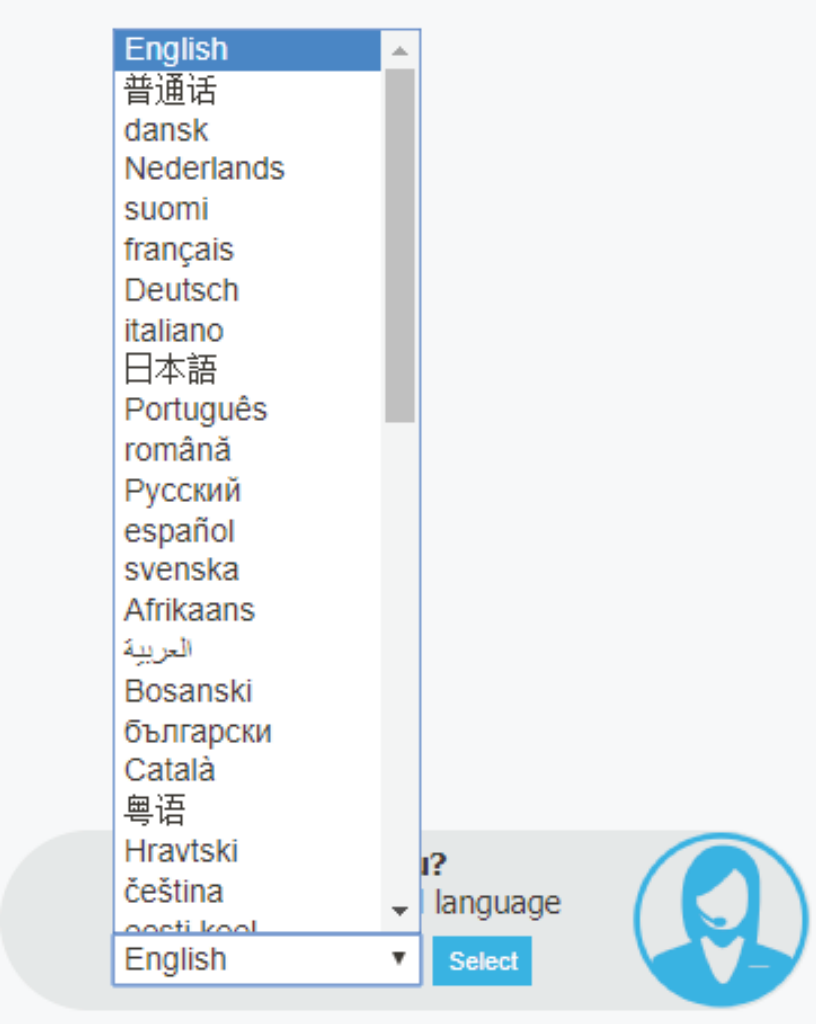


3) You can open the web-chat, available in 60+ languages, by clicking the blue widget in the lower left corner of the screen to start your live chat with one of our Support Agents.

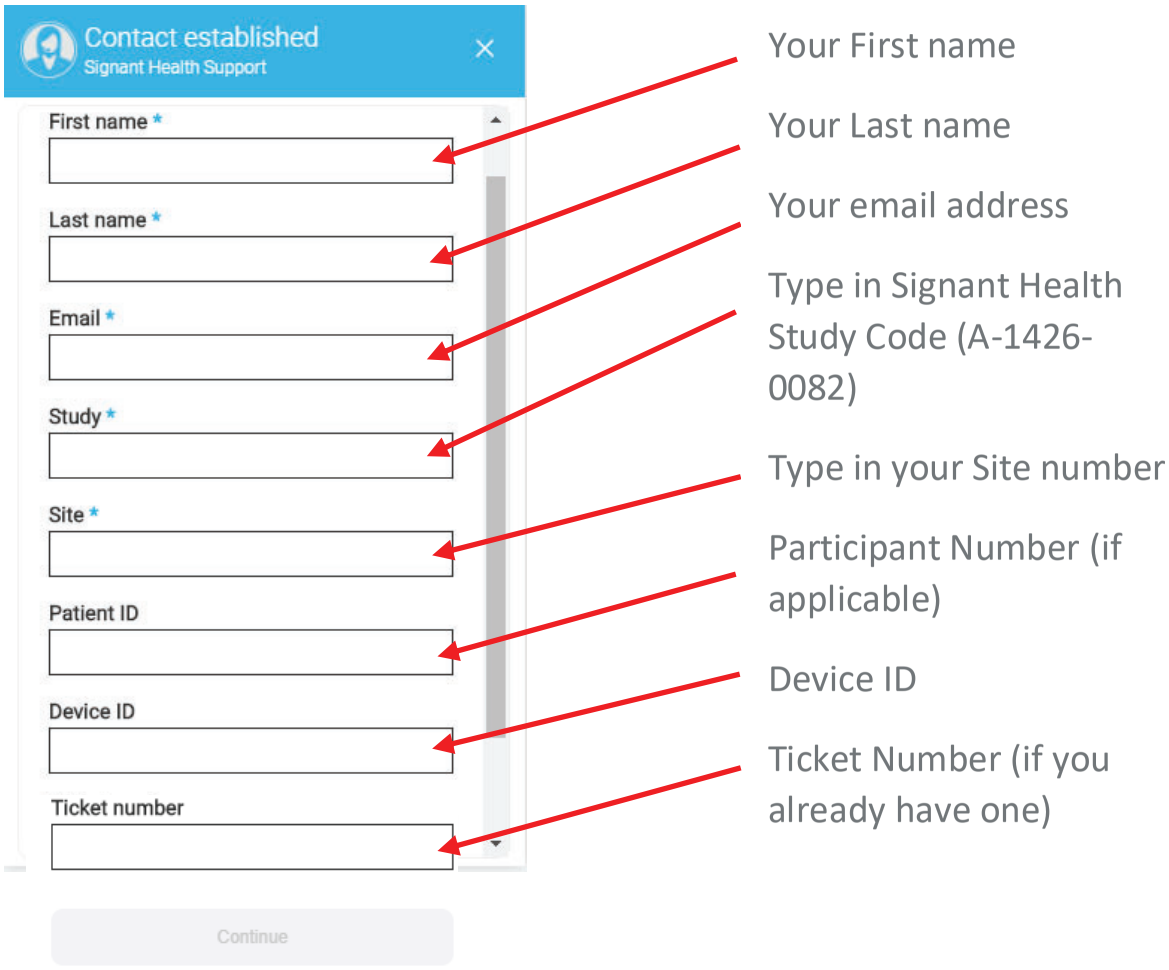


4) Once you click on this widget, you will be able to select your preferred language from the drop-down menu.





5) After selecting your language, you will need to complete the necessary information in the below screen and click the Continue button, then you will be connected to the next available support agent.



Fields with an asterisk (*) are required.

Once you click on "Continue", you will be connected to the Signant Health Helpdesk specialist, who will discuss your issue with you.

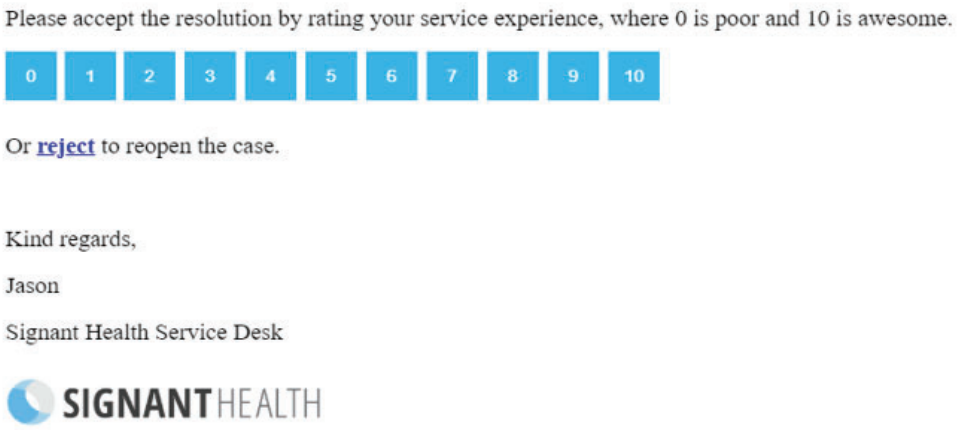
Please note that if a telephone call has already been placed make sure that you enter the Ticket Number you received from your telephone call into the web chat the ensure the background information is linked. If the ticket number is not entered, it will be counted as 2 separate calls.

Providing feedback about Helpdesk performance

Each time you request support from the Helpdesk, you can rate the level of your satisfaction from the provided service. This is important, as it helps us continuously improve to exceed your expectations.

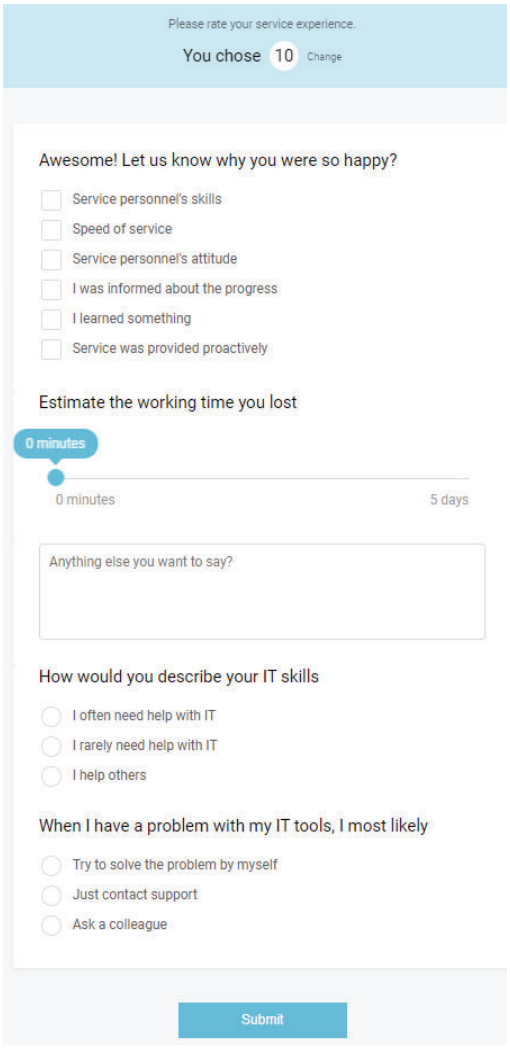
You can provide the feedback in 2 ways:

- Each time you have spoken to the Helpdesk on the phone you can remain on the line and rate your experience on the scale 0 to 5, where 5 is awesome and 0 poor.
- When your request has been completed, you will receive an email, enabling you to evaluate the service or reject the resolution of the incident.

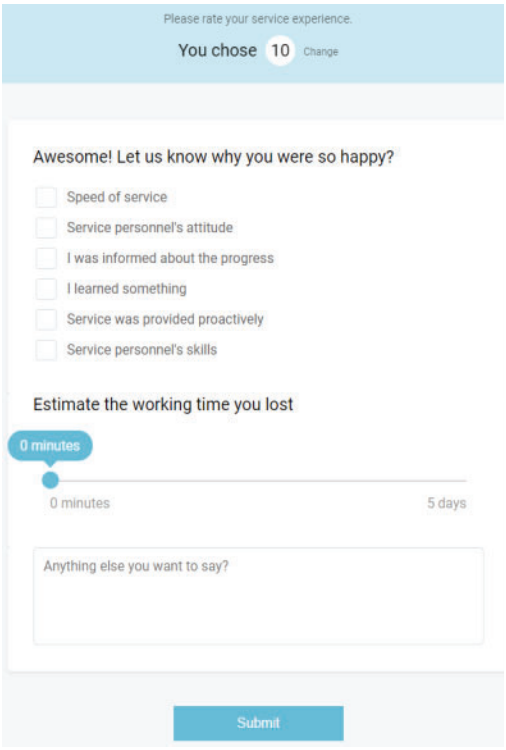


To provide feedback, you would click one of the numbered boxes (0-10), where 0 means poor and 10 awesome. Selecting any rating will take you to a form, where additional information can be provided. The form is a bit longer when you use it the first time and will be shorter with every further use (IT profile information needs only to be provided once).

Evaluation form 1st use

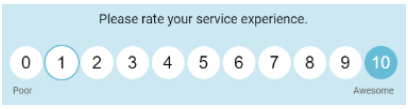


Evaluation form consecutive uses



Please remember that only 9 and 10 mean positive feedback, 7-8 average, 6 and below means negative feedback.

You can change your rating on the top of the form any time before submitting it.



3 Equipment

3.1 Supplies for participant

Provisioned device supplies -

- Samsung device with TrialMax App installed (if not using personal iOS or Android device), accompanied by an incorporated SD memory card (this backs up the data for recovery if needed) and a SIM card installed for mobile data sending.
- A device charger (power-cord and charging brick)
- TrialMax App sticker with country specific Helpdesk number
- Quick Reference Guide in the participant's language
- App Activation Guide in the participant's language
  Participant card with App activation details to be sent via email or SMS

Bring Your Own Device supplies -

- TrialMax App sticker with country specific Helpdesk number
- Quick Reference Guide in the participant's language
- App Activation Guide in the participant's language
- Participant card with App activation details to be sent via email or SMS

3.2 Provisioned Device Basics

Each TrialMax App device has a sticker applied to it that contains the country specific Helpdesk phone number.

Please contact the Signant Health Helpdesk if a device is not working properly. The Helpdesk agents will assist you or the participant with technical questions.

3.3 How to turn on the Provisioned device

Press the power button on the side

The Samsung device is the provisioned device for this study.

Turn the Device on by pressing the power button on the right side of the device.

If the Device is left on for ten (10) minutes without use, it will hibernate and perform automatic log out.

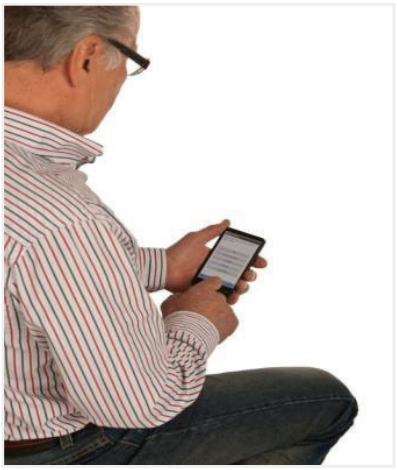
3.4 How to charge the Provisioned Device

The device has a rechargeable battery. Please remember to instruct the participant to **charge the battery <u>every day</u>.** If the device prompts the participant with a message that the battery is low, they should charge the device immediately. When the device is powered on it will display a battery status symbol on the top right side of the screen that indicates the amount of charge remaining in the device.

The participant can use the device while it is being charged but if discharged fully, it may take a little time to charge before use.

Connect the power charger cable to the provisioned device.
The device will usually fully charge in approximately 2 hours.

3.5 Device Navigation



Use your finger to navigate through the device.

Please do not use a stylus or sharp points as these will not function on the device and will damage the screen.

3.6 Additional Site Supplies

- This Manual
- Quick Reference Guide for the participant and TrialMax App device sticker
- App Activation Guide

4 TrialManager

TrialManager is an online, internet-based application used by investigators, coordinators, monitors and study personnel to view and monitor study progress. TrialManager enables the users to follow overall participant compliance and view the participant's Daily Diary data.

TrialManager supports the following Internet browsers:

- Firefox 33 and up
- Internet Explorer 11 and up
- Chrome 32 and up
- Apple Safari v9 and up

4.1 Functions of TrialManager

After answering the questions on the electronic device, the participant will need to send their answers to the study database (TrialManager). Within minutes of sending data, you can view the data (and reports of the data) sent.

By using TrialManager, you can:

- View the participant's Daily Diary answers
- Monitor participant compliance and other reports
- Monitor the number of days since the participant has last completed their Daily Diary
- Raise Data Clarification Forms (DCFs) and monitor their progression through to closure
- View data audit trails for questionnaire entries (including changes to forms)
- Deactivate the participant

Note: You should be logging in to TrialManager only with your own login details (which will be sent to your email). Do not share your password with your colleagues. It is also important to note that while the term "Participant" is used to describe the patient in this study, you will see the terms "Subjects" and "Participants" used interchangeably throughout the App and TrialManager platforms.

4.2 Accessing the TrialManager website

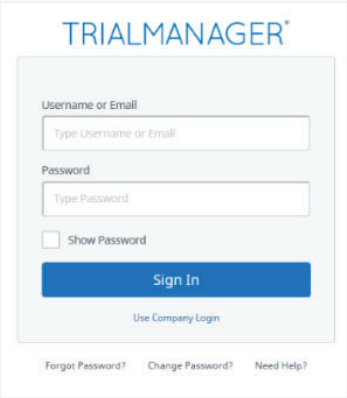
All people will have separate access based on their role within the study.

Your TrialManager username and initial password will be emailed to you. You will be prompted to change this password at your first login (see How to change your TrialManager password for more information). Your TrialManager password has no relation to the Site personnel PIN codes on the TrialMax App.

Note: If you have access to TrialManager for another Clinical Study, then you will be able to use the same Username and Password for each TrialManager. Please note that this feature is only available for the studies that started after September 1st, 2019. If you have a TrialManager account for older studies, you will not be able to use the same Username and Password for each TrialManager unless you change them manually to match with the rest of your credentials.

Type the following address into your web browser:

http://trialmax.crfhealth.net/c4591001



A login window will open. Bookmark this address for easy future access. Next, enter the username and password that was emailed to you.

4.2.1 How to change your TrialManager password

If you need to change your password, select 'My settings' in the top right-hand corner of the screen or "Change Password" from the Login Screen. There you will find an option to change your password.

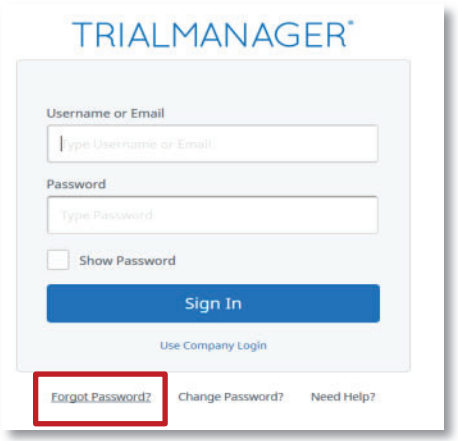
When you decide to change your password, you will be asked to type in your current password, your new password, and verify your new password by typing it in again. Click the 'Change' button to activate your new password.

Rules for creating new password:

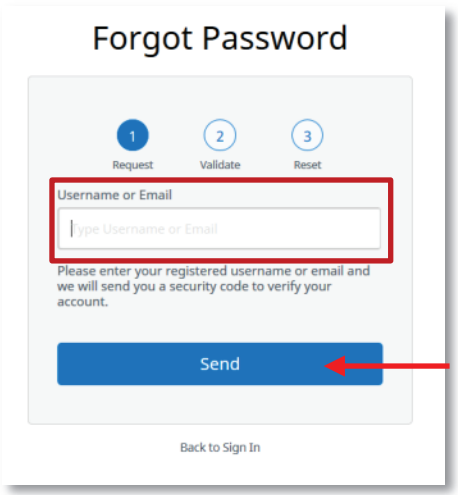
- Must be at least 8 characters.
- Must contain at least one lower case character.
- Must contain at least one upper case character.
- Must contain at least one number.
- Must not contain Unicode characters.
- Special characters in password are not necessary.
- Must not contain spaces, line breaks or new lines.

4.2.2 How to Reset your TrialManager Password

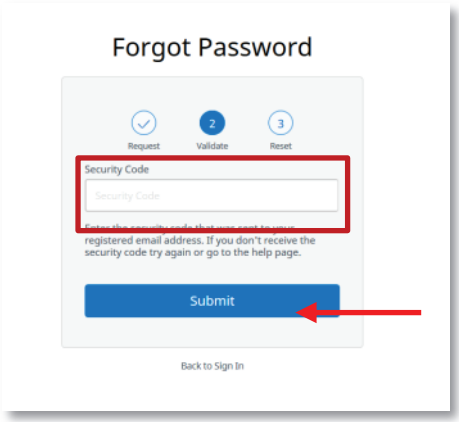
If you have forgotten your password to your TrialManager Account, you are able to reset the password directly within the TrialManager Portal.



From the log in page, select "Forgot Password"



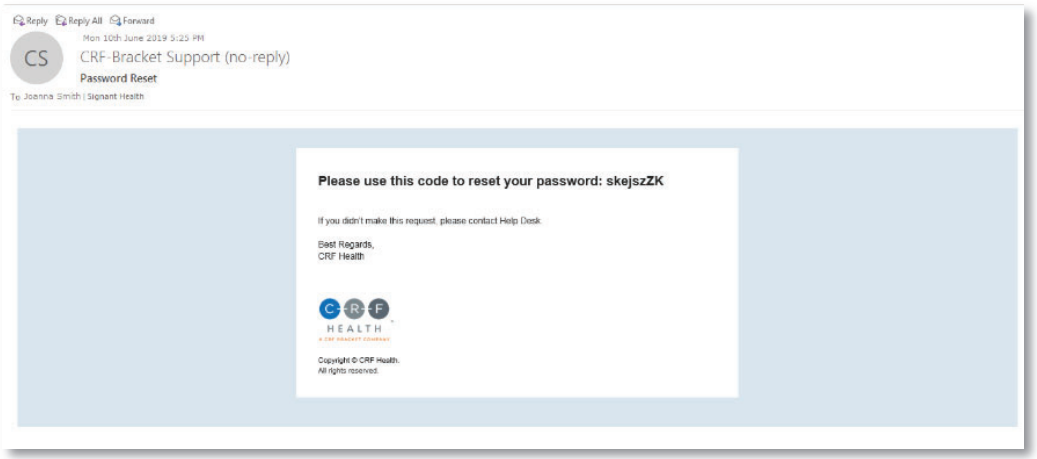
You will be asked to enter your email address so that the system can send you a security code for the password reset

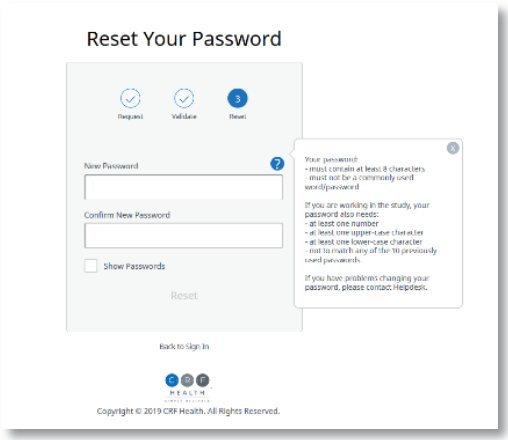


You will be taken to this screen

Check your email inbox and enter the security code, which has been sent to you

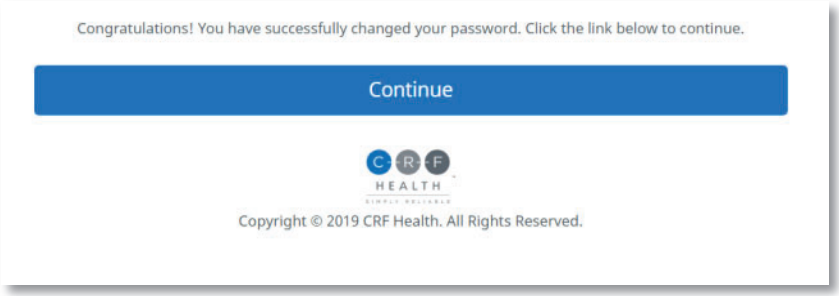
This is an example of the email which will be sent to you:





Enter a new password following the guidance on the screen

Once your reset has been successful, then you should see this screen:



4.2.3 How to request TrialManager access for new team members

In order to request TrialManager accounts for new team members you should add their information into the 'TrialManager User Order Form' and send the updated form to the Signant Health 'TM accounts' team, collating requests into 1 email per week.

Allow 5 business days to create new TrialManager accounts/make updates.

Urgent TrialManager requests can be requested via Helpdesk or directly contacting the Pfizer Study Team via your CRA/Monitor.

4.3 How to navigate the TrialManager website

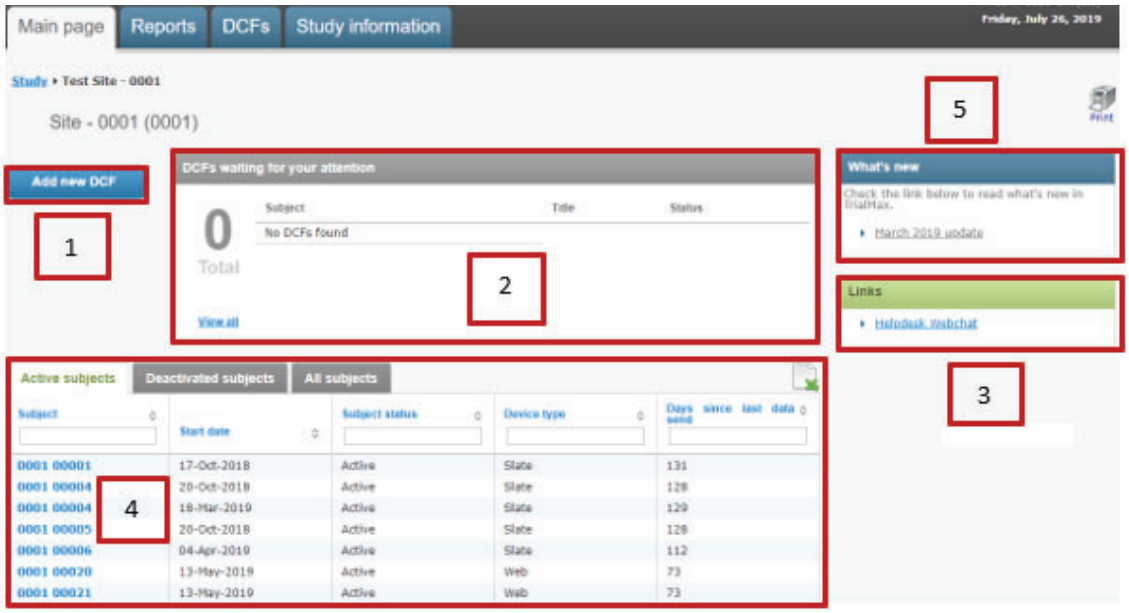
Investigators and Study Coordinators will see several tabs at the top of the screen. They are the 'Main Page', 'Reports', 'DCFs', and 'Study Information' tabs. These are selected by clicking on them.

The points below highlight the main functions and features of the tabs:

- **Main Page:** View a list of all your participants, navigate to individual participant pages, view open DCFs and navigate to the DCF tool, view the latest TrialMax updates
- **Reports:** Review, filter, and print information associated with your site and participants, such as compliance, DCFs, and administrative data
- **DCFs:** Create, approve, and monitor all requested data changes for your participants
- **Study Information:** Access supplemental reference content, such as electronic versions of the Site User Manual and DCF Guide

4.3.1 Main Page Tab

When you select “Main page” the following screen appears:



1. With this button, you are able to add DCFs (see Where to create DCFs in TrialManager).
2. This section is called the DCF Notice Board and will display all DCFs for your site that require your action. Simply click on the title of a particular DCF to see further details displayed. All DCFs created by you or anyone else will also need to be approved by a site user with DCF approval rights. Signant Health will be the one to implement the corrections requested in the DCFs.
3. Some useful web links for the study are displayed on the right-hand side of the screen, including the Helpdesk web chat.
4. The participant list section at the bottom of the screen will display all participants at your site.
    a. By default, this will display Active participants at the site. Click on the ‘Deactivated subjects’ or ‘All subjects’ to also

view participants that have already been deactivated from the TrialMax App.

b. You are able to sort and filter by any of the column headings by typing into the text boxes below the column headings.

c. Clicking on a subject number will take you to more detailed information regarding that participant (see Participant Details Card).

5. You can see the latest updates regarding any TrialManager system updates.

4.4 Add a new participant

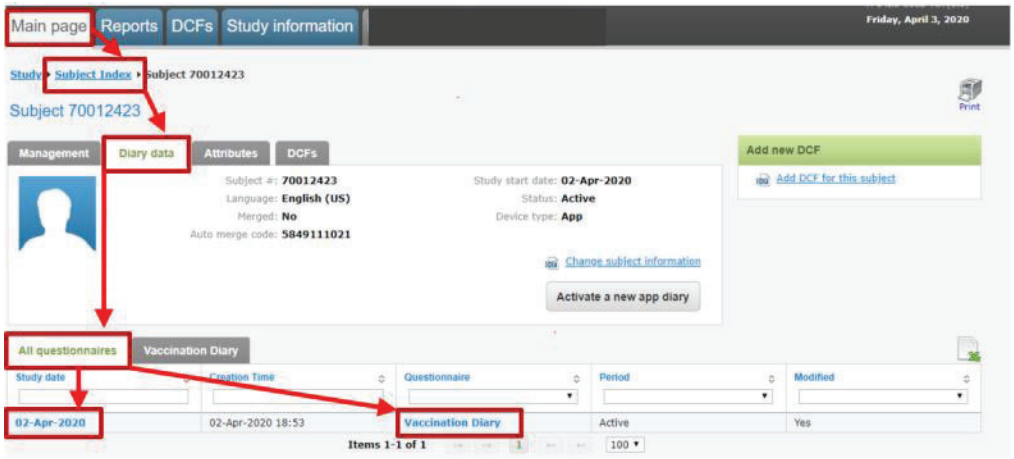
Please see **'How to set up a participant in TrialManager'**.

4.4.1 Participant Details Card

Upon clicking on a participant from the main page, the participant/subject's information card will display:

This will show details for the participant including: language, participant status, study start date, device type, and the participant's auto merge code, which is necessary for replacement devices.

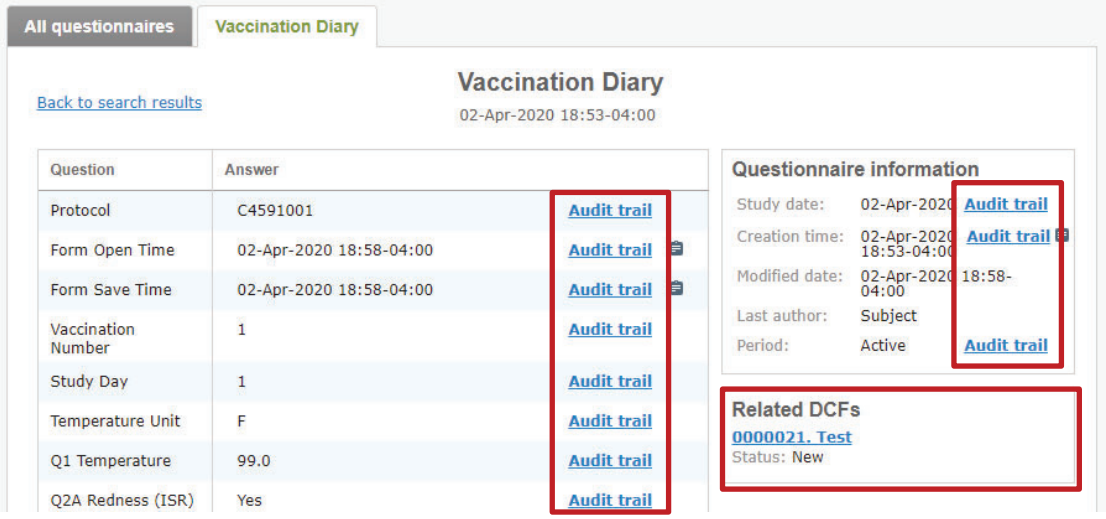
Below the participant details card, you will be able to review the Daily Diary forms submitted by the participant on the TrialMax App.



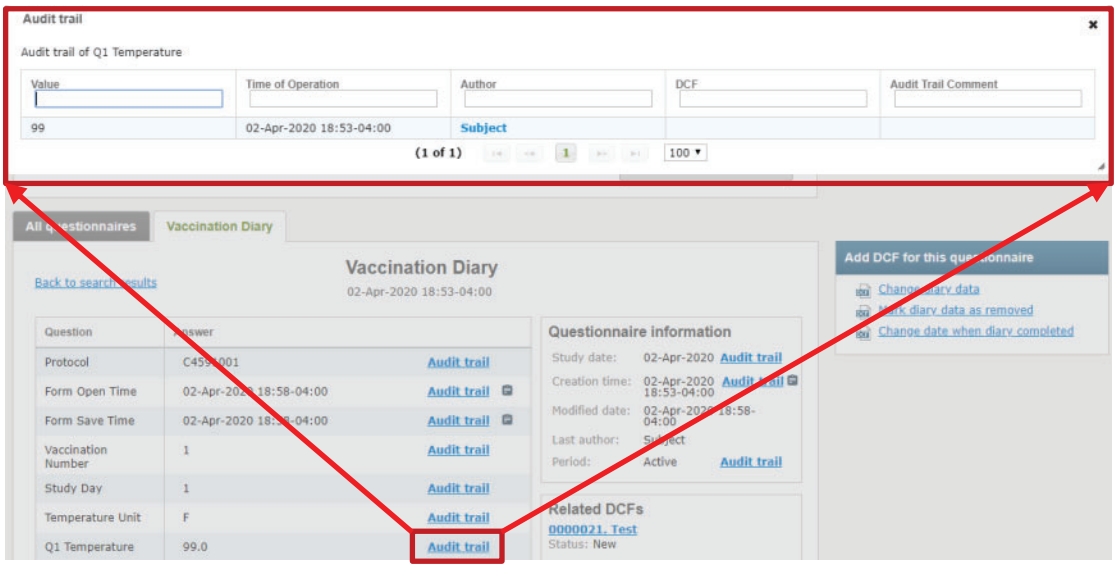
'All questionnaires' tab which contains 'Study date' and 'Questionnaire' links to each completed form. Each column can be filtered and sorted. Upon selecting a form link the form will open, displaying a list of all form data items, including the questionnaire items and responses completed by the participant, and administrative items such as the date and time a completed form was saved.

4.4.2 Data Item Audit Trails

You will also be able to view the audit trails for each questionnaire data item from within these form pages. You can use the audit trails to review the original values and a full change history of any data item if changes were made via the TrialManager DCF tool If there was a DCF associated with a questionnaire form, this will be displayed to the right of the form with a direct link to the DCF itself and the current DCF status.



To view the full audit trail of any available form item, including the original value and any changes, click the 'Audit trail' link to the right of the desired item. An audit trail of the item will open displaying a list of the data item elements, sorted newest to oldest from top to bottom. If only 1 row is displayed, this indicates that this is the original value of the data item, and that it has not been modified.



The Audit trail column headers are defined as follows:

- **Value:** the value of the data item itself
- **Time of Operation:** the date and time associated with the data item entry or modification
- **Author:** the user that committed the associated operation (participant, site, or Signant Health Data Management)
- **DCF:** the DCF ID number if a DCF was used to execute a change to the form
- **Audit Trail Comment:** free text field where the Signant Health data change implementer may post the DCF number, an external DCR number (if DCF was not used), or other useful reference information

Note: if a data item was modified via DCF within TrialManager, it will display a small clipboard icon to its right. Hovering with the mouse over the clipboard icon will trigger a pop-up with a brief summary of the change.

4.5 Reports Tab

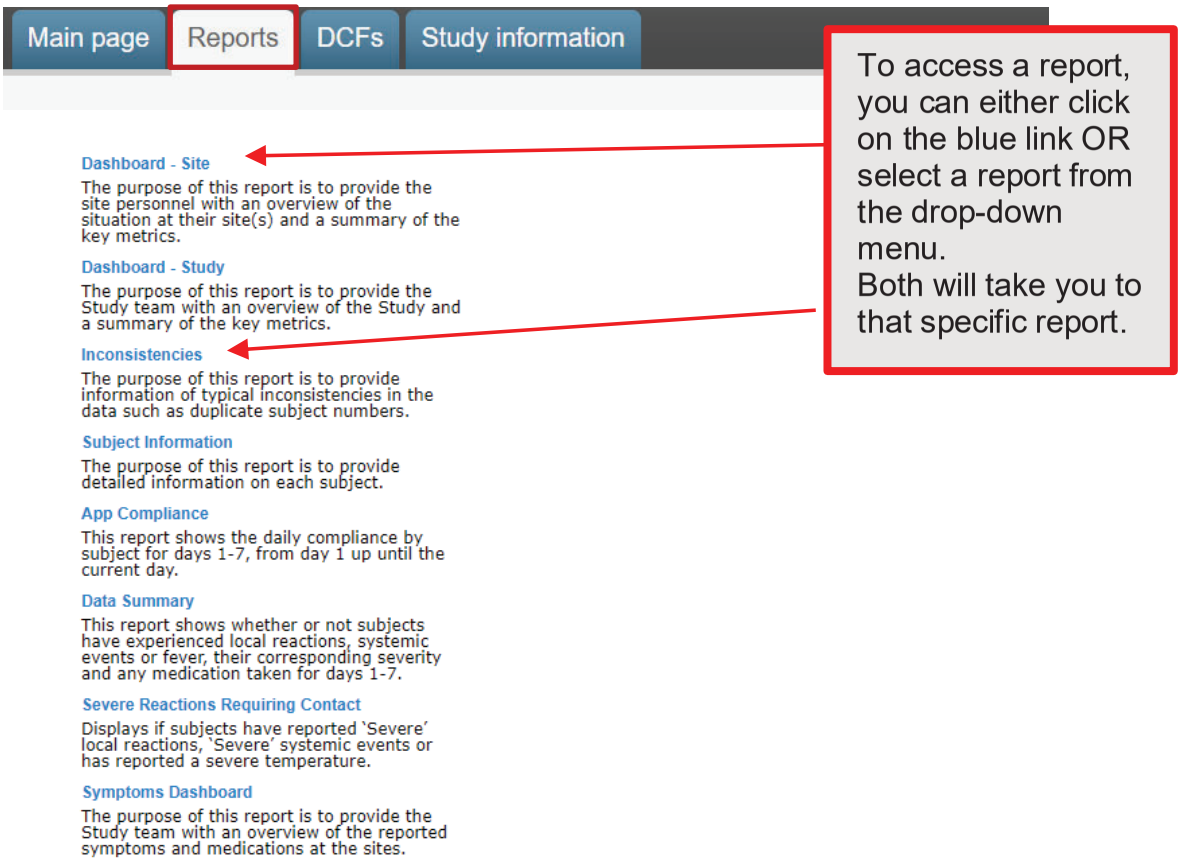
The 'Reports' tab will contain reports for you to view. These reports should be reviewed on a regular basis to ensure the participants are completing the questionnaires correctly with good compliance.

Note: TrialManager reports accessibility may not be available on the initial login of the user. The user may have to logout and log back in to view these reports.

The following reports will be available for this study:

- **Dashboard - Site:** The purpose of this report is to provide the site personnel with an overview of the situation at their site(s) and a summary of the key metrics.
- **Dashboard – Study:** The purpose of this report is to provide the Study team with an overview of the Study and a summary of the key metrics.
- **Inconsistencies:** The purpose of this report is to provide information of typical inconsistencies in the data such as duplicate participant numbers.
- **Subject Information:** The purpose of this report is to provide detailed information on each participant.
- **Compliance**: This report shows the daily compliance by participant for days 1-7, from day 1 up until the current day following each vaccination.
- **Data Summary**: This report shows whether or not participants have experienced local reactions, systemic events or fever, their corresponding severity and any medication taken for days 1-7 following each vaccination.
- **Severe Reactions**: Displays if participants have reported 'Severe' local reactions, 'Severe' systemic events or have reported a severe temperature.

- **Symptoms Dashboard**: The purpose of this report is to provide the Study team with an overview of the reported symptoms and medications at the sites.

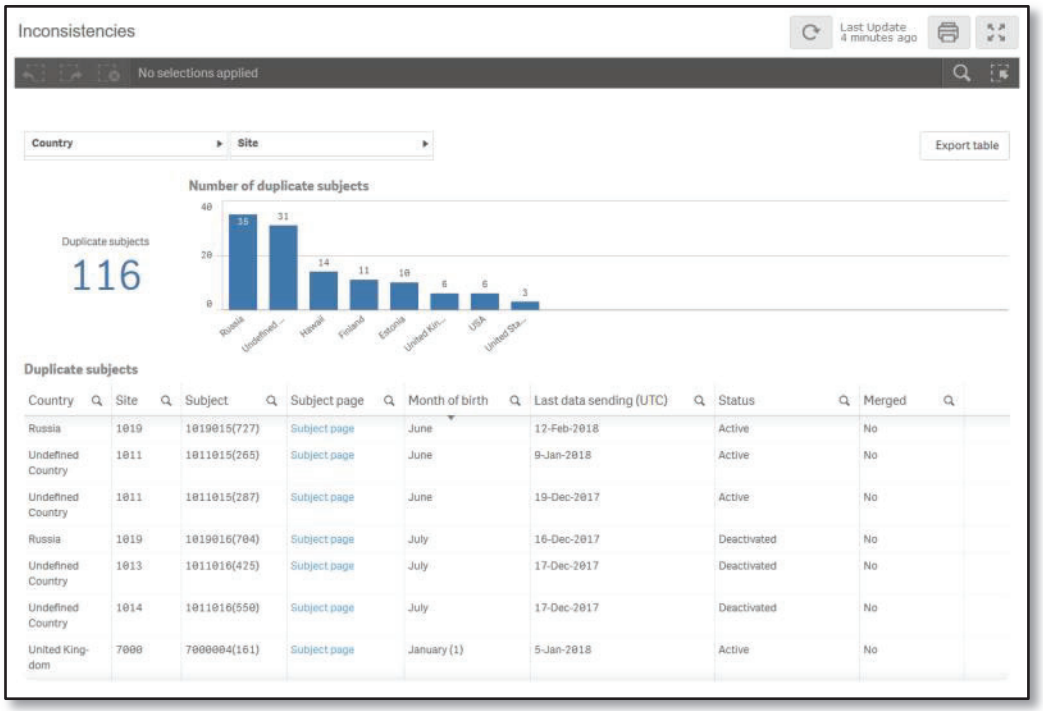


4.6 How To Review Reports

For monitoring purposes, you can view near real-time, graphical reports about the state of the study right inside TrialManager. Graphical visualizations allow you to identify quickly any deviations from the study protocol and take corrective action. For example, you can verify which study participants are still compliant (if they are completing their questionnaires on schedule) or verify the progress on resolving DCFs.

4.6.1 Reports User Guide

The Signant Health Reporting Solution supports a variety of visualizations, including bar charts and data tables. Below is an example of the Inconsistencies Report.



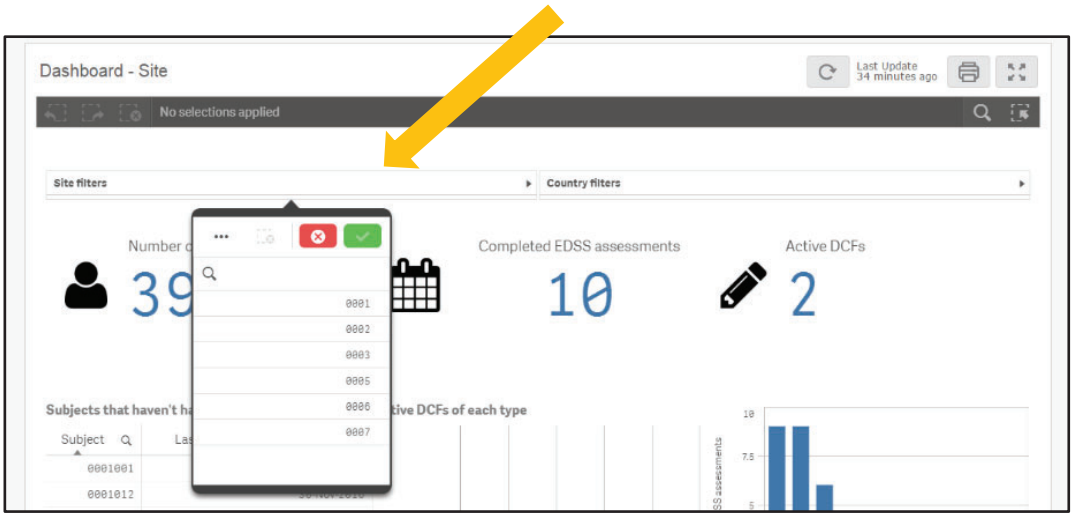
These report visualizations are interactive. When you select parts of the displayed data in report, all other sections update to filter for the selection automatically. This even works between reports in the same drop-down list and allows the user to ask questions about the data. Depending on your user role, you can select your site and/or participant number from the drop-down options at the top of the page. The report will automatically repopulate using the criteria selected. Clicking on the drop-down options will automatically filter the whole report.

4.6.2 Hints and Tips for Viewing Reports

The reports used in this study are designed to give you easy access to key study details. Below are some hints and tips on how to get the best from the reports available in the study:

Filtering

Reports can be filtered in several ways. One way is by selecting from the drop-down filters appearing at the top of the reports, as shown below.



To use the drop-down filters, select an item or items, from the list and select the green tick to apply the filter. Select the red cross to close the filter list without applying the change.

Reports can also be filtered by selecting part of a table or chart, for example selecting a participant from a list, or selecting a bar in a chart.

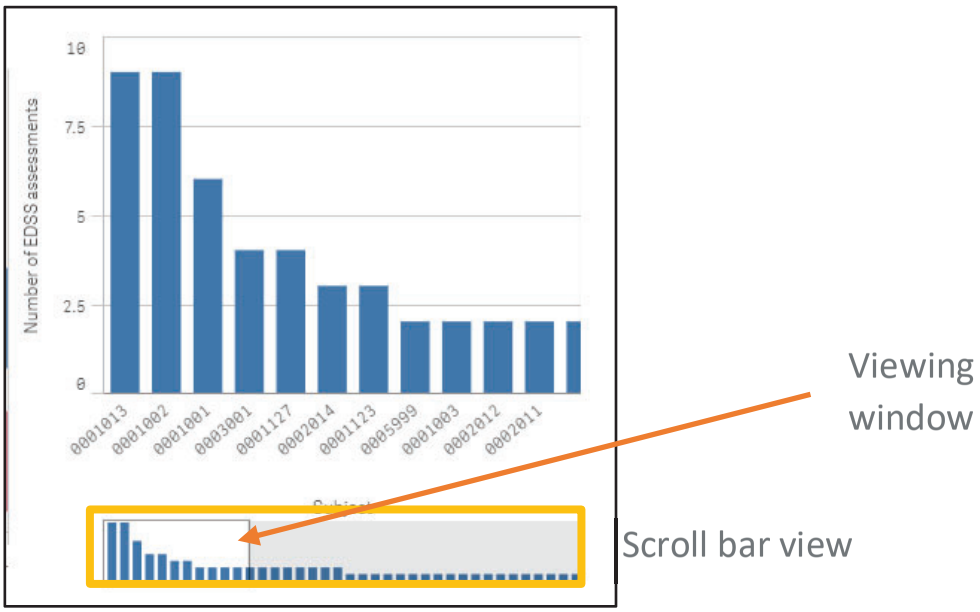
Selecting the icon in column headings can also be used to filter reports.

Once a filter selection has been made, all parts of the report and other reports viewed, will have this filter applied. All filters that are applied can be seen in the banner at the top of the report.

To remove a filter, select the “X” next to the filter in the banner at the top of the screen, as per the image below:

Viewing Bar Charts

Some reports contain bar charts to display specific data information. For bar charts with many data bars, it may not be possible to view all bars at the same time. When this is the case, a smaller ‘scroll bar’ version of the report can be seen. Move the white ‘viewing area’ box to the left or right on the scroll bar view to change the data shown in the main part of the report.



Hovering over a bar within a bar chart will display additional information.

Viewing Reports with Tables

For reports with large tables, you may wish to resize columns to ensure the best view in your browser. To do this, simply select the line between columns, and resize as required to fit all the columns in the view. If a column name is too wide to be displayed fully, hover over the column name with the mouse to view the full name.

You can rearrange the order that the columns will appear in by clicking on and dragging a column header into a different position, allowing you to focus on the columns you require.

You can select column headings to sort the report by that item. One click will sort the report in ascending order, a second click will sort the report in descending order. An arrow will appear on the column header to indicate the sorting applied.

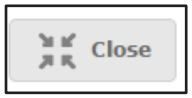
Select the 

button, where seen, to export information in a table to excel.

Standard Report Icons

The icons seen below can be found at the top left corner of all reports in the study.


This icon can be used to expand the viewing area for any report to full screen.



This icon will be seen to exit the full screen view.

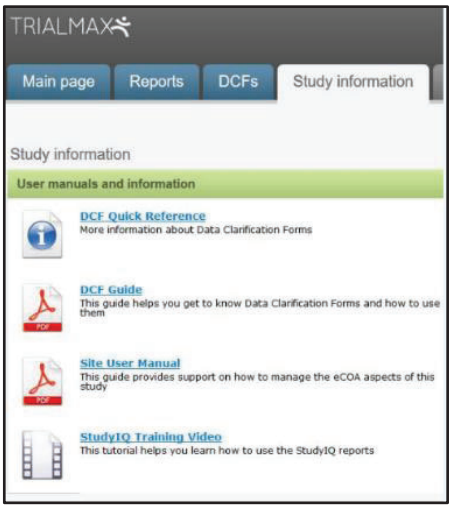

This icon can be used to print to pdf the report being viewed. This pdf copy of the report can be printed or saved, as required.


This icon can be used to reload of the data within the report.

To switch between reports, you can either return to the full list of reports by selecting the 'All Reports' option, or you can switch between reports using the drop-down options 'Standard reports' and 'Study reports'.

Note: Any filters applied to one report will also remain active on other reports viewed in the same drop-down list, unless specifically removed.

Further information and video training on how to use the reports can be found in the 'Study information' tab in Trial Manager.

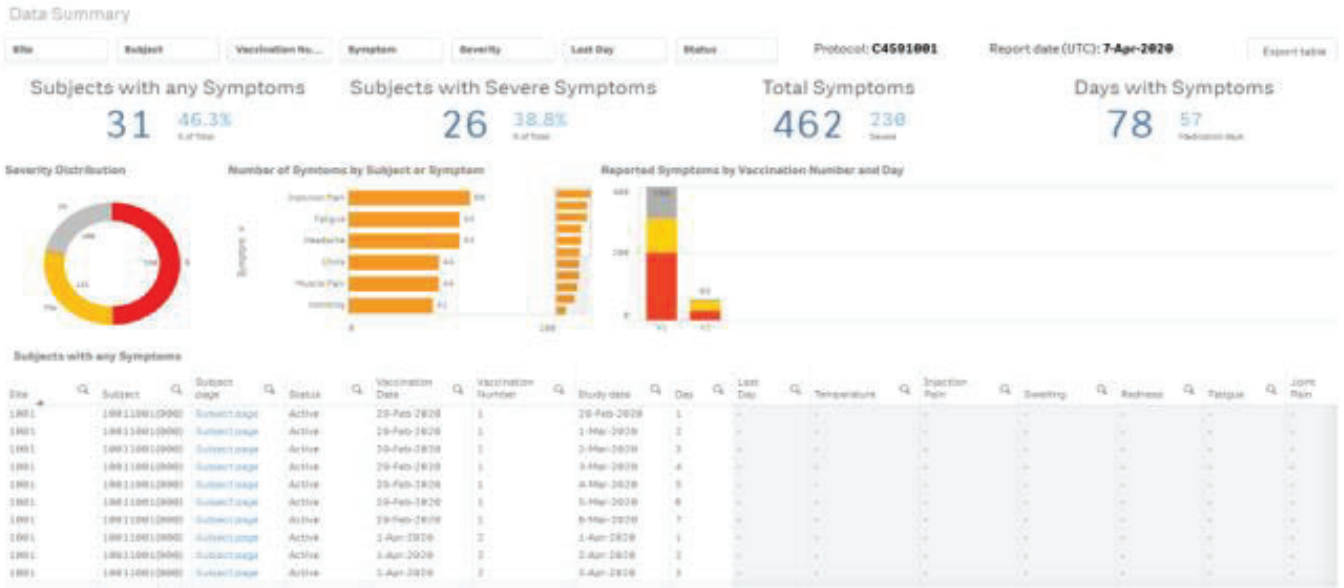


4.7 C4591001 Custom reports

4.7.1 Daily Diary Data Summary Report

This report shows whether or not participants have experienced local reactions, systemic events or fever, their corresponding severity and any medication taken for days 1-7.

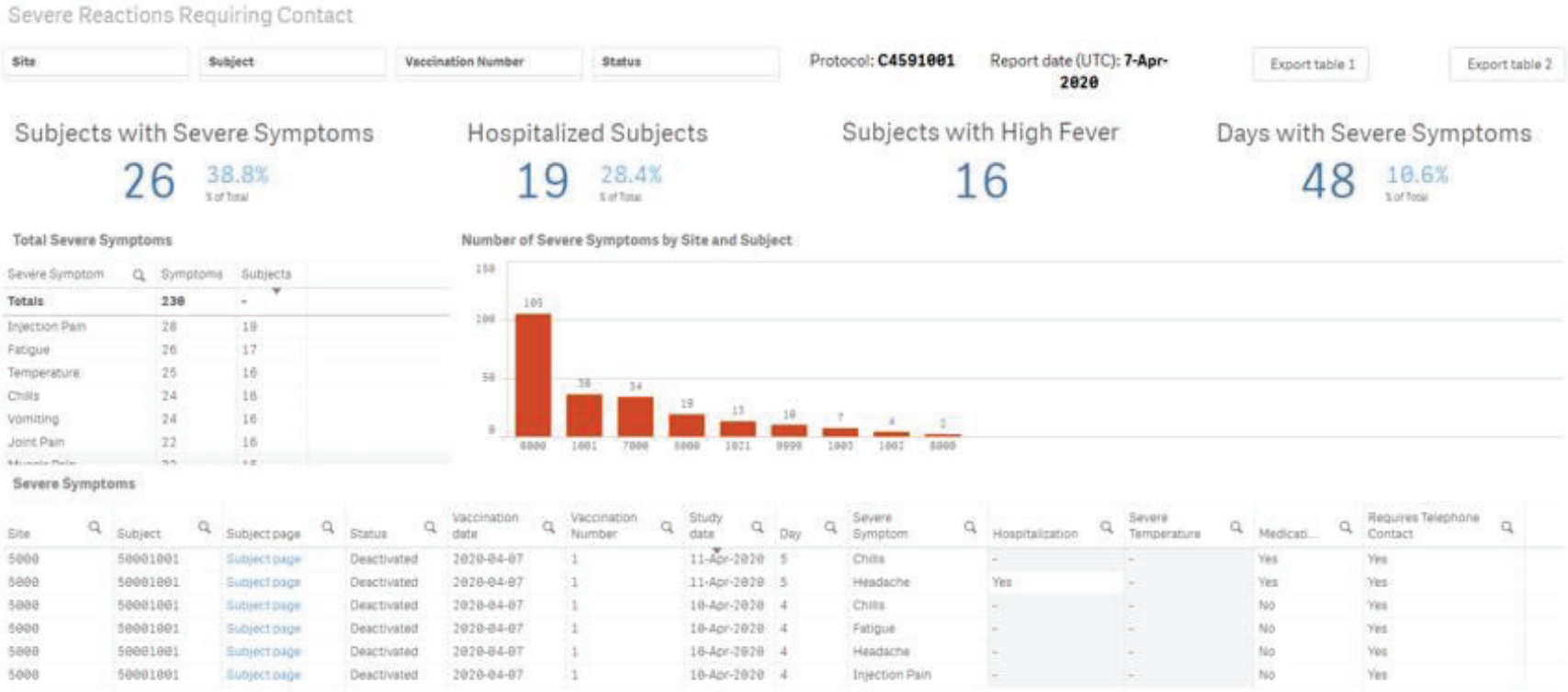
Columns will include: “Site”, “Participant”, “Participant page” (hyperlink which takes you to the participant page in TrialManager), “Status”, “Vaccination Date”, “Vaccination Number” (displays the vaccination number entered in the TrialManager), “Study Date” (displays date when daily diary form was opened. Future/ uncompleted diary dates will appear as [blank]), “Study Day” (fixed column listing ‘1’ – ‘7’ representing each of the study days for each participant), “Temperature”, “Injection Site Pain”, “Swelling”, “Redness”, “Fatigue”, “Chills”, “Diarrhea”, “Vomiting”, “Headache”, “Joint Pain”, “Muscle Pain”, and “Medication”.



4.7.2 Severe Reactions Requiring Contact Report

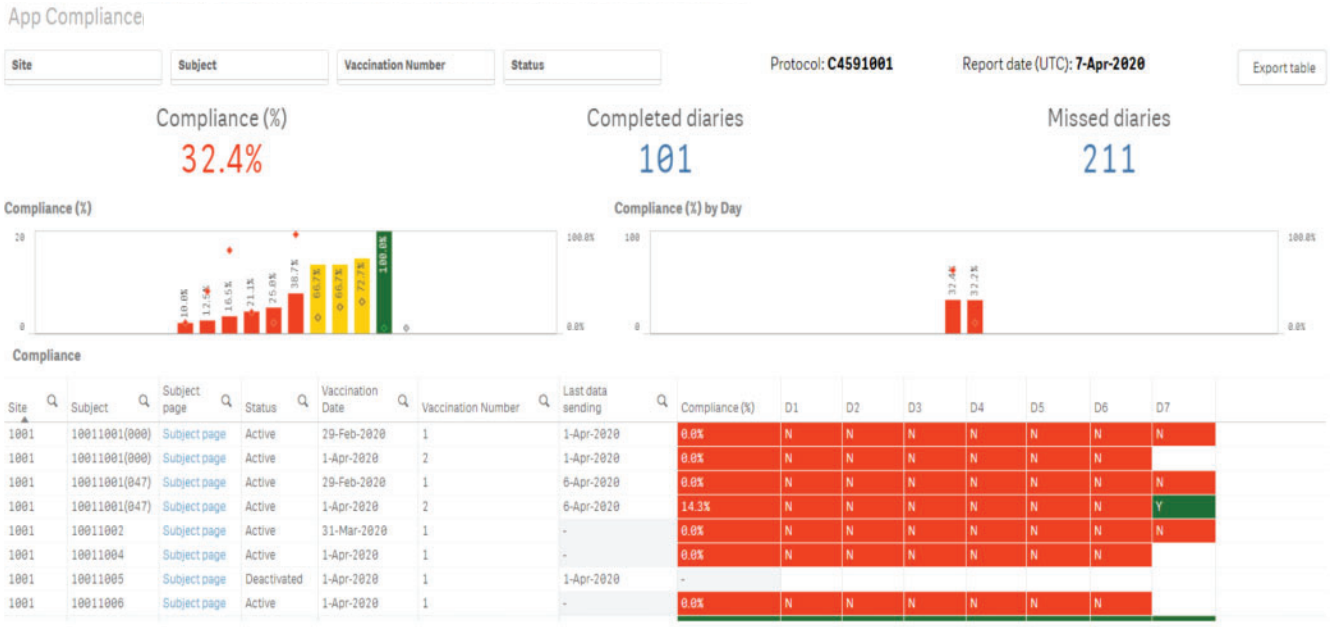
Displays if participant have reported 'Severe' local reactions, 'Severe' systemic events or has reported a severe temperature.

Columns will include: "Site", "Participant"," Participant page" (hyperlink which takes you to the participant page in TrialManager), "Vaccination date", "Vaccination number" (displays the vaccination number entered in the TrialManager), "Study date", (displays date when daily diary form was opened. Future/ uncompleted diary dates will appear as [blank]) "Study Day" (fixed column listing '1' – '7' representing each of the study days for each participant), "Severe Symptoms", "Hospitalization", "Severe Temperature" (Any Temperature higher than 102°F), "Medication", and "Require Telephone Contact" .



4.7.3 Daily Diary Compliance Report

This report shows the daily compliance by participant for days 1-7, from day 1 up until the current day.



Columns will include: “Site”, “Participant”, ”Participant page”, “Status”, “Vaccination date”, “Vaccination number”, “Last data sending” , & “% Compliance”.

Compliance (%): Displays the compliance rate.

D1-D7: represent the study days and will display the status of the participant’s diary completion for each day.

Color scheme display for the Compliance (%):

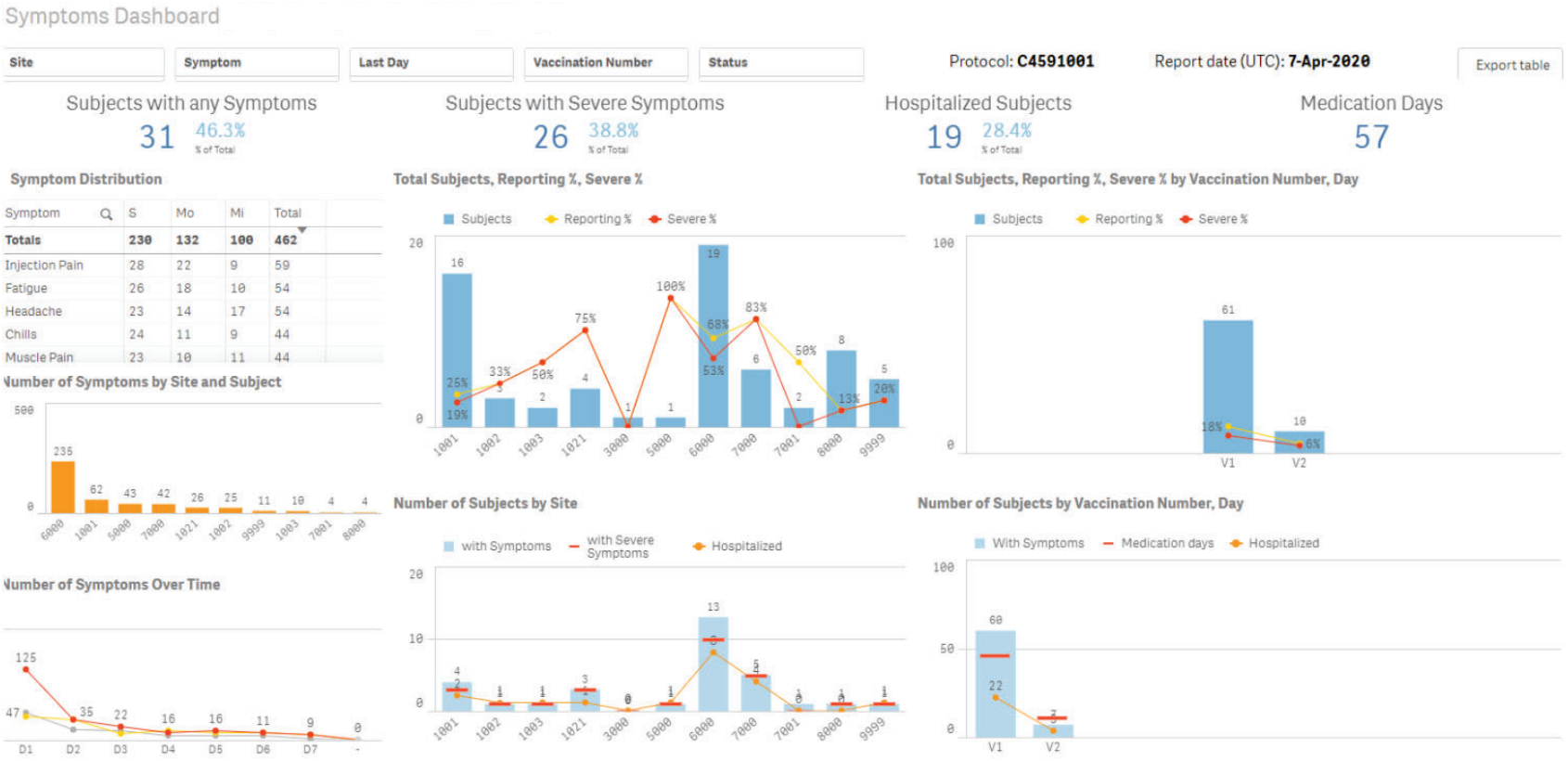
- Red: <40%
- Yellow: ≥ 40% - < 80%
- Green: ≥ 80%

Expected diary compliance will follow the standard color-coding scheme and thresholds. For active participants, diary completion expectations will be based on the current date. Once a participant is vaccinated, the participant will be expected to complete the diary every day for 7 days including on the day of the vaccination, for the participant. As each study day passes, the previous study days become expected and should have one daily diary completed. For deactivated participants, diary completion expectations will be based on the deactivation date. The participant will thus be expected to have completed one diary for each study day starting from the vaccination day and until the day before the Deactivation date. The exception here is that if the participant completed a diary on the day they were deactivated, that day will also be considered as expected.

4.7.4 Symptoms Dashboard Report

The purpose of this report is to provide the Study team with an overview of the reported symptoms and medications at the sites.

Symptom Distribution columns will include: “Symptom”, “S” (Severe), “Mo” (Moderate), “Mi” (Mild), & “Total”.

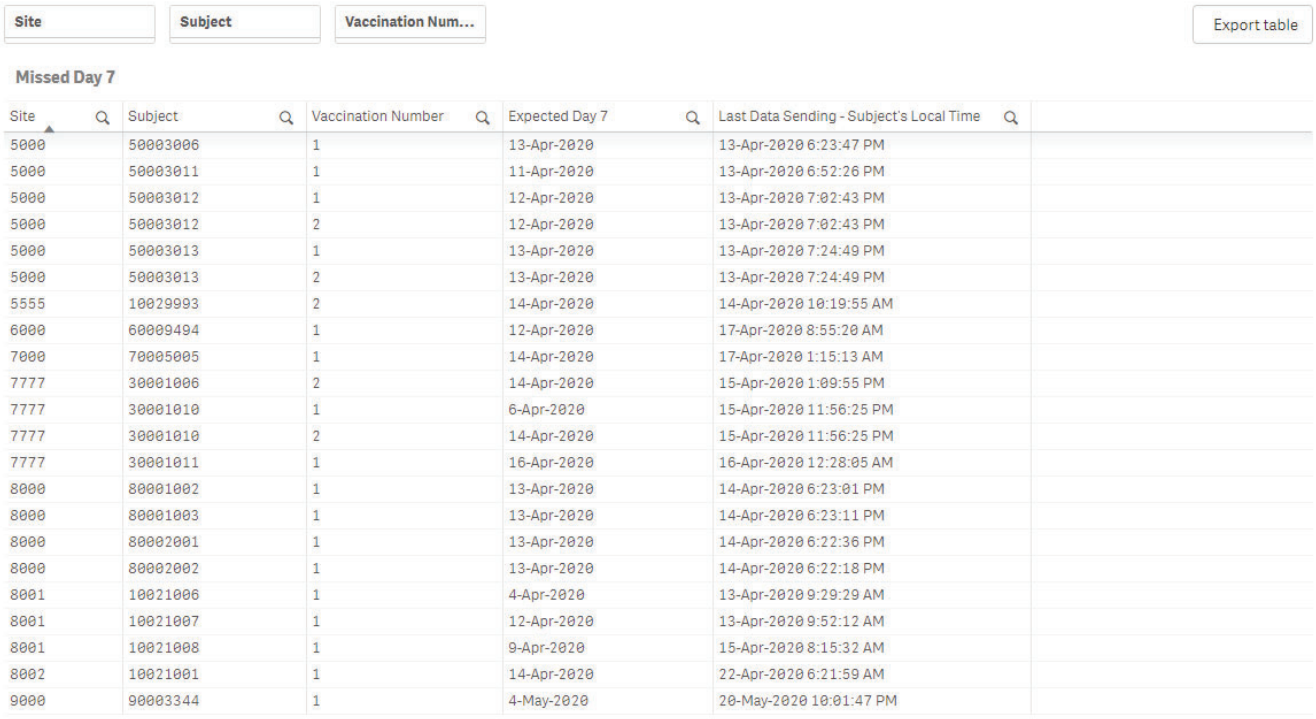


4.7.5 Missed Day 7 Transfer Report

The purpose of this report is to flag any participants who are missing diary data for day 7, following vaccination 1 or vaccination 2, and have not sent data for day 7 or thereafter.

The table will list the site number, participant (subject) number Vaccination number, the date day 7 diary was expected, and the last date and time the participant's App connected to the server (in the participant's local time).

The report can be filtered by: Site number, Subject (participant) number, Vaccination number.



Site	Subject	Vaccination Number	Expected Day 7	Last Data Sending - Subject's Local Time
5000	50003006	1	13-Apr-2020	13-Apr-2020 6:23:47 PM
5000	50003011	1	11-Apr-2020	13-Apr-2020 6:52:26 PM
5000	50003012	1	12-Apr-2020	13-Apr-2020 7:02:43 PM
5000	50003012	2	12-Apr-2020	13-Apr-2020 7:02:43 PM
5000	50003013	1	13-Apr-2020	13-Apr-2020 7:24:49 PM
5000	50003013	2	13-Apr-2020	13-Apr-2020 7:24:49 PM
5555	10029993	2	14-Apr-2020	14-Apr-2020 10:19:55 AM
6000	60009494	1	12-Apr-2020	17-Apr-2020 8:55:20 AM
7000	70005005	1	14-Apr-2020	17-Apr-2020 1:15:13 AM
7777	30001006	2	14-Apr-2020	15-Apr-2020 1:09:55 PM
7777	30001010	1	6-Apr-2020	15-Apr-2020 11:56:25 PM
7777	30001010	2	14-Apr-2020	15-Apr-2020 11:56:25 PM
7777	30001011	1	16-Apr-2020	16-Apr-2020 12:28:05 AM
8000	80001002	1	13-Apr-2020	14-Apr-2020 6:23:01 PM
8000	80001003	1	13-Apr-2020	14-Apr-2020 6:23:11 PM
8000	80002001	1	13-Apr-2020	14-Apr-2020 6:22:36 PM
8000	80002002	1	13-Apr-2020	14-Apr-2020 6:22:18 PM
8001	10021006	1	4-Apr-2020	13-Apr-2020 9:29:29 AM
8001	10021007	1	12-Apr-2020	13-Apr-2020 9:52:12 AM
8001	10021008	1	9-Apr-2020	15-Apr-2020 8:15:32 AM
8002	10021001	1	14-Apr-2020	22-Apr-2020 6:21:59 AM
9000	90003344	1	4-May-2020	20-May-2020 10:01:47 PM

5 DATA CLARIFICATION FORM (DCF)

5.1 What is a DCF

TrialManager allows authorized personnel to request modifications to certain data items via the DCF process. The data reported by the sites and participant is considered to be the original electronic source data. This data is very rarely, if ever, changed, however, in some situations data changes are needed. The DCF is the audit trail for data changes. Each DCF and its full history are available for review during the study via TrialManager and will be provided to the sites and client at the end of the study via the site archive.

5.2 Types of data changes allowed:

The following data modifications are permitted for this study:

- Changes to data previously reported by the participant, i.e., increase or decrease in the severity of a local reaction or systemic event previously reported on a given day. It is the investigational sites responsibility to ensure such changes are only requested if supported by appropriate source documentation, e.g., telephone contact report detailing the initial data entered and the corrected data.

- Changes to device set-up information, i.e., corrections to the following when previously entered incorrectly:
    - Site number
    - Participant number
    - Vaccination number or date of vaccination

- Other administrative changes, i.e.:
    - Merging participant data and removal of duplicate data – allows cleaning of data issues that may result

from replacement or multiple devices being issued to participants.
    - Modifying timestamps - allow cleaning of data issues arising from when the diary device internal clock is inaccurate.
    - Changing participant status

When data is modified or duplicate data removed, no data is ever fully deleted, all data will remain in the data base audit trail.

The following data modifications are not permitted for this study:

- Addition of a form, e.g., addition of a daily diary that has previously been reported as missed, or if the device fails and the participant is unable to record their daily diary.

5.3 Where to create DCFs in TrialManager

You can add a new DCF for any participant where ever you see the 'Add new DCF' button in TrialManager.

It is also possible to add a DCF for a specific participant from the participant page (so the participant instance will be preselected), or from a participant's form view while reviewing data (so the participant instance and the specific form will be preselected).

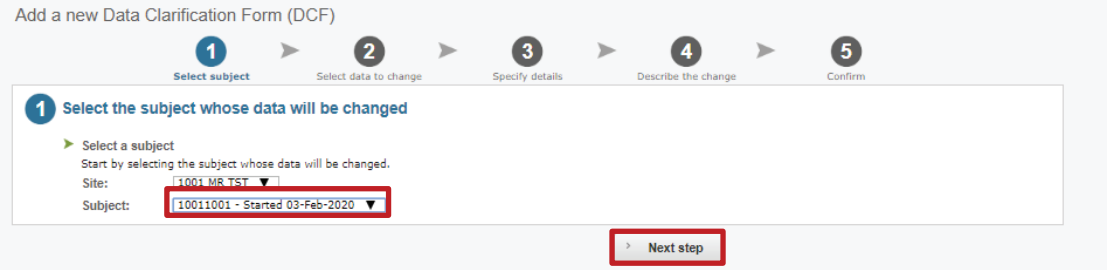
5.4 How to create a DCF

The steps required to complete a new DCF are detailed below. For certain DCFs, additional steps may be required to provide the necessary level of information. The system will guide you to select the necessary information, where this is required.

After initiating the DCF as outlined in Where to create DCFs in TrialManager:

1. **Select Site and Participant**

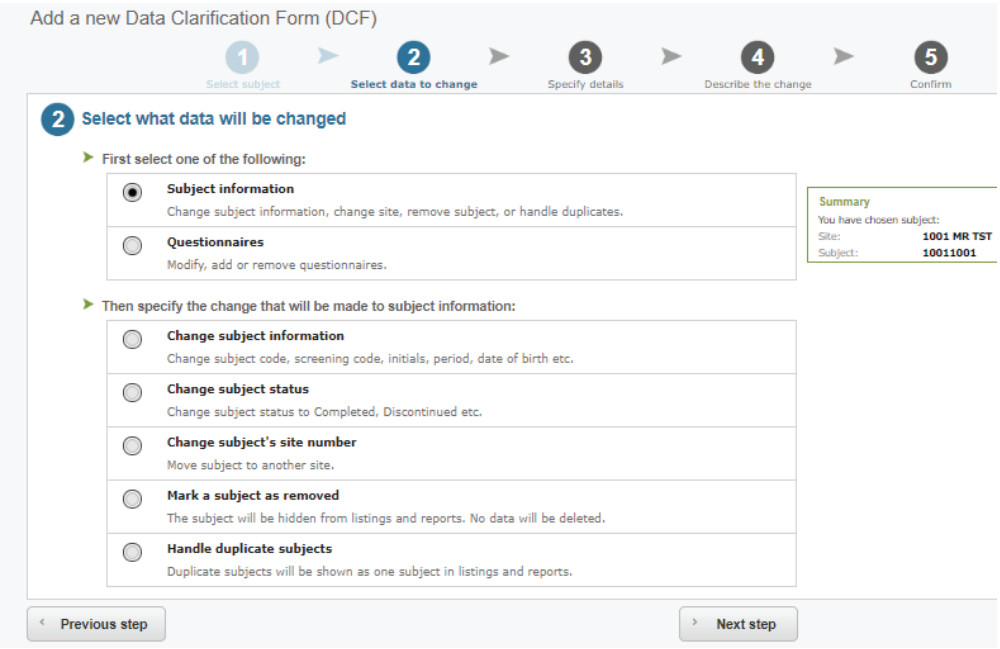
Note: If the DCF was raised at the participant or form level, entering the site and participant in the dropdown will not be necessary.



If there are multiple instances for the participant (i.e. multiple Daily Diary instance) you must select the correct one based on the start date (found in the site index). Alternatively, raise the DCF from the participant level of the correct instance to pre-select the participant details.

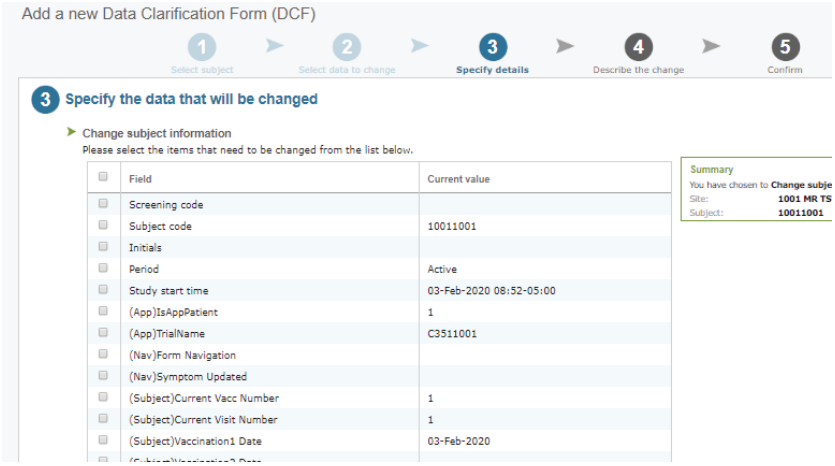
2. Select data to change

Select the data to be changed, either Participant Information or Questionnaires. Based on the selection a further list will appear, as per the example screenshots below. Select the option that best fits the change, then select 'Next step' to proceed to step 3.



3. Specify details (required for some DCF types)

Based on the options selected in the previous step, additional information may be required.



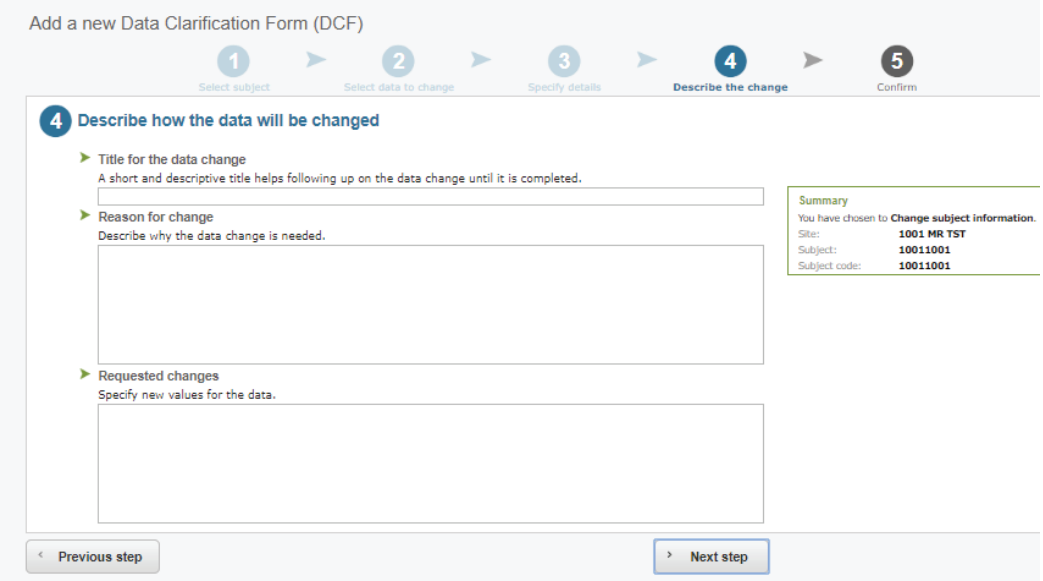
4. Describe the change

Fill in the 3 required free text boxes to describe the change, in as much detail as you can provide. When finished, click 'Next step':

a. **Title for the data change:** Give the DCF a brief title that describes the change (*e.g. 'Update participant number'*).

b. **Reason for change:** Describe the issue with as many details as possible. If this is not specific, processing may be delayed. This should not simply outline what change must be made but rather provide reason for the change explicitly, to act as the audit trail. (*e.g. 'Participant number was entered incorrectly on the device'*)

c. **Requested changes:** Detail the requested changes. Specify any values that need to be changed, including the original value and new value *(e.g. 'Please change X to Y.')*.



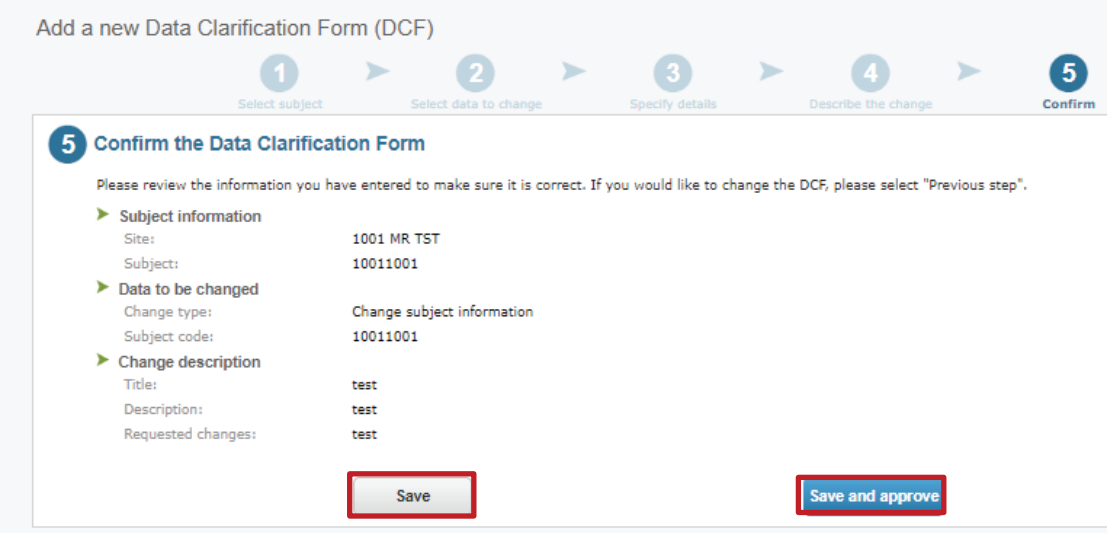
Additional information required for some DCF types:

- Requesting to change a participant's status: be sure to include the date of when the participant status has changed in Step 4 (Describe the change). This DCF type cannot be processed without a date when the new status started.

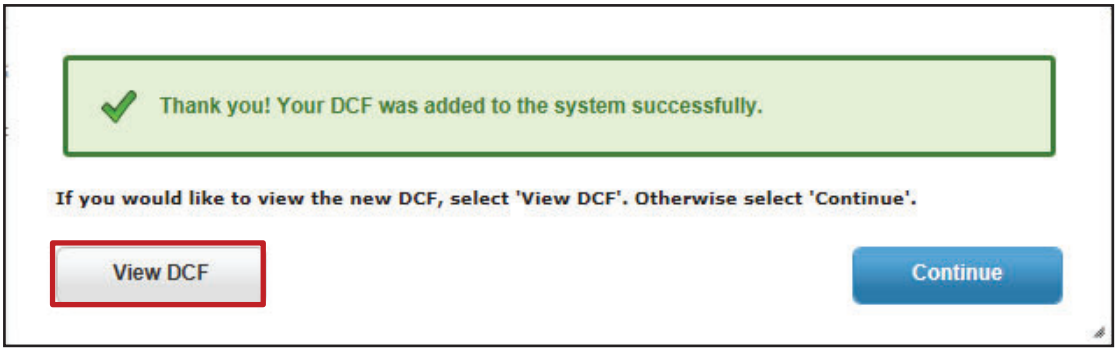
Marking a participant as removed: be sure to specify if forms saved under the participant should also be marked as 'removed' in Step 4 (Requested changes).

5. Confirm

When the DCF has been drafted, you will see a screen where you can review the information entered and click 'Save' to save the information required; or press 'Previous Step' to return to the last step and amend the information. The 'Save and approve' button can also be seen if your user role allows you to approve the DCF request. This button should only be used if you are sure the data entered in the DCF is correct and the request does not need to be reviewed by anyone else before sending to Signant Health Data Management.



You will get a confirmation that the DCF was created successfully after pressing either 'Save' or 'Save and approve'. Select 'View DCF' to change the status of the DCF for processing by the Signant Health Data Management Team, if 'Save and approve' was not selected.



5.5 Approval of DCFs

When to approve DCFs

DCFs must be approved once they have been created and confirmed to have all the necessary and required information. This may be completed separately, once the DCF is created, or during the DCF creation process if the user has DCF approval rights. **Before Signant Health can implement a DCF, it must first be approved by the Site**.

How to Approve DCFs

DCFs pending site approval can be monitored in the weekly DCF notification emails, which will include links to each DCF, or by reviewing the DCF Dashboard on the study's TrialManager Main Page.

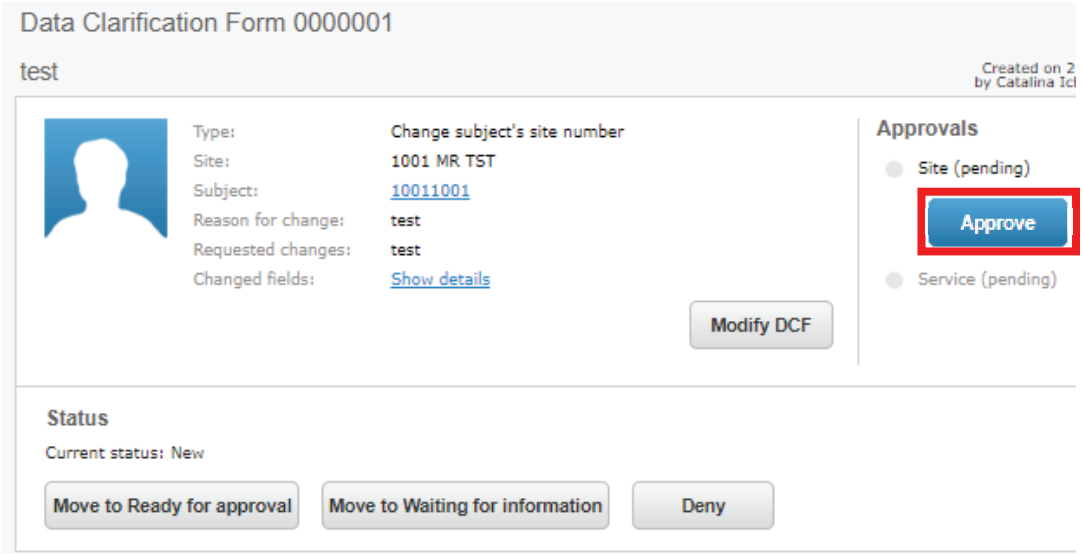
After clicking the DCF link from the email notification, the user will be taken directly to the page where the status of the DCF can be changed. User can also select the appropriate DCF from DCF Dashboard on TrialManager home page by clicking on the DCF title.

Before the change requested can be implemented, the DCF must be approved by the following levels:

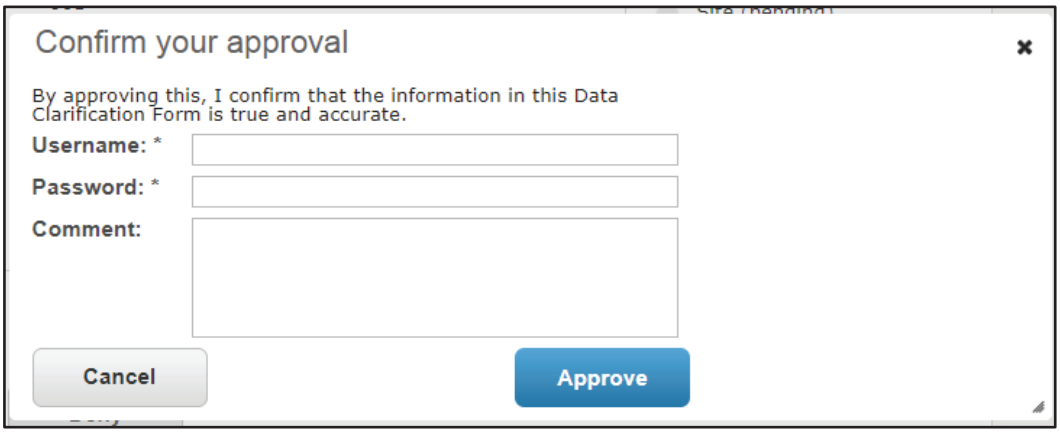
> **Level 1 (Site):** The first level of approval is the Site/Investigator approval. Steps below describe how site personnel can approve DCFs.
>
> **Level 2 (Service):** Finally, Signant Health Data Management Team approval is added once all approvals are received, and Signant Health have confirmed that the DCF includes all necessary information to implement the requested changes.

Follow the instructions below in order to ensure the DCF is approved for processing:

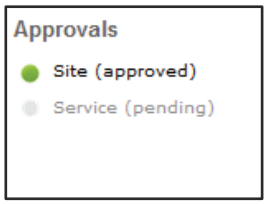
1. Navigate to the DCF and select the **'Approve'** button.



2. Next, a confirmation screen will appear which allows you to add a comment (*optional*) and approve the DCF. After entering your credentials, you can select approve. Please note only Investigator and Study Coordinator (DCF) roles can approve DCF.



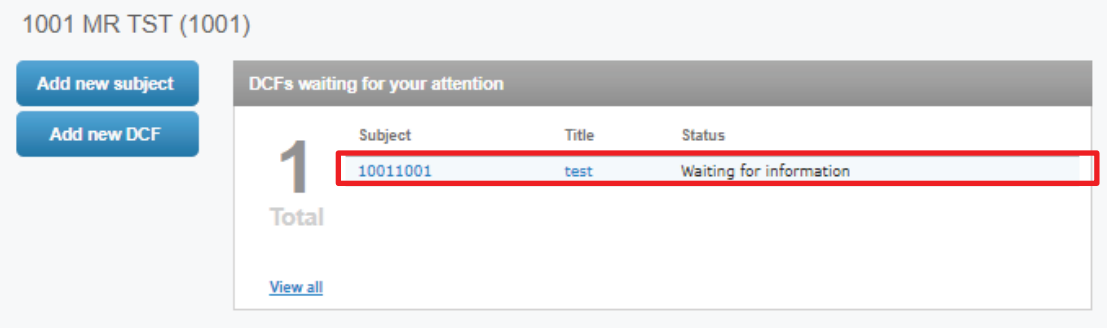
3. The DCF is now approved by the site; approval status is listed on the upper right corner of the DCF. Signant Health can now approve the DCF and implement the changes. **Note: Signant Health may change the status and request additional information see How to Answer Comments: Waiting for Information.)**



You can follow the progress by selecting the DCF and checking the status in the 'DCF' tab of TrialManager and the comments within the DCF.

5.6 Adding Additional Information to DCFs

How to Answer Comments: Waiting for Information



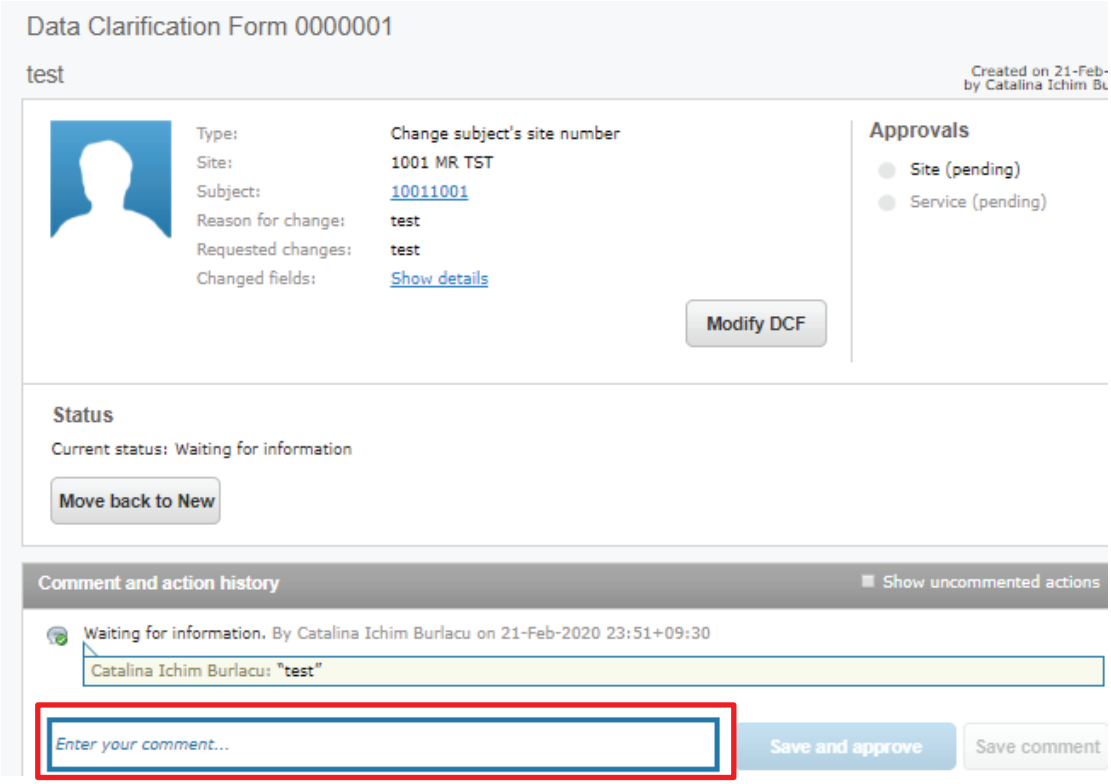
Sometimes, DCFs will need additional clarification and will be changed to the 'Waiting for information' status with questions that the site will need to answer. The DCFs waiting for information can be found on the 'Main page' tab of the TrialManager.

DCFs may be placed in a 'Waiting for information' status for the following reasons:

- DCF wording is unclear
- Wrong type of DCF was selected
- There is missing information that needs to be confirmed

The following steps will be required in order to add comments to DCFs in a 'Waiting for information' status:

1. Click on the Title link to review and read the comment history for the DCF in the 'Waiting for information' status.
2. Review the comments that details the information that needs to be clarified. Enter a clarifying comment in the 'Enter your comment…' text box. Try to respond to all questions raised with as much detail as possible**. If you are still unsure about what information is needed, please state this in your comment**. Press the 'Save comment' button when finished.



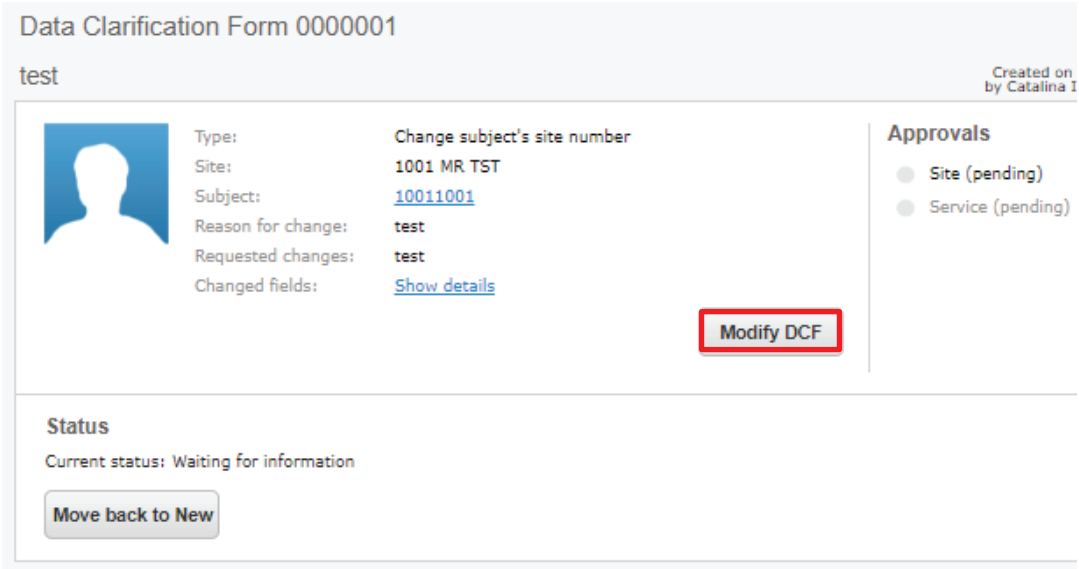
3. Once the necessary additional information has been added via a comment, **the DCF must be approved again**. Follow the steps outlined in How to Approve DCFs above.

You will notice that the DCF no longer appears on the DCF Notice Board on the Main page – this means that no further action is needed on that DCF. Continue the process with all remaining DCFs in your notice board until no DCFs appear in the DCF Notice Board. **Note: The DCF may be moved to a 'Waiting for information' status again if the comments in the DCF are not clear or do not clearly answer the questions from the Signant Health Data Management Team.**

How to Modify DCFs

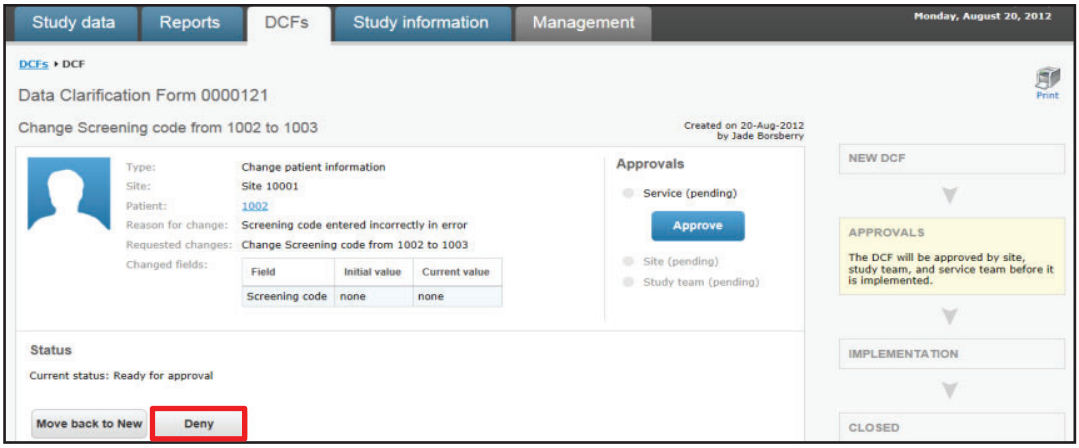
Until a DCF is either under 'Ready for approval' or any 'Approved' status, the site is able to modify the DCF. This can be accomplished by simply selecting the **'Modify DCF'** button on the DCF itself.

When making modifications, be sure to save all updates made to the DCF and move to 'Ready for approval' for processing.



How to Cancel/Deny DCFs

The site can cancel their entered DCF at any time prior to their first approval, by selecting the **'Deny'** button on the DCF page.

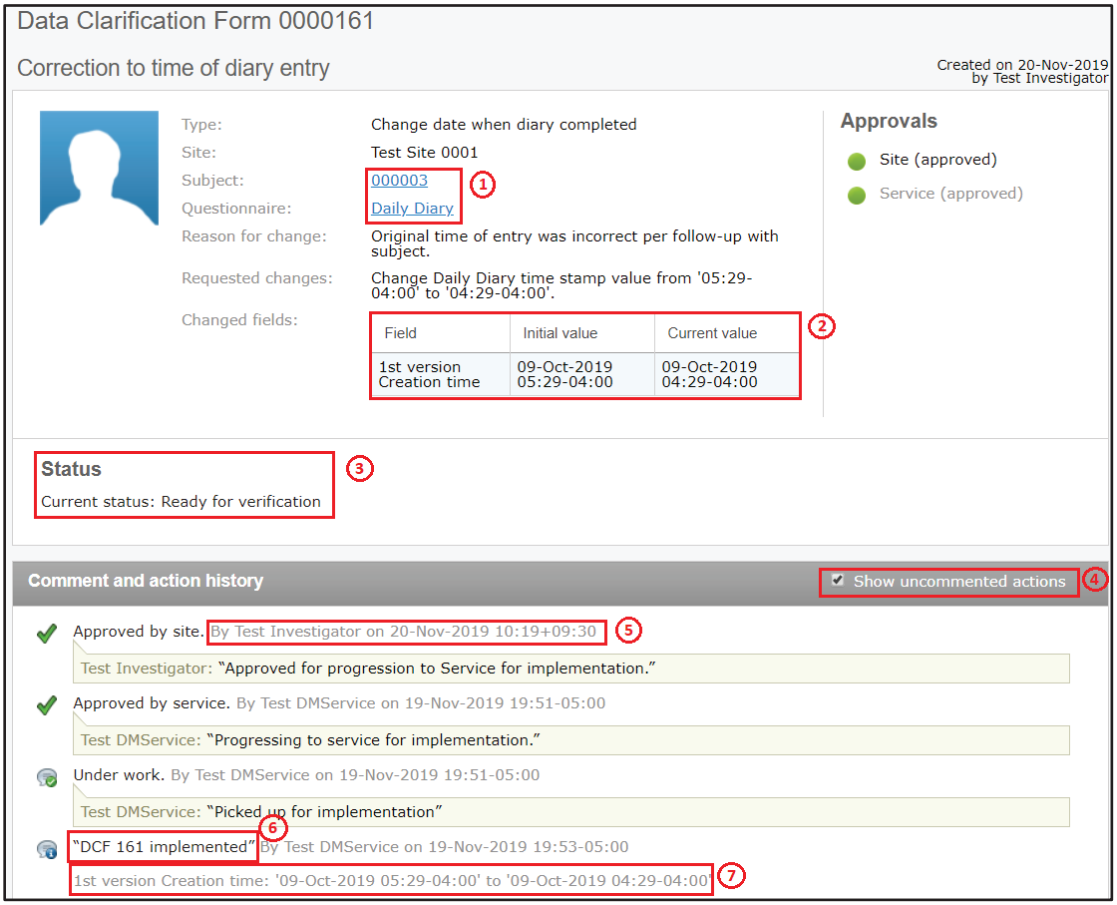


By selecting the 'Deny' button, this signals to the Signant Health Data Management Team that the change requested in the DCF should not be processed.

Note: The Signant Heath Data Management Team may deny DCFs that are not applicable for your protocol or are duplicate requests.

5.7 Viewing DCF Comment and Action History

A DCF will always retain the full history of all comments and actions committed. To view the latest activity for a DCF, navigate to the 'DCFs' tab, select the sub-tab, 'All', and then click the desired DCF link to view the DCF detail. Select the check box, 'Show uncommented actions', and the full history of actions committed in that DCF will be displayed in order of oldest to newest, top-to-bottom.



The elements of the DCF detail view pictured above are defined as follows:

1. Direct links to Participant card and the questionnaire under change, as applicable to the DCF
2. Changed fields will be displayed if specific fields were selected for change during DCF creation. 'Field' will display the data item, 'Initial value' will display the original data item value captured via the TrialMax device, and 'Current value' will display the data item's present value (this may match the 'Initial value' if the DCF has not been implemented yet)
3. The current status of the DCF will be displayed
4. Check box to show uncommented actions, such as a status change can be selected for a comprehensive view of the DCF's history or deselected for a reduced listing. The checkbox will default to unchecked when first opening the DCF
5. The name of the individual committing the action and the commit timestamp will display next to each committed comment or action
6. Comments entered will display within quotation marks
7. Committed changes directly associated with the DCF will display in grey text without quotations

Note: DCF comment and action history items comprise an audit trail of all comments and actions committed in the DCF and cannot be modified once committed.

5.8 DCF Timelines and Tips for Success

DCF Timelines

Once a DCF has been approved, Signant Health Data Management will review and implement the request within 5 working days. If a DCF must go to "Waiting for information" status, then the implementation time will restart on re-approval of the updated DCF.

Tips for Success

It is important that all the data that has been uploaded be reviewed and cleaned throughout the study. Please find below some important guidelines on best practices below:

1. It is highly important that data is reviewed and DCFs are raised and approved on an ongoing basis to avoid high volumes of DCFs ahead of interim and final database locks.
   For example, you can use the **Inconsistencies report** to identify participants with potentially incorrect participant numbers, or who may need to be merged, and you should check the participant data to ensure visits are labelled correctly.
2. Sites should continuously review any DCFs waiting for more information to provide Signant Health with the information required to implement prior to lock dates. Regularly review the 'DCFs waiting for your attention' noticeboard on the TrialManager Main Page to find any DCFs that need action to be taken.
3. Sites should ensure that all devices at site have sent data so that all data is uploaded and visible in TrialManager.
4. Please be aware that Signant Health does not review data or raise DCFs.

6 Setting up SMS notifications

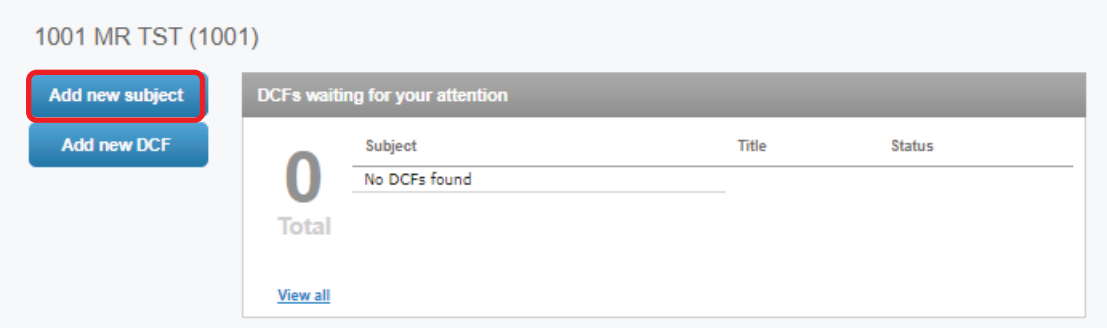
As part of participant setup, you can choose to enter a participant's personal mobile number to receive activation details via SMS. **US participants will need to** subscribe with the mobile phone number they wish to receive this message on. **This should be completed before setting up a participant.**

To opt-in to receive SMS activation code, send a text message with the word **SUBSCRIBE** to phone number **42526**. When you opt-in to the service, you will receive a reply confirming your signup. Once confirmation of subscription message is received, the participant will be able to receive SMS activation code.

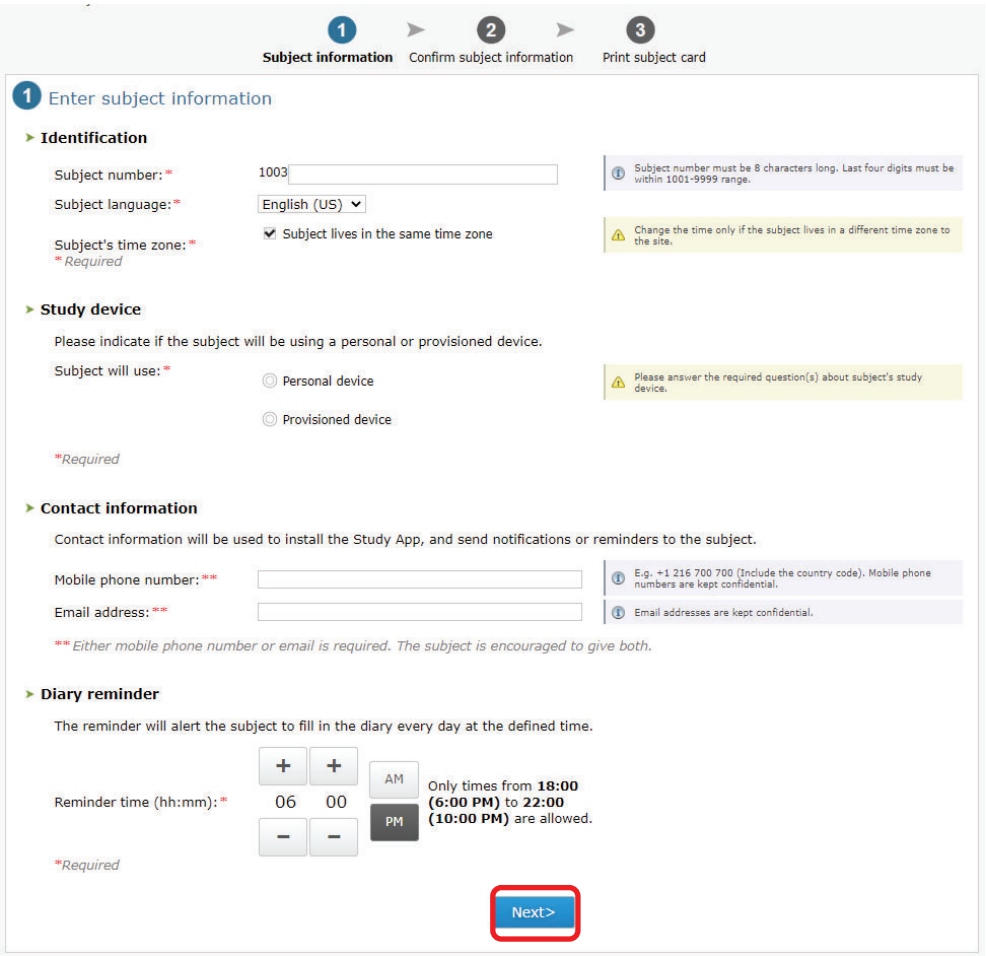
7 How to set up a participant in TrialManager

Participant setup must be performed by site staff through TrialManager for all participants. This must be done when the participant is at your site for their first study visit and not prior as it is a prerequisite for the participant to start entering data in the App. Login to TrialManager to begin.

Select 'Add new participant'



You will then be taken to a screen where you will need to enter the participant number and provide participant information; including their language, time zone, device type, contact information (for receiving activation details), and Daily Diary reminder time.



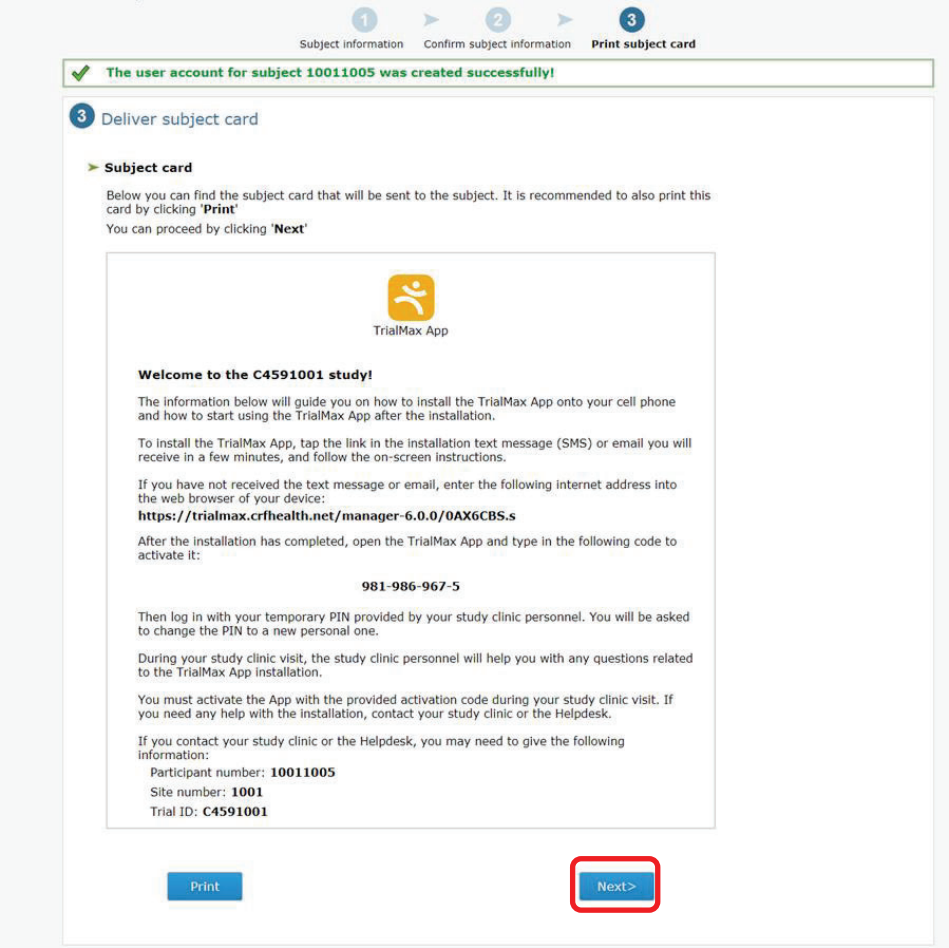
Select “Next” once all the required fields have been filled out.

Note: Mobile phone number and email address are used by the TrialMax system to send an activation code to participant. Therefore, it is important that this information is entered correctly. The participant should enter either their personal email address and/or mobile number to receive the activation code.

Next you will see a confirmation screen, where you will be able to review the participant contact information (mobile phone number and email address) you have entered. Carefully check the details and then select “Confirm”. This will lead you to another page confirming the other participant information that has been entered. Carefully check this information as well, then select “Confirm”.

You will then receive a message on screen that will confirm that the participant was created successfully. You will also see displayed a Participant Card that is sent to the participant via email/SMS. This participant card contains their activation code and applicable instructions for getting set up with the App.

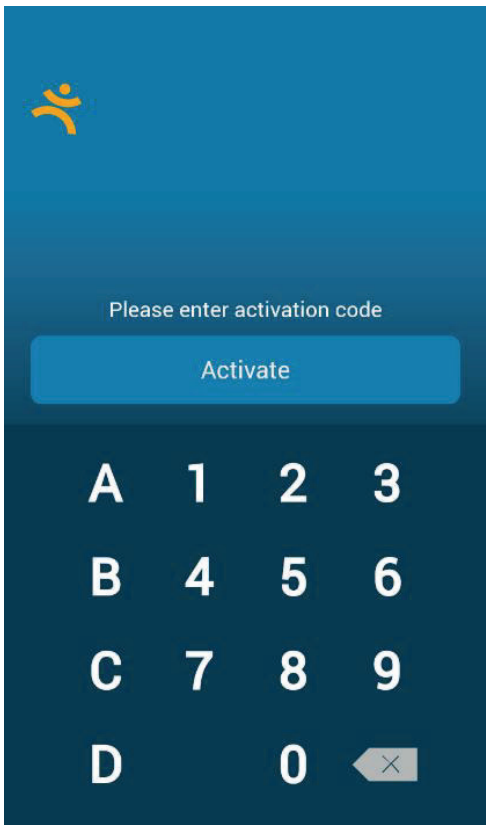
TrialManager will also display a copy of the participant's card on screen and this should be printed if possible, to make it more convenient for the participant. **Be sure to write down the Activation Code displayed on screen and provide this to the participant.**



Press "Next" to conclude setup.

7.1 How to Activate the App

When the participant setup is complete and the participant receives their participant card with the welcome message and activation code, the participant should also be provided with a fully charged Samsung device (provisioned device) to use in the study.



The activation screen is the first screen presented when the provisioned device is turned on. Here, the participant will need to enter the activation code provided in the participant card/ SMS/email message.

Once the activation code has been entered appropriately, the participant will be taken to the login screen where they should enter the default PIN code '**1234**' to login for the first time.

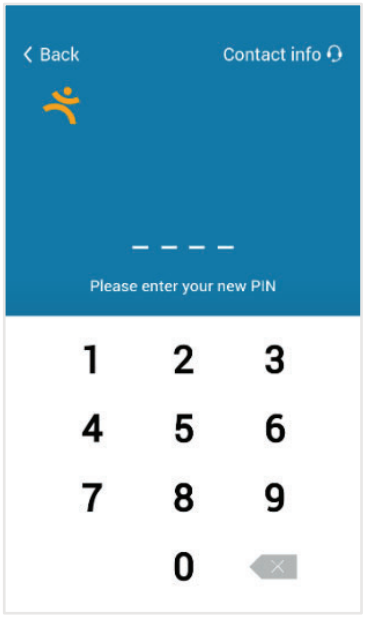
7.1.1 How to setup WiFi on the Provisioned Device

WiFi can be configured on the provisioned devices. To access the WiFi Settings on the provisioned device please follow these steps:

1. Press the 'home' button on the device.
2. Next, press the 'gear' symbol in the top right-hand corner of the screen.
3. Select 'WiFi settings' to display a list of available networks.
4. Select the appropriate network from the list and enter the password if required. *Once the connection is authenticated, the WiFi will connect.*
5. You can then return by clicking the 'home' button, and the App will automatically open.

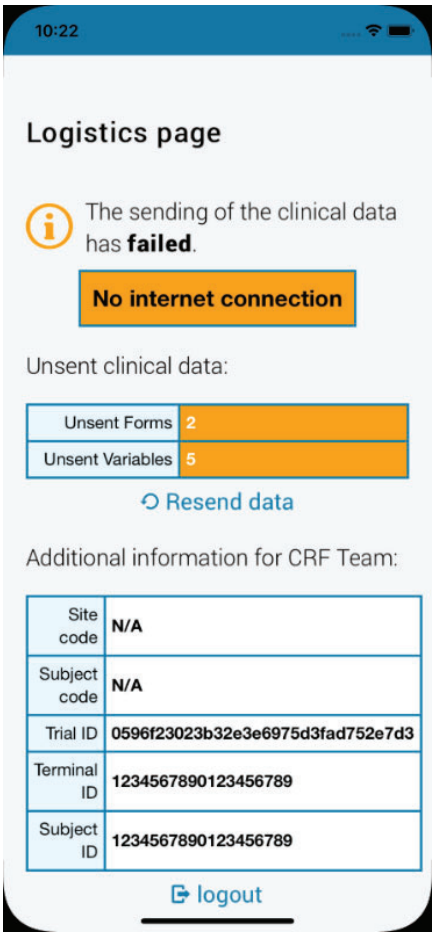
7.1.2 Instructions for reusing the Provisioned Device

The App supports the reuse of the Provisioned Devices, meaning that when one participant has finished using the device, it can be setup for a subsequent participant. To reuse the Provisioned Device for another participant, all unsent clinical data must first be sent to Signant Health.



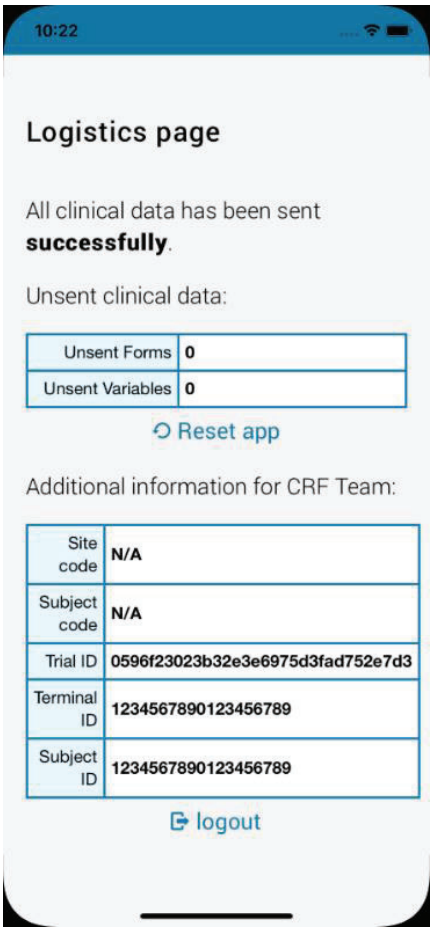
In order to do this, you will first need to login to the Logistics Page on the device.

- From the login screen, first enter the **'Special Code', 8888** to ready the device for the logistics pIN
- Then enter the **'Logistics PIN', 4422**
- Once both PINs have been entered in succession, you will be taken to the Logistics Page



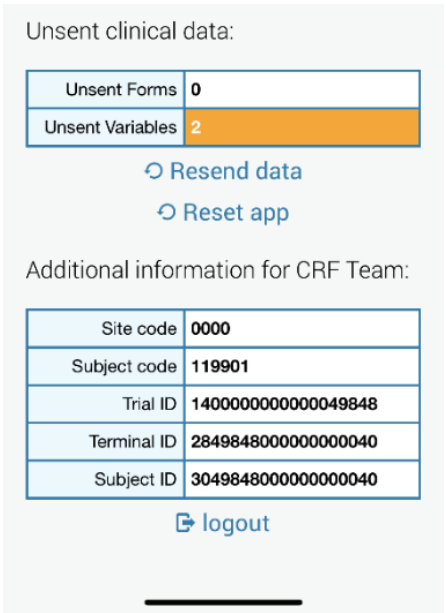
- From the Logistics Page, select 'Resend data' to send any unsent clinical data to Signant Health

The device cannot be reset until all clinical data has successfully been sent.

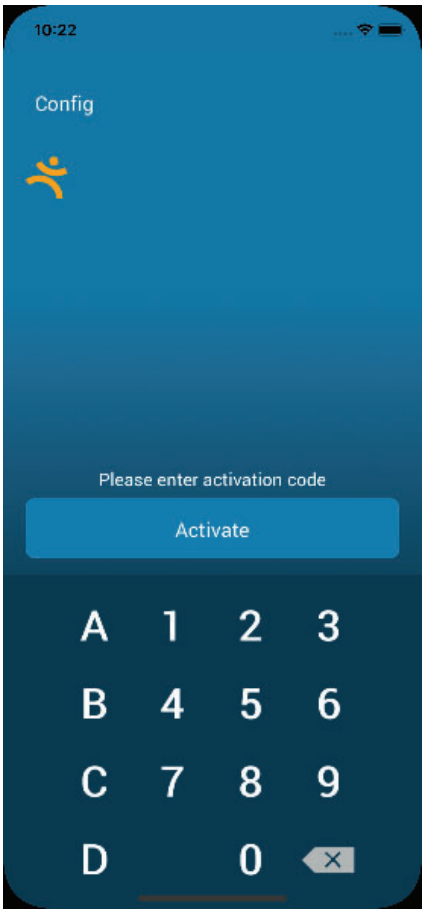


If there is no unsent data, or once all unsent data has successfully been sent, the 'Reset app' button will appear

Selecting 'Reset app Button will reset the App for the next participant



Note: if there are new unsent variables after the data send (due to protocol), but all Daily Diary data has successfully been sent, then the App can still be reset



Selecting the 'Reset app' Button will reset the App; the App will do one more final data sync, then is reset and returns to pre-activated state, ready for another participant to be setup

7.2 Selecting a TrialMax App PIN

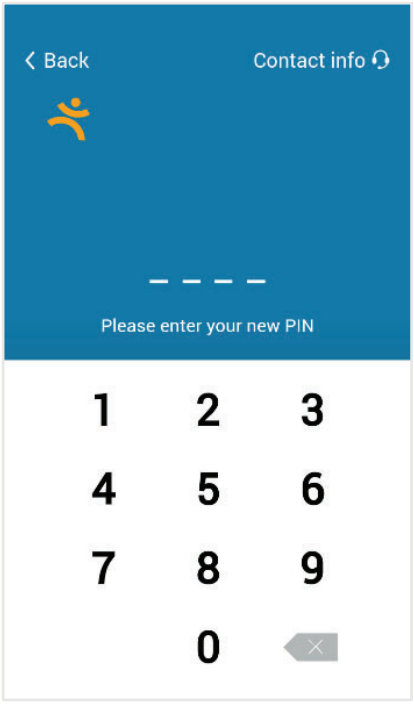
The TrialMax app has certain restrictions for PIN codes:

- Easily remembered by the user (ex: memorable date)
- It cannot be the same as the default PIN code
- It must be four digits
- It must not contain running numbers, e.g. 2345, 5678 will not be accepted
- It must not contain more than three consecutively repeated numbers, e.g. 1111, 2222 will not be accepted

The participant should not share their PIN code with anyone, not even with study staff. The new PIN code must remain confidential, with only the participant knowing the PIN code.

If a participant forgets their PIN code, they will need to contact the helpdesk who will be able to reset the PIN code.

7.3 Logging In & Setting Security Question



After the activation code is entered, the participant will be asked to log in to the App. The user will have to enter the default four-digit PIN code (**1234**) to access the App and will then be prompted to change their PIN to a unique 4-digit PIN.

The participant should not share his/her PIN code with anyone, not even with study staff. The new PIN code must remain confidential, with only the participant knowing the PIN code.

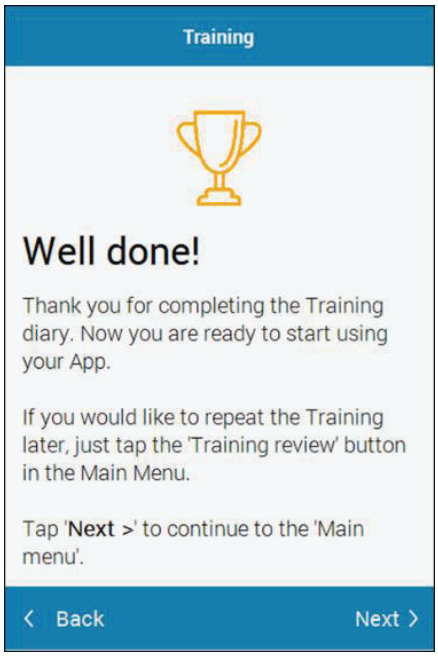
Once the participant has changed their PIN, they will be prompted to select and answer a security question which will assist the helpdesk in resetting their PIN code should they forget it during the study.

After PIN code change and security question selection is fully complete, the participant will be led straight into training on how to use the App.

7.4 Training on the TrialMax App

This initial, mandatory training is required to be completed before the participant can access any other portions of the App (including the Daily Diary).

The training is brief and provides helpful information on App usage as well as a sampling of the types of questions they will encounter while using the App over the course of the study.



Once the participant has concluded the Training, they will receive this screen confirming their completion.

By tapping 'Next' the participant will then be directed to the main menu of the App where they will be able complete their Daily Diary and modify their settings.

***Please note** – any activities performed while logged into the App should be performed by the participant only. Site staff will not need to login to the App for any purposes.*

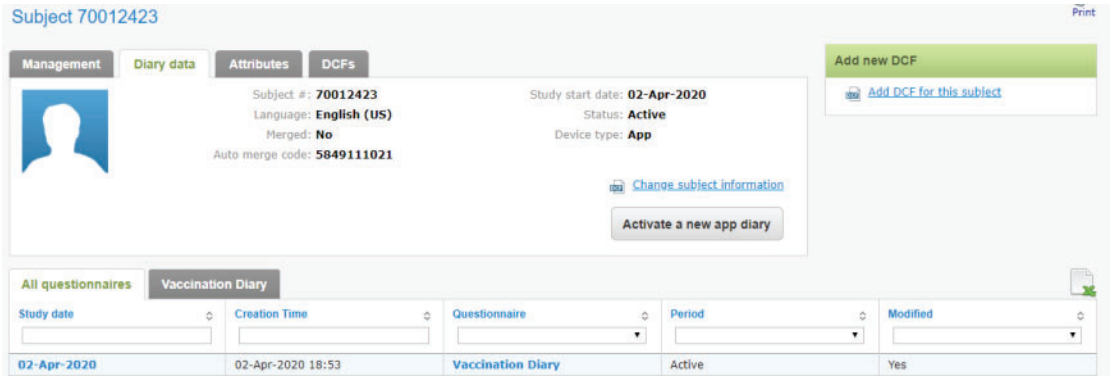
7.5 Software Updates

Site users/participants do not need to take any special action to perform a software update during the course of the study; any available update is automatically downloaded when the TrialMax App is opened and logged in. The login process may appear to take longer than usual when there is a software update, however a percentage will be displayed on the device indicating progress.

8 Managing Participants in TrialManager

8.1 Participant Card

Upon clicking on a participant number from the main page in TrialManager, the participant/subject's information card will display:



This will show details for the participant, including: language, participant status, study group, study start date, and the status of App installation.

Here is where you will activate a new App for a participant due to loss, theft, or change in provision device over the course of the study.

8.2 Activating a new App for an Existing Participant

This section will explain how the participant and site will handle activating new Apps for existing participants.

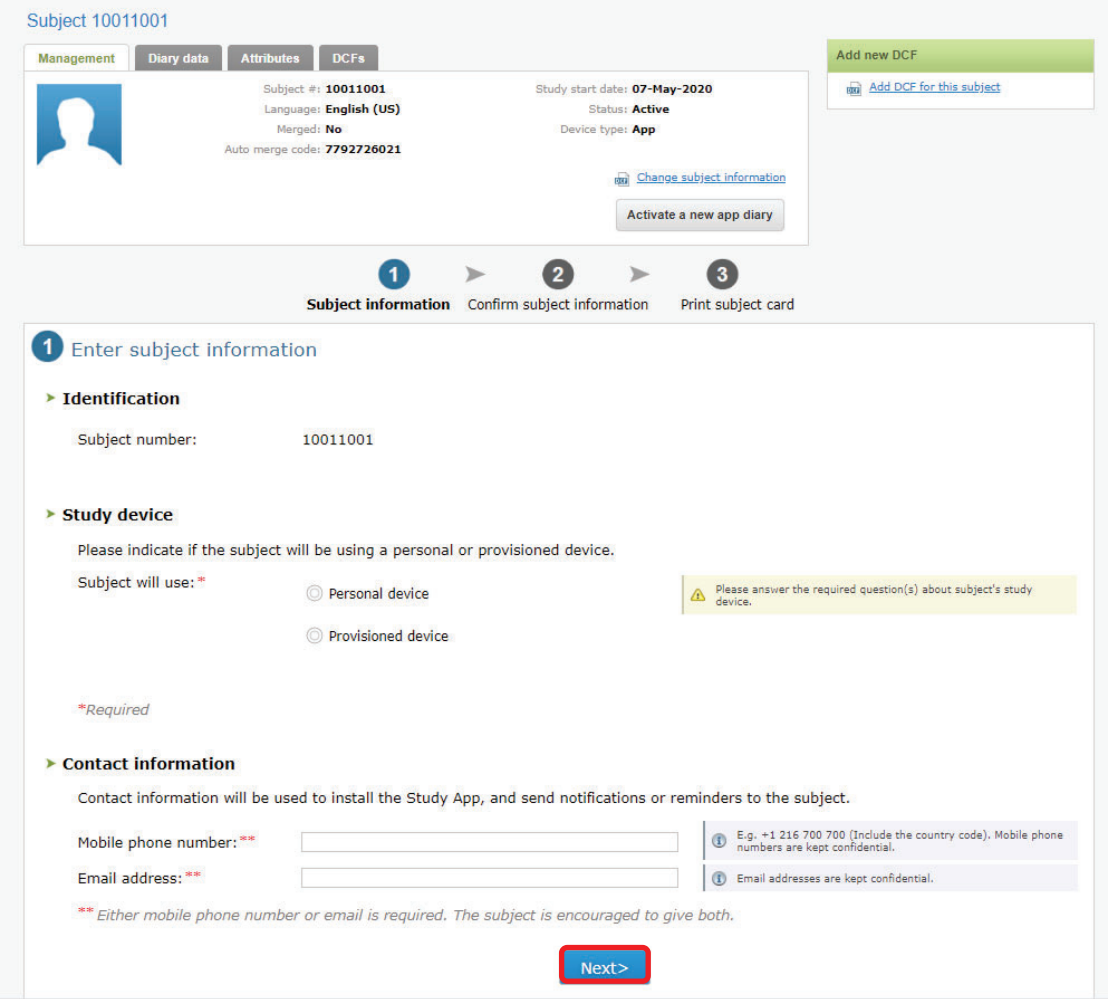
There are three instances in which a new App activation may be needed:

1) If the participant needs a new activation code due broken device, loss or theft of device, changing device during the study, or
2) If the participant has not used their provided activation code within 72 hours which is the expiration limit. This should not occur since the participant is to activate the app as soon as possible at the visit, or
3) If the subject is switching between using their personal device and a provisioned device.

The steps to handle either of these situations are the same:

Login to TrialManager and select the appropriate participant. From the participant card screen, select the 'Activate a new app diary' button

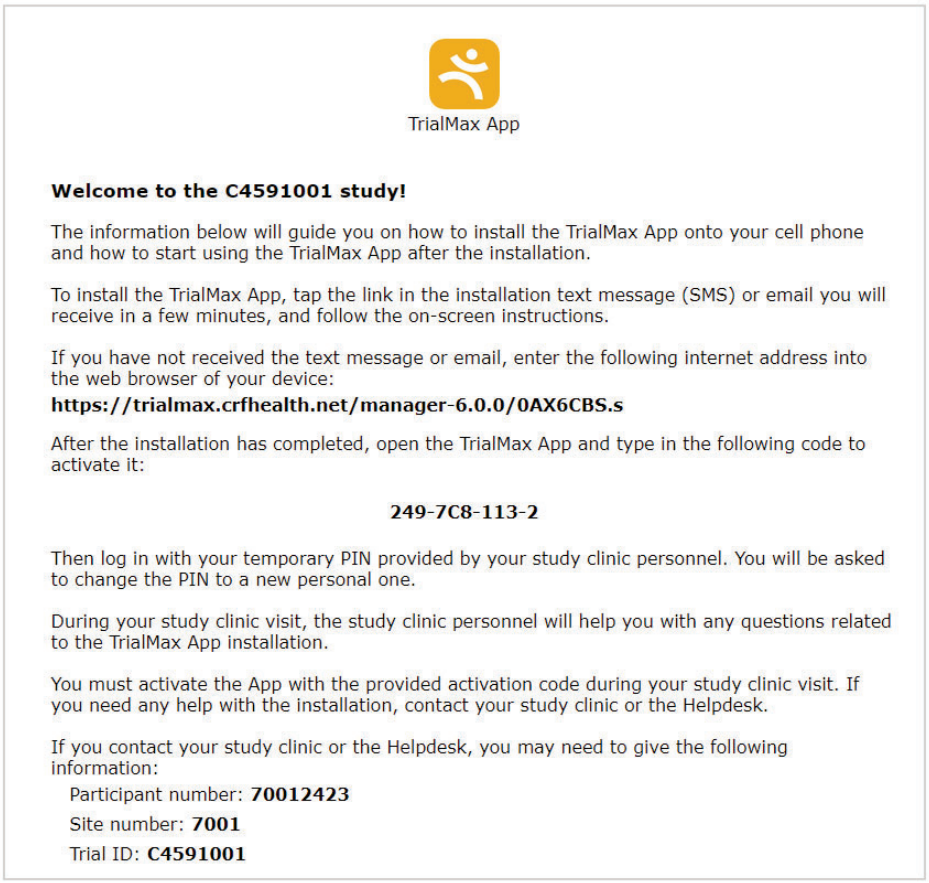
You will be required to select the participant's mobile phone number and/or email address. Once entered, select 'Next'.



On the next page, make sure the entered information is correct, then select “Confirm”.

You will then receive a message on screen that will confirm that the participant was created successfully. You will also see displayed a Participant card that is sent to the participant via email/SMS (if provided). This Participant card contains their new activation code and applicable instructions for getting set up with the App. TrialManager will also display a copy of the card which can be printed to make it more convenient for the participant.

Press ‘Exit’ to return to your site in TrialManager.



TrialMax App

Welcome to the C4591001 study!

The information below will guide you on how to install the TrialMax App onto your cell phone and how to start using the TrialMax App after the installation.

To install the TrialMax App, tap the link in the installation text message (SMS) or email you will receive in a few minutes, and follow the on-screen instructions.

If you have not received the text message or email, enter the following internet address into the web browser of your device:
https://trialmax.crfhealth.net/manager-6.0.0/0AX6CBS.s

After the installation has completed, open the TrialMax App and type in the following code to activate it:

249-7C8-113-2

Then log in with your temporary PIN provided by your study clinic personnel. You will be asked to change the PIN to a new personal one.

During your study clinic visit, the study clinic personnel will help you with any questions related to the TrialMax App installation.

You must activate the App with the provided activation code during your study clinic visit. If you need any help with the installation, contact your study clinic or the Helpdesk.

If you contact your study clinic or the Helpdesk, you may need to give the following information:

Participant number: **70012423**
Site number: **7001**
Trial ID: **C4591001**

The participant should then follow the appropriate steps to install and/or activate their App as outlined in the **Participant Setup** section of this guide.

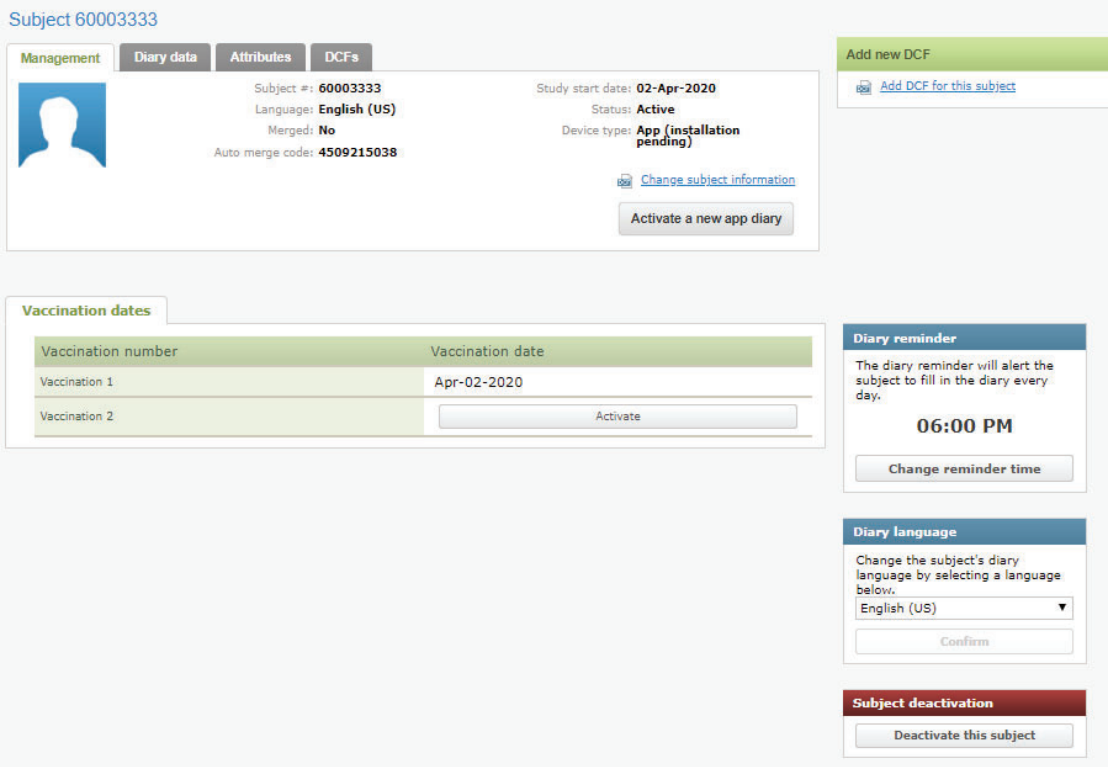
8.3 Management tab

Upon clicking on a participant number from the main page in TrialManager, the participant's information card will display. Clicking on the button titled 'Management' will bring you to a page displaying several options/settings for that participant. Here you can log vaccination dates, update Daily Diary reminder times, change participant language for the App, add or update participant information, and deactivate a participant from the study. Details for each activity are provided in the following sections.

8.3.1 Activating a New Vaccination

When a participant comes in for the first vaccination the participant needs to be set up on TrialManager. The vaccination is automatically activated on the day of a new participant set up, for instance, in the example below, the participant was set up on TrialManager, and vaccinated on 02-Apr-2020.

****If their vaccination date is not set in TrialManager before they leave the site office, they will NOT be able to complete their Daily Diary. Please be sure this is done before they leave.****

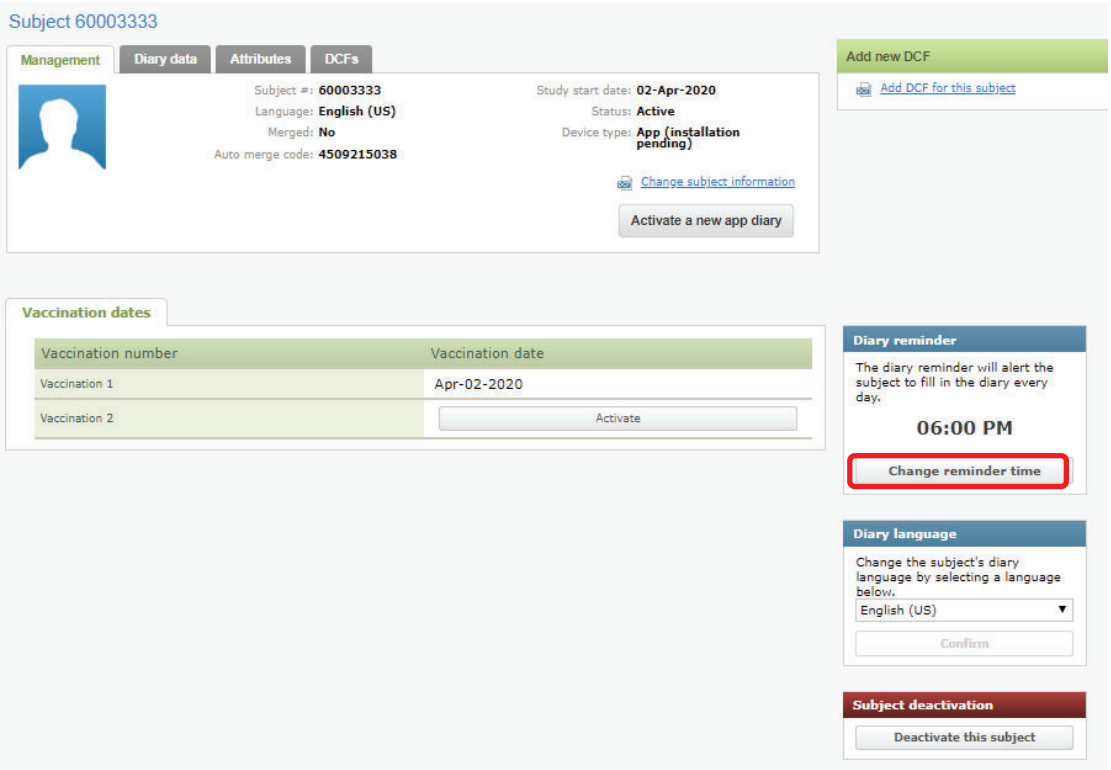


To activate subsequent diaries, click 'Activate' next to the appropriate visit. You will then be asked to select the date of the next vaccination. In the example above, Vaccination 2 still requires activation.

8.3.2 Changing Daily Diary Reminder Time

Site staff have the ability to adjust the time that reminder notifications will be sent to participants to complete their Daily Diary each day (during the post-vaccination periods). This can be modified by accessing the 'Management' tab in TrialManager for the particular participant.

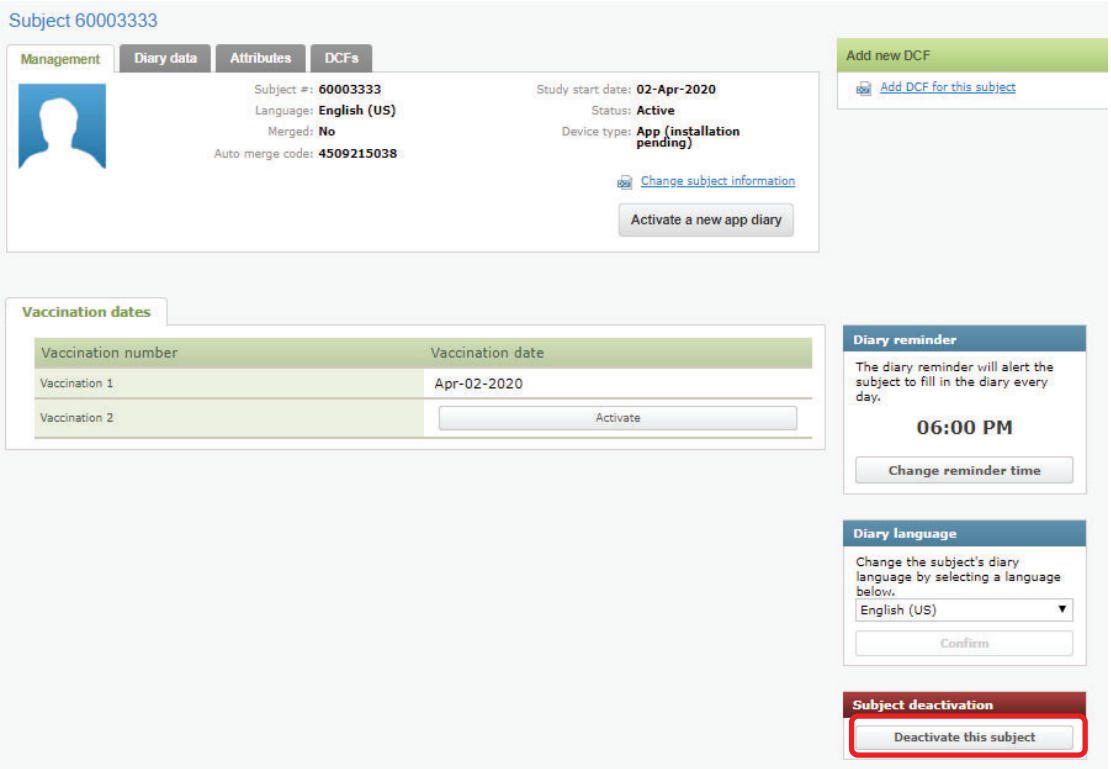
Additionally, participants may change this on their own by logging into the App and selecting 'Information and Settings' from the main menu screen. This will lead them to several options including 'Diary Reminder' which will allow them to adjust the time. The permitted window for reminders to be sent is between 6:00pm and 10:00pm in 15-minute increments.



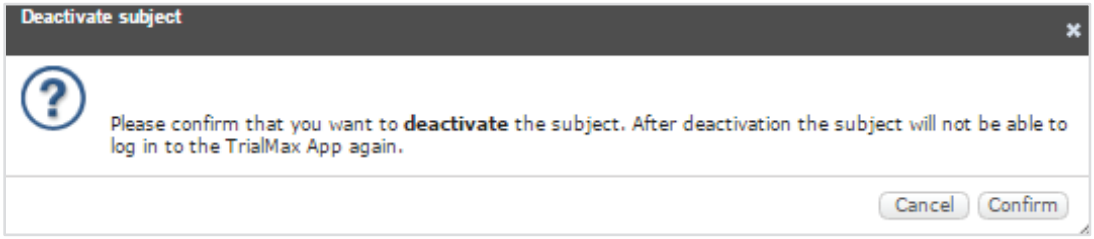
8.4 Deactivating a Participant from the Study

Whether the participant needs to be terminated early or has reached end of study, the participant must be deactivated by the site in TrialManager so that they can no longer login to the App and record study data.

This can be handled by accessing the 'Management' tab in TrialManager for the particular participant. Selecting 'Deactivate this participant' at the very bottom of the page (red header) will deactivate the participant and prevent further login to the App.



Upon clicking this button, you will be asked to confirm this is the desired action:



Selecting “Confirm” will successfully deactivate the participant while clicking “Cancel” will return you to the management tab for that participant.

Once deactivated, participants will no longer display on the ‘Active Participants’ tab in your main page of TrialManager. There is a separate tab titled ‘Deactivated Participants’ that will list any participants who have been deactivated.

8.5 Participant Travel

All provisioned devices will update the time zone automatically if the participant travels between different time zones.

9 How to Request Additional Supplies

If a Site requires device re-supply (for example more provisioned devices than initially allocated in their first shipment), they can request it via the Helpdesk (see Helpdesk phone number in Helpdesk Operating Hours). The request must be approved by the Pfizer Study Team, as all initial site allocations are predetermined.

IMPORTANT NOTE: Remember that provisioned devices can be reused after one participant has finished using the device.

Once approved, it will take 5 business days to prepare any additional shipments. These will be shipped with standard delivery service.

Replacement device requests (for example for devices that are lost or broken during use) should be requested via the Helpdesk. A return shipment label will be provided, along with a Faulty Device Return form to indicate why a replacement is needed.

10 How to return the provisioned devices

At the end of the study ALL devices must be returned to Signant Health.

When returning devices to Signant Health, UPS will need to pick them up. If the site does not have a regular pickup, they will have to call their local UPS office for a pickup. The UPS number is different in each country. The UPS driver can bring a manual waybill to the site if they do not have one. Please see Appendix A for US Logistics device returns instructions.

If you need to return a faulty device to Signant Health, make sure to include a completed Faulty Device Return Form (refer to Signant Health Helpdesk for a form) with the return. Only devices with a Faulty Device Return Form included will be investigated for any unsent data.

11 Frequently Asked Questions

Q: Where can I get more help?

A: Please contact the Signant Health Helpdesk. The Helpdesk is available 24/7 via the phone number provided at the beginning of this guide or on the participant's Quick Reference Guide or Device Label. Please make sure to provide as much information as you can about the problem. For any protocol or health-related questions, please contact your study monitor.

Q: How often should the provisioned device be charged?

A: Please be sure to leave the provisioned device plugged into the charger when not in use to keep it fully charged.

Q: What do I do if my provisioned device does not switch on?

A: Charge the provisioned device for two (2) hours. After charging, turn the device on. If the home screen with message and App icons does not appear, call the Helpdesk.

Q: A participant forgot their PIN code and cannot use their provisioned device. How can the PIN code be retrieved?

A: The participant's PIN code can be retrieved. The participant should call the helpdesk who will retrieve their original PIN code.

Q: How will the participant know how to send data?

A: The App will do it automatically, as long as the device is online. The App will send data each time the participant logs in, and also when saving study answers.

Q: A participant forgot to complete their Daily Diary on one day. Can that be added later on?

A: No. Data cannot be entered retrospectively. However, the participant can update their symptoms – both experience and severity within the same day.

Q: What should be done if the device is unable to send data?

A: As soon as the participant logs into the App, unsent data will be sent immediately once a connection is established. If the participant cannot seem to access a connection, please remind them that all data will be saved and automatically sent the next time they use the device online. If they continue to have issues with data sending, please contact helpdesk.

Q: Is the participant able to change the time and/or settings on a provisioned device?

A: The provisioned device is locked to only enable usage of the App and WiFi setup. The participant cannot change the time or make any other changes to the settings. Also, the device uses the network-provided date and time, so if the participant travels to a different time zone or there are changes in daylight savings, the time will automatically be updated.

Q: Can the participant send data while away on vacation in another country or region?

A: Yes, as long as they can connect to a network. Because of time zone differences, the time of entry may appear different.

Q: What happens if the participant forgets to log out of the App?

A: If the participant does not log out of the App, the App will automatically log the participant out. Please note that any unsaved answers will be deleted from the App at that time.

Q: Will the Helpdesk answer questions related to the Daily Diary itself?

A: The Helpdesk can provide answers on how the Daily Diary functions, but for any vaccine or study-related questions, the participant needs to contact the site.

Q: The participant does not understand the questions. What should I do?

A: If the participant does not understand the questions in the TrialMax App, you may have to explain what is being asked. The Helpdesk cannot answer any health-related questions. For further assistance with the questions, please contact your study monitor.

12 APPENDIX A: US LOGISTICS DEVICE RETURNS

US Logistics Device Returns

- When returning devices to Signant Health, UPS will need to pick them up.
- If the site does not have a regular pickup, they will have to call their local UPS office for a pickup. The number is different in each country.
- When calling for a pickup, the site will need to provide the **CRF Health (note CRF not Signant due to how account is set up with UPS) UPS account number 37V198 and postal code 19462** for the pickup charge to be billed on CRF Health(Signant Health)'s account. Sites with regular pickups will not have any issues with pickup charge.
- For returns from USA based sites can request their own return airway bill, quickly and easily. Using this portal sites will be able to choose a pick-up time which best suits their needs The site address is:

  https://row.ups.com/Ship/Ship/StandardShipGuest
- The UPS driver can bring a manual waybill to the site if they do not have one. Please complete the UPS Manual Waybill using the instructions below.
- For returns from outside of the USA or where a commercial invoice is required please email us-logistics@crfhealth.com please include all the information below and a UPS waybill will be emailed back to you.
  - Protocol Number/CRF Project code:
  - Name of sender:
  - Email address of person to be emailed the labels:
  - Contact number for sender:
  - Site Number:
  - Full Site Address:
  - How many electronic devices are being returned:
  - How many boxes will be used for the return of the devices:

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1003 10031122 (USA/NEW YORK/48/M)	Placebo	Dose 2/77	05NOV2020	24NOV2020	Neg/Neg/Neg	Fever	Pos/Neg, 06NOV2020, B.1.280
						New or increased cough	
						Chills	
C4591001 1003 10031167 (USA/NEW YORK/57/F)	Placebo	Dose 2/67	02NOV2020	11DEC2020	Neg/Neg/Neg	New or increased cough	Neg/, 06NOV2020, NS
						New or increased shortness of breath	
						Sore throat	
		Dose 2/112	17DEC2020	16JAN2021	Neg/Neg/Neg	Fever	Pos/Pos, 19DEC2020, B.1.404
						New or increased cough	
						New or increased shortness of breath	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1003 10031204 (USA/NEW YORK/39/F)	Placebo	Dose 2/95	07DEC2020	12JAN2021	Neg/Neg/Neg	Chills New or increased muscle pain New loss of taste or smell Sore throat New or increased cough New or increased shortness of breath Chills New or increased muscle pain New loss of taste or smell Sore throat Diarrhea	Pos/Pos, 11DEC2020, B.1.349
C4591001 1005 10051358 (USA/NEW YORK/52/F)	Placebo	Dose 2/59	10JAN2021	20JAN2021	Neg/Neg/Neg	Fever	Pos/, 12JAN2021, B.1.243

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Sore throat	
C4591001 1005 10051360 (USA/NEW YORK/77/M)	Placebo	Dose 2/29	10DEC2020	26DEC2020	Neg/Neg/Neg	Fever	Pos/, 12DEC2020, B.1.243
						New or increased cough	
						Sore throat	
C4591001 1006 10061012 (USA/UTAH/53/M)	Placebo	Dose 2/68	06NOV2020	16NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 06NOV2020, B.1.2
						New or increased shortness of breath	
						New or increased muscle pain	
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1006 10061025 (USA/UTAH/65/F)	Placebo	Dose 2/82	21NOV2020	02DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 24NOV2020, B.1.2
						New or increased shortness of breath	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1006 10061066 (USA/UTAH/39/F)	Placebo	Dose 2/59	11NOV2020		Neg/Neg/Neg	New or increased cough	Pos/, 11NOV2020, B.1.2
						Sore throat	
C4591001 1006 10061075 (USA/UTAH/42/F)	Placebo	Dose 2/69	16NOV2020	04JAN2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 16NOV2020, B.1.2
						Sore throat	
C4591001 1006 10061076 (USA/UTAH/61/F)	Placebo	Dose 2/123	11JAN2021	16JAN2021	Neg/Neg/Neg	New or increased	Pos/, 12JAN2021, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						shortness of breath	
						Sore throat	
C4591001 1006 10061084 (USA/UTAH/27/F)	Placebo	Dose 2/48	27OCT2020	10NOV2020	Neg/Neg/Neg	Fever	Pos/, 28OCT2020, B.1.2
						New or increased cough	
C4591001 1006 10061091 (USA/UTAH/20/F)	Placebo	Dose 2/50	30OCT2020	10NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 01NOV2020, B.1.2
						Sore throat	
C4591001 1006 10061114 (USA/UTAH/21/M)	Placebo	Dose 2/35	20OCT2020	03NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 23OCT2020, B.1.443
						New or increased shortness of breath	
						New or increased muscle pain	
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						Sore throat	
C4591001 1006 10061206 (USA/UTAH/12/M)	Placebo	Dose 2/10	01JAN2021	03JAN2021	Neg/Neg/Neg	Fever	Pos/, 01JAN2021, B.1.400
C4591001 1006 10061260 (USA/UTAH/12/F)	Placebo	Dose 2/17	21JAN2021	27JAN2021	Neg/Neg/Neg	Sore throat	Pos/, 21JAN2021, B.1.1.29
C4591001 1006 10061284 (USA/UTAH/14/M)	Placebo	Dose 2/8	15JAN2021	16JAN2021	Neg/Neg/Pos	Diarrhea	Pos/, 18JAN2021, B.1.142
C4591001 1007 10071163 (USA/OHIO/80/F)	Placebo	Dose 2/76	14NOV2020	28NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 27NOV2020, B.1.2
C4591001 1007 10071246 (USA/OHIO/30/F)	Placebo	Dose 2/129	16JAN2021	19JAN2021	Neg/Neg/Neg	Sore throat	Pos/, 19JAN2021, B.1.2
C4591001 1007 10071306 (USA/OHIO/58/F)	Placebo	Dose 2/60	31DEC2020	16JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 01JAN2021, B.1.2
						New or increased shortness of breath	
						Chills	
						Sore throat	
						Diarrhea	
C4591001 1007 10071425 (USA/OHIO/50/F)	Placebo	Dose 2/25	06DEC2020	11DEC2020	Neg/Neg/Neg	Sore throat	Pos/, 11DEC2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1007 10071448 (USA/OHIO/16/M)	Placebo	Dose 2/46	16JAN2021	24JAN2021	Neg/Neg/Neg	Fever	Pos/, 19JAN2021, B.1.234
C4591001 1007 10071456 (USA/OHIO/17/F)	Placebo	Dose 2/35	10JAN2021	14JAN2021	Neg/Neg/Neg	Sore throat	Pos/, 13JAN2021, B.1.240
C4591001 1007 10071527 (USA/OHIO/12/M)	Placebo	Dose 2/10	07JAN2021	10JAN2021	Neg/Neg/Pos	Sore throat	Pos/Pos, 10JAN2021, B.1.2
C4591001 1007 10071559 (USA/OHIO/14/F)	Placebo	Dose 2/11	14JAN2021	26JAN2021	Neg/Neg/Neg	Fever Sore throat	Pos/, 15JAN2021, B.1.2
C4591001 1007 10071603 (USA/OHIO/13/M)	Placebo	Dose 2/35	22FEB2021	28FEB2021	Neg/Neg/Neg	Fever New loss of taste or smell Sore throat	Pos/, 23FEB2021, B.1.2
C4591001 1008 10081011 (USA/MISSOURI/55/F)	Placebo	Dose 2/52	22OCT2020	31OCT2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 26OCT2020, B.1.2
C4591001 1008 10081015 (USA/MISSOURI/33/M)	Placebo	Dose 2/97	07DEC2020	12DEC2020	Neg/Neg/Neg	New or increased muscle pain Sore throat	Pos/, 14DEC2020, B.1.2
C4591001 1008 10081044 (USA/MISSOURI/58/F)	Placebo	Dose 2/66	12NOV2020	17NOV2020	Neg/Neg/Neg	Fever	Pos/, 13NOV2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						New or increased shortness of breath	
						New or increased muscle pain	
						Sore throat	
						Diarrhea	
C4591001 1008 10081048 (USA/MISSOURI/38/F)	Placebo	Dose 2/60	07NOV2020	27NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 11NOV2020, B.1.1.222
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1008 10081060 (USA/MISSOURI/71/F)	Placebo	Dose 2/78	25NOV2020	04DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 01DEC2020, B.1.2
						New loss of taste or smell	
C4591001 1008 10081069 (USA/MISSOURI/57/F)	Placebo	Dose 2/97	15DEC2020	22DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 16DEC2020, B.1.2
						Sore throat	
C4591001 1008 10081092 (USA/MISSOURI/62/F)	Placebo	Dose 2/76	29NOV2020	12DEC2020	Neg/Neg/Neg	Fever	Pos/, 30NOV2020, B.1.2
						New or increased cough	
						Sore throat	
						Diarrhea	
C4591001 1008 10081103 (USA/MISSOURI/35/F)	Placebo	Dose 2/86	10DEC2020	17DEC2020	Neg/Neg/Neg	Fever	Pos/, 17DEC2020, B.1.1.304
						New or increased cough	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 1008 10081123 (USA/MISSOURI/57/F)	Placebo	Dose 2/103	28DEC2020	22JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 30DEC2020, B.1.2
						New or increased shortness of breath	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1008 10081130 (USA/MISSOURI/52/F)	Placebo	Dose 2/32	17OCT2020	29OCT2020	Neg/Neg/Neg	New or increased shortness of breath	Pos/, 23OCT2020, INDETERMINATE
C4591001 1008 10081145 (USA/MISSOURI/78/M)	Placebo	Dose 2/97	26DEC2020	31DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 30DEC2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1008 10081153 (USA/MISSOURI/31/F)	Placebo	Dose 2/71	01DEC2020	04DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 02DEC2020, B.1.2
						New loss of taste or smell	
C4591001 1008 10081210 (USA/MISSOURI/57/F)	Placebo	Dose 2/58	25NOV2020	13DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 30NOV2020, B.1.311
						New or increased muscle pain	
C4591001 1008 10081214 (USA/MISSOURI/62/M)	Placebo	Dose 2/42	09NOV2020	13NOV2020	Neg/Neg/Neg	Fever	Pos/, 09NOV2020, B.1.2
						New or increased cough	
						New or increased shortness of breath	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1008 10081232 (USA/MISSOURI/53/F)	Placebo	Dose 2/79	16DEC2020	27DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 18DEC2020, B.1.311
						Sore throat	
C4591001 1008 10081281 (USA/MISSOURI/20/F)	Placebo	Dose 2/99	06JAN2021	19JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 08JAN2021, B.1.2
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1008 10081285 (USA/MISSOURI/60/F)	Placebo	Dose 2/57	27NOV2020	06DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 27NOV2020, B.1.2
						New or increased shortness of breath	
C4591001 1008 10081319 (USA/MISSOURI/79/F)	Placebo	Dose 2/31	04NOV2020	08NOV2020	Neg/Neg/Neg	Chills	Pos/, 06NOV2020, B.1.509
C4591001 1008 10081356 (USA/MISSOURI/63/M)	Placebo	Dose 2/25	31OCT2020	10NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 04NOV2020, B.1.311

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
C4591001 1008 10081415 (USA/MISSOURI/56/M)	Placebo	Dose 2/53	04DEC2020	14DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 07DEC2020, B.1.2
C4591001 1008 10081493 (USA/MISSOURI/19/M)	Placebo	Dose 2/47	29NOV2020	04DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 01DEC2020, B.1.428
						Chills	
						New or increased muscle pain	
C4591001 1008 10081563 (USA/MISSOURI/72/M)	Placebo	Dose 2/14	08NOV2020	20NOV2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 17NOV2020, B.1.2
C4591001 1008 10081596 (USA/MISSOURI/38/F)	Placebo	Dose 2/61	02JAN2021	09JAN2021	Neg/Neg/Neg	Fever	Pos/, 04JAN2021, B.1.1.222
						New or increased cough	
						Chills	
C4591001 1008 10081612 (USA/MISSOURI/38/F)	Placebo	Dose 2/24	27NOV2020	05DEC2020	Neg/Neg/Neg	Fever	Pos/, 30NOV2020, B.1.1.7

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Chills	
C4591001 1008 10081664 (USA/MISSOURI/49/F)	Placebo	Dose 2/22	02DEC2020	14DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 04DEC2020, B.1.243
						Sore throat	
C4591001 1009 10091005 (USA/UTAH/31/M)	Placebo	Dose 2/66	06NOV2020	11NOV2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 03NOV2020, B.1.2
C4591001 1009 10091018 (USA/UTAH/70/M)	Placebo	Dose 2/89	01DEC2020		Neg/Neg/Neg	New or increased cough	Pos/, 04DEC2020, B.1.2
						New loss of taste or smell	
C4591001 1009 10091102 (USA/UTAH/22/F)	Placebo	Dose 2/115	08JAN2021	20JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 13JAN2021, B.1.429
C4591001 1009 10091110 (USA/UTAH/46/F)	Placebo	Dose 2/69	21NOV2020	09DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 20NOV2020, B.1.2
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1009 10091114 (USA/UTAH/77/F)	Placebo	Dose 2/105	27DEC2020	15JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 31DEC2020, B.1.2
						Diarrhea	
C4591001 1009 10091115 (USA/UTAH/78/M)	Placebo	Dose 2/108	30DEC2020	17JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 04JAN2021, B.1.2
C4591001 1009 10091128 (USA/UTAH/51/M)	Placebo	Dose 2/30	15OCT2020	24FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 20OCT2020, B.1.2
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1009 10091129 (USA/UTAH/38/M)	BNT162b2 (30 µg)	Dose 2/135	28JAN2021		Neg/Neg/Neg	Fever	Pos/, 08FEB2021, B.1.427

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1009 10091153 (USA/UTAH/68/M)	Placebo	Dose 2/66	29NOV2020	06DEC2020	Unk/Neg/Neg	New or increased cough	Pos/, 01DEC2020, B.1.1.161
						Sore throat	
C4591001 1009 10091208 (USA/UTAH/15/M)	Placebo	Dose 2/66	10JAN2021	14JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 10JAN2021, B.1.2
						New or increased shortness of breath	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Sore throat	
C4591001 1009 10091214 (USA/UTAH/47/F)	Placebo	Dose 2/24	27NOV2020	09DEC2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 30NOV2020, B.1.210
C4591001 1009 10091235 (USA/UTAH/16/M)	Placebo	Dose 2/17	27NOV2020	01DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 30NOV2020, B.1.2
						Sore throat	
						Diarrhea	
C4591001 1009 10091236 (USA/UTAH/45/F)	Placebo	Dose 2/16	26NOV2020	03DEC2020	Neg/Neg/Neg	Sore throat	Pos/, 30NOV2020, B.1
C4591001 1009 10091282 (USA/UTAH/14/M)	Placebo	Dose 2/42	01FEB2021	02FEB2021	Neg/Neg/Neg	Chills	Pos/, 02FEB2021, B.1.427
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1009 10091412 (USA/UTAH/15/M)	Placebo	Dose 2/29	01MAR2021		Neg/Neg/Neg	New or increased cough	Pos/, 01MAR2021, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						Sore throat	
C4591001 1012 10121006 (USA/ARIZONA/52/M)	Placebo	Dose 2/71	06NOV2020	23NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 15NOV2020, B.1.2
C4591001 1012 10121042 (USA/ARIZONA/63/M)	Placebo	Dose 2/71	18NOV2020		Neg/Neg/Neg	Fever	Pos/, 23NOV2020, B.1.2
						New or increased cough	
						New loss of taste or smell	
						Diarrhea	
C4591001 1012 10121059 (USA/ARIZONA/28/F)	Placebo	Dose 2/95	13DEC2020	10FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 15DEC2020, B.1.2
						New or increased shortness of breath	
						New loss of taste or smell	
						Sore throat	
C4591001 1012 10121164 (USA/ARIZONA/37/M)	Placebo	Dose 2/84	23DEC2020	02JAN2021	Neg/Neg/Neg	Fever	Pos/, 24DEC2020, B.1.189

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Diarrhea	
C4591001 1013 10131014 (USA/FLORIDA/29/M)	Placebo	Dose 2/131	29DEC2020	05JAN2021	Neg/Neg/Neg	Fever	Pos/, 05JAN2021, B.1.234
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Diarrhea	
C4591001 1013 10131064 (USA/FLORIDA/28/F)	Placebo	Dose 2/155	25JAN2021	03FEB2021	Neg/Neg/Neg	Fever	Pos/, 28JAN2021, B.1
						New or increased cough	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Sore throat	
C4591001 1013 10131166 (USA/FLORIDA/50/M)	Placebo	Dose 2/117	28DEC2020	13JAN2021	Neg/Neg/Unk	New or increased cough	Pos/, 05JAN2021, B.1.2
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1013 10131167 (USA/FLORIDA/50/F)	Placebo	Dose 2/119	30DEC2020	13JAN2021	Neg/Neg/Neg	Chills	Pos/, 05JAN2021, B.1.2
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1013 10131257 (USA/FLORIDA/61/F)	Placebo	Dose 2/89	11DEC2020	30DEC2020	Neg/Neg/Neg	New or increased cough Chills New or increased muscle pain Sore throat Diarrhea Vomiting	Pos/, 13DEC2020, B.1.2
C4591001 1013 10131288 (USA/FLORIDA/53/M)	Placebo	Dose 2/11	25SEP2020	06OCT2020	Neg/Neg/Neg	New or increased cough New or increased shortness of breath Chills New or increased muscle pain New loss of taste or smell	Pos/, 28SEP2020, B.1.396

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1013 10131296 (USA/FLORIDA/44/M)	Placebo	Dose 2/72	25NOV2020	11DEC2020	Neg/Neg/Neg	Fever	Pos/, 30NOV2020, B.1.1.122
						New or increased cough	
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						Sore throat	
						Diarrhea	
C4591001 1013 10131396 (USA/FLORIDA/41/M)	Placebo	Dose 2/75	05DEC2020	09DEC2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 08DEC2020, B.1.2
C4591001 1013 10131398 (USA/FLORIDA/36/M)	Placebo	Dose 2/86	16DEC2020	21DEC2020	Pos/Neg/Neg	New or increased cough	Pos/, 17DEC2020, B.1.234
						Chills	
						Sore throat	
C4591001 1013 10131409 (USA/FLORIDA/35/M)	Placebo	Dose 2/90	21DEC2020	03JAN2021	Neg/Neg/Neg	Fever	Pos/, 30DEC2020, B.1

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Chills	
						Sore throat	
C4591001 1013 10131460 (USA/FLORIDA/56/F)	BNT162b2 (30 µg)	Dose 2/93	30DEC2020	27JAN2021	Neg/Neg/Neg	Chills	Pos/, 04JAN2021, B.1.1.222
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1013 10131471 (USA/FLORIDA/20/M)	Placebo	Dose 2/46	13NOV2020	16NOV2020	Neg/Neg/Neg	Fever	Pos/, 17NOV2020, B.1.280
						Chills	
						New or increased muscle pain	
C4591001 1013 10131475 (USA/FLORIDA/49/F)	Placebo	Dose 2/23	22OCT2020	25OCT2020	Neg/Neg/Neg	New or increased cough	Pos/, 26OCT2020, B.1.369

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Sore throat	
C4591001 1013 10131539 (USA/FLORIDA/70/F)	Placebo	Dose 2/94	07JAN2021	17JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 08JAN2021, B.1.2
						Sore throat	
C4591001 1013 10131540 (USA/FLORIDA/71/M)	Placebo	Dose 2/91	04JAN2021	06JAN2021	Neg/Neg/Neg	Fever	Pos/, 06JAN2021, B.1.2
						Chills	
C4591001 1013 10131720 (USA/FLORIDA/55/M)	BNT162b2 (30 µg)	Dose 2/93	05FEB2021	03MAR2021	Neg/Neg/Neg	New or increased cough	Pos/, 09FEB2021, A.2.4
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						Sore throat	
						Diarrhea	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						Vomiting	
C4591001 1013 10131758 (USA/FLORIDA/60/M)	Placebo	Dose 2/48	28DEC2020		Neg/Neg/Neg	New or increased shortness of breath	Pos/, 30DEC2020, B.1.1.222
						Chills	
						New or increased muscle pain	
C4591001 1015 10151094 (USA/MASSACHUSETTS/50/F)	Placebo	Dose 2/123	14JAN2021		Neg/Neg/Neg	Fever	Pos/, 19JAN2021, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1016 10161003 (USA/KENTUCKY/23/F)	Placebo	Dose 2/57	14OCT2020	26OCT2020	Neg/Neg/Neg	Fever	Pos/, 16OCT2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Chills	
						New loss of taste or smell	
C4591001 1016 10161004 (USA/KENTUCKY/51/F)	BNT162b2 (30 µg)	Dose 2/58	15OCT2020	22OCT2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 17OCT2020, B.1.2
						Sore throat	
C4591001 1016 10161017 (USA/KENTUCKY/18/F)	Placebo	Dose 2/19	07SEP2020	29OCT2020	Neg/Neg/Neg	Fever	Pos/, 09SEP2020, B.1.1.4
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1016 10161035 (USA/KENTUCKY/70/F)	Placebo	Dose 2/67	29OCT2020	29OCT2020	Neg/Neg/Neg	New or increased cough	Pos/, 30OCT2020, B.1.2
C4591001 1016 10161048 (USA/KENTUCKY/52/F)	Placebo	Dose 2/75	06NOV2020	31JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 06NOV2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1016 10161114 (USA/KENTUCKY/22/F)	BNT162b2 (30 µg)	Dose 2/122	02JAN2021	08JAN2021	Neg/Neg/Neg	Chills	Pos/, 04JAN2021, B.1.2
						New or increased muscle pain	
C4591001 1016 10161123 (USA/KENTUCKY/48/F)	Placebo	Dose 2/98	09DEC2020	25DEC2020	Neg/Neg/Neg	Fever	Pos/, 11DEC2020, B.1.2
						Chills	
C4591001 1016 10161146 (USA/KENTUCKY/59/F)	Placebo	Dose 2/89	07DEC2020	20DEC2020	Neg/Neg/Neg	Fever	Pos/, 10DEC2020, B.1.2
						New or increased cough	
						New or increased muscle pain	
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1016 10161183 (USA/KENTUCKY/31/F)	Placebo	Dose 2/32	16OCT2020	01NOV2020	Neg/Neg/Neg	Sore throat Fever New or increased cough Chills New or increased muscle pain New loss of taste or smell Sore throat Diarrhea Vomiting	Pos/ (R1 Pos), 16OCT2020 (23OCT2020), B.1.2 (B.1.2)
C4591001 1016 10161207 (USA/KENTUCKY/62/F)	Placebo	Dose 2/27	14OCT2020	01NOV2020	Neg/Neg/Neg	New or increased cough Chills New or increased muscle pain	Pos/, 16OCT2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						Sore throat	
C4591001 1016 10161209 (USA/KENTUCKY/33/F)	Placebo	Dose 2/98	28DEC2020	05JAN2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 04JAN2021, B.1.2
C4591001 1016 10161305 (USA/KENTUCKY/16/M)	Placebo	Dose 2/8	09NOV2020	13NOV2020	Neg/Neg/Pos	New or increased cough	Pos/, 11NOV2020, QNS
						New loss of taste or smell	
C4591001 1016 10161317 (USA/KENTUCKY/17/M)	Placebo	Dose 2/51	26DEC2020	03JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 29DEC2020, B.1.2
						New or increased muscle pain	
C4591001 1018 10181083 (USA/TEXAS/45/M)	Placebo	Dose 2/72	06NOV2020	16NOV2020	Neg/Neg/Neg	Fever	Pos/, 15NOV2020, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						Diarrhea	
						Vomiting	
C4591001 1018 10181107 (USA/TEXAS/26/F)	BNT162b2 (30 µg)	Dose 2/125	02JAN2021		Neg/Neg/Neg	New or increased cough	Pos/, 05JAN2021, B.1.2
						New loss of taste or smell	
C4591001 1018 10181198 (USA/TEXAS/50/F)	Placebo	Dose 2/55	04NOV2020	05NOV2020	Neg/Neg/Neg	Fever	Pos/, 05NOV2020, B.1.234
						New or increased cough	
C4591001 1018 10181289 (USA/TEXAS/49/M)	Placebo	Dose 2/88	31DEC2020	13JAN2021	Neg/Neg/Neg	Fever	Pos/, 03JAN2021, B.1.2
						New or increased cough	
						New or increased muscle pain	
C4591001 1019 10191038 (USA/TEXAS/47/F)	Placebo	Dose 2/61	03NOV2020	18NOV2020	Neg/Neg/Neg	Fever	Pos/, 09NOV2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						New loss of taste or smell	
						Diarrhea	
C4591001 1019 10191184 (USA/TEXAS/52/M)	Placebo	Dose 2/36	05NOV2020	08DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 05NOV2020, B.1.2
						New or increased muscle pain	
						Vomiting	
C4591001 1019 10191200 (USA/TEXAS/67/M)	Placebo	Dose 2/77	22DEC2020	19JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 28DEC2020, B.1.2
C4591001 1019 10191242 (USA/TEXAS/28/F)	Placebo	Dose 2/70	29DEC2020	05JAN2021	Neg/Neg/Neg	Fever	Pos/, 31DEC2020, B.1.2
						New or increased cough	
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1019 10191251 (USA/TEXAS/19/M)	Placebo	Dose 2/45	06DEC2020	16DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 10DEC2020, B.1
						New loss of taste or smell	
C4591001 1019 10191256 (USA/TEXAS/49/M)	Placebo	Dose 2/41	08DEC2020	15DEC2020	Neg/Neg/Neg	Fever	Pos/, 11DEC2020, B.1.403
						New or increased cough	
						Chills	
						Sore throat	
C4591001 1021 10211093 (USA/NORTH CAROLINA/72/M)	Placebo	Dose 2/99	21DEC2020		Neg/Neg/Neg	New or increased cough	Pos/, 10JAN2021, B.1.1.244
C4591001 1021 10211122 (USA/NORTH CAROLINA/57/F)	Placebo	Dose 2/114	12JAN2021	12FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 14JAN2021, B.1.2
						Sore throat	
C4591001 1022 10221053 (USA/WASHINGTON/64/F)	Placebo	Dose 2/112	03JAN2021	10JAN2021	Neg/Neg/Neg	Chills	Pos/, 04JAN2021, B.1.2
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1024 10241080 (USA/NEW JERSEY/54/M)	Placebo	Dose 2/142	03FEB2021	21FEB2021	Neg/Neg/Neg	Vomiting Chills New or increased muscle pain New loss of taste or smell Sore throat	Pos/, 04FEB2021, A.2.4
C4591001 1024 10241092 (USA/NEW JERSEY/53/F)	Placebo	Dose 2/86	10DEC2020	13DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 11DEC2020, B.1.509
C4591001 1027 10271086 (USA/NORTH CAROLINA/46/F)	Placebo	Dose 2/77	03DEC2020	18DEC2020	Neg/Neg/Neg	New or increased cough Sore throat	Pos/, 07DEC2020, B.1
C4591001 1027 10271202 (USA/NORTH CAROLINA/57/F)	Placebo	Dose 2/68	19DEC2020	01JAN2021	Neg/Neg/Neg	New or increased cough New or increased muscle pain	Pos/Pos, 21DEC2020, B.1.1.139
C4591001 1028 10281038 (USA/NORTH DAKOTA/53/F)	Placebo	Dose 2/31	10OCT2020	22OCT2020	Neg/Neg/Neg	Fever	Pos/, 13OCT2020, B.1

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Sore throat	
C4591001 1028 10281054 (USA/NORTH DAKOTA/51/M)	Placebo	Dose 2/63	16NOV2020	18DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 20NOV2020, B.1.2
						Chills	
C4591001 1028 10281057 (USA/NORTH DAKOTA/63/M)	Placebo	Dose 2/93	29DEC2020	08JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 30DEC2020, B.1.2
						New or increased muscle pain	
						Sore throat	
C4591001 1028 10281100 (USA/NORTH DAKOTA/47/F)	Placebo	Dose 2/19	11OCT2020	21OCT2020	Neg/Neg/Neg	New or increased cough	Pos/, 13OCT2020, B.1.240
C4591001 1028 10281122 (USA/NORTH DAKOTA/44/F)	Placebo	Dose 2/53	15NOV2020	27NOV2020	Neg/Neg/Neg	Fever	Pos/, 18NOV2020, B.1.2
						New or increased cough	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Vomiting	
C4591001 1028 10281132 (USA/NORTH DAKOTA/61/M)	Placebo	Dose 2/14	11OCT2020	21OCT2020	Neg/Neg/Neg	Fever	Pos/, 13OCT2020, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1028 10281138 (USA/NORTH DAKOTA/38/F)	Placebo	Dose 2/25	23OCT2020	03NOV2020	Neg/Neg/Neg	Fever	Pos/, 27OCT2020, B.1.400
						Chills	
						Sore throat	
						Diarrhea	
C4591001 1028 10281152 (USA/NORTH DAKOTA/51/M)	Placebo	Dose 2/94	30DEC2020	06JAN2021	Neg/Neg/Neg	Fever	Pos/, 02JAN2021, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1028 10281187 (USA/NORTH DAKOTA/82/M)	Placebo	Dose 2/59	09DEC2020	30DEC2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 09DEC2020, B.1
C4591001 1028 10281269 (USA/NORTH DAKOTA/29/F)	Placebo	Dose 2/9	19NOV2020	24NOV2020	Neg/Neg/Neg	Fever	Pos/, 19NOV2020, B.1
						New or increased cough	
						New or increased muscle pain	
						Sore throat	
C4591001 1030 10301025 (USA/OHIO/66/F)	Placebo	Dose 2/85	15DEC2020	24DEC2020	Neg/Neg/Neg	Sore throat	Pos/, 16DEC2020, B.1.2
C4591001 1030 10301048 (USA/OHIO/33/M)	Placebo	Dose 2/74	05DEC2020	11DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 06DEC2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1030 10301069 (USA/OHIO/29/F)	Placebo	Dose 2/64	04DEC2020	10DEC2020	Neg/Neg/Neg	Sore throat New or increased cough New loss of taste or smell	Pos/, 05DEC2020, B.1.2
C4591001 1030 10301088 (USA/OHIO/39/F)	Placebo	Dose 2/87	30DEC2020	12JAN2021	Neg/Neg/Neg	Fever New or increased cough Chills New or increased muscle pain	Pos/, 02JAN2021, B.1.2
C4591001 1030 10301113 (USA/OHIO/30/F)	Placebo	Dose 2/35	12NOV2020	17NOV2020	Neg/Neg/Neg	New or increased cough New loss of taste or smell Diarrhea	Pos/, 19NOV2020, B.1.2
C4591001 1030 10301123 (USA/OHIO/45/F)	Placebo	Dose 2/64	15DEC2020	30DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 21DEC2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						Sore throat	
C4591001 1036 10361035 (USA/TENNESSEE/63/M)	BNT162b2 (30 µg)	Dose 2/71	24NOV2020	29NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 01DEC2020, B.1.265
						New loss of taste or smell	
						Diarrhea	
C4591001 1037 10371004 (USA/TENNESSEE/57/F)	Placebo	Dose 2/69	16NOV2020	03FEB2021	Neg/Neg/Neg	Chills	Pos/, 19NOV2020, B.1.2
C4591001 1037 10371016 (USA/TENNESSEE/84/M)	Placebo	Dose 2/88	05DEC2020	11DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 10DEC2020, B.1.2
						New or increased muscle pain	
C4591001 1037 10371036 (USA/TENNESSEE/62/M)	Placebo	Dose 2/52	31OCT2020	11DEC2020	Neg/Neg/Neg	Fever	Pos/, 05NOV2020, B.1.361
						New or increased cough	
						Chills	
C4591001 1037 10371113 (USA/TENNESSEE/71/F)	Placebo	Dose 2/70	29NOV2020	09DEC2020	Neg/Neg/Neg	Fever	Pos/, 02DEC2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Chills	
C4591001 1037 10371146 (USA/TENNESSEE/78/M)	Placebo	Dose 2/96	27DEC2020		Neg/Neg/Neg	New or increased cough	Pos/, 30DEC2020, B.1.2
						New or increased shortness of breath	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1037 10371155 (USA/TENNESSEE/55/M)	Placebo	Dose 2/75	12DEC2020		Unk/Neg/Neg	Fever	Pos/, 14DEC2020, B.1.2
						New or increased cough	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
						Sore throat	
C4591001 1037 10371187 (USA/TENNESSEE/78/M)	Placebo	Dose 2/69	06DEC2020	14DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 14DEC2020, B.1.2
						Chills	
C4591001 1037 10371193 (USA/TENNESSEE/76/F)	Placebo	Dose 2/36	05NOV2020	15NOV2020	Neg/Neg/Neg	Fever	Pos/, 17NOV2020, B.1.234
						New or increased shortness of breath	
						Chills	
						Diarrhea	
C4591001 1037 10371200 (USA/TENNESSEE/29/F)	Placebo	Dose 2/70	15DEC2020	27DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 16DEC2020, B.1.2
						New or increased shortness of breath	
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1037 10371280 (USA/TENNESSEE/58/M)	Placebo	Dose 2/28	10NOV2020	04DEC2020	Neg/Neg/Neg	Fever	Pos/, 11NOV2020, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Diarrhea	
C4591001 1037 10371307 (USA/TENNESSEE/43/F)	Placebo	Dose 2/59	16DEC2020	25DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 18DEC2020, B.1.2
						New or increased muscle pain	
C4591001 1037 10371323 (USA/TENNESSEE/48/F)	Placebo	Dose 2/36	02DEC2020	06DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 02DEC2020, B.1.2
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1037 10371353 (USA/TENNESSEE/37/M)	Placebo	Dose 2/18	28NOV2020	21DEC2020	Neg/Neg/Neg	Fever	Pos/, 03DEC2020, B.1.1.231
						New or increased cough	
						New or increased shortness of breath	
						Chills	
						New loss of taste or smell	
						Diarrhea	
C4591001 1038 10381044 (USA/TENNESSEE/32/F)	Placebo	Dose 2/79	02DEC2020	13DEC2020	Pos/Neg/Neg	New or increased shortness of breath	Pos/, 07DEC2020, INDETERMINATE
						Chills	
C4591001 1038 10381051 (USA/TENNESSEE/69/M)	Placebo	Dose 2/51	07NOV2020	25NOV2020	Neg/Neg/Neg	Fever	Pos/, 09NOV2020, B.1.361
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased shortness of breath	
						Sore throat	
C4591001 1039 10391025 (USA/TEXAS/55/F)	Placebo	Dose 2/40	25OCT2020	15NOV2020	Neg/Neg/Neg	Sore throat	Pos/, 28OCT2020, B.1.2
C4591001 1039 10391268 (USA/TEXAS/13/F)	Placebo	Dose 2/33	29JAN2021	03MAR2021	Neg/Neg/Neg	Fever	Pos/, 29JAN2021, B.1
						New or increased cough	
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
C4591001 1042 10421133 (USA/TEXAS/61/F)	Placebo	Dose 2/142	28JAN2021	11FEB2021	Neg/Neg/Neg	Fever	Pos/, 01FEB2021, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Chills	
						New or increased muscle pain	
						Sore throat	
						Diarrhea	
C4591001 1042 10421168 (USA/TEXAS/59/F)	Placebo	Dose 2/76	30NOV2020	21DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 02DEC2020, B.1.2
						New loss of taste or smell	
C4591001 1042 10421223 (USA/TEXAS/71/F)	Placebo	Dose 2/90	27DEC2020	16JAN2021	Neg/Neg/Neg	Fever	Pos/, 28DEC2020, B.1.2
						New or increased cough	
						New or increased muscle pain	
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1044 10441138 (USA/VIRGINIA/63/M)	Placebo	Dose 2/102	22JAN2021	23JAN2021	Neg/Neg/Neg	Fever	Pos/, 25JAN2021, B.1.351
C4591001 1044 10441167 (USA/VIRGINIA/42/F)	Placebo	Dose 2/103	05FEB2021	25FEB2021	Neg/Neg/Neg	New or increased shortness of breath	Pos/, 09FEB2021, B.1.2
						New loss of taste or smell	
C4591001 1044 10441242 (USA/VIRGINIA/17/M)	Placebo	Dose 2/49	01FEB2021	07FEB2021	Neg/Neg/Neg	Fever	Pos/, 04FEB2021, B.1.2
						Chills	
						New or increased muscle pain	
C4591001 1044 10441374 (USA/VIRGINIA/15/M)	Placebo	Dose 2/13	14FEB2021	17FEB2021	Neg/Neg/Neg	Chills	Pos/, 16FEB2021, B.1.243
						New loss of taste or smell	
						Vomiting	
C4591001 1046 10461037 (USA/ALABAMA/60/M)	BNT162b2 (30 µg)	Dose 2/109	21DEC2020	28DEC2020	Neg/Neg/Neg	Fever	Pos/, 22DEC2020, B.1
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 1046 10461058 (USA/ALABAMA/44/F)	Placebo	Dose 2/62	09NOV2020	16NOV2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 09NOV2020, B.1.240
C4591001 1046 10461101 (USA/ALABAMA/31/F)	Placebo	Dose 2/98	21DEC2020	24DEC2020	Neg/Neg/Neg	Fever	Pos/, 21DEC2020, B.1.2
						New or increased cough	
						New or increased muscle pain	
C4591001 1046 10461124 (USA/ALABAMA/36/F)	Placebo	Dose 2/105	29DEC2020	04JAN2021	Neg/Neg/Neg	Fever	Pos/, 29DEC2020, B.1.2
						New or increased cough	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1046 10461203 (USA/ALABAMA/55/F)	Placebo	Dose 2/53	23NOV2020	30NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 24NOV2020, B.1.2
						New or increased muscle pain	
C4591001 1046 10461204 (USA/ALABAMA/54/M)	Placebo	Dose 2/55	23NOV2020	27NOV2020	Neg/Neg/Neg	Fever	Pos/, 24NOV2020, B.1.2
						New or increased cough	
						New or increased muscle pain	
C4591001 1046 10461235 (USA/ALABAMA/59/M)	BNT162b2 (30 µg)	Dose 2/86	23DEC2020	29DEC2020	Neg/Neg/Neg	Fever	Pos/, 23DEC2020, B.1.2
						New or increased cough	
						New or increased muscle pain	
C4591001 1046 10461334 (USA/ALABAMA/53/F)	Placebo	Dose 2/28	16DEC2020	17DEC2020	Neg/Neg/Neg	Fever	Pos/, 16DEC2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1047 10471024 (USA/ALABAMA/63/F)	BNT162b2 (30 µg)	Dose 2/37	16OCT2020	18OCT2020	Neg/Neg/Neg	Fever	Pos/, 17OCT2020, B.1.139
						Diarrhea	
						Vomiting	
C4591001 1047 10471079 (USA/ALABAMA/21/F)	Placebo	Dose 2/87	13DEC2020	25DEC2020	Neg/Neg/Neg	Fever	Pos/, 15DEC2020, B.1.2
						Sore throat	
C4591001 1047 10471080 (USA/ALABAMA/43/F)	Placebo	Dose 2/56	12NOV2020	20NOV2020	Neg/Neg/Neg	New loss of taste or smell	Pos/Pos, 13NOV2020, B.1.2
C4591001 1047 10471170 (USA/ALABAMA/63/M)	BNT162b2 (30 µg)	Dose 2/62	01DEC2020	15JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 03DEC2020, QNS
C4591001 1047 10471217 (USA/ALABAMA/49/F)	Placebo	Dose 2/72	19DEC2020	22DEC2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 22DEC2020, B.1.240
C4591001 1047 10471327 (USA/ALABAMA/35/M)	Placebo	Dose 2/59	09JAN2021	13JAN2021	Neg/Neg/Neg	Fever	Pos/, 15JAN2021, B.1.366
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1048 10481027 (USA/ARIZONA/46/M)	Placebo	Dose 2/112	05JAN2021	19JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 11JAN2021, B.1.2
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1048 10481064 (USA/ARIZONA/52/F)	Placebo	Dose 2/107	06JAN2021	10JAN2021	Neg/Neg/Neg	Fever	Pos/, 08JAN2021, B.1.2
						New or increased cough	
						New or increased muscle pain	
C4591001 1048 10481104 (USA/ARIZONA/57/F)	Placebo	Dose 2/43	11NOV2020	16DEC2020	Neg/Neg/Neg	Fever	Pos/, 13NOV2020, B.1.2
						Chills	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1048 10481118 (USA/ARIZONA/67/F)	Placebo	Dose 2/32	02NOV2020	11NOV2020	Neg/Neg/Neg	New or increased cough New loss of taste or smell Sore throat	Pos/, 13NOV2020, B.1.2
C4591001 1052 10521082 (USA/CALIFORNIA/38/F)	Placebo	Dose 2/110	09JAN2021	10JAN2021	Neg/Neg/Neg	Fever	Pos/, 12JAN2021, B.1.429
C4591001 1052 10521110 (USA/CALIFORNIA/53/F)	Placebo	Dose 2/112	13JAN2021	13JAN2021	Neg/Neg/Neg	New or increased cough New or increased muscle pain Sore throat	Pos/, 13JAN2021, B.1.2
C4591001 1054 10541001 (USA/CALIFORNIA/50/F)	Placebo	Dose 2/134	19JAN2021	09FEB2021	Neg/Neg/Neg	New or increased cough New or increased shortness of breath Chills	Pos/, 24JAN2021, B.1.409

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						New loss of taste or smell	
						Vomiting	
C4591001 1054 10541002 (USA/CALIFORNIA/51/M)	BNT162b2 (30 µg)	Dose 2/134	19JAN2021	25JAN2021	Neg/Neg/Neg	Fever	Pos/, 26JAN2021, B.1.409
						New or increased cough	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1054 10541035 (USA/CALIFORNIA/29/M)	BNT162b2 (30 µg)	Dose 2/81	29NOV2020		Neg/Neg/Neg	New or increased cough	Pos/, 04DEC2020, B.1.1.29
						New or increased	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						shortness of breath	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1054 10541038 (USA/CALIFORNIA/27/F)	Placebo	Dose 2/88	10DEC2020	04FEB2021	Neg/Neg/Neg	Fever	Pos/, 12DEC2020, B.1.2
						New or increased cough	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1054 10541137 (USA/CALIFORNIA/42/M)	Placebo	Dose 2/100	07JAN2021	13JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 08JAN2021, B.1.2
C4591001 1054 10541146 (USA/CALIFORNIA/65/F)	BNT162b2 (30 µg)	Dose 2/62	09DEC2020	12DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 11DEC2020, B.1.399

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1054 10541194 (USA/CALIFORNIA/58/F)	Placebo	Dose 2/29	03DEC2020	17DEC2020	Neg/Neg/Neg	Sore throat	Pos/ (R1 Pos), 05DEC2020 (04JAN2021), B.1.2 (B.1.525)
C4591001 1054 10541202 (USA/CALIFORNIA/57/M)	Placebo	Dose 2/60	11JAN2021		Neg/Neg/Neg	Fever	Pos/, 12JAN2021, INDETERMINATE
						New or increased cough	
						New or increased shortness of breath	
						New or increased muscle pain	
C4591001 1055 10551016 (USA/CALIFORNIA/38/F)	BNT162b2 (30 µg)	Dose 2/104	12DEC2020	18DEC2020	Neg/Neg/Neg	Sore throat	Pos/, 16DEC2020, B.1.241
C4591001 1055 10551099 (USA/CALIFORNIA/30/M)	Placebo	Dose 2/100	22DEC2020	28DEC2020	Neg/Neg/Neg	Fever	Pos/, 27DEC2020, B.1.429
						New loss of taste or smell	
C4591001 1055 10551123 (USA/CALIFORNIA/67/M)	Placebo	Dose 2/64	19NOV2020	29NOV2020	Neg/Neg/Neg	Fever	Pos/, 20NOV2020, B.1

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
C4591001 1055 10551203 (USA/CALIFORNIA/49/M)	Placebo	Dose 2/48	17NOV2020	27NOV2020	Neg/Neg/Neg	New or increased cough	Pos/Pos, 18NOV2020, B.1.2
						Chills	
						New or increased muscle pain	
C4591001 1055 10551228 (USA/CALIFORNIA/39/F)	Placebo	Dose 2/48	21NOV2020	14DEC2020	Neg/Neg/Neg	Fever	Pos/, 22NOV2020, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1055 10551243 (USA/CALIFORNIA/18/M)	Placebo	Dose 2/67	20DEC2020	29DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 22DEC2020, B.1.2
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1056 10561041 (USA/FLORIDA/49/F)	BNT162b2 (30 µg)	Dose 2/116	10JAN2021	01FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 15JAN2021, B.1.1.143
						New loss of taste or smell	
C4591001 1056 10561349 (USA/FLORIDA/59/F)	Placebo	Dose 2/72	05JAN2021	13JAN2021	Neg/Neg/Neg	Fever	Pos/, 11JAN2021, B.1.375
						New or increased cough	
						New or increased shortness of breath	
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1056 10561502 (USA/FLORIDA/64/F)	Placebo	Dose 2/65	05JAN2021	17JAN2021	Neg/Neg/Neg	Sore throat New or increased cough New or increased muscle pain	Pos/, 07JAN2021, B.1.2
C4591001 1056 10561514 (USA/FLORIDA/30/F)	Placebo	Dose 2/9	13NOV2020	18NOV2020	Neg/Neg/Neg	Sore throat Diarrhea	Pos/, 17NOV2020, B.1.2
C4591001 1057 10571238 (USA/FLORIDA/49/F)	Placebo	Dose 2/60	13DEC2020	21DEC2020	Neg/Neg/Neg	New or increased muscle pain New loss of taste or smell	Pos/, 15DEC2020, B.1.2
C4591001 1057 10571363 (USA/FLORIDA/17/F)	Placebo	Dose 2/48	24JAN2021	01FEB2021	Neg/Neg/Neg	Sore throat Fever New or increased cough Chills	Pos/, 26JAN2021, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Sore throat	
C4591001 1066 10661050 (USA/IDAHO/59/M)	Placebo	Dose 2/116	03JAN2021	18JAN2021	Neg/Neg/Neg	Fever	Pos/, 04JAN2021, B.1
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1066 10661129 (USA/IDAHO/44/F)	Placebo	Dose 2/73	28NOV2020	21DEC2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 30NOV2020, B.1.2
C4591001 1066 10661163 (USA/IDAHO/24/M)	Placebo	Dose 2/56	16NOV2020	28NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 18NOV2020, B.1.2
						New loss of taste or smell	
C4591001 1066 10661167 (USA/IDAHO/50/F)	Placebo	Dose 2/81	12DEC2020	05JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 17DEC2020, B.1.2
C4591001 1066 10661176 (USA/IDAHO/61/M)	Placebo	Dose 2/99	31DEC2020	03JAN2021	Neg/Neg/Neg	Fever	Pos/, 05JAN2021, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 1066 10661242 (USA/IDAHO/54/M)	Placebo	Dose 2/90	30DEC2020	08JAN2021	Neg/Neg/Neg	Chills	Pos/, 04JAN2021, B.1.2
						New or increased muscle pain	
C4591001 1066 10661313 (USA/IDAHO/66/F)	Placebo	Dose 2/34	17NOV2020	28NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 19NOV2020, B.1.2
						Chills	
						New or increased muscle pain	
C4591001 1068 10681003 (USA/MONTANA/42/F)	Placebo	Dose 2/108	25DEC2020	11JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 31DEC2020, B.1.2
						New loss of taste or smell	
C4591001 1068 10681037 (USA/MONTANA/22/F)	Placebo	Dose 2/116	07JAN2021	09JAN2021	Neg/Neg/Neg	Sore throat	Pos/Pos, 12JAN2021, B.1.2
C4591001 1068 10681082 (USA/MONTANA/58/M)	Placebo	Dose 2/42	01NOV2020	25NOV2020	Neg/Neg/Neg	Fever	Pos/, 02NOV2020, B.1.395

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						New or increased shortness of breath	
						Sore throat	
C4591001 1068 10681083 (USA/MONTANA/26/F)	Placebo	Dose 2/105	03JAN2021	08JAN2021	Neg/Neg/Neg	New or increased cough	Pos/Pos, 06JAN2021, B.1.2
C4591001 1068 10681110 (USA/MONTANA/30/F)	Placebo	Dose 2/22	16OCT2020	02NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 21OCT2020, B.1.2
						New loss of taste or smell	
C4591001 1068 10681115 (USA/MONTANA/28/M)	Placebo	Dose 2/93	31DEC2020	08JAN2021	Neg/Neg/Neg	Sore throat	Pos/Pos, 04JAN2021, B.1.2
C4591001 1071 10711022 (USA/NEBRASKA/47/M)	Placebo	Dose 2/72	10NOV2020	16NOV2020	Neg/Neg/Neg	Fever	Pos/, 11NOV2020, B.1.139
						Chills	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1071 10711028 (USA/NEBRASKA/54/F)	Placebo	Dose 2/93	03DEC2020	09DEC2020	Neg/Neg/Neg	Sore throat Fever New or increased cough New loss of taste or smell	Pos/, 11DEC2020, B.1.311
C4591001 1071 10711034 (USA/NEBRASKA/49/F)	Placebo	Dose 2/111	20DEC2020	27DEC2020	Neg/Neg/Neg	New or increased cough New loss of taste or smell	Pos/, 24DEC2020, B.1.234
C4591001 1071 10711058 (USA/NEBRASKA/72/F)	Placebo	Dose 2/60	06NOV2020	25NOV2020	Neg/Neg/Neg	New or increased cough Sore throat	Pos/, 07NOV2020, B.1.2
C4591001 1071 10711147 (USA/NEBRASKA/70/M)	Placebo	Dose 2/86	22DEC2020	24DEC2020	Neg/Neg/Neg	New or increased cough New or increased muscle pain	Pos/, 27DEC2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1071 10711197 (USA/NEBRASKA/61/M)	Placebo	Dose 2/31	13NOV2020	15NOV2020	Neg/Neg/Neg	Fever	Pos/, 16NOV2020, B.1.2
						Chills	
C4591001 1071 10711198 (USA/NEBRASKA/54/F)	Placebo	Dose 2/31	13NOV2020	15NOV2020	Neg/Neg/Neg	Fever	Pos/, 16NOV2020, B.1.2
						New or increased cough	
C4591001 1071 10711249 (USA/NEBRASKA/44/M)	Placebo	Dose 2/59	15JAN2021		Neg/Neg/Neg	New or increased cough	Pos/, 19JAN2021, B.1.2
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1072 10721004 (USA/ALABAMA/59/M)	Placebo	Dose 2/129	15JAN2021	12FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 20JAN2021, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1072 10721024 (USA/ALABAMA/51/F)	BNT162b2 (30 µg)	Dose 2/137	25JAN2021		Neg/Neg/Neg	New or increased cough	Pos/Pos, 26JAN2021, B.1.2
C4591001 1072 10721057 (USA/ALABAMA/70/M)	Placebo	Dose 2/41	26OCT2020	16NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 05NOV2020, B.1.2
C4591001 1072 10721064 (USA/ALABAMA/77/M)	Placebo	Dose 2/85	09DEC2020	26DEC2020	Neg/Neg/Neg	Fever New or increased cough	Pos/Pos, 15DEC2020, B.1.2
C4591001 1072 10721089 (USA/ALABAMA/19/F)	Placebo	Dose 2/157	26FEB2021		Neg/Neg/Neg	New or increased cough	Pos/, 01MAR2021, B.1.1.7
C4591001 1072 10721096 (USA/ALABAMA/70/M)	Placebo	Dose 2/93	31DEC2020	05FEB2021	Neg/Neg/Neg	New or increased cough Sore throat	Pos/, 01JAN2021, B.1
C4591001 1073 10731029 (USA/ARIZONA/43/F)	Placebo	Dose 2/104	07DEC2020	11DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 09DEC2020, B.1.2
C4591001 1073 10731036 (USA/ARIZONA/50/F)	Placebo	Dose 2/82	17NOV2020	02DEC2020	Neg/Neg/Neg	Fever	Pos/, 19NOV2020, B.1.234

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
						Sore throat	
C4591001 1073 10731060 (USA/ARIZONA/78/F)	Placebo	Dose 2/127	04JAN2021	10JAN2021	Neg/Neg/Neg	Fever	Pos/, 07JAN2021, B.1.243
						New or increased cough	
						New or increased muscle pain	
C4591001 1073 10731067 (USA/ARIZONA/24/F)	Placebo	Dose 2/127	06JAN2021	09JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 08JAN2021, B.1
						New or increased muscle pain	
C4591001 1073 10731068 (USA/ARIZONA/39/M)	Placebo	Dose 2/126	05JAN2021	08JAN2021	Neg/Neg/Neg	New or increased shortness of breath	Pos/, 06JAN2021, B.1
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1073 10731085 (USA/ARIZONA/51/F)	Placebo	Dose 2/105	14DEC2020	16DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 16DEC2020, B.1.2
						New loss of taste or smell	
C4591001 1073 10731093 (USA/ARIZONA/48/F)	BNT162b2 (30 µg)	Dose 2/77	24NOV2020	05DEC2020	Neg/Neg/Neg	Chills	Pos/, 27NOV2020, B.1.2
						New or increased muscle pain	
C4591001 1073 10731098 (USA/ARIZONA/70/M)	Placebo	Dose 2/100	16DEC2020	20DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 17DEC2020, B.1.2
C4591001 1073 10731103 (USA/ARIZONA/49/M)	Placebo	Dose 2/133	18JAN2021	22JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 20JAN2021, B.1.2
						New loss of taste or smell	
C4591001 1073 10731123 (USA/ARIZONA/73/F)	Placebo	Dose 2/69	22NOV2020	25NOV2020	Neg/Neg/Neg	Fever	Pos/, 25NOV2020, B.1.2
						Sore throat	
C4591001 1073 10731124 (USA/ARIZONA/76/M)	Placebo	Dose 2/67	20NOV2020	25NOV2020	Neg/Neg/Neg	Fever	Pos/, 25NOV2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Sore throat	
C4591001 1077 10771175 (USA/NEW YORK/61/M)	Placebo	Dose 2/85	15DEC2020	05JAN2021	Neg/Neg/Neg	Fever	Pos/, 21DEC2020, B.1.240
						New or increased cough	
						Chills	
						New loss of taste or smell	
C4591001 1077 10771176 (USA/NEW YORK/61/F)	BNT162b2 (30 µg)	Dose 2/90	20DEC2020	03JAN2021	Neg/Neg/Neg	Fever	Pos/, 21DEC2020, B.1.240
						New or increased cough	
C4591001 1077 10771189 (USA/NEW YORK/51/M)	Placebo	Dose 2/51	11NOV2020	01DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 15NOV2020, B.1.110.3
						Diarrhea	
C4591001 1077 10771195 (USA/NEW YORK/73/F)	Placebo	Dose 2/40	01NOV2020	29NOV2020	Neg/Neg/Neg	Fever	Pos/, 07NOV2020, B.1.110.3

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						New or increased muscle pain	
C4591001 1077 10771239 (USA/NEW YORK/59/M)	Placebo	Dose 2/58	04DEC2020	07DEC2020	Neg/Neg/Neg	Fever	Pos/, 07DEC2020, B.1.404
						New or increased cough	
						New or increased muscle pain	
C4591001 1079 10791046 (USA/NORTH CAROLINA/55/F)	Placebo	Dose 2/62	26OCT2020	17DEC2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 30OCT2020, B.1
C4591001 1079 10791054 (USA/NORTH CAROLINA/28/F)	Placebo	Dose 2/63	29OCT2020	14NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 30OCT2020, B.1.1.29
C4591001 1079 10791098 (USA/NORTH CAROLINA/53/M)	Placebo	Dose 2/111	22DEC2020	04JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 07JAN2021, B.47
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1079 10791123 (USA/NORTH CAROLINA/61/F)	Placebo	Dose 2/135	13JAN2021	18JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 22JAN2021, B.1.2
						New or increased muscle pain	
C4591001 1079 10791230 (USA/NORTH CAROLINA/19/M)	Placebo	Dose 2/83	13DEC2020	20DEC2020	Neg/Pos/Neg	New or increased cough	Pos/, 18DEC2020, B.1.1.244
						New or increased muscle pain	
						Sore throat	
C4591001 1079 10791255 (USA/NORTH CAROLINA/58/M)	Placebo	Dose 2/96	01JAN2021	03JAN2021	Neg/Neg/Neg	Fever	Pos/, 04JAN2021, B.1.2
						Chills	
C4591001 1079 10791257 (USA/NORTH CAROLINA/45/M)	Placebo	Dose 2/98	05JAN2021	08FEB2021	Neg/Neg/Neg	Fever	Pos/, 06JAN2021, B.1.2
						New or increased cough	
						New or increased	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						shortness of breath	
						Chills	
						New or increased muscle pain	
						Diarrhea	
C4591001 1079 10791296 (USA/NORTH CAROLINA/40/F)	Placebo	Dose 2/29	26NOV2020	10DEC2020	Neg/Neg/Neg	New or increased cough	Pos/Pos, 01DEC2020, B.1.2
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1080 10801135 (USA/FLORIDA/28/M)	Placebo	Dose 2/126	28JAN2021	17FEB2021	Neg/Neg/Neg	Fever	Pos/, 11FEB2021, QNS
						New or increased cough	
						New or increased shortness of breath	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1081 10811014 (USA/OHIO/63/M)	Placebo	Dose 2/103	12DEC2020	20FEB2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 15DEC2020, B.1.2
C4591001 1081 10811043 (USA/OHIO/58/F)	Placebo	Dose 2/90	06DEC2020	21DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 08DEC2020, B.1.2
C4591001 1081 10811077 (USA/OHIO/50/F)	Placebo	Dose 2/132	19JAN2021	02FEB2021	Neg/Neg/Neg	Fever	Pos/, 23JAN2021, B.1.1.222
						New or increased cough	
						Chills	
C4591001 1081 10811086 (USA/OHIO/45/F)	Placebo	Dose 2/117	09JAN2021	05FEB2021	Neg/Neg/Neg	Fever	Pos/, 14JAN2021, B.1.438
						New or increased cough	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 1081 10811151 (USA/OHIO/79/F)	Placebo	Dose 2/10	30SEP2020	14OCT2020	Neg/Neg/Neg	New or increased cough	Pos/, 14OCT2020, QNS
C4591001 1081 10811173 (USA/OHIO/66/M)	Placebo	Dose 2/99	31DEC2020		Neg/Neg/Neg	New or increased cough	Pos/, 04JAN2021, B.1.2
						Diarrhea	
C4591001 1081 10811196 (USA/OHIO/48/F)	Placebo	Dose 2/90	29DEC2020	26JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 31DEC2020, B.1.2
						New loss of taste or smell	
						Sore throat	
C4591001 1081 10811210 (USA/OHIO/51/M)	BNT162b2 (30 µg)	Dose 2/85	31DEC2020	21JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/ (R1 Pos), 02JAN2021 (03JAN2021), B.1.2 (B.1.2)
C4591001 1082 10821016 (USA/TENNESSEE/46/F)	Placebo	Dose 2/44	06OCT2020	27OCT2020	Neg/Neg/Neg	Fever	Pos/, 07OCT2020, B.1.400

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1082 10821026 (USA/TENNESSEE/48/M)	Placebo	Dose 2/81	13NOV2020	24DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 18NOV2020, B.1.2
C4591001 1082 10821143 (USA/TENNESSEE/41/M)	Placebo	Dose 2/48	11NOV2020	05DEC2020	Neg/Neg/Neg	Fever	Pos/, 13NOV2020, B.1
						New or increased cough	
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1082 10821162 (USA/TENNESSEE/72/M)	Placebo	Dose 2/50	27NOV2020	23DEC2020	Neg/Neg/Neg	Fever	Pos/, 03DEC2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						Chills	
C4591001 1083 10831181 (USA/TEXAS/35/F)	Placebo	Dose 2/99	28DEC2020	03JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 30DEC2020, B.1.2
						New or increased shortness of breath	
						New loss of taste or smell	
C4591001 1084 10841016 (USA/TEXAS/43/M)	Placebo	Dose 2/130	31DEC2020	05JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 07JAN2021, B.1.2
						Sore throat	
C4591001 1084 10841089 (USA/TEXAS/28/M)	Placebo	Dose 2/85	20NOV2020	02DEC2020	Neg/Neg/Neg	Fever	Pos/, 24NOV2020, B.1.2
						New or increased cough	
C4591001 1084 10841188 (USA/TEXAS/48/F)	Placebo	Dose 2/83	25NOV2020	07DEC2020	Neg/Neg/Neg	Fever	Pos/, 30NOV2020, B.1.2
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased shortness of breath	
						Vomiting	
C4591001 1084 10841302 (USA/TEXAS/65/F)	Placebo	Dose 2/56	12NOV2020	30NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 16NOV2020, B.1.2
						New or increased shortness of breath	
C4591001 1084 10841392 (USA/TEXAS/72/F)	Placebo	Dose 2/80	25DEC2020	27DEC2020	Neg/Neg/Neg	Fever	Pos/, 29DEC2020, B.1.2
						New or increased cough	
						Chills	
						New loss of taste or smell	
C4591001 1085 10851004 (USA/TEXAS/49/F)	Placebo	Dose 2/120	17DEC2020	18DEC2020	Neg/Neg/Neg	Sore throat	Pos/, 18DEC2020, B.1.509
C4591001 1085 10851027 (USA/TEXAS/50/F)	Placebo	Dose 2/101	02DEC2020	25FEB2021	Neg/Neg/Neg	New or increased	Pos/, 04DEC2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						shortness of breath	
						New or increased muscle pain	
C4591001 1085 10851177 (USA/TEXAS/70/M)	Placebo	Dose 2/107	01JAN2021	05JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 05JAN2021, B.1.2
C4591001 1085 10851258 (USA/TEXAS/58/M)	Placebo	Dose 2/100	30DEC2020	03JAN2021	Neg/Neg/Neg	Chills	Pos/, 04JAN2021, B.1.2
C4591001 1085 10851293 (USA/TEXAS/63/F)	Placebo	Dose 2/37	07NOV2020	27NOV2020	Neg/Neg/Neg	Fever	Pos/, 10NOV2020, INDETERMINATE
						New or increased cough	
						New loss of taste or smell	
C4591001 1085 10851347 (USA/TEXAS/77/F)	Placebo	Dose 2/75	22DEC2020	29DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 29DEC2020, B.1.2
C4591001 1085 10851374 (USA/TEXAS/17/F)	Placebo	Dose 2/48	03JAN2021	07JAN2021	Neg/Neg/Neg	Chills	Pos/, 04JAN2021, NS
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1087 10871572 (USA/NORTH CAROLINA/54/M)	Placebo	Dose 2/88	31JAN2021	15FEB2021	Neg/Neg/Neg	Fever	Pos/, 01FEB2021, B.1.243
						New or increased cough	
						New or increased muscle pain	
C4591001 1088 10881011 (USA/NORTH CAROLINA/48/F)	Placebo	Dose 2/89	27NOV2020	19DEC2020	Neg/Neg/Neg	Fever	Pos/, 03DEC2020, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
						Sore throat	
						Diarrhea	
C4591001 1088 10881016 (USA/NORTH CAROLINA/50/F)	Placebo	Dose 2/119	28DEC2020	02JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 29DEC2020, B.1.2
C4591001 1088 10881024 (USA/NORTH CAROLINA/32/F)	Placebo	Dose 2/96	06DEC2020	20DEC2020	Neg/Neg/Neg	Fever	Pos/, 09DEC2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						Chills	
						Sore throat	
C4591001 1088 10881075 (USA/NORTH CAROLINA/68/F)	Placebo	Dose 2/83	02DEC2020	13DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 07DEC2020, B.1.2
C4591001 1088 10881086 (USA/NORTH CAROLINA/69/F)	Placebo	Dose 2/106	28DEC2020	04JAN2021	Neg/Neg/Neg	Fever	Pos/, 29DEC2020, B.1.2
						New or increased cough	
						New or increased muscle pain	
						Sore throat	
C4591001 1088 10881091 (USA/NORTH CAROLINA/66/F)	Placebo	Dose 2/132	25JAN2021	03MAR2021	Neg/Neg/Unk	Fever	Pos/, 28JAN2021, B.1.243
						Chills	
C4591001 1088 10881097 (USA/NORTH CAROLINA/57/M)	Placebo	Dose 2/83	07DEC2020	17DEC2020	Neg/Neg/Neg	Fever	Pos/, 08DEC2020, B.1.2
						New or increased cough	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 1088 10881126 (USA/NORTH CAROLINA/65/M)	Placebo	Dose 2/68	29NOV2020	01DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 30NOV2020, B.1.2
C4591001 1088 10881142 (USA/NORTH CAROLINA/61/F)	Placebo	Dose 2/94	25DEC2020	29DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 29DEC2020, B.1.2
C4591001 1088 10881148 (USA/NORTH CAROLINA/28/F)	Placebo	Dose 2/73	04DEC2020	10DEC2020	Neg/Neg/Neg	Fever	Pos/, 09DEC2020, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1088 10881164 (USA/NORTH CAROLINA/58/F)	Placebo	Dose 2/46	13NOV2020	03DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 18NOV2020, B.1.2
						New or increased muscle pain	
						Sore throat	
C4591001 1088 10881188 (USA/NORTH CAROLINA/67/F)	Placebo	Dose 2/84	21DEC2020	15JAN2021	Neg/Neg/Neg	Fever	Pos/, 23DEC2020, B.1.2
						New or increased muscle pain	
C4591001 1088 10881219 (USA/NORTH CAROLINA/63/M)	Placebo	Dose 2/17	25OCT2020	16NOV2020	Neg/Neg/Neg	Fever	Pos/, 26OCT2020, B.1.2
						New or increased cough	
						New or increased muscle pain	
C4591001 1088 10881233 (USA/NORTH CAROLINA/47/M)	Placebo	Dose 2/15	02NOV2020	12NOV2020	Neg/Neg/Neg	Fever	Pos/, 04NOV2020, B.1

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Chills	
						Sore throat	
C4591001 1089 10891100 (USA/NORTH CAROLINA/33/F)	Placebo	Dose 2/115	24DEC2020	05FEB2021	Neg/Neg/Neg	Fever	Pos/, 28DEC2020, B.1.361
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1089 10891110 (USA/NORTH CAROLINA/59/F)	Placebo	Dose 2/158	04FEB2021	20FEB2021	Neg/Neg/Neg	Fever	Pos/, 11FEB2021, B.1.2
						New or increased cough	
						Diarrhea	
						Vomiting	
C4591001 1089 10891115 (USA/NORTH CAROLINA/55/M)	BNT162b2 (30 µg)	Dose 2/140	21JAN2021	25FEB2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 26JAN2021, B.1.210

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1089 10891235 (USA/NORTH CAROLINA/29/F)	Placebo	Dose 2/47	08NOV2020	18NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 12NOV2020, B.1.2
						Sore throat	
C4591001 1089 10891314 (USA/NORTH CAROLINA/57/F)	Placebo	Dose 2/56	30NOV2020	11DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 30NOV2020, B.1.2
						Sore throat	
						Diarrhea	
C4591001 1090 10901022 (USA/NORTH CAROLINA/52/F)	BNT162b2 (30 µg)	Dose 2/114	19DEC2020	07JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 31DEC2020, B.1.1.222
C4591001 1090 10901075 (USA/NORTH CAROLINA/73/M)	Placebo	Dose 2/96	01DEC2020	18DEC2020	Neg/Neg/Neg	Diarrhea	Pos/, 21DEC2020, B.1.2
C4591001 1090 10901086 (USA/NORTH CAROLINA/55/M)	Placebo	Dose 2/165	08FEB2021		Neg/Neg/Neg	New or increased muscle pain	Pos/, 10FEB2021, B.1.429
C4591001 1090 10901121 (USA/NORTH CAROLINA/58/F)	Placebo	Dose 2/49	18OCT2020	22OCT2020	Neg/Neg/Neg	Fever	Pos/, 20OCT2020, B.1.369
						New loss of taste or smell	
C4591001 1090 10901278 (USA/NORTH CAROLINA/46/M)	Placebo	Dose 2/81	10DEC2020	22DEC2020	Neg/Neg/Neg	Fever	Pos/, 14DEC2020, B.1.239

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Diarrhea	
C4591001 1090 10901349 (USA/NORTH CAROLINA/53/M)	Placebo	Dose 2/105	11JAN2021	16JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 12JAN2021, B.1.1.244
C4591001 1090 10901353 (USA/NORTH CAROLINA/63/M)	Placebo	Dose 2/40	08NOV2020	29NOV2020	Neg/Neg/Neg	Fever	Pos/, 09NOV2020, B.1.349
						New or increased cough	
C4591001 1090 10901528 (USA/NORTH CAROLINA/53/F)	Placebo	Dose 2/43	24DEC2020	24JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 28DEC2020, B.1.2
C4591001 1091 10911003 (USA/OHIO/59/M)	Placebo	Dose 2/135	01JAN2021	10JAN2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 14JAN2021, B.1
C4591001 1091 10911071 (USA/OHIO/66/F)	Placebo	Dose 2/164	10FEB2021	27FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 18FEB2021, B.1.2
						Chills	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1091 10911119 (USA/OHIO/44/F)	Placebo	Dose 2/121	31DEC2020	21JAN2021	Neg/Neg/Neg	Sore throat	Pos/Pos, 05JAN2021, B.1.2
C4591001 1091 10911183 (USA/OHIO/26/M)	Placebo	Dose 2/62	17NOV2020	26NOV2020	Neg/Neg/Neg	Fever	Pos/, 18NOV2020, B.1.1.253
						New or increased cough	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1091 10911198 (USA/OHIO/34/M)	Placebo	Dose 2/93	17DEC2020	30DEC2020	Neg/Neg/Neg	Fever	Pos/, 18DEC2020, B.1.400
						New or increased cough	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
C4591001 1091 10911203 (USA/43/M)	Placebo	Dose 2/44	05NOV2020		Neg/Neg/Neg	New or increased cough	Unk/Pos, 05NOV2020, NS
						New or increased muscle pain	
C4591001 1091 10911327 (USA/OHIO/40/F)	Placebo	Dose 2/38	18NOV2020	25NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 20NOV2020, B.1.2
						New or increased shortness of breath	
						New loss of taste or smell	
C4591001 1091 10911365 (USA/OHIO/73/F)	Placebo	Dose 2/50	24DEC2020	07JAN2021	Neg/Neg/Neg	Fever	Pos/, 26DEC2020, B.1.2
						New or increased cough	
						Sore throat	
						Diarrhea	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1091 10911371 (USA/OHIO/31/M)	Placebo	Dose 2/14	24NOV2020	09DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 26NOV2020, B.1.2
						New or increased muscle pain	
C4591001 1091 10911404 (USA/OHIO/13/F)	Placebo	Dose 2/27	23JAN2021		Neg/Neg/Neg	New or increased shortness of breath	Pos/, 25JAN2021, B.1.361
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1092 10921021 (USA/OHIO/60/F)	Placebo	Dose 2/48	27OCT2020	17NOV2020	Neg/Neg/Neg	Fever	Pos/, 29OCT2020, B.1.2
						New or increased cough	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 1092 10921055 (USA/OHIO/19/F)	Placebo	Dose 2/88	10DEC2020	20DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 14DEC2020, B.1.2
						New loss of taste or smell	
C4591001 1092 10921079 (USA/OHIO/67/M)	Placebo	Dose 2/122	15JAN2021	04FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 03FEB2021, NS
C4591001 1092 10921089 (USA/OHIO/63/F)	BNT162b2 (30 µg)	Dose 2/101	25DEC2020	01JAN2021	Neg/Neg/Neg	Chills	Pos/, 27DEC2020, B.1.2
C4591001 1092 10921092 (USA/OHIO/66/M)	Placebo	Dose 2/66	21NOV2020	11DEC2020	Neg/Neg/Neg	Fever	Pos/, 25NOV2020, B.1.2
						New or increased cough	
						New or increased shortness of breath	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Sore throat	
						Vomiting	
C4591001 1092 10921130 (USA/OHIO/53/M)	Placebo	Dose 2/18	09OCT2020		Neg/Neg/Neg	Fever	Pos/, 12OCT2020, B.1.2
						New or increased cough	
						New or increased shortness of breath	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1092 10921176 (USA/OHIO/68/M)	Placebo	Dose 2/86	24DEC2020	17JAN2021	Neg/Neg/Neg	Fever	Pos/, 28DEC2020, B.1.2
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
C4591001 1092 10921242 (USA/OHIO/69/M)	Placebo	Dose 2/9	12NOV2020	10JAN2021	Neg/Neg/Neg	New or increased cough	Pos/ (R1 Pos), 17NOV2020 (01DEC2020), B.1.2 (B.1)
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1092 10921258 (USA/OHIO/60/F)	Placebo	Dose 2/52	01JAN2021	14JAN2021	Neg/Neg/Neg	Fever	Pos/, 06JAN2021, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1093 10931019 (USA/IOWA/28/M)	Placebo	Dose 2/87	03DEC2020	12DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 04DEC2020, B.1.234

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased shortness of breath	
						Chills	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
						Vomiting	
C4591001 1093 10931028 (USA/IOWA/38/M)	Placebo	Dose 2/69	17NOV2020	23NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 18NOV2020, B.1.240
						Sore throat	
C4591001 1093 10931081 (USA/IOWA/67/F)	Placebo	Dose 2/19	05OCT2020	19OCT2020	Neg/Neg/Neg	Sore throat	Pos/, 06OCT2020, B.1.2
C4591001 1093 10931121 (USA/IOWA/37/F)	Placebo	Dose 2/50	23NOV2020	01DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 30NOV2020, B.1.234
						Chills	
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1093 10931177 (USA/IOWA/55/F)	Placebo	Dose 2/15	23NOV2020	27NOV2020	Neg/Neg/Neg	New or increased shortness of breath Chills New or increased muscle pain	Pos/, 30NOV2020, B.1.234
C4591001 1093 10931189 (USA/IOWA/74/M)	Placebo	Dose 2/26	04DEC2020	15DEC2020	Neg/Neg/Neg	Fever New or increased cough Chills New or increased muscle pain	Pos/, 07DEC2020, B.1.240
C4591001 1093 10931216 (USA/IOWA/35/M)	Placebo	Dose 2/11	30NOV2020	02DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 02DEC2020, B.1
C4591001 1094 10941056 (USA/TEXAS/58/F)	Placebo	Dose 2/68	21NOV2020	22DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 25NOV2020, NS

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1094 10941163 (USA/TEXAS/53/F)	Placebo	Dose 2/61	19DEC2020	19JAN2021	Neg/Neg/Neg	Sore throat	Pos/, 22DEC2020, B.1.2
C4591001 1094 10941171 (USA/TEXAS/71/M)	Placebo	Dose 2/60	25DEC2020	12JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 28DEC2020, B.1.2
C4591001 1095 10951002 (USA/TEXAS/20/F)	Placebo	Dose 2/140	07JAN2021	08JAN2021	Neg/Neg/Neg	Fever	Pos/, 11JAN2021, B.1.2
						Chills	
C4591001 1095 10951060 (USA/TEXAS/36/M)	Placebo	Dose 2/104	08DEC2020	07JAN2021	Neg/Neg/Neg	Fever	Pos/, 09DEC2020, B.1.2
						New or increased cough	
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						Diarrhea	
						Vomiting	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1095 10951098 (USA/TEXAS/59/F)	Placebo	Dose 2/71	06NOV2020	17DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 10NOV2020, B.1.2
						Chills	
						New or increased muscle pain	
						Sore throat	
						Diarrhea	
C4591001 1095 10951117 (USA/TEXAS/70/M)	Placebo	Dose 2/96	15DEC2020	02JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 19DEC2020, B.1
C4591001 1095 10951196 (USA/TEXAS/50/M)	Placebo	Dose 2/88	18DEC2020	21DEC2020	Neg/Neg/Neg	Fever	Pos/, 21DEC2020, NS
						New or increased cough	
C4591001 1095 10951223 (USA/TEXAS/42/M)	Placebo	Dose 2/95	27DEC2020	01JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 30DEC2020, B.1.243
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1095 10951238 (USA/TEXAS/63/F)	Placebo	Dose 2/19	02NOV2020	20DEC2020	Neg/Neg/Neg	New or increased cough New or increased shortness of breath Chills New or increased muscle pain Sore throat Diarrhea	Pos/, 09NOV2020, B.1.2
C4591001 1095 10951260 (USA/TEXAS/25/M)	Placebo	Dose 2/9	05NOV2020	05NOV2020	Neg/Neg/Neg	New or increased cough Chills New or increased muscle pain Sore throat	Pos/, 09NOV2020, B.1
C4591001 1096 10961021 (USA/TEXAS/67/F)	Placebo	Dose 2/98	08DEC2020	09JAN2021	Neg/Neg/Neg	Chills	Pos/, 18DEC2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Sore throat	
						Diarrhea	
C4591001 1096 10961072 (USA/TEXAS/49/M)	Placebo	Dose 2/98	22DEC2020	08JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 28DEC2020, INDETERMINATE
						Chills	
C4591001 1096 10961164 (USA/TEXAS/62/F)	BNT162b2 (30 µg)	Dose 2/104	29DEC2020	25JAN2021	Neg/Neg/Neg	New or increased shortness of breath	Pos/, 05JAN2021, B.1.2
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1096 10961172 (USA/TEXAS/51/M)	Placebo	Dose 2/49	06NOV2020	08NOV2020	Neg/Neg/Neg	Fever	Pos/, 10NOV2020, B.1.361
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1096 10961258 (USA/TEXAS/55/F)	Placebo	Dose 2/25	22OCT2020	26OCT2020	Neg/Neg/Neg	New or increased cough	Pos/Pos, 26OCT2020, B.1.2
						New or increased muscle pain	
						Sore throat	
C4591001 1097 10971038 (USA/SOUTH CAROLINA/64/M)	Placebo	Dose 2/79	04DEC2020	15DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 08DEC2020, B.1.110.3
						Sore throat	
C4591001 1098 10981028 (USA/TEXAS/58/M)	Placebo	Dose 2/102	21DEC2020	02JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 22DEC2020, B.1.2
						New or increased muscle pain	
						Sore throat	
C4591001 1098 10981046 (USA/TEXAS/66/F)	BNT162b2 (30 µg)	Dose 2/70	23NOV2020	23NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 25NOV2020, B.1.1.29
C4591001 1098 10981058 (USA/TEXAS/69/F)	Placebo	Dose 2/130	23JAN2021	06FEB2021	Neg/Neg/Neg	Fever	Pos/, 04FEB2021, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 1098 10981062 (USA/TEXAS/63/F)	Placebo	Dose 2/32	17OCT2020	20OCT2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 19OCT2020, B.1.2
C4591001 1098 10981187 (USA/TEXAS/23/M)	Placebo	Dose 2/124	07FEB2021	18FEB2021	Neg/Neg/Neg	Fever	Pos/, 10FEB2021, B.1.429
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1098 10981216 (USA/TEXAS/52/M)	Placebo	Dose 2/42	23NOV2020	29NOV2020	Neg/Neg/Neg	Sore throat	Pos/, 25NOV2020, B.1.2
C4591001 1101 11011041 (USA/NEBRASKA/54/F)	Placebo	Dose 2/107	15JAN2021	21JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 19JAN2021, B.1.2
C4591001 1101 11011095 (USA/NEBRASKA/60/M)	Placebo	Dose 2/20	02NOV2020	06NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 04NOV2020, B.1.2
C4591001 1101 11011105 (USA/NEBRASKA/22/F)	Placebo	Dose 2/18	19NOV2020	27NOV2020	Neg/Neg/Neg	Fever	Pos/, 24NOV2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						New or increased shortness of breath	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1107 11071037 (USA/ALABAMA/59/M)	Placebo	Dose 2/124	26DEC2020	29JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 03JAN2021, B.1.2
						New or increased muscle pain	
C4591001 1107 11071121 (USA/ALABAMA/77/M)	Placebo	Dose 2/98	14DEC2020	30DEC2020	Neg/Neg/Neg	Chills	Pos/, 27DEC2020, B.1.2
C4591001 1107 11071170 (USA/ALABAMA/61/F)	Placebo	Dose 2/101	23DEC2020	02JAN2021	Neg/Neg/Neg	Sore throat	Pos/, 27DEC2020, B.1.349

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1107 11071171 (USA/ALABAMA/39/M)	Placebo	Dose 2/58	10NOV2020	20NOV2020	Neg/Neg/Neg	Fever	Pos/, 11NOV2020, B.1
						Chills	
C4591001 1107 11071190 (USA/ALABAMA/42/F)	Placebo	Dose 2/82	13DEC2020	28DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 14DEC2020, B.1.234
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1109 11091067 (USA/FLORIDA/42/M)	Placebo	Dose 2/84	11NOV2020	28NOV2020	Neg/Neg/Neg	New or increased shortness of breath	Pos/, 11NOV2020, B.1.311
						Sore throat	
C4591001 1109 11091092 (USA/FLORIDA/18/M)	Placebo	Dose 2/70	31OCT2020	24NOV2020	Neg/Neg/Neg	Fever	Pos/, 10NOV2020, B.1.240
						New or increased cough	
						Sore throat	
C4591001 1109 11091147 (USA/FLORIDA/46/F)	Placebo	Dose 2/151	20JAN2021	26JAN2021	Neg/Neg/Neg	Sore throat	Pos/, 22JAN2021, B.1.306

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1109 11091229 (USA/FLORIDA/69/F)	Placebo	Dose 2/82	26NOV2020	12JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 28NOV2020, B.1.2
C4591001 1109 11091233 (USA/FLORIDA/59/F)	BNT162b2 (30 µg)	Dose 2/115	26DEC2020	28DEC2020	Neg/Neg/Neg	Sore throat	Pos/, 29DEC2020, B.1.311
C4591001 1109 11091309 (USA/FLORIDA/24/F)	Placebo	Dose 2/124	11JAN2021	21JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 15JAN2021, B.1
						New or increased shortness of breath	
						New loss of taste or smell	
C4591001 1109 11091316 (USA/FLORIDA/47/M)	Placebo	Dose 2/115	05JAN2021		Neg/Neg/Neg	New or increased cough	Pos/, 08JAN2021, B.1.2
						New or increased shortness of breath	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 1109 11091323 (USA/FLORIDA/64/M)	Placebo	Dose 2/47	31OCT2020	02NOV2020	Neg/Neg/Neg	Fever	Pos/, 03NOV2020, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
C4591001 1109 11091346 (USA/FLORIDA/64/M)	Placebo	Dose 2/99	24DEC2020		Neg/Neg/Neg	New or increased cough	Pos/, 04JAN2021, INDETERMINATE
						New loss of taste or smell	
C4591001 1109 11091415 (USA/FLORIDA/48/F)	Placebo	Dose 2/93	27DEC2020	18JAN2021	Neg/Neg/Neg	Fever	Pos/, 29DEC2020, B.1.2
						New or increased cough	
						New or increased	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						shortness of breath	
						Chills	
						Sore throat	
C4591001 1109 11091416 (USA/FLORIDA/46/F)	Placebo	Dose 2/41	03NOV2020	17NOV2020	Neg/Neg/Neg	Fever	Pos/, 11NOV2020, B.1.2
						New or increased cough	
						Sore throat	
C4591001 1109 11091448 (USA/FLORIDA/46/F)	Placebo	Dose 2/9	06OCT2020	28OCT2020	Neg/Neg/Neg	Fever	Pos/ (R1 Pos), 09OCT2020 (23OCT2020), B.1.2 (B.1.2)
						New or increased cough	
						New or increased shortness of breath	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1109 11091482 (USA/FLORIDA/63/M)	Placebo	Dose 2/28	29OCT2020	13NOV2020	Neg/Neg/Neg	Sore throat New or increased cough New loss of taste or smell	Pos/, 03NOV2020, B.1.369
C4591001 1110 11101050 (USA/FLORIDA/47/M)	BNT162b2 (30 µg)	Dose 2/76	10NOV2020	12JAN2021	Neg/Neg/Neg	New or increased cough Chills	Pos/, 12NOV2020, B.1.2
C4591001 1110 11101079 (USA/FLORIDA/71/F)	Placebo	Dose 2/88	28NOV2020	13DEC2020	Neg/Neg/Neg	Sore throat New or increased cough New or increased muscle pain New loss of taste or smell	Pos/, 04DEC2020, B.1.2
C4591001 1110 11101108 (USA/FLORIDA/58/M)	Placebo	Dose 2/95	11DEC2020	15JAN2021	Neg/Neg/Neg	Fever Chills	Pos/, 15DEC2020, B.1.1.143

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1110 11101111 (USA/FLORIDA/45/M)	Placebo	Dose 2/108	25DEC2020	06JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 02JAN2021, B.1.2
						New or increased shortness of breath	
						New or increased muscle pain	
						New loss of taste or smell	
						Diarrhea	
C4591001 1110 11101136 (USA/FLORIDA/62/M)	Placebo	Dose 2/52	04NOV2020	15JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 06NOV2020, B.1
						Chills	
						Diarrhea	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1110 11101162 (USA/FLORIDA/51/M)	BNT162b2 (30 µg)	Dose 2/34	24OCT2020	04NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 26OCT2020, B.1.2
						New loss of taste or smell	
C4591001 1110 11101232 (USA/FLORIDA/62/M)	BNT162b2 (30 µg)	Dose 2/113	21JAN2021	15FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 22JAN2021, B.1.2
						New loss of taste or smell	
C4591001 1110 11101325 (USA/FLORIDA/42/F)	Placebo	Dose 2/75	04JAN2021	26JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 07JAN2021, B.1.2
						New or increased muscle pain	
C4591001 1111 11111010 (USA/FLORIDA/75/M)	Placebo	Dose 2/45	04OCT2020	05OCT2020	Neg/Neg/Neg	Fever	Pos/, 06OCT2020, B.1.2
						Chills	
C4591001 1111 11111128 (USA/FLORIDA/60/F)	Placebo	Dose 2/127	12JAN2021	19JAN2021	Neg/Neg/Neg	Fever	Pos/, 15JAN2021, B.1.2
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1111 11111150 (USA/FLORIDA/57/M)	Placebo	Dose 2/43	02NOV2020	17NOV2020	Neg/Neg/Neg	Sore throat Chills New or increased muscle pain	Pos/, 17NOV2020, B.1.311
C4591001 1111 11111186 (USA/FLORIDA/88/M)	Placebo	Dose 2/79	29DEC2020	05JAN2021	Neg/Neg/Neg	Sore throat Diarrhea	Pos/, 05JAN2021, B.1.2
C4591001 1112 11121003 (USA/GEORGIA/64/F)	Placebo	Dose 2/116	12DEC2020	28DEC2020	Neg/Neg/Neg	Fever New or increased cough	Pos/, 15DEC2020, B.1.1.222
C4591001 1112 11121064 (USA/GEORGIA/42/M)	Placebo	Dose 2/131	02JAN2021	18JAN2021	Neg/Neg/Neg	Sore throat Diarrhea New or increased cough	Pos/, 06JAN2021, B.1.2
C4591001 1112 11121210 (USA/GEORGIA/69/F)	Placebo	Dose 2/88	21DEC2020	06JAN2021	Neg/Neg/Neg	Diarrhea New loss of taste or smell	Pos/, 21DEC2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1112 11121224 (USA/GEORGIA/45/F)	Placebo	Dose 2/76	07DEC2020	28DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 15DEC2020, B.1.2
						New loss of taste or smell	
C4591001 1112 11121245 (USA/GEORGIA/41/F)	Placebo	Dose 2/91	30DEC2020	02JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 04JAN2021, B.1.2
						Chills	
C4591001 1112 11121301 (USA/GEORGIA/47/M)	Placebo	Dose 2/27	28NOV2020	19DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 29NOV2020, B.1.280
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1114 11141008 (USA/KANSAS/22/M)	Placebo	Dose 2/80	19NOV2020	23NOV2020	Neg/Neg/Neg	Fever	Pos/, 20NOV2020, B.1.2
C4591001 1114 11141014 (USA/KANSAS/20/F)	BNT162b2 (30 µg)	Dose 2/123	01JAN2021	21JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 06JAN2021, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1114 11141024 (USA/KANSAS/18/F)	Placebo	Dose 2/126	07JAN2021	31JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 11JAN2021, B.1.2
C4591001 1114 11141075 (USA/KANSAS/40/F)	Placebo	Dose 2/110	28DEC2020	16FEB2021	Neg/Neg/Neg	Fever	Pos/, 04JAN2021, QNS
						New or increased cough	
						New or increased shortness of breath	
						New or increased muscle pain	
C4591001 1116 11161072 (USA/MISSISSIPPI/52/F)	Placebo	Dose 2/81	10DEC2020		Neg/Neg/Neg	New or increased cough	Pos/, 14DEC2020, B.1.2
						New loss of taste or smell	
C4591001 1116 11161075 (USA/MISSISSIPPI/73/M)	Placebo	Dose 2/43	03NOV2020	19JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 05NOV2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased shortness of breath	
						Chills	
C4591001 1116 11161104 (USA/MISSISSIPPI/38/F)	Placebo	Dose 2/140	07FEB2021	01MAR2021	Neg/Neg/Neg	New or increased cough	Pos/, 09FEB2021, B.1.2
C4591001 1116 11161111 (USA/MISSISSIPPI/71/F)	Placebo	Dose 2/111	12JAN2021	04FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 21JAN2021, INDETERMINATE
C4591001 1116 11161160 (USA/MISSISSIPPI/47/M)	Placebo	Dose 2/103	08JAN2021	18JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 13JAN2021, B.1.2
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1116 11161184 (USA/MISSISSIPPI/77/M)	Placebo	Dose 2/72	09DEC2020	24DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 15DEC2020, B.1.2
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1116 11161207 (USA/MISSISSIPPI/58/F)	Placebo	Dose 2/64	02DEC2020	25DEC2020	Neg/Neg/Neg	Fever	Pos/, 03DEC2020, B.1.243
						New or increased cough	
						Chills	
						New or increased muscle pain	
C4591001 1116 11161224 (USA/MISSISSIPPI/52/F)	Placebo	Dose 2/46	14NOV2020	20NOV2020	Neg/Neg/Neg	Fever	Pos/, 16NOV2020, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1116 11161250 (USA/MISSISSIPPI/62/F)	Placebo	Dose 2/55	01DEC2020	11DEC2020	Neg/Neg/Neg	New or increased cough Chills New or increased muscle pain Sore throat	Pos/, 03DEC2020, B.1.234
C4591001 1116 11161275 (USA/MISSISSIPPI/58/F)	Placebo	Dose 2/80	01JAN2021	09JAN2021	Neg/Neg/Neg	Fever Chills Diarrhea	Pos/, 03JAN2021, B.1.234
C4591001 1116 11161283 (USA/MISSISSIPPI/72/F)	Placebo	Dose 2/39	20NOV2020	02DEC2020	Neg/Neg/Neg	Sore throat	Pos/, 02DEC2020, B.1.361
C4591001 1117 11171010 (USA/MISSOURI/72/F)	Placebo	Dose 2/34	11OCT2020	19OCT2020	Neg/Neg/Neg	Fever New or increased cough	Pos/, 11OCT2020, B.1.2
C4591001 1117 11171028 (USA/MISSOURI/67/M)	Placebo	Dose 2/62	10NOV2020	01DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 13NOV2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 1117 11171031 (USA/MISSOURI/74/F)	Placebo	Dose 2/82	29NOV2020	07DEC2020	Neg/Neg/Neg	Sore throat	Pos/, 05DEC2020, B.1.2
C4591001 1117 11171120 (USA/MISSOURI/60/M)	Placebo	Dose 2/67	11DEC2020	16DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 15DEC2020, B.1.2
						Chills	
						New loss of taste or smell	
C4591001 1117 11171121 (USA/MISSOURI/34/F)	Placebo	Dose 2/42	16NOV2020	11JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 22NOV2020, B.1.2
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1117 11171141 (USA/MISSOURI/73/F)	Placebo	Dose 2/53	04DEC2020	25DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 06DEC2020, INDETERMINATE

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased shortness of breath	
						New or increased muscle pain	
						Diarrhea	
C4591001 1117 11171173 (USA/MISSOURI/61/M)	Placebo	Dose 2/38	22NOV2020	09DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 30NOV2020, B.1.2
						Sore throat	
C4591001 1118 11181014 (USA/NEW YORK/38/F)	Placebo	Dose 2/119	28DEC2020	13JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 30DEC2020, B.1.243
						Chills	
						New loss of taste or smell	
						Sore throat	
C4591001 1118 11181076 (USA/NEW YORK/33/F)	Placebo	Dose 2/110	27DEC2020	08JAN2021	Neg/Neg/Neg	Fever	Pos/, 28DEC2020, B.1.2
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						Sore throat	
						Diarrhea	
C4591001 1118 11181088 (USA/NEW YORK/73/M)	Placebo	Dose 2/36	20OCT2020	10NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 29OCT2020, INDETERMINATE
						New or increased muscle pain	
C4591001 1120 11201091 (USA/GEORGIA/67/F)	Placebo	Dose 2/135	15JAN2021	19JAN2021	Neg/Neg/Neg	Fever	Pos/, 20JAN2021, B.1.243
						New or increased muscle pain	
C4591001 1120 11201101 (USA/GEORGIA/48/F)	Placebo	Dose 2/133	04JAN2021	07FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 06JAN2021, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Diarrhea	
						Vomiting	
C4591001 1120 11201115 (USA/GEORGIA/19/F)	Placebo	Dose 2/73	06NOV2020	12NOV2020	Neg/Neg/Neg	Fever	Pos/, 09NOV2020, B.1
						New or increased muscle pain	
						Sore throat	
						Diarrhea	
C4591001 1120 11201154 (USA/GEORGIA/35/F)	Placebo	Dose 2/168	17FEB2021		Neg/Neg/Neg	Fever	Pos/, 19FEB2021, B.1.2
C4591001 1120 11201191 (USA/GEORGIA/23/M)	Placebo	Dose 2/86	26NOV2020	28NOV2020	Neg/Neg/Neg	Fever	Pos/, 27NOV2020, B.1.1.222
						New or increased cough	
						Chills	
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1120 11201353 (USA/GEORGIA/59/F)	Placebo	Dose 2/98	18FEB2021	10MAR2021	Neg/Neg/Neg	New or increased cough	Pos/, 04MAR2021, B.1
						New or increased muscle pain	
						Sore throat	
						Diarrhea	
C4591001 1120 11201374 (USA/GEORGIA/71/F)	Placebo	Dose 2/49	28DEC2020	04JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 30DEC2020, B.1.2
C4591001 1121 11211069 (USA/ILLINOIS/45/M)	Placebo	Dose 2/71	01DEC2020	20DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 04DEC2020, QNS
C4591001 1121 11211070 (USA/ILLINOIS/43/F)	Placebo	Dose 2/56	16NOV2020	20DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 27NOV2020, B.1.369
						New or increased muscle pain	
C4591001 1121 11211094 (USA/ILLINOIS/28/M)	Placebo	Dose 2/86	23DEC2020		Neg/Neg/Neg	New or increased shortness of breath	Pos/, 23DEC2020, B.1.139

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
C4591001 1121 11211105 (USA/ILLINOIS/52/M)	Placebo	Dose 2/39	05NOV2020	10DEC2020	Neg/Neg/Neg	Fever	Pos/, 06NOV2020, B.1.2
						New or increased cough	
						Sore throat	
C4591001 1122 11221025 (USA/OHIO/40/M)	Placebo	Dose 2/32	01NOV2020	16NOV2020	Neg/Neg/Neg	Fever	Pos/, 03NOV2020, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1123 11231025 (USA/NEBRASKA/60/F)	Placebo	Dose 2/77	08NOV2020	13DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 11NOV2020, B.1.234
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1123 11231073 (USA/NEBRASKA/25/F)	Placebo	Dose 2/10	10SEP2020	25SEP2020	Neg/Neg/Neg	Sore throat New or increased cough Chills New or increased muscle pain	Pos/Pos, 11SEP2020, B.1.369
C4591001 1123 11231086 (USA/NEBRASKA/35/F)	Placebo	Dose 2/57	27OCT2020	18NOV2020	Neg/Neg/Neg	Sore throat New or increased cough New or increased muscle pain	Pos/, 28OCT2020, B.1.2
C4591001 1123 11231102 (USA/NEBRASKA/52/F)	Placebo	Dose 2/88	28NOV2020	11DEC2020	Neg/Neg/Neg	Diarrhea	Pos/, 01DEC2020, B.1.509
C4591001 1123 11231103 (USA/NEBRASKA/63/M)	BNT162b2 (30 µg)	Dose 2/105	15DEC2020	26DEC2020	Neg/Neg/Neg	Fever New or increased cough Diarrhea	Pos/, 23DEC2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1123 11231117 (USA/NEBRASKA/55/F)	Placebo	Dose 2/64	10NOV2020	22NOV2020	Neg/Neg/Neg	Chills	Pos/, 11NOV2020, B.1.234
						New or increased muscle pain	
C4591001 1123 11231123 (USA/NEBRASKA/47/F)	Placebo	Dose 2/84	01DEC2020	11DEC2020	Neg/Neg/Neg	Fever	Pos/, 07DEC2020, B.1.2
						New or increased cough	
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Diarrhea	
						Vomiting	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1123 11231132 (USA/NEBRASKA/32/F)	Placebo	Dose 2/99	15DEC2020	26DEC2020	Neg/Neg/Neg	New or increased cough Chills New or increased muscle pain	Pos/, 16DEC2020, QNS
C4591001 1123 11231156 (USA/NEBRASKA/33/F)	Placebo	Dose 2/55	07NOV2020	30NOV2020	Neg/Neg/Neg	New or increased cough New or increased shortness of breath New or increased muscle pain New loss of taste or smell	Pos/, 12NOV2020, B.1.2
C4591001 1123 11231182 (USA/NEBRASKA/65/M)	Placebo	Dose 2/108	30DEC2020	08JAN2021	Neg/Neg/Neg	New loss of taste or smell Sore throat	Pos/, 30DEC2020, B.1.324

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1123 11231214 (USA/NEBRASKA/60/F)	Placebo	Dose 2/34	26OCT2020	01DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 05NOV2020, B.1.2
						New or increased shortness of breath	
						Chills	
						New loss of taste or smell	
						Sore throat	
C4591001 1123 11231232 (USA/NEBRASKA/39/F)	BNT162b2 (30 µg)	Dose 2/83	21DEC2020	08JAN2021	Neg/Neg/Neg	New or increased shortness of breath	Pos/, 23DEC2020, B.1.2
						New loss of taste or smell	
C4591001 1123 11231234 (USA/NEBRASKA/29/M)	Placebo	Dose 2/32	02NOV2020	12NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 03NOV2020, B.1.2
						New or increased muscle pain	
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1123 11231255 (USA/NEBRASKA/76/M)	Placebo	Dose 2/20	24OCT2020	01NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 02NOV2020, B.1.349
C4591001 1123 11231256 (USA/NEBRASKA/72/F)	Placebo	Dose 2/20	24OCT2020	25NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 02NOV2020, B.1.349
C4591001 1123 11231284 (USA/NEBRASKA/67/M)	Placebo	Dose 2/12	24OCT2020	24NOV2020	Neg/Neg/Neg	Fever	Pos/, 26OCT2020, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1123 11231339 (USA/NEBRASKA/35/F)	Placebo	Dose 2/38	02DEC2020	15JAN2021	Neg/Neg/Neg	Fever	Pos/, 09DEC2020, B.1.369
						New or increased cough	
						New or increased	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						shortness of breath	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1123 11231357 (USA/NEBRASKA/51/F)	Placebo	Dose 2/44	11DEC2020	18FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 15DEC2020, B.1
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1124 11241007 (USA/RHODE ISLAND/60/F)	Placebo	Dose 2/85	23NOV2020	03DEC2020	Neg/Neg/Neg	Fever	Pos/, 24NOV2020, B.1.517

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1124 11241052 (USA/RHODE ISLAND/39/F)	Placebo	Dose 2/101	18DEC2020	31DEC2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 21DEC2020, B.1
C4591001 1124 11241117 (USA/RHODE ISLAND/57/F)	Placebo	Dose 2/60	14NOV2020	19NOV2020	Neg/Neg/Neg	New or increased shortness of breath	Pos/, 15NOV2020, B.1.2
C4591001 1124 11241128 (USA/RHODE ISLAND/67/M)	Placebo	Dose 2/88	17DEC2020		Neg/Neg/Neg	Fever	Pos/, 18JAN2021, B.1.361
						New or increased cough	
						New or increased shortness of breath	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1124 11241176 (USA/RHODE ISLAND/49/M)	Placebo	Dose 2/72	03DEC2020	20DEC2020	Neg/Neg/Neg	Fever	Pos/, 04DEC2020, B.1.517
						New or increased cough	
						Chills	
						New or increased muscle pain	
C4591001 1125 11251006 (USA/NEBRASKA/35/M)	Placebo	Dose 2/42	11OCT2020	12OCT2020	Neg/Neg/Neg	Fever	Pos/, 11OCT2020, B.1.139
						New or increased cough	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1125 11251014 (USA/NEBRASKA/45/F)	Placebo	Dose 2/59	30OCT2020	17NOV2020	Neg/Neg/Neg	Fever	Pos/, 10NOV2020, B.1.413
						New or increased cough	
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						Diarrhea	
C4591001 1125 11251023 (USA/NEBRASKA/49/M)	Placebo	Dose 2/56	27OCT2020	18NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 06NOV2020, B.1.2
						New or increased shortness of breath	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 1125 11251028 (USA/NEBRASKA/39/F)	Placebo	Dose 2/27	29SEP2020	02OCT2020	Neg/Neg/Neg	Fever	Pos/, 01OCT2020, B.1
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1125 11251038 (USA/NEBRASKA/28/M)	Placebo	Dose 2/74	16NOV2020		Neg/Neg/Neg	Diarrhea	Pos/, 23NOV2020, B.1.240
C4591001 1125 11251049 (USA/NEBRASKA/52/M)	Placebo	Dose 2/50	27OCT2020	24DEC2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 02NOV2020, B.1.2
						Sore throat	
C4591001 1125 11251088 (USA/NEBRASKA/67/M)	Placebo	Dose 2/92	14DEC2020	10JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 23DEC2020, B.1
						New or increased shortness of breath	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1125 11251098 (USA/NEBRASKA/33/F)	Placebo	Dose 2/78	02DEC2020		Neg/Neg/Neg	New or increased cough	Pos/, 03DEC2020, B.1.2
C4591001 1125 11251106 (USA/NEBRASKA/44/F)	Placebo	Dose 2/68	20NOV2020	04DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 20NOV2020, B.1.2
						Sore throat	
C4591001 1125 11251109 (USA/NEBRASKA/46/F)	Placebo	Dose 2/51	04NOV2020	18NOV2020	Neg/Neg/Neg	Fever	Pos/, 05NOV2020, B.1.2
						New or increased shortness of breath	
						New or increased muscle pain	
						Diarrhea	
C4591001 1125 11251114 (USA/NEBRASKA/59/M)	Placebo	Dose 2/38	22OCT2020	26OCT2020	Neg/Neg/Neg	Fever	Pos/Pos, 28OCT2020, B.1.2
C4591001 1125 11251124 (USA/NEBRASKA/39/M)	Placebo	Dose 2/53	08NOV2020	10NOV2020	Neg/Neg/Neg	Fever	Pos/, 10NOV2020, B.1.139
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 1125 11251177 (USA/NEBRASKA/50/F)	BNT162b2 (30 µg)	Dose 2/68	29NOV2020	13DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 03DEC2020, B.1.2
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						Sore throat	
						Diarrhea	
C4591001 1125 11251208 (USA/NEBRASKA/51/F)	Placebo	Dose 2/43	13NOV2020	18NOV2020	Neg/Neg/Neg	New or increased cough	Pos/Pos, 19NOV2020, B.1.139
						New loss of taste or smell	
C4591001 1125 11251215 (USA/NEBRASKA/43/M)	Placebo	Dose 2/25	06NOV2020	13NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 11NOV2020, B.1.361

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1125 11251218 (USA/NEBRASKA/41/F)	Placebo	Dose 2/37	20NOV2020	04DEC2020	Neg/Neg/Neg	Chills	Pos/, 23NOV2020, B.1.2
						New loss of taste or smell	
C4591001 1126 11261017 (USA/CALIFORNIA/34/F)	Placebo	Dose 2/50	20OCT2020	20NOV2020	Neg/Neg/Neg	Fever	Pos/, 21OCT2020, B.1.2
						New or increased muscle pain	
C4591001 1126 11261179 (USA/CALIFORNIA/60/M)	Placebo	Dose 2/85	30DEC2020	28JAN2021	Neg/Neg/Neg	Fever	Pos/, 04JAN2021, B.1.311
						New or increased cough	
						Chills	
						New or increased muscle pain	
C4591001 1128 11281156 (USA/TEXAS/53/M)	Placebo	Dose 2/115	31DEC2020	15JAN2021	Neg/Neg/Neg	Fever	Pos/, 06JAN2021, B.1.2
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						Diarrhea	
C4591001 1128 11281165 (USA/TEXAS/26/F)	Placebo	Dose 2/46	29OCT2020	03NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 02NOV2020, B.1.2
						Sore throat	
C4591001 1128 11281194 (USA/TEXAS/82/M)	Placebo	Dose 2/112	05JAN2021	19JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 21JAN2021, A.2
						Vomiting	
C4591001 1128 11281224 (USA/TEXAS/46/M)	Placebo	Dose 2/88	14DEC2020	29DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 17DEC2020, B.1.2
						New or increased shortness of breath	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1128 11281281 (USA/TEXAS/36/F)	Placebo	Dose 2/51	12NOV2020	13NOV2020	Neg/Neg/Neg	Fever	Pos/, 13NOV2020, B.1.2
						New or increased muscle pain	
						Sore throat	
C4591001 1128 11281312 (USA/TEXAS/40/M)	Placebo	Dose 2/66	04DEC2020	15JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 08DEC2020, B.1.2
						New loss of taste or smell	
						Sore throat	
C4591001 1128 11281375 (USA/TEXAS/57/F)	Placebo	Dose 2/81	27DEC2020	29DEC2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 28DEC2020, B.1.2
C4591001 1129 11291044 (USA/FLORIDA/62/F)	Placebo	Dose 2/92	24NOV2020	09DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 24NOV2020, B.1
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						Diarrhea	
C4591001 1131 11311036 (USA/OHIO/62/F)	Placebo	Dose 2/112	29DEC2020	13JAN2021	Neg/Neg/Neg	Fever	Pos/, 30DEC2020, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1131 11311039 (USA/OHIO/69/F)	Placebo	Dose 2/107	23DEC2020	26DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 28DEC2020, B.1.2
						Diarrhea	
C4591001 1131 11311045 (USA/OHIO/40/M)	Placebo	Dose 2/143	31JAN2021	07FEB2021	Neg/Neg/Neg	Fever	Pos/, 01FEB2021, B.1.2
						New or increased cough	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						Diarrhea	
						Vomiting	
C4591001 1131 11311100 (USA/OHIO/64/M)	Placebo	Dose 2/58	12NOV2020	30NOV2020	Neg/Neg/Neg	Fever	Pos/, 13NOV2020, B.1.2
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1131 11311113 (USA/OHIO/40/F)	Placebo	Dose 2/59	21NOV2020	23NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 23NOV2020, B.1.2
						New or increased shortness of breath	
C4591001 1131 11311138 (USA/OHIO/45/F)	Placebo	Dose 2/45	07NOV2020	01DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 10NOV2020, B.1
						New or increased shortness of breath	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1131 11311160 (USA/OHIO/27/F)	Placebo	Dose 2/52	18NOV2020	02DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 23NOV2020, B.1.2
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1131 11311170 (USA/OHIO/60/F)	BNT162b2 (30 µg)	Dose 2/58	27NOV2020	22FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 29NOV2020, B.1.2
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1131 11311241 (USA/OHIO/50/M)	Placebo	Dose 2/63	03JAN2021	10JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 11JAN2021, B.1.361

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
C4591001 1131 11311269 (USA/OHIO/16/M)	Placebo	Dose 2/45	28JAN2021	04FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 28JAN2021, B.1.429
						New or increased shortness of breath	
						Chills	
C4591001 1133 11331097 (USA/FLORIDA/46/F)	Placebo	Dose 2/143	18JAN2021	08FEB2021	Neg/Neg/Neg	Fever	Pos/, 02FEB2021, QNS
						New or increased cough	
						New or increased	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						shortness of breath	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1133 11331209 (USA/FLORIDA/30/M)	Placebo	Dose 2/32	10OCT2020	15OCT2020	Neg/Neg/Neg	New or increased cough	Pos/, 13OCT2020, B.1
						Sore throat	
C4591001 1133 11331333 (USA/FLORIDA/46/F)	Placebo	Dose 2/108	08JAN2021	09FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 18JAN2021, B.1.1.29
						New or increased muscle pain	
C4591001 1133 11331335 (USA/FLORIDA/51/M)	Placebo	Dose 2/108	08JAN2021	27JAN2021	Neg/Neg/Neg	Fever	Pos/, 18JAN2021, B.1.1.29

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						New or increased muscle pain	
C4591001 1133 11331445 (USA/FLORIDA/61/F)	Placebo	Dose 2/73	18DEC2020	15JAN2021	Neg/Neg/Neg	Fever	Pos/, 11JAN2021, QNS
						Chills	
						New or increased muscle pain	
						Diarrhea	
C4591001 1133 11331511 (USA/FLORIDA/30/M)	BNT162b2 (30 µg)	Dose 2/50	02DEC2020	10DEC2020	Neg/Neg/Neg	New or increased shortness of breath	Pos/, 07DEC2020, B.1.1
						New loss of taste or smell	
C4591001 1133 11331525 (USA/FLORIDA/45/M)	Placebo	Dose 2/16	26NOV2020	27NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 01DEC2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 1133 11331526 (USA/FLORIDA/55/M)	Placebo	Dose 2/20	30NOV2020	16DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 01DEC2020, B.1.2
						New or increased muscle pain	
C4591001 1133 11331604 (USA/FLORIDA/54/M)	Placebo	Dose 2/19	07DEC2020	15DEC2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 14DEC2020, B.1.2
C4591001 1134 11341022 (USA/NORTH CAROLINA/66/M)	Placebo	Dose 2/29	29SEP2020	03OCT2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 30SEP2020, B.1.369
						Sore throat	
C4591001 1134 11341031 (USA/NORTH CAROLINA/31/M)	Placebo	Dose 2/92	30NOV2020	05DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 01DEC2020, B.1.2
						New loss of taste or smell	
C4591001 1134 11341035 (USA/NORTH CAROLINA/59/F)	Placebo	Dose 2/114	23DEC2020	06JAN2021	Neg/Neg/Neg	Fever	Pos/, 24DEC2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Diarrhea	
C4591001 1134 11341086 (USA/NORTH CAROLINA/41/F)	Placebo	Dose 2/134	19JAN2021	15FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 20JAN2021, B.1.2
C4591001 1134 11341190 (USA/NORTH CAROLINA/52/F)	Placebo	Dose 2/94	19DEC2020	31DEC2020	Neg/Neg/Neg	Fever	Pos/, 20DEC2020, INDETERMINATE
						New or increased cough	
						Chills	
						New or increased muscle pain	
C4591001 1134 11341254 (USA/NORTH CAROLINA/29/F)	Placebo	Dose 2/106	07JAN2021	03FEB2021	Neg/Neg/Neg	New or increased cough	Neg/ (R1 Pos), (19JAN2021), (B.1.2)
						New or increased shortness of breath	
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1134 11341406 (USA/NORTH CAROLINA/48/M)	Placebo	Dose 2/43	14DEC2020	07JAN2021	Neg/Neg/Neg	Fever	Pos/, 28DEC2020, B.1.2
						New or increased cough	
						New or increased shortness of breath	
						Chills	
C4591001 1134 11341411 (USA/NORTH CAROLINA/69/M)	Placebo	Dose 2/18	20NOV2020	21NOV2020	Neg/Neg/Neg	Fever	Pos/, 21NOV2020, B.1.2
C4591001 1135 11351001 (USA/CALIFORNIA/18/M)	Placebo	Dose 2/83	15NOV2020	07DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 17NOV2020, B.1
						New loss of taste or smell	
						Sore throat	
C4591001 1135 11351023 (USA/CALIFORNIA/37/F)	Placebo	Dose 2/128	30DEC2020	06JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 02JAN2021, B.1.429
						New or increased	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						shortness of breath	
C4591001 1135 11351029 (USA/CALIFORNIA/27/M)	Placebo	Dose 2/84	18NOV2020	24NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 20NOV2020, B.1.2
C4591001 1135 11351038 (USA/CALIFORNIA/48/M)	Placebo	Dose 2/97	07DEC2020	15DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 08DEC2020, B.1.438
						Chills	
						New or increased muscle pain	
C4591001 1135 11351041 (USA/CALIFORNIA/29/F)	Placebo	Dose 2/122	27DEC2020	22JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 29DEC2020, B.1.404
						New or increased shortness of breath	
						Diarrhea	
C4591001 1135 11351045 (USA/CALIFORNIA/57/F)	Placebo	Dose 2/106	08DEC2020	22FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 10DEC2020, B.1.400

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
C4591001 1135 11351082 (USA/CALIFORNIA/39/F)	Placebo	Dose 2/116	21DEC2020	08JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 24DEC2020, B.1.177
						New or increased shortness of breath	
						New or increased muscle pain	
						Diarrhea	
						Vomiting	
C4591001 1135 11351111 (USA/CALIFORNIA/53/F)	Placebo	Dose 2/128	05JAN2021	12JAN2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 06JAN2021, B.1.429
C4591001 1135 11351177 (USA/CALIFORNIA/46/F)	Placebo	Dose 2/70	18NOV2020	28NOV2020	Neg/Neg/Neg	Fever	Pos/, 19NOV2020, B.1.311
						New or increased cough	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Sore throat	
						Vomiting	
C4591001 1135 11351207 (USA/CALIFORNIA/33/F)	Placebo	Dose 2/30	13OCT2020	28OCT2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 19OCT2020, B.1.1.63
						New loss of taste or smell	
						Diarrhea	
C4591001 1135 11351230 (USA/CALIFORNIA/38/M)	Placebo	Dose 2/48	15NOV2020	18NOV2020	Neg/Neg/Neg	Fever	Pos/, 17NOV2020, B.1.239
						New or increased cough	
						Chills	
						New or increased muscle pain	
C4591001 1135 11351237 (USA/CALIFORNIA/75/F)	Placebo	Dose 2/99	28DEC2020	31DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 29DEC2020, B.1.427

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1135 11351294 (USA/CALIFORNIA/42/M)	Placebo	Dose 2/95	26DEC2020	29DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 29DEC2020, B.1.429
						New or increased muscle pain	
C4591001 1135 11351361 (USA/CALIFORNIA/24/F)	Placebo	Dose 2/106	20JAN2021	28JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 25JAN2021, B.1.2
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1135 11351388 (USA/CALIFORNIA/63/F)	Placebo	Dose 2/65	12DEC2020	30DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 15DEC2020, B.1.2
						Chills	
						New or increased muscle pain	
C4591001 1135 11351390 (USA/CALIFORNIA/60/M)	Placebo	Dose 2/56	03DEC2020	15DEC2020	Neg/Neg/Neg	Fever	Pos/, 04DEC2020, B.1.189

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1135 11351400 (USA/CALIFORNIA/37/M)	Placebo	Dose 2/57	08DEC2020	01JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 11DEC2020, B.1.429
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Vomiting	
C4591001 1135 11351426 (USA/CALIFORNIA/57/M)	Placebo	Dose 2/69	23DEC2020	02JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 02JAN2021, B.1.429
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
C4591001 1135 11351451 (USA/CALIFORNIA/50/F)	Placebo	Dose 2/30	08DEC2020	21DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 09DEC2020, B.1.1.29
						Chills	
						New or increased muscle pain	
C4591001 1135 11351527 (USA/CALIFORNIA/43/M)	Placebo	Dose 2/81	01FEB2021		Neg/Neg/Neg	New or increased cough	Pos/, 04FEB2021, B.1.427
C4591001 1135 11351534 (USA/CALIFORNIA/37/F)	Placebo	Dose 2/30	15DEC2020	11JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 21DEC2020, B.1.2
C4591001 1136 11361011 (USA/NEVADA/72/M)	Placebo	Dose 2/62	18NOV2020	02DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 25NOV2020, B.47
C4591001 1136 11361012 (USA/NEVADA/39/M)	Placebo	Dose 2/82	28NOV2020	21DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 30NOV2020, B.1.403
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Sore throat	
						Diarrhea	
C4591001 1140 11401028 (USA/NEW YORK/53/F)	Placebo	Dose 2/91	09DEC2020	18DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 10DEC2020, B.1.243
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1140 11401039 (USA/NEW YORK/53/F)	Placebo	Dose 2/121	22DEC2020	03JAN2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 25DEC2020, B.1.240
C4591001 1140 11401063 (USA/NEW YORK/49/M)	BNT162b2 (30 µg)	Dose 2/108	11DEC2020	23DEC2020	Neg/Neg/Neg	Sore throat	Pos/, 13DEC2020, B.1.234
C4591001 1140 11401135 (USA/NEW YORK/54/M)	Placebo	Dose 2/110	26DEC2020	29DEC2020	Neg/Neg/Neg	Fever	Pos/, 29DEC2020, B.1.243
						Chills	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1140 11401263 (USA/NEW YORK/66/F)	Placebo	Dose 2/67	31DEC2020		Neg/Neg/Neg	Sore throat New loss of taste or smell	Pos/, 02JAN2021, B.1.2
C4591001 1140 11401281 (USA/NEW YORK/23/M)	Placebo	Dose 2/65	05JAN2021	31JAN2021	Neg/Neg/Neg	Sore throat Fever New or increased cough Chills	Pos/, 06JAN2021, B.1.2
C4591001 1141 11411006 (USA/IOWA/25/M)	BNT162b2 (30 µg)	Dose 2/119	17DEC2020	19DEC2020	Pos/Neg/Neg	Sore throat New or increased cough New or increased shortness of breath Chills New or increased muscle pain Sore throat	Pos/, 20DEC2020, QNS

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1141 11411032 (USA/IOWA/22/F)	Placebo	Dose 2/72	20NOV2020	29NOV2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 24NOV2020, B.1.2
						Sore throat	
C4591001 1141 11411045 (USA/IOWA/46/F)	Placebo	Dose 2/81	16NOV2020	05JAN2021	Neg/Neg/Neg	Fever	Neg/ (R1 Pos), (20DEC2020), (B.1.2)
						New or increased cough	
						Chills	
						New loss of taste or smell	
						Sore throat	
C4591001 1141 11411088 (USA/IOWA/52/M)	Placebo	Dose 2/29	07OCT2020	10OCT2020	Neg/Neg/Neg	Fever	Pos/, 08OCT2020, B.1.2
						Chills	
						Sore throat	
C4591001 1141 11411161 (USA/IOWA/25/F)	Placebo	Dose 2/47	08NOV2020	15NOV2020	Neg/Neg/Neg	Fever	Pos/, 10NOV2020, B.1.2
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Diarrhea	
						Vomiting	
C4591001 1141 11411162 (USA/IOWA/20/M)	Placebo	Dose 2/44	05NOV2020	09NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 08NOV2020, B.1.139
						Sore throat	
C4591001 1141 11411175 (USA/IOWA/28/F)	Placebo	Dose 2/51	14NOV2020	30NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 17NOV2020, B
						Chills	
						New or increased muscle pain	
C4591001 1141 11411195 (USA/IOWA/36/F)	Placebo	Dose 2/94	15JAN2021		Neg/Neg/Neg	Fever	Pos/ (R1 Pos), 26JAN2021 (03FEB2021), B.1.2 (B.1)
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1141 11411204 (USA/IOWA/21/F)	Placebo	Dose 2/61	30NOV2020	13DEC2020	Neg/Neg/Neg	Fever	Pos/, 07DEC2020, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1141 11411221 (USA/IOWA/46/F)	Placebo	Dose 2/76	21DEC2020	02JAN2021	Neg/Neg/Neg	Fever	Pos/, 22DEC2020, B.1.311
						Chills	
						New or increased muscle pain	
C4591001 1141 11411242 (USA/IOWA/22/F)	Placebo	Dose 2/25	08NOV2020	30NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 20NOV2020, B.1.139
						New or increased muscle pain	
						New loss of taste or smell	
						Diarrhea	
C4591001 1142 11421120 (USA/TEXAS/68/M)	Placebo	Dose 2/96	12DEC2020	31DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 15DEC2020, B.1.2
						New or increased muscle pain	
C4591001 1142 11421148 (USA/TEXAS/59/M)	Placebo	Dose 2/59	11NOV2020	20NOV2020	Neg/Neg/Neg	Fever	Pos/, 16NOV2020, B.1.405
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1142 11421197 (USA/TEXAS/48/F)	Placebo	Dose 2/70	08DEC2020	14DEC2020	Neg/Neg/Neg	Fever	Pos/, 09DEC2020, B.1.2
						New or increased shortness of breath	
						Chills	
C4591001 1142 11421255 (USA/TEXAS/48/M)	Placebo	Dose 2/68	20DEC2020	10JAN2021	Neg/Neg/Neg	New or increased shortness of breath	Pos/, 23DEC2020, B.1.2
						New or increased muscle pain	
C4591001 1142 11421388 (USA/TEXAS/15/M)	Placebo	Dose 2/25	19FEB2021		Neg/Neg/Neg	Sore throat	Pos/, 19FEB2021, B.1.2
C4591001 1145 11451056 (USA/MARYLAND/67/F)	Placebo	Dose 2/59	14NOV2020	20NOV2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 16NOV2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1146 11461004 (USA/NEW JERSEY/40/F)	Placebo	Dose 2/84	24NOV2020	28DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 27NOV2020, B.1.1.207
						New loss of taste or smell	
						Sore throat	
C4591001 1146 11461070 (USA/NEW JERSEY/54/F)	Placebo	Dose 2/116	03JAN2021	08JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 07JAN2021, B.1.243
						New loss of taste or smell	
						Diarrhea	
C4591001 1146 11461071 (USA/NEW JERSEY/54/M)	BNT162b2 (30 µg)	Dose 2/116	03JAN2021	08JAN2021	Neg/Neg/Neg	Sore throat	Pos/, 11JAN2021, QNS
C4591001 1146 11461156 (USA/NEW JERSEY/60/M)	Placebo	Dose 2/54	09NOV2020	23NOV2020	Neg/Neg/Neg	Fever	Pos/, 16NOV2020, B.1.240
						New or increased cough	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1146 11461235 (USA/65/M)	Placebo	Dose 2/60	03DEC2020	08DEC2020	Neg/Neg/Neg	New or increased cough	Unk/Pos, 03DEC2020, NS
						New or increased muscle pain	
C4591001 1146 11461268 (USA/NEW JERSEY/42/M)	Placebo	Dose 2/73	20JAN2021	27JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 21JAN2021, B.1.1.220
						Sore throat	
C4591001 1146 11461309 (USA/NEW JERSEY/52/F)	Placebo	Dose 2/17	28NOV2020	02DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 28NOV2020, B.1.234
						Sore throat	
C4591001 1146 11461379 (USA/NEW JERSEY/45/M)	Placebo	Dose 2/17	03DEC2020		Neg/Neg/Neg	Sore throat	Pos/, 05DEC2020, B.1
						Diarrhea	
C4591001 1147 11471021 (USA/LOUISIANA/35/F)	Placebo	Dose 2/108	13DEC2020	20DEC2020	Neg/Neg/Neg	New loss of taste or smell	Pos/Pos, 24DEC2020, B.1.234
C4591001 1147 11471025 (USA/LOUISIANA/35/M)	Placebo	Dose 2/101	04DEC2020	18DEC2020	Neg/Neg/Neg	Fever	Pos/, 05DEC2020, B.1.240
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						Chills	
						New or increased muscle pain	
C4591001 1147 11471176 (USA/LOUISIANA/20/M)	Placebo	Dose 2/106	23DEC2020	28DEC2020	Neg/Neg/Neg	Fever	Pos/, 26DEC2020, B.1.234
						New or increased cough	
						Chills	
C4591001 1147 11471205 (USA/LOUISIANA/57/M)	Placebo	Dose 2/79	08DEC2020	11DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 09DEC2020, B.1.243
C4591001 1147 11471228 (USA/LOUISIANA/59/F)	BNT162b2 (30 µg)	Dose 2/74	11DEC2020	18DEC2020	Neg/Neg/Neg	Sore throat	Pos/, 13DEC2020, B.1.243
C4591001 1149 11491113 (USA/CALIFORNIA/69/M)	BNT162b2 (30 µg)	Dose 2/44	23OCT2020	24OCT2020	Neg/Neg/Neg	Fever	Pos/, 26OCT2020, B.1
						Chills	
						Vomiting	
C4591001 1149 11491135 (USA/CALIFORNIA/71/M)	Placebo	Dose 2/76	28NOV2020	23JAN2021	Neg/Neg/Neg	Fever	Pos/, 01DEC2020, B.1
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						Chills	
						New or increased muscle pain	
						Sore throat	
						Diarrhea	
C4591001 1149 11491160 (USA/CALIFORNIA/34/F)	Placebo	Dose 2/112	06JAN2021	22JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 08JAN2021, B.1.215
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1149 11491260 (USA/CALIFORNIA/60/M)	Placebo	Dose 2/77	24DEC2020	01JAN2021	Neg/Neg/Neg	New or increased shortness of breath	Pos/, 04JAN2021, B.1.429
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1149 11491263 (USA/CALIFORNIA/24/F)	BNT162b2 (30 µg)	Dose 2/96	12JAN2021	26JAN2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 14JAN2021, B.1.2
						Sore throat	
						Diarrhea	
C4591001 1149 11491265 (USA/CALIFORNIA/59/M)	Placebo	Dose 2/107	26JAN2021	13FEB2021	Neg/Neg/Neg	Fever	Pos/, 03FEB2021, B.1.2
						New or increased cough	
						New or increased shortness of breath	
						New or increased muscle pain	
C4591001 1149 11491340 (USA/CALIFORNIA/47/F)	Placebo	Dose 2/30	18DEC2020	20DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 19DEC2020, B.1.429
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1150 11501009 (USA/OHIO/29/M)	Placebo	Dose 2/123	09JAN2021	17JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 11JAN2021, B.1.2
						New loss of taste or smell	
C4591001 1150 11501055 (USA/OHIO/42/F)	Placebo	Dose 2/107	30DEC2020	08JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 30DEC2020, B.1.429
						Sore throat	
C4591001 1150 11501093 (USA/OHIO/45/F)	Placebo	Dose 2/84	16DEC2020	09JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 28DEC2020, B.1.2
C4591001 1150 11501204 (USA/OHIO/14/M)	Placebo	Dose 2/32	04FEB2021		Neg/Neg/Neg	New or increased cough	Pos/, 05FEB2021, B.1.2
						Sore throat	
C4591001 1152 11521010 (USA/CALIFORNIA/34/F)	Placebo	Dose 2/87	27NOV2020	27DEC2020	Neg/Neg/Neg	Fever	Pos/, 07DEC2020, INDETERMINATE
						New or increased shortness of breath	
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1152 11521032 (USA/CALIFORNIA/22/F)	Placebo	Dose 2/113	22DEC2020	16JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 28DEC2020, B.1.1.222
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1152 11521039 (USA/CALIFORNIA/39/F)	Placebo	Dose 2/93	03DEC2020	20DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 15DEC2020, B.1.1.222
						New or increased shortness of breath	
						New loss of taste or smell	
C4591001 1152 11521063 (USA/CALIFORNIA/35/F)	Placebo	Dose 2/117	26DEC2020	10JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 06JAN2021, B.1.427
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1152 11521082 (USA/CALIFORNIA/62/F)	Placebo	Dose 2/115	25DEC2020	20JAN2021	Neg/Neg/Neg	New or increased cough	Unk/Pos, 07JAN2021, B.1.2
						Diarrhea	
C4591001 1152 11521226 (USA/CALIFORNIA/47/M)	Placebo	Dose 2/68	21NOV2020	10DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 24NOV2020, B.1.1.222
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1152 11521265 (USA/CALIFORNIA/77/M)	BNT162b2 (30 µg)	Dose 2/53	12NOV2020	30NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 24NOV2020, B.1.2
C4591001 1152 11521309 (USA/CALIFORNIA/31/F)	Placebo	Dose 2/69	29NOV2020	15DEC2020	Neg/Neg/Neg	New or increased shortness of breath	Pos/, 30NOV2020, B.1.2
						Chills	
						Sore throat	
						Diarrhea	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1152 11521322 (USA/CALIFORNIA/20/M)	Placebo	Dose 2/109	08JAN2021	22JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 12JAN2021, B.1.429
						Sore throat	
C4591001 1152 11521339 (USA/CALIFORNIA/35/M)	Placebo	Dose 2/64	26NOV2020	12DEC2020	Neg/Neg/Neg	Fever	Pos/, 30NOV2020, B.1.2
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1152 11521342 (USA/CALIFORNIA/57/F)	Placebo	Dose 2/98	28DEC2020		Neg/Neg/Neg	New or increased cough	Pos/, 06JAN2021, B.1.404
						Sore throat	
C4591001 1152 11521363 (USA/CALIFORNIA/19/M)	Placebo	Dose 2/9	06OCT2020	10OCT2020	Neg/Neg/Neg	New or increased cough	Pos/, 07OCT2020, B.1.232
C4591001 1152 11521372 (USA/CALIFORNIA/28/F)	Placebo	Dose 2/32	29OCT2020	07NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 31OCT2020, B.1.243
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Sore throat	
C4591001 1152 11521413 (USA/CALIFORNIA/27/F)	Placebo	Dose 2/105	11JAN2021		Neg/Neg/Neg	Fever	Pos/, 14JAN2021, B.1.429
						New or increased cough	
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Diarrhea	
C4591001 1152 11521455 (USA/CALIFORNIA/53/F)	Placebo	Dose 2/83	28DEC2020	13JAN2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 14JAN2021, B.1

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
C4591001 1152 11521473 (USA/CALIFORNIA/60/M)	Placebo	Dose 2/76	28DEC2020	19FEB2021	Neg/Neg/Neg	Chills	Pos/, 13JAN2021, B.1.404
						New loss of taste or smell	
						Sore throat	
C4591001 1152 11521501 (USA/CALIFORNIA/27/F)	Placebo	Dose 2/13	10NOV2020	12NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 16NOV2020, B.1.1.152
C4591001 1152 11521573 (USA/CALIFORNIA/59/F)	Placebo	Dose 2/48	03JAN2021		Neg/Neg/Neg	New or increased cough	Pos/, 06JAN2021, B.1.404
						Chills	
						New or increased muscle pain	
						Diarrhea	
C4591001 1152 11521666 (USA/CALIFORNIA/15/F)	Placebo	Dose 2/17	15JAN2021	23JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 21JAN2021, B.1.427
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
C4591001 1156 11561067 (USA/FLORIDA/63/F)	Placebo	Dose 2/98	27DEC2020	14JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 29DEC2020, B.1.2
						Sore throat	
C4591001 1156 11561178 (USA/FLORIDA/50/F)	Placebo	Dose 2/73	27DEC2020	31DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 28DEC2020, B.1.2
C4591001 1156 11561260 (USA/FLORIDA/15/F)	Placebo	Dose 2/82	01FEB2021	05FEB2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 01FEB2021, B.1.2
C4591001 1156 11561263 (USA/FLORIDA/15/M)	Placebo	Dose 2/41	20DEC2020	25DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 22DEC2020, B.1.369
C4591001 1157 11571098 (USA/CALIFORNIA/65/F)	Placebo	Dose 2/70	23NOV2020	27NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 25NOV2020, B.1.311
C4591001 1157 11571147 (USA/CALIFORNIA/67/F)	Placebo	Dose 2/14	12NOV2020	03DEC2020	Neg/Neg/Neg	Fever	Pos/, 13NOV2020, B.1.119
						New or increased cough	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Vomiting	
C4591001 1157 11571148 (USA/CALIFORNIA/61/F)	Placebo	Dose 2/22	20NOV2020	03DEC2020	Neg/Neg/Unk	New or increased cough	Pos/, 27NOV2020, B.1.2
C4591001 1157 11571166 (USA/CALIFORNIA/26/M)	Placebo	Dose 2/50	30DEC2020	06JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 31DEC2020, B.1.404
C4591001 1162 11621011 (USA/GEORGIA/56/M)	Placebo	Dose 2/150	21JAN2021		Neg/Neg/Neg	Chills	Pos/, 22JAN2021, B.1.2
						Diarrhea	
C4591001 1162 11621075 (USA/GEORGIA/40/F)	Placebo	Dose 2/67	06NOV2020	08NOV2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 09NOV2020, B.1.2
C4591001 1162 11621103 (USA/GEORGIA/39/F)	Placebo	Dose 2/97	09DEC2020		Neg/Neg/Neg	New or increased shortness of breath	Pos/, 11DEC2020, B.1.2
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1162 11621124 (USA/GEORGIA/36/M)	Placebo	Dose 2/112	29DEC2020	04JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 04JAN2021, B.1.2
C4591001 1162 11621241 (USA/GEORGIA/68/M)	Placebo	Dose 2/102	02JAN2021	09JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 08JAN2021, B.1.139
						Sore throat	
						Vomiting	
C4591001 1162 11621281 (USA/GEORGIA/56/M)	Placebo	Dose 2/97	29DEC2020	01JAN2021	Neg/Neg/Neg	Fever	Pos/, 04JAN2021, B.1.2
						New or increased cough	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1162 11621554 (USA/GEORGIA/49/F)	Placebo	Dose 2/44	24DEC2020		Neg/Neg/Neg	New or increased cough	Pos/, 08JAN2021, B.1.2
						New loss of taste or smell	
C4591001 1163 11631009 (USA/LOUISIANA/72/F)	BNT162b2 (30 µg)	Dose 2/93	24NOV2020	04DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 01DEC2020, B.1.2
						New or increased shortness of breath	
						New or increased muscle pain	
C4591001 1163 11631014 (USA/LOUISIANA/66/M)	BNT162b2 (30 µg)	Dose 2/80	13NOV2020	18NOV2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 16NOV2020, B.1.234
C4591001 1163 11631037 (USA/LOUISIANA/37/M)	Placebo	Dose 2/118	19DEC2020	28DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 21DEC2020, INDETERMINATE
						Chills	
						Diarrhea	
C4591001 1163 11631113 (USA/LOUISIANA/25/M)	Placebo	Dose 2/43	14OCT2020	22OCT2020	Neg/Neg/Neg	Fever	Pos/, 19OCT2020, B.1.265

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Chills	
						Sore throat	
C4591001 1163 11631135 (USA/LOUISIANA/42/M)	Placebo	Dose 2/21	30SEP2020	02OCT2020	Neg/Neg/Neg	Fever	Pos/, 30SEP2020, B.1.243
						New or increased muscle pain	
						Diarrhea	
C4591001 1166 11661005 (USA/OHIO/40/M)	Placebo	Dose 2/79	26NOV2020	02DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 30NOV2020, B.1.265
						Chills	
						New or increased muscle pain	
						Diarrhea	
C4591001 1166 11661025 (USA/OHIO/31/M)	BNT162b2 (30 µg)	Dose 2/69	17NOV2020	09DEC2020	Neg/Neg/Neg	Fever	Pos/, 01DEC2020, QNS
						New or increased	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						shortness of breath	
						Chills	
						New or increased muscle pain	
C4591001 1166 11661035 (USA/OHIO/38/M)	Placebo	Dose 2/66	12NOV2020	31DEC2020	Neg/Neg/Neg	Fever	Pos/, 17NOV2020, B.1.2
						New loss of taste or smell	
						Sore throat	
C4591001 1166 11661094 (USA/OHIO/54/M)	Placebo	Dose 2/51	03DEC2020	11DEC2020	Neg/Neg/Neg	Fever	Pos/, 08DEC2020, B.1
						New or increased cough	
						Chills	
						New or increased muscle pain	
C4591001 1167 11671031 (USA/TENNESSEE/72/M)	Placebo	Dose 2/90	08DEC2020	12DEC2020	Neg/Neg/Neg	Sore throat	Pos/, 08DEC2020, B.1.2
C4591001 1167 11671046 (USA/TENNESSEE/54/M)	Placebo	Dose 2/113	01JAN2021	11JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 04JAN2021, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1167 11671152 (USA/TENNESSEE/41/F)	Placebo	Dose 2/26	20OCT2020	10NOV2020	Neg/Neg/Neg	Fever	Pos/Pos, 26OCT2020, B.1.1.29
						New or increased cough	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1167 11671157 (USA/TENNESSEE/58/M)	Placebo	Dose 2/16	14OCT2020	26OCT2020	Neg/Neg/Neg	Fever	Pos/, 15OCT2020, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
C4591001 1167 11671171 (USA/TENNESSEE/59/F)	Placebo	Dose 2/55	22NOV2020	04JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 07DEC2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1167 11671186 (USA/TENNESSEE/66/M)	Placebo	Dose 2/72	18DEC2020	20DEC2020	Neg/Neg/Neg	Fever	Pos/, 23DEC2020, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
C4591001 1167 11671211 (USA/TENNESSEE/54/M)	BNT162b2 (30 µg)	Dose 2/65	15DEC2020	30JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 17DEC2020, INDETERMINATE
C4591001 1168 11681004 (USA/OKLAHOMA/54/M)	Placebo	Dose 2/67	07NOV2020	19NOV2020	Neg/Neg/Neg	Fever	Pos/, 11NOV2020, B.1.243
						New or increased cough	
						New or increased muscle pain	
C4591001 1168 11681007 (USA/OKLAHOMA/33/F)	Placebo	Dose 2/36	06OCT2020	28FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 08OCT2020, B.1
						New or increased	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						shortness of breath	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1168 11681008 (USA/OKLAHOMA/37/M)	Placebo	Dose 2/35	05OCT2020	20NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 06OCT2020, B.1
						New loss of taste or smell	
C4591001 1168 11681078 (USA/OKLAHOMA/20/M)	Placebo	Dose 2/77	29NOV2020	15DEC2020	Neg/Neg/Neg	Fever	Pos/, 06DEC2020, B.1.234
						New or increased cough	
						New or increased shortness of breath	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1168 11681079 (USA/OKLAHOMA/41/M)	BNT162b2 (30 µg)	Dose 2/114	06JAN2021		Neg/Neg/Neg	Chills	Pos/, 07JAN2021, B.1.1.222
						New loss of taste or smell	
C4591001 1168 11681080 (USA/OKLAHOMA/37/F)	Placebo	Dose 2/108	31DEC2020	12FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 07JAN2021, B.1.1.222
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Diarrhea	
C4591001 1168 11681090 (USA/OKLAHOMA/18/F)	Placebo	Dose 2/107	01JAN2021	15JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 07JAN2021, B.1.1.29
						New or increased	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						shortness of breath	
						New loss of taste or smell	
C4591001 1168 11681114 (USA/OKLAHOMA/46/F)	Placebo	Dose 2/23	13OCT2020		Neg/Neg/Neg	Fever	Pos/, 13OCT2020, B.1.311
						New or increased cough	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1168 11681117 (USA/OKLAHOMA/37/M)	Placebo	Dose 2/45	04NOV2020	08NOV2020	Neg/Neg/Neg	Fever	Pos/, 05NOV2020, B.1.2
						New or increased muscle pain	
C4591001 1168 11681147 (USA/OKLAHOMA/66/M)	Placebo	Dose 2/96	02JAN2021		Neg/Neg/Neg	Fever	Pos/, 03JAN2021, B.1.240

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1168 11681187 (USA/OKLAHOMA/34/F)	Placebo	Dose 2/40	17NOV2020	25DEC2020	Neg/Neg/Neg	Sore throat Fever New or increased muscle pain New loss of taste or smell	Pos/, 19NOV2020, NS
C4591001 1168 11681202 (USA/OKLAHOMA/24/M)	Placebo	Dose 2/88	08JAN2021	22JAN2021	Neg/Neg/Neg	Sore throat Diarrhea New or increased cough New or increased shortness of breath Chills New or increased muscle pain New loss of taste or smell Sore throat	Pos/, 11JAN2021, B.1.1

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1168 11681230 (USA/OKLAHOMA/61/M)	BNT162b2 (30 µg)	Dose 2/57	04JAN2021	10JAN2021	Neg/Neg/Neg	Vomiting New or increased cough Chills New or increased muscle pain Sore throat	Pos/, 06JAN2021, B.1.2
C4591001 1168 11681232 (USA/OKLAHOMA/67/F)	BNT162b2 (30 µg)	Dose 2/60	07JAN2021	14JAN2021	Neg/Neg/Neg	Fever New loss of taste or smell	Pos/, 08JAN2021, B.1.2
C4591001 1169 11691007 (USA/PENNSYLVANIA/28/F)	Placebo	Dose 2/19	11OCT2020	11NOV2020	Neg/Neg/Neg	New or increased shortness of breath New loss of taste or smell	Pos/, 13OCT2020, B.1.234
C4591001 1170 11701060 (USA/TEXAS/30/F)	Placebo	Dose 2/84	01DEC2020	15DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 07DEC2020, B.1.234
C4591001 1170 11701089 (USA/TEXAS/25/F)	Placebo	Dose 2/16	01OCT2020	05OCT2020	Neg/Neg/Neg	Fever	Pos/, 03OCT2020, B.1.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1170 11701149 (USA/TEXAS/27/F)	Placebo	Dose 2/74	04DEC2020	12DEC2020	Neg/Neg/Neg	Sore throat Fever New or increased cough New or increased muscle pain	Pos/, 07DEC2020, B.1.2
C4591001 1170 11701195 (USA/TEXAS/54/F)	Placebo	Dose 2/68	30NOV2020	14DEC2020	Neg/Neg/Neg	Fever New or increased cough	Pos/, 04DEC2020, B.1.2
C4591001 1170 11701221 (USA/TEXAS/48/M)	Placebo	Dose 2/43	10NOV2020	30NOV2020	Neg/Neg/Neg	Sore throat New or increased cough New or increased shortness of breath Chills	Pos/, 16NOV2020, B.1.361

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 1170 11701312 (USA/TEXAS/41/F)	Placebo	Dose 2/77	20DEC2020	15JAN2021	Neg/Neg/Neg	Sore throat	Pos/, 26DEC2020, B.1.2
C4591001 1170 11701479 (USA/TEXAS/28/M)	Placebo	Dose 2/45	31DEC2020		Neg/Neg/Neg	Fever	Pos/, 31DEC2020, B.1.2
						New or increased cough	
						New or increased muscle pain	
C4591001 1171 11711056 (USA/TEXAS/24/F)	Placebo	Dose 2/56	08NOV2020	09NOV2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 13NOV2020, B.1.2
						Sore throat	
C4591001 1171 11711081 (USA/TEXAS/36/F)	Placebo	Dose 2/71	18NOV2020	30NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 20NOV2020, B.1.2
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
C4591001 1171 11711117 (USA/TEXAS/60/M)	Placebo	Dose 2/109	01JAN2021	04JAN2021	Neg/Neg/Neg	Sore throat	Pos/, 04JAN2021, B.1.2
C4591001 1171 11711161 (USA/TEXAS/42/M)	Placebo	Dose 2/107	05JAN2021	08JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 08JAN2021, INDETERMINATE
C4591001 1171 11711199 (USA/TEXAS/58/M)	Placebo	Dose 2/77	15DEC2020	30DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 22DEC2020, B.1.1
						New loss of taste or smell	
C4591001 1171 11711212 (USA/TEXAS/33/M)	Placebo	Dose 2/50	04DEC2020	30DEC2020	Neg/Neg/Neg	Fever	Pos/, 07DEC2020, B.1.2
						Chills	
						Sore throat	
C4591001 1177 11771026 (USA/HAWAII/29/F)	Placebo	Dose 2/114	01JAN2021	09FEB2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 18JAN2021, B.1.235
						New loss of taste or smell	
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1177 11771170 (USA/HAWAII/19/M)	BNT162b2 (30 µg)	Dose 2/113	07JAN2021	10JAN2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 07JAN2021, B.1.2
C4591001 1178 11781058 (USA/TENNESSEE/36/M)	Placebo	Dose 2/86	16DEC2020	30DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 17DEC2020, B.1.324
						New or increased shortness of breath	
						New loss of taste or smell	
C4591001 1178 11781065 (USA/TENNESSEE/48/M)	Placebo	Dose 2/23	13OCT2020	25OCT2020	Neg/Neg/Neg	Fever	Pos/, 14OCT2020, B.1.361
						New or increased cough	
						Chills	
						New or increased muscle pain	
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1178 11781085 (USA/TENNESSEE/60/F)	Placebo	Dose 2/72	03DEC2020	18DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 14DEC2020, B.1.2
						Sore throat	
C4591001 1178 11781124 (USA/TENNESSEE/59/M)	Placebo	Dose 2/70	07DEC2020	21DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 08DEC2020, B.1.234
						New loss of taste or smell	
C4591001 1178 11781238 (USA/TENNESSEE/60/F)	Placebo	Dose 2/16	29OCT2020	03NOV2020	Neg/Neg/Neg	Fever	Pos/, 30OCT2020, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1178 11781251 (USA/TENNESSEE/28/F)	Placebo	Dose 2/89	11JAN2021	19JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 13JAN2021, B.1.2
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Sore throat	
C4591001 1178 11781280 (USA/TENNESSEE/58/M)	Placebo	Dose 2/9	03NOV2020	24NOV2020	Neg/Neg/Neg	Fever	Pos/, 04NOV2020, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1178 11781282 (USA/TENNESSEE/65/F)	Placebo	Dose 2/32	26NOV2020	12DEC2020	Neg/Neg/Neg	Sore throat	Pos/, 27NOV2020, B.1.2
C4591001 1179 11791054 (USA/MICHIGAN/51/F)	Placebo	Dose 2/69	01DEC2020		Neg/Neg/Neg	New or increased cough	Pos/, 07DEC2020, B.1.2
						New or increased muscle pain	
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1179 11791073 (USA/MICHIGAN/62/M)	Placebo	Dose 2/61	01DEC2020		Neg/Neg/Neg	New or increased muscle pain	Pos/, 02DEC2020, B.1.2
C4591001 1179 11791079 (USA/MICHIGAN/26/F)	Placebo	Dose 2/42	10NOV2020	20NOV2020	Neg/Neg/Neg	Chills	Pos/, 12NOV2020, B.1.2
						New loss of taste or smell	
						Sore throat	
C4591001 1179 11791080 (USA/MICHIGAN/68/F)	Placebo	Dose 2/104	11JAN2021	21JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 12JAN2021, B.1.2
						Chills	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1179 11791085 (USA/MICHIGAN/34/M)	Placebo	Dose 2/34	09NOV2020		Neg/Neg/Neg	Fever	Pos/, 10NOV2020, B.1.2
						New or increased cough	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1179 11791107 (USA/MICHIGAN/29/M)	Placebo	Dose 2/37	26NOV2020		Neg/Neg/Neg	New loss of taste or smell	Pos/, 30NOV2020, B.1.2
C4591001 1179 11791118 (USA/MICHIGAN/30/F)	Placebo	Dose 2/16	14NOV2020		Neg/Neg/Neg	Sore throat	Pos/, 16NOV2020, B.1.2
C4591001 1194 11941017 (DEU/69/M)	Placebo	Dose 2/64	06JAN2021	27JAN2021	Neg/Neg/Neg	New or increased cough New or increased shortness of breath Chills Diarrhea	Pos/Pos, 13JAN2021, B.1.177
C4591001 1205 12051070 (TUR/68/M)	Placebo	Dose 2/28	28DEC2020	28DEC2020	Neg/Neg/Neg	Sore throat	Pos/, 30DEC2020, B.1
C4591001 1207 12071025 (TUR/55/M)	Placebo	Dose 2/20	07DEC2020	21DEC2020	Neg/Neg/Neg	Fever	Pos/, 08DEC2020, B.1.1.54
C4591001 1207 12071042 (TUR/44/F)	Placebo	Dose 2/26	19DEC2020	27DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 21DEC2020, B.1.1.105
C4591001 1212 12121004 (TUR/38/M)	Placebo	Dose 2/30	11DEC2020	12DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 11DEC2020, B.1.177

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1212 12121019 (TUR/43/M)	Placebo	Dose 2/9	28NOV2020	31DEC2020	Neg/Neg/Neg	Fever	Pos/, 01DEC2020, B.1.1.29
						New or increased muscle pain	
C4591001 1217 12171003 (TUR/34/M)	Placebo	Dose 2/16	27NOV2020	04JAN2021	Neg/Neg/Unk	Fever	Pos/, 01DEC2020, B.1.1.120
C4591001 1223 12231005 (USA/CONNECTICUT/20/F)	Placebo	Dose 2/51	06NOV2020	16NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 07NOV2020, B.1.1.220
						Chills	
						Sore throat	
C4591001 1223 12231008 (USA/CONNECTICUT/24/F)	Placebo	Dose 2/61	16NOV2020	25NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 19NOV2020, NS
						New or increased muscle pain	
C4591001 1223 12231096 (USA/CONNECTICUT/77/F)	Placebo	Dose 2/48	11NOV2020	30DEC2020	Neg/Neg/Neg	New or increased cough	Pos/ (R1 Pos), 11NOV2020 (14NOV2020), B.1.265 (B.1.1.220)
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1223 12231224 (USA/CONNECTICUT/41/M)	Placebo	Dose 2/109	12FEB2021		Neg/Neg/Neg	Fever	Pos/, 15FEB2021, B.1.526
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Diarrhea	
C4591001 1223 12231252 (USA/CONNECTICUT/48/M)	Placebo	Dose 2/68	10JAN2021	25JAN2021	Neg/Neg/Neg	Fever	Pos/, 11JAN2021, B.1.409
C4591001 1224 12241004 (USA/COLORADO/63/M)	Placebo	Dose 2/74	12NOV2020	25NOV2020	Neg/Neg/Neg	Fever	Pos/, 16NOV2020, B.1.2
						New or increased muscle pain	
C4591001 1224 12241105 (USA/COLORADO/36/F)	Placebo	Dose 2/65	25NOV2020	21DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 29NOV2020, B.1.2
						New loss of taste or smell	
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1224 12241142 (USA/COLORADO/63/F)	Placebo	Dose 2/57	18NOV2020	19NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 18NOV2020, B.1.234
						New or increased muscle pain	
C4591001 1226 12261005 (BRA/45/M)	Placebo	Dose 2/121	22DEC2020	06JAN2021	Neg/Neg/Neg	Fever	Pos/, 23DEC2020, P.2
						New or increased muscle pain	
C4591001 1226 12261064 (BRA/74/F)	Placebo	Dose 2/135	12JAN2021	25JAN2021	Neg/Neg/Neg	New or increased shortness of breath	Pos/, 13JAN2021, B.1.1.33
						Chills	
C4591001 1226 12261137 (BRA/52/M)	Placebo	Dose 2/126	06JAN2021	08JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 11JAN2021, B.1.1.34
						New or increased muscle pain	
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1226 12261218 (BRA/38/M)	BNT162b2 (30 µg)	Dose 2/87	03DEC2020	15DEC2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 08DEC2020, B.1.1.33
C4591001 1226 12261219 (BRA/68/M)	Placebo	Dose 2/83	29NOV2020	20DEC2020	Neg/Neg/Neg	Fever	Pos/, 01DEC2020, P.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1226 12261226 (BRA/30/M)	Placebo	Dose 2/120	05JAN2021	20JAN2021	Neg/Neg/Neg	New or increased shortness of breath	Pos/, 14JAN2021, B.1.1.28
						New loss of taste or smell	
						Sore throat	
C4591001 1226 12261309 (BRA/61/M)	Placebo	Dose 2/40	20OCT2020	26OCT2020	Neg/Neg/Neg	New or increased cough	Pos/, 27OCT2020, B.1.1.28

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1226 12261322 (BRA/49/M)	Placebo	Dose 2/131	19JAN2021	21JAN2021	Neg/Neg/Neg	Fever	Pos/, 20JAN2021, B.1.1.28
						New or increased cough	
						Chills	
C4591001 1226 12261354 (BRA/46/M)	Placebo	Dose 2/72	21NOV2020	30NOV2020	Neg/Neg/Neg	New or increased shortness of breath	Pos/, 23NOV2020, B.1.1.28
						New loss of taste or smell	
						Diarrhea	
C4591001 1226 12261363 (BRA/48/F)	Placebo	Dose 2/23	03OCT2020	15DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 06OCT2020, P.2
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Vomiting	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1226 12261383 (BRA/39/F)	Placebo	Dose 2/78	30NOV2020	08DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 01DEC2020, B.1.1.28
						New or increased muscle pain	
C4591001 1226 12261384 (BRA/36/M)	Placebo	Dose 2/111	02JAN2021	15FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 11JAN2021, B.1.1.28
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1226 12261400 (BRA/45/M)	Placebo	Dose 2/75	28NOV2020	04DEC2020	Neg/Neg/Neg	Fever	Pos/, 30NOV2020, P.2
						New or increased muscle pain	
C4591001 1226 12261497 (BRA/26/M)	Placebo	Dose 2/70	27NOV2020	06DEC2020	Neg/Neg/Neg	Fever	Pos/, 02DEC2020, P.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
						Sore throat	
C4591001 1226 12261521 (BRA/32/M)	Placebo	Dose 2/111	12JAN2021	10FEB2021	Neg/Neg/Neg	Fever	Pos/, 19JAN2021, P.2
						New or increased cough	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1226 12261548 (BRA/37/F)	Placebo	Dose 2/63	25NOV2020	02DEC2020	Neg/Neg/Neg	Chills	Pos/, 30NOV2020, B.1.1.28
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1226 12261549 (BRA/41/M)	Placebo	Dose 2/65	27NOV2020	20DEC2020	Neg/Neg/Neg	Chills	Pos/, 30NOV2020, B.1.1.28

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
C4591001 1226 12261559 (BRA/49/M)	BNT162b2 (30 µg)	Dose 2/108	10JAN2021	12JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 12JAN2021, B.1.1.28
						New or increased muscle pain	
C4591001 1226 12261575 (BRA/41/M)	Placebo	Dose 2/95	31DEC2020	22JAN2021	Neg/Neg/Neg	New or increased shortness of breath	Pos/, 05JAN2021, QNS
C4591001 1226 12261586 (BRA/37/M)	Placebo	Dose 2/47	13NOV2020	22NOV2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 16NOV2020, QNS
						Diarrhea	
C4591001 1226 12261587 (BRA/42/M)	Placebo	Dose 2/49	15NOV2020	26NOV2020	Neg/Neg/Neg	Fever	Pos/, 17NOV2020, B.1.1.33
						New or increased cough	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1226 12261599 (BRA/41/F)	BNT162b2 (30 µg)	Dose 2/36	06NOV2020	13NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 07NOV2020, B.1.1.94
						New loss of taste or smell	
						Sore throat	
C4591001 1226 12261624 (BRA/52/M)	Placebo	Dose 2/34	02NOV2020	14NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 05NOV2020, B.1.1.143
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1226 12261660 (BRA/27/F)	Placebo	Dose 2/37	05NOV2020	10NOV2020	Neg/Neg/Neg	Fever	Pos/, 06NOV2020, B.1.1.33
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1226 12261682 (BRA/32/F)	Placebo	Dose 2/102	11JAN2021	26JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 13JAN2021, B.1.182
						New or increased muscle pain	
						Sore throat	
						Diarrhea	
C4591001 1226 12261732 (BRA/31/M)	Placebo	Dose 2/64	08DEC2020	15DEC2020	Neg/Neg/Neg	Fever	Pos/, 10DEC2020, B.1.1.33
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 1226 12261743 (BRA/36/F)	Placebo	Dose 2/103	16JAN2021	22JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 20JAN2021, B.1.1.143
						Sore throat	
C4591001 1226 12261778 (BRA/41/F)	BNT162b2 (30 µg)	Dose 2/100	14JAN2021	20JAN2021	Pos/Pos/Pos	New or increased muscle pain	Pos/, 18JAN2021, QNS
						Diarrhea	
						Vomiting	
C4591001 1226 12261780 (BRA/43/M)	Placebo	Dose 2/35	10NOV2020	18NOV2020	Neg/Neg/Neg	Fever	Pos/, 13NOV2020, P.2
						New loss of taste or smell	
C4591001 1226 12261790 (BRA/43/F)	BNT162b2 (30 µg)	Dose 2/106	20JAN2021	22JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 21JAN2021, P.2
C4591001 1226 12261800 (BRA/34/M)	BNT162b2 (30 µg)	Dose 2/89	03JAN2021	11JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 07JAN2021, P.2
						Sore throat	
						Diarrhea	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1226 12261803 (BRA/33/M)	Placebo	Dose 2/93	06JAN2021	13JAN2021	Neg/Neg/Neg	Fever	Pos/, 07JAN2021, P.2
						Chills	
						New or increased muscle pain	
C4591001 1226 12261885 (BRA/30/F)	Placebo	Dose 2/32	17NOV2020	05DEC2020	Neg/Neg/Neg	Chills	Pos/, 19NOV2020, P.2
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1226 12261888 (BRA/49/M)	BNT162b2 (30 µg)	Dose 2/96	18JAN2021	21JAN2021	Neg/Neg/Neg	Fever	Pos/, 20JAN2021, P.2
						New or increased cough	
C4591001 1226 12261920 (BRA/28/M)	Placebo	Dose 2/36	24NOV2020	29NOV2020	Pos/Neg/Neg	New or increased muscle pain	Pos/, 27NOV2020, QNS
C4591001 1226 12261927 (BRA/38/M)	Placebo	Dose 2/12	16NOV2020		Neg/Neg/Neg	Fever	Pos/, 18NOV2020, INDETERMINATE

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 1226 12261964 (BRA/27/F)	Placebo	Dose 2/9	29OCT2020	13NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 04NOV2020, N.1
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1226 12261995 (BRA/55/M)	BNT162b2 (30 µg)	Dose 2/70	30DEC2020	15JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 05JAN2021, B.1.1.33
						Sore throat	
C4591001 1226 12262020 (BRA/60/M)	BNT162b2 (30 µg)	Dose 2/28	18NOV2020	23NOV2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 25NOV2020, P.2
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1226 12262028 (BRA/42/F)	Placebo	Dose 2/50	10DEC2020	20DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 11DEC2020, B.1.1.143
						New or increased muscle pain	
						Sore throat	
C4591001 1226 12262111 (BRA/51/M)	Placebo	Dose 2/12	10NOV2020	09DEC2020	Neg/Neg/Neg	Fever	Pos/, 12NOV2020, P.2
						New or increased cough	
C4591001 1226 12262183 (BRA/29/M)	Placebo	Dose 2/61	03JAN2021	10JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 06JAN2021, B.1.1.1
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Diarrhea	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1226 12262187 (BRA/43/M)	BNT162b2 (30 µg)	Dose 2/47	20DEC2020	30DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 23DEC2020, B.1.1.143
						New loss of taste or smell	
						Diarrhea	
C4591001 1226 12262196 (BRA/51/M)	Placebo	Dose 2/59	01JAN2021	17JAN2021	Neg/Neg/Neg	Fever	Pos/, 06JAN2021, P.2
						New or increased cough	
						Sore throat	
C4591001 1226 12262204 (BRA/38/M)	Placebo	Dose 2/64	06JAN2021	05FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 11JAN2021, P.2
						New loss of taste or smell	
C4591001 1226 12262211 (BRA/39/F)	Placebo	Dose 2/23	28NOV2020	15DEC2020	Neg/Neg/Neg	Fever	Pos/, 30NOV2020, P.2
						New or increased muscle pain	
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						Sore throat	
C4591001 1226 12262226 (BRA/39/F)	Placebo	Dose 2/63	08JAN2021	13JAN2021	Neg/Neg/Neg	Sore throat	Pos/, 11JAN2021, B.1.1.34
						Diarrhea	
C4591001 1226 12262287 (BRA/46/M)	Placebo	Dose 2/8	16NOV2020	28NOV2020	Neg/Neg/Neg	Fever	Pos/, 18NOV2020, P.2
						New or increased cough	
						New or increased muscle pain	
						Diarrhea	
C4591001 1226 12262298 (BRA/42/F)	Placebo	Dose 2/58	03JAN2021	13JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 07JAN2021, P.2
						Chills	
						New or increased muscle pain	
C4591001 1226 12262314 (BRA/31/F)	Placebo	Dose 2/47	27DEC2020	29DEC2020	Neg/Neg/Neg	Fever	Pos/, 29DEC2020, P.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						New or increased muscle pain	
C4591001 1226 12262318 (BRA/26/F)	Placebo	Dose 2/34	10DEC2020	27DEC2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 18DEC2020, B.1.1.44
C4591001 1229 12291102 (ZAF/63/F)†	Placebo	Dose 2/66	30DEC2020	17JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 08JAN2021, NS
						New loss of taste or smell	
						Sore throat	
C4591001 1231 12311014 (ARG/62/F)	Placebo	Dose 2/134	06JAN2021	14JAN2021	Neg/Neg/Neg	New or increased shortness of breath	Pos/, 08JAN2021, B.1.1.33
C4591001 1231 12311043 (ARG/46/M)	Placebo	Dose 2/40	10OCT2020	11OCT2020	Neg/Neg/Neg	New or increased cough	Pos/, 11OCT2020, B.1.499
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1231 12311069 (ARG/41/M)	Placebo	Dose 2/117	27DEC2020	12JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 27DEC2020, B.1.1.33
						New loss of taste or smell	
C4591001 1231 12311083 (ARG/51/F)	BNT162b2 (30 µg)	Dose 2/160	08FEB2021	15FEB2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 11FEB2021, B.1.1.70
C4591001 1231 12311205 (ARG/29/F)	Placebo	Dose 2/87	28NOV2020	14DEC2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 01DEC2020, B.1.1.33
C4591001 1231 12311224 (ARG/35/M)	Placebo	Dose 2/117	28DEC2020	29DEC2020	Neg/Neg/Neg	Fever	Pos/, 02JAN2021, B.1.1.33
						New or increased cough	
						Sore throat	
C4591001 1231 12311267 (ARG/67/M)	Placebo	Dose 2/24	26SEP2020	07OCT2020	Neg/Neg/Neg	Fever	Pos/, 02OCT2020, B.1.1.33
						New or increased cough	
						Sore throat	
C4591001 1231 12311285 (ARG/26/F)	Placebo	Dose 2/151	01FEB2021	19FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 03FEB2021, B.1.1.33

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 1231 12311297 (ARG/49/M)	Placebo	Dose 2/98	13DEC2020	25DEC2020	Neg/Neg/Neg	Fever	Pos/, 15DEC2020, B.1.1.33
						New loss of taste or smell	
C4591001 1231 12311407 (ARG/63/M)	Placebo	Dose 2/24	27SEP2020	06OCT2020	Neg/Neg/Neg	Fever	Pos/, 01OCT2020, B.1.499
						Chills	
						New or increased muscle pain	
						Diarrhea	
C4591001 1231 12311480 (ARG/40/M)	BNT162b2 (30 µg)	Dose 2/147	27JAN2021	06FEB2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 29JAN2021, B.1.1.33
						Sore throat	
C4591001 1231 12311520 (ARG/29/M)	BNT162b2 (30 µg)	Dose 2/130	14JAN2021	21JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 18JAN2021, B.1.499
C4591001 1231 12311531 (ARG/35/M)	Placebo	Dose 2/9	16SEP2020	27SEP2020	Neg/Neg/Neg	Fever	Pos/, 19SEP2020, B.1
						New or increased	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						shortness of breath	
						New or increased muscle pain	
C4591001 1231 12311556 (ARG/24/M)	Placebo	Dose 2/45	21OCT2020	09NOV2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 22OCT2020, B.1.499
C4591001 1231 12311560 (ARG/44/M)	Placebo	Dose 2/70	12NOV2020	19NOV2020	Neg/Neg/Neg	Fever	Pos/, 12NOV2020, B.1.1.33
						New or increased cough	
C4591001 1231 12311599 (ARG/34/M)	Placebo	Dose 2/139	23JAN2021	18FEB2021	Neg/Neg/Neg	Fever	Pos/, 23JAN2021, B.1.1.33
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1231 12311609 (ARG/25/M)	BNT162b2 (30 µg)	Dose 2/113	28DEC2020	08JAN2021	Neg/Neg/Neg	Fever	Pos/, 30DEC2020, B.1.428
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1231 12311648 (ARG/50/F)	Placebo	Dose 2/140	25JAN2021	01FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 28JAN2021, B.1.1.33
						New loss of taste or smell	
C4591001 1231 12311651 (ARG/52/F)	Placebo	Dose 2/8	14SEP2020	01OCT2020	Neg/Neg/Neg	New or increased cough	Pos/, 20SEP2020, N.3
						Chills	
						New or increased muscle pain	
						Sore throat	
						Vomiting	
C4591001 1231 12311664 (ARG/34/F)	Placebo	Dose 2/9	15SEP2020	03OCT2020	Neg/Neg/Neg	Fever	Pos/, 17SEP2020, B.1
						New or increased cough	
C4591001 1231 12311728 (ARG/59/F)	Placebo	Dose 2/101	18DEC2020	14JAN2021	Neg/Neg/Neg	Fever	Pos/, 22DEC2020, P.2
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1231 12311754 (ARG/54/M)	Placebo	Dose 2/38	14OCT2020	25OCT2020	Neg/Neg/Neg	Fever	Pos/, 16OCT2020, B.1.1.33
						New or increased muscle pain	
						Sore throat	
C4591001 1231 12311764 (ARG/34/M)	Placebo	Dose 2/63	09NOV2020	09NOV2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 10NOV2020, B.1
C4591001 1231 12311793 (ARG/43/M)	Placebo	Dose 2/131	15JAN2021	01FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 19JAN2021, B.1.1.33
						Sore throat	
C4591001 1231 12311809 (ARG/28/M)	Placebo	Dose 2/161	14FEB2021	20FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 15FEB2021, B.1.1.33
C4591001 1231 12311841 (ARG/24/M)	BNT162b2 (30 µg)	Dose 2/77	22NOV2020	06DEC2020	Neg/Neg/Neg	Sore throat	Pos/, 27NOV2020, B.1.1.35
C4591001 1231 12311866 (ARG/21/F)	Placebo	Dose 2/137	21JAN2021	03FEB2021	Neg/Neg/Neg	Fever	Pos/, 22JAN2021, B.1

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1231 12311982 (ARG/41/F)	Placebo	Dose 2/37	14OCT2020	24OCT2020	Neg/Neg/Neg	New or increased cough	Pos/, 20OCT2020, B.1.1.33
						New or increased muscle pain	
						Sore throat	
C4591001 1231 12312119 (ARG/32/M)	Placebo	Dose 2/139	23JAN2021	03FEB2021	Neg/Neg/Neg	Fever	Pos/, 24JAN2021, B.1.1.33
						New or increased cough	
						New or increased muscle pain	
						New loss of taste or smell	
						Diarrhea	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1231 12312133 (ARG/38/M)	Placebo	Dose 2/119	04JAN2021	28JAN2021	Neg/Neg/Neg	Fever	Pos/, 05JAN2021, B.1.1.33
						New or increased cough	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1231 12312188 (ARG/36/M)	Placebo	Dose 2/147	02FEB2021	13FEB2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 03FEB2021, B.1.1.28
C4591001 1231 12312223 (ARG/61/F)	Placebo	Dose 2/133	18JAN2021	30JAN2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 23JAN2021, B.1.1.33
C4591001 1231 12312275 (ARG/21/F)	Placebo	Dose 2/148	02FEB2021	05FEB2021	Neg/Neg/Neg	Fever	Pos/, 04FEB2021, B.1.1.33
						New or increased cough	
C4591001 1231 12312282 (ARG/19/F)	BNT162b2 (30 µg)	Dose 2/133	18JAN2021	24JAN2021	Neg/Neg/Neg	Fever	Pos/, 19JAN2021, B.1.1.33

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Sore throat	
C4591001 1231 12312349 (ARG/24/F)	Placebo	Dose 2/116	01JAN2021	10JAN2021	Neg/Neg/Neg	Sore throat	Pos/, 04JAN2021, B.1.1.33
C4591001 1231 12312479 (ARG/43/M)	Placebo	Dose 2/30	09OCT2020	07NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 11OCT2020, B.1.1.33
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1231 12312492 (ARG/70/M)	Placebo	Dose 2/153	07FEB2021	12FEB2021	Neg/Neg/Neg	Fever	Pos/, 10FEB2021, B.1.499
						New or increased cough	
						Sore throat	
C4591001 1231 12312507 (ARG/47/F)	Placebo	Dose 2/10	17SEP2020	28SEP2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 19SEP2020, B.1.499

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1231 12312572 (ARG/46/M)	Placebo	Dose 2/111	27DEC2020	25JAN2021	Neg/Neg/Neg	Sore throat Fever New or increased cough	Pos/, 29DEC2020, B.1.1.200
C4591001 1231 12312617 (ARG/27/M)	BNT162b2 (30 µg)	Dose 2/122	09JAN2021	26JAN2021	Neg/Neg/Neg	New or increased cough New or increased muscle pain New loss of taste or smell	Pos/, 12JAN2021, P.2
C4591001 1231 12312630 (ARG/39/F)	Placebo	Dose 2/44	23OCT2020	14NOV2020	Neg/Neg/Neg	Sore throat Fever New or increased cough New or increased shortness of breath	Pos/, 26OCT2020, B.1.499

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Sore throat	
C4591001 1231 12312635 (ARG/71/M)	Placebo	Dose 2/27	04OCT2020	26OCT2020	Neg/Neg/Neg	Fever	Pos/, 06OCT2020, B.1.1.33
						New or increased cough	
						Chills	
						Sore throat	
C4591001 1231 12312663 (ARG/34/F)	Placebo	Dose 2/110	26DEC2020	15FEB2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 27DEC2020, B.1
						Sore throat	
C4591001 1231 12312675 (ARG/41/M)	BNT162b2 (30 µg)	Dose 2/161	15FEB2021	25FEB2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 20FEB2021, B.1.1.33
						Sore throat	
C4591001 1231 12312680 (ARG/31/M)	BNT162b2 (30 µg)	Dose 2/171	25FEB2021	02MAR2021	Neg/Neg/Neg	Sore throat	Pos/, 28FEB2021, B.1.1.1
C4591001 1231 12312702 (ARG/30/F)	Placebo	Dose 2/114	02JAN2021	13FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 07JAN2021, B.1.1.33

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1231 12312704 (ARG/49/M)	Placebo	Dose 2/110	28DEC2020	06FEB2021	Neg/Neg/Neg	Fever	Pos/, 09JAN2021, QNS
						New or increased cough	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1231 12312769 (ARG/47/M)	Placebo	Dose 2/63	12NOV2020	14NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 13NOV2020, B.1.1.33
C4591001 1231 12312867 (ARG/40/F)	Placebo	Dose 2/35	14OCT2020	01NOV2020	Neg/Neg/Neg	Fever	Pos/, 16OCT2020, B.1
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1231 12312901 (ARG/28/M)	Placebo	Dose 2/140	27JAN2021	19FEB2021	Neg/Neg/Neg	Diarrhea Fever New or increased cough New or increased muscle pain New loss of taste or smell Sore throat	Pos/, 31JAN2021, P.2
C4591001 1231 12312914 (ARG/50/M)	Placebo	Dose 2/43	26OCT2020	17NOV2020	Neg/Neg/Neg	Diarrhea Fever New or increased cough New or increased muscle pain Sore throat	Pos/, 29OCT2020, B.1.1.33

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1231 12313040 (ARG/51/M)	Placebo	Dose 2/137	28JAN2021	11FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 30JAN2021, B.1.1.33
						New loss of taste or smell	
						Sore throat	
C4591001 1231 12313085 (ARG/23/F)	Placebo	Dose 2/148	07FEB2021	14FEB2021	Neg/Neg/Neg	Fever	Pos/, 10FEB2021, B.1.1.33
						New or increased cough	
						Sore throat	
C4591001 1231 12313182 (ARG/33/M)	Placebo	Dose 2/10	20SEP2020	19OCT2020	Neg/Neg/Neg	New or increased shortness of breath	Pos/, 25SEP2020, B.1.1.33
						New loss of taste or smell	
C4591001 1231 12313244 (ARG/21/F)	Placebo	Dose 2/121	12JAN2021	27JAN2021	Neg/Neg/Neg	Fever	Pos/, 17JAN2021, B.1.1.33
						New loss of taste or smell	
						Diarrhea	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1231 12313259 (ARG/41/M)	Placebo	Dose 2/153	09FEB2021	15FEB2021	Neg/Neg/Neg	Sore throat	Pos/, 14FEB2021, B.1.1.1
C4591001 1231 12313296 (ARG/49/F)	Placebo	Dose 2/25	04OCT2020	20OCT2020	Neg/Neg/Neg	New or increased cough	Pos/, 06OCT2020, B.1.1.289
						New loss of taste or smell	
C4591001 1231 12313372 (ARG/24/F)	Placebo	Dose 2/119	07JAN2021	02FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 11JAN2021, B.1.1.33
						Chills	
						New or increased muscle pain	
						Sore throat	
						Diarrhea	
C4591001 1231 12313400 (ARG/46/M)	Placebo	Dose 2/37	19OCT2020	28OCT2020	Neg/Neg/Neg	New or increased cough	Pos/, 21OCT2020, B.1.499
						New or increased shortness of breath	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1231 12313422 (ARG/34/M)	Placebo	Dose 2/44	28OCT2020	27DEC2020	Neg/Neg/Neg	Fever	Pos/, 29OCT2020, B.1.2
						New or increased cough	
						New or increased shortness of breath	
						Diarrhea	
C4591001 1231 12313437 (ARG/36/F)	Placebo	Dose 2/172	03MAR2021	14MAR2021	Neg/Neg/Neg	Fever	Pos/, 04MAR2021, B.1.1.33
						New or increased cough	
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1231 12313470 (ARG/54/F)	Placebo	Dose 2/159	27FEB2021	11MAR2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 01MAR2021, B.1.1.1
						Sore throat	
C4591001 1231 12313504 (ARG/36/M)	Placebo	Dose 2/94	15DEC2020	24DEC2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 16DEC2020, B.1.1.33
						Diarrhea	
C4591001 1231 12313520 (ARG/28/F)	Placebo	Dose 2/8	22SEP2020	09OCT2020	Neg/Neg/Neg	New or increased cough	Pos/, 25SEP2020, B.1.499
						New loss of taste or smell	
						Sore throat	
C4591001 1231 12313596 (ARG/41/M)	Placebo	Dose 2/106	27DEC2020	07JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 30DEC2020, B.1.1.33
						New loss of taste or smell	
						Sore throat	
C4591001 1231 12313668 (ARG/33/M)	Placebo	Dose 2/12	24SEP2020	02OCT2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 25SEP2020, B.1.499
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1231 12313697 (ARG/55/M)	Placebo	Dose 2/119	11JAN2021		Neg/Neg/Neg	Fever	Pos/, 14JAN2021, P.2
						New or increased cough	
C4591001 1231 12313787 (ARG/58/M)	Placebo	Dose 2/48	02NOV2020	05NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 04NOV2020, B.1.1.33
						Sore throat	
C4591001 1231 12313801 (ARG/55/F)	Placebo	Dose 2/127	19JAN2021	30JAN2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 28JAN2021, QNS
C4591001 1231 12313881 (ARG/36/M)	Placebo	Dose 2/149	10FEB2021	19FEB2021	Neg/Neg/Neg	Fever	Pos/, 11FEB2021, B.1.1.33
						Sore throat	
C4591001 1231 12313895 (ARG/50/F)	Placebo	Dose 2/21	03OCT2020	17OCT2020	Neg/Neg/Neg	New or increased cough	Pos/, 07OCT2020, B.1
						New or increased muscle pain	
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1231 12313996 (ARG/50/F)	Placebo	Dose 2/68	20NOV2020	03DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 21NOV2020, B.1.1.33
						New loss of taste or smell	
C4591001 1231 12314112 (ARG/52/M)	Placebo	Dose 2/42	28OCT2020	02NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 29OCT2020, B.1
C4591001 1231 12314123 (ARG/37/F)	Placebo	Dose 2/147	09FEB2021	21FEB2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 11FEB2021, B.1.1.33
						New loss of taste or smell	
C4591001 1231 12314193 (ARG/36/M)	Placebo	Dose 2/104	29DEC2020	31DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 30DEC2020, B.1.499
C4591001 1231 12314209 (ARG/68/M)	Placebo	Dose 2/66	18NOV2020	04DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 21NOV2020, INDETERMINATE
						Sore throat	
C4591001 1231 12314213 (ARG/66/M)	Placebo	Dose 2/133	25JAN2021	20FEB2021	Neg/Neg/Neg	Fever	Pos/, 27JAN2021, B.1.1.33

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						New loss of taste or smell	
C4591001 1231 12314308 (ARG/31/F)	Placebo	Dose 2/15	30SEP2020	11OCT2020	Neg/Neg/Neg	New or increased cough	Pos/, 01OCT2020, B.1.1.33
						New or increased muscle pain	
						Sore throat	
						Vomiting	
C4591001 1231 12314329 (ARG/52/M)	Placebo	Dose 2/97	19DEC2020	29DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 21DEC2020, B.1.1.33
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1231 12314477 (ARG/36/M)	Placebo	Dose 2/16	03OCT2020	15OCT2020	Pos/Neg/Neg	New or increased cough	Pos/, 06OCT2020, B.1.499

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
C4591001 1231 12314499 (ARG/52/F)	Placebo	Dose 2/141	03FEB2021	17FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 05FEB2021, B.1
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1231 12314534 (ARG/18/F)	Placebo	Dose 2/21	05OCT2020	09OCT2020	Neg/Neg/Neg	New or increased cough	Pos/, 08OCT2020, B.1.499
						New or increased muscle pain	
						Sore throat	
C4591001 1231 12314551 (ARG/76/M)	Placebo	Dose 2/137	29JAN2021	12FEB2021	Neg/Neg/Neg	Fever	Pos/, 01FEB2021, B.1.1.33
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
						Sore throat	
C4591001 1231 12314565 (ARG/41/F)	BNT162b2 (30 µg)	Dose 2/104	29DEC2020	19JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 30DEC2020, B.1.1.33
						New loss of taste or smell	
						Sore throat	
C4591001 1231 12314583 (ARG/20/F)	Placebo	Dose 2/134	26JAN2021	03FEB2021	Neg/Neg/Neg	Fever	Pos/, 27JAN2021, B.1.1.33
						New loss of taste or smell	
C4591001 1231 12314622 (ARG/32/F)	Placebo	Dose 2/15	01OCT2020	07OCT2020	Neg/Neg/Neg	Fever	Pos/, 03OCT2020, B.1.499
						New or increased cough	
						New or increased shortness of breath	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1231 12314681 (ARG/66/F)	Placebo	Dose 2/104	28DEC2020	28DEC2020	Neg/Neg/Neg	Fever	Pos/, 29DEC2020, B.1.1.33
						New or increased cough	
						New or increased shortness of breath	
						Sore throat	
C4591001 1231 12314746 (ARG/21/M)	Placebo	Dose 2/107	01JAN2021	10FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 12JAN2021, B.1.1.33
C4591001 1231 12314912 (ARG/31/F)	BNT162b2 (30 µg)	Dose 2/123	18JAN2021	02FEB2021	Neg/Neg/Neg	Fever	Pos/, 20JAN2021, B.1.1.33
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1231 12314941 (ARG/60/F)	Placebo	Dose 2/109	02JAN2021	13JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 04JAN2021, B.1.499
C4591001 1231 12315003 (ARG/76/M)	Placebo	Dose 2/90	14DEC2020	18DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 19DEC2020, B.1.499
C4591001 1231 12315038 (ARG/56/F)	Placebo	Dose 2/147	09FEB2021	19FEB2021	Neg/Neg/Neg	Fever	Pos/, 10FEB2021, B.1
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1231 12315062 (ARG/25/M)	Placebo	Dose 2/107	01JAN2021	06JAN2021	Neg/Neg/Neg	Fever	Pos/, 04JAN2021, B.1.499
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Diarrhea	
C4591001 1231 12315074 (ARG/36/M)	Placebo	Dose 2/169	04MAR2021	16MAR2021	Neg/Neg/Neg	Fever	Pos/, 05MAR2021, B.1.1.33
						New or increased muscle pain	
C4591001 1231 12315136 (ARG/23/M)	Placebo	Dose 2/123	18JAN2021	14FEB2021	Neg/Neg/Neg	Fever	Pos/, 21JAN2021, B.1.1.33
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1231 12315216 (ARG/52/M)	Placebo	Dose 2/94	19DEC2020	08JAN2021	Neg/Neg/Neg	Fever	Pos/, 27DEC2020, B.1.1.33
						New or increased cough	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
						Sore throat	
C4591001 1231 12315247 (ARG/34/F)	Placebo	Dose 2/174	10MAR2021	20MAR2021	Neg/Neg/Neg	New or increased cough	Pos/, 11MAR2021, B.1.1.33
						New or increased muscle pain	
C4591001 1231 12315287 (ARG/46/F)	Placebo	Dose 2/127	21JAN2021	01FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 27JAN2021, B.1.1.33
						New loss of taste or smell	
						Sore throat	
C4591001 1231 12315299 (ARG/20/F)	BNT162b2 (30 µg)	Dose 2/101	26DEC2020	14JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 29DEC2020, B.1.1.33
						New loss of taste or smell	
C4591001 1231 12315324 (ARG/58/F)	Placebo	Dose 2/99	25DEC2020	31JAN2021	Neg/Neg/Neg	Fever	Pos/, 26DEC2020, B.1.1.291

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased cough	
						Chills	
C4591001 1231 12315349 (ARG/39/F)	Placebo	Dose 2/110	04JAN2021	23JAN2021	Neg/Neg/Neg	Fever	Pos/, 08JAN2021, B.1
						New or increased cough	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1231 12315392 (ARG/64/F)	Placebo	Dose 2/75	02DEC2020	15DEC2020	Neg/Neg/Neg	Fever	Pos/, 04DEC2020, B.1.1.33
						New or increased cough	
						Diarrhea	
						Vomiting	
C4591001 1231 12315497 (ARG/34/F)	Placebo	Dose 2/139	03FEB2021	28FEB2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 06FEB2021, B.1.1.33

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
						Sore throat	
C4591001 1231 12315500 (ARG/57/F)	Placebo	Dose 2/88	14DEC2020	30JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 17DEC2020, B.1.1.33
						New loss of taste or smell	
						Diarrhea	
C4591001 1231 12315553 (ARG/42/F)	Placebo	Dose 2/83	10DEC2020	21DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 11DEC2020, B.1.1.33
						New loss of taste or smell	
C4591001 1231 12315624 (ARG/44/M)	Placebo	Dose 2/87	17DEC2020	21DEC2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 19DEC2020, B.1
C4591001 1231 12315628 (ARG/55/M)	Placebo	Dose 2/115	11JAN2021	16JAN2021	Neg/Neg/Neg	Fever	Pos/, 14JAN2021, B.1.1.33
						New or increased cough	
C4591001 1231 12315636 (ARG/53/F)	Placebo	Dose 2/35	23OCT2020	21NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 26OCT2020, B.1.302

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						Sore throat	
C4591001 1231 12315637 (ARG/40/F)	Placebo	Dose 2/11	29SEP2020	08OCT2020	Neg/Neg/Neg	Fever	Pos/, 01OCT2020, B.1.1.33
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1232 12321046 (USA/GEORGIA/39/M)	Placebo	Dose 2/109	26DEC2020	04JAN2021	Neg/Neg/Neg	Chills	Pos/, 30DEC2020, B.1.2
C4591001 1232 12321301 (USA/GEORGIA/44/M)	Placebo	Dose 2/65	29DEC2020	10FEB2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 04JAN2021, B.1.2
						New loss of taste or smell	
C4591001 1232 12321426 (USA/GEORGIA/37/F)	Placebo	Dose 2/29	22DEC2020	06JAN2021	Neg/Neg/Neg	Sore throat	Pos/, 23DEC2020, B.1.2
C4591001 1235 12351024 (USA/LOUISIANA/27/M)	Placebo	Dose 2/48	11NOV2020	12NOV2020	Neg/Neg/Neg	Chills	Pos/, 16NOV2020, B.1.2
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1235 12351064 (USA/LOUISIANA/25/F)	Placebo	Dose 2/47	17NOV2020	25NOV2020	Neg/Neg/Neg	Fever	Pos/, 18NOV2020, B.1.2
						Chills	
						New or increased muscle pain	
C4591001 1235 12351093 (USA/LOUISIANA/30/F)	BNT162b2 (30 µg)	Dose 2/32	08NOV2020	14NOV2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 11NOV2020, B.1.2
C4591001 1235 12351112 (USA/LOUISIANA/24/F)	Placebo	Dose 2/86	02JAN2021	13JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 08JAN2021, B.1
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1235 12351140 (USA/LOUISIANA/72/M)	Placebo	Dose 2/55	09DEC2020	13DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 11DEC2020, B.1.1.222

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1235 12351243 (USA/LOUISIANA/15/M)	Placebo	Dose 2/42	09FEB2021	11FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 11FEB2021, B.1.2
						Sore throat	
						Diarrhea	
C4591001 1241 12411043 (BRA/33/F)	Placebo	Dose 2/116	25DEC2020	29DEC2020	Neg/Neg/Neg	New or increased cough	Pos/Pos, 27DEC2020, B.1.1.28
						New loss of taste or smell	
C4591001 1241 12411252 (BRA/57/F)	Placebo	Dose 2/123	09JAN2021	18JAN2021	Neg/Neg/Neg	New or increased cough	Pos/Pos, 13JAN2021, P.2
						New loss of taste or smell	
						Sore throat	
C4591001 1241 12411277 (BRA/42/F)	Placebo	Dose 2/121	07JAN2021	20JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 11JAN2021, B.1.1.28
						New or increased shortness of breath	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
						Vomiting	
C4591001 1241 12411319 (BRA/52/F)	Placebo	Dose 2/69	18NOV2020	30NOV2020	Neg/Neg/Neg	New loss of taste or smell	Pos/Pos, 24NOV2020, B.1.1.33
						Sore throat	
C4591001 1241 12411347 (BRA/23/F)	Placebo	Dose 2/86	04DEC2020	17DEC2020	Neg/Neg/Neg	New or increased cough	Pos/Pos, 06DEC2020, B.1.1.33
						Sore throat	
C4591001 1241 12411404 (BRA/58/F)	Placebo	Dose 2/61	10NOV2020	20NOV2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 14NOV2020, B.1.1.33
C4591001 1241 12411410 (BRA/45/F)	Placebo	Dose 2/117	08JAN2021	18JAN2021	Neg/Neg/Neg	Sore throat	Pos/Pos, 13JAN2021, INDETERMINATE
C4591001 1241 12411421 (BRA/37/F)	Placebo	Dose 2/58	10NOV2020	17NOV2020	Neg/Neg/Neg	New or increased cough	Pos/Pos, 13NOV2020, B.1.1.28
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1241 12411433 (BRA/29/M)	Placebo	Dose 2/126	17JAN2021	19JAN2021	Neg/Neg/Neg	Fever	Pos/Pos, 19JAN2021, B.1.1.143
						New or increased cough	
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1241 12411478 (BRA/39/F)	Placebo	Dose 2/91	14DEC2020	26DEC2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 15DEC2020, P.2
						Sore throat	
C4591001 1241 12411481 (BRA/27/F)	Placebo	Dose 2/74	28NOV2020	12JAN2021	Neg/Neg/Neg	Fever	Pos/Pos, 04DEC2020, B.1
						New or increased cough	
						Diarrhea	
C4591001 1241 12411566 (BRA/18/F)	Placebo	Dose 2/116	15JAN2021	20JAN2021	Neg/Neg/Neg	Fever	Pos/, 17JAN2021, P.2
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
						Sore throat	
C4591001 1241 12411581 (BRA/52/M)	Placebo	Dose 2/125	24JAN2021	05FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 26JAN2021, P.2
						Chills	
C4591001 1241 12411617 (BRA/47/M)	Placebo	Dose 2/84	15DEC2020	05JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 17DEC2020, B.1.1.34
						Chills	
C4591001 1241 12411625 (BRA/34/M)	Placebo	Dose 2/102	02JAN2021	08JAN2021	Neg/Neg/Neg	New or increased muscle pain	Pos/Pos, 04JAN2021, P.2
						New loss of taste or smell	
						Diarrhea	
C4591001 1241 12411658 (BRA/35/F)	BNT162b2 (30 µg)	Dose 2/105	11JAN2021	15FEB2021	Neg/Neg/Neg	New or increased cough	Pos/Pos, 13JAN2021, P.2
						Chills	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1241 12411659 (BRA/32/M)	Placebo	Dose 2/95	01JAN2021	16JAN2021	Neg/Neg/Neg	Sore throat New or increased cough Chills New or increased muscle pain	Pos/Pos, 09JAN2021, P.2
C4591001 1241 12411661 (BRA/34/M)	Placebo	Dose 2/84	21DEC2020	24DEC2020	Neg/Neg/Neg	Sore throat Fever New or increased cough Chills	Pos/Pos, 22DEC2020, P.2
C4591001 1241 12411746 (BRA/58/M)	Placebo	Dose 2/54	28NOV2020	10DEC2020	Neg/Neg/Neg	Diarrhea Fever Chills New or increased muscle pain	Pos/Pos, 01DEC2020, P.2

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
						Sore throat	
C4591001 1241 12411747 (BRA/31/M)	Placebo	Dose 2/106	19JAN2021	23JAN2021	Neg/Neg/Neg	Fever	Pos/, 21JAN2021, P.2
						New or increased cough	
						Chills	
						New loss of taste or smell	
C4591001 1241 12411768 (BRA/42/F)	Placebo	Dose 2/94	07JAN2021	21JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/Pos, 10JAN2021, P.2
C4591001 1241 12411770 (BRA/69/F)	Placebo	Dose 2/94	07JAN2021	14JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/Pos, 10JAN2021, P.2
C4591001 1241 12411787 (BRA/54/M)	Placebo	Dose 2/103	19JAN2021	27JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/Pos, 22JAN2021, P.2
						Sore throat	
C4591001 1241 12411788 (BRA/62/M)	Placebo	Dose 2/68	14DEC2020	04JAN2021	Neg/Neg/Neg	Fever	Pos/, 17DEC2020, P.2
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Sore throat	
C4591001 1241 12411837 (BRA/53/M)	BNT162b2 (30 µg)	Dose 2/110	25JAN2021	01FEB2021	Neg/Neg/Neg	Sore throat	Pos/Pos, 27JAN2021, P.1
C4591001 1241 12411845 (BRA/43/F)	Placebo	Dose 2/111	26JAN2021	10FEB2021	Neg/Neg/Neg	Fever	Pos/Pos, 29JAN2021, P.1
						New or increased cough	
						New loss of taste or smell	
C4591001 1241 12411858 (BRA/18/M)	Placebo	Dose 2/90	03JAN2021	10JAN2021	Neg/Neg/Neg	New or increased muscle pain	Pos/Pos, 07JAN2021, B.1.1.28
						Sore throat	
						Diarrhea	
C4591001 1241 12411885 (BRA/23/M)	BNT162b2 (30 µg)	Dose 2/14	22OCT2020	24OCT2020	Pos/Neg/Neg	Sore throat	Pos/Neg, 23OCT2020, QNS
C4591001 1241 12411896 (BRA/62/F)	Placebo	Dose 2/39	16NOV2020	24NOV2020	Neg/Neg/Neg	New or increased muscle pain	Pos/Neg, 18NOV2020, QNS
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1241 12411950 (BRA/34/M)	BNT162b2 (30 µg)	Dose 2/95	09JAN2021	21JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 11JAN2021, B.1.1.143
C4591001 1241 12411991 (BRA/29/F)	Placebo	Dose 2/67	18DEC2020	26DEC2020	Neg/Neg/Neg	Fever	Pos/, 20DEC2020, B.1.1.28
						New or increased cough	
						Chills	
C4591001 1241 12411998 (BRA/53/F)	Placebo	Dose 2/39	20NOV2020	05DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 24NOV2020, B.1
C4591001 1241 12412017 (BRA/59/M)	Placebo	Dose 2/9	29OCT2020	02NOV2020	Neg/Neg/Neg	Fever	Pos/Pos, 30OCT2020, B.1.1.28
						New or increased muscle pain	
C4591001 1241 12412018 (BRA/55/F)	Placebo	Dose 2/8	28OCT2020	15NOV2020	Neg/Neg/Neg	Fever	Pos/Pos, 30OCT2020, B.1.1.28
						New loss of taste or smell	
						Sore throat	
C4591001 1241 12412087 (BRA/37/M)	Placebo	Dose 2/31	21NOV2020	02DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/Pos, 25NOV2020, B.1.1.28

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
C4591001 1241 12412111 (BRA/44/F)	Placebo	Dose 2/82	10JAN2021	20JAN2021	Neg/Neg/Neg	New or increased cough	Pos/Pos, 13JAN2021, P.2
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1241 12412114 (BRA/24/F)	Placebo	Dose 2/98	27JAN2021	08FEB2021	Neg/Neg/Neg	New or increased cough	Pos/Pos, 31JAN2021, P.2
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						Diarrhea	
C4591001 1241 12412140 (BRA/16/F)	Placebo	Dose 2/76	09JAN2021	18JAN2021	Neg/Neg/Neg	Sore throat	Pos/, 12JAN2021, P.2
C4591001 1241 12412170 (BRA/27/F)	Placebo	Dose 2/60	01JAN2021	11JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 06JAN2021, P.2
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1241 12412235 (BRA/38/M)	Placebo	Dose 2/42	16DEC2020	20DEC2020	Neg/Neg/Neg	Fever	Pos/Pos, 19DEC2020, B.1.1.34
						New or increased cough	
						Chills	
						Sore throat	
C4591001 1241 12412259 (BRA/35/M)	Placebo	Dose 2/41	15DEC2020	28DEC2020	Neg/Neg/Neg	New or increased cough	Pos/Pos, 18DEC2020, B.1.1.28
						New or increased	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						shortness of breath	
						New or increased muscle pain	
						Sore throat	
						Diarrhea	
C4591001 1241 12412334 (BRA/41/M)	Placebo	Dose 2/26	04DEC2020	14DEC2020	Neg/Neg/Neg	Fever	Pos/, 07DEC2020, B.1.1.33
						Chills	
						New or increased muscle pain	
C4591001 1241 12412397 (BRA/24/F)	Placebo	Dose 2/10	19NOV2020	29NOV2020	Neg/Neg/Neg	New or increased cough	Pos/Pos, 20NOV2020, P.2
						New loss of taste or smell	
C4591001 1241 12412458 (BRA/28/F)	Placebo	Dose 2/8	18NOV2020	20NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 20NOV2020, P.2
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1241 12412512 (BRA/47/F)	Placebo	Dose 2/37	18DEC2020	30DEC2020	Neg/Neg/Neg	Fever	Pos/Pos, 20DEC2020, B.1
						New or increased cough	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1246 12461072 (ZAF/39/F)	Placebo	Dose 2/82	12JAN2021	16FEB2021	Neg/Neg/Neg	Fever	Pos/, 26JAN2021, B.1.351
						New or increased cough	
						Chills	
						New or increased muscle pain	
						Sore throat	
						Diarrhea	
						Vomiting	
C4591001 1246 12461110 (ZAF/19/M)	Placebo	Dose 2/68	03JAN2021	27JAN2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 06JAN2021, B.1.351

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1246 12461126 (ZAF/22/M)	Placebo	Dose 2/63	31DEC2020	17JAN2021	Neg/Neg/Neg	Fever	Pos/, 11JAN2021, B.1.351
						New or increased cough	
						Sore throat	
C4591001 1247 12471016 (ZAF/30/F)	Placebo	Dose 2/80	01JAN2021	12JAN2021	Neg/Neg/Neg	Fever	Pos/, 05JAN2021, B.1.351
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1247 12471053 (ZAF/30/M)	Placebo	Dose 2/78	31DEC2020	09JAN2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 02JAN2021, B.1.351
						Sore throat	
C4591001 1247 12471070 (ZAF/58/M)	Placebo	Dose 2/107	02FEB2021	08FEB2021	Neg/Neg/Neg	Fever	Pos/, 02FEB2021, B.1.351
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						Sore throat	
C4591001 1247 12471085 (ZAF/54/F)	Placebo	Dose 2/12	30OCT2020	03NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 02NOV2020, QNS
						Chills	
						Diarrhea	
C4591001 1247 12471091 (ZAF/39/F)	Placebo	Dose 2/69	27DEC2020	03JAN2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 29DEC2020, B.1.351
						New loss of taste or smell	
C4591001 1247 12471092 (ZAF/37/M)	Placebo	Dose 2/49	16DEC2020	06JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 23DEC2020, B.1.351
						New or increased shortness of breath	
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1247 12471141 (ZAF/27/F)	Placebo	Dose 2/53	13DEC2020	06JAN2021	Pos/Neg/Neg	New or increased cough	Pos/, 17DEC2020, P.2
						New or increased shortness of breath	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1251 12511032 (USA/FLORIDA/25/F)	Placebo	Dose 2/142	30JAN2021	17FEB2021	Neg/Neg/Neg	New loss of taste or smell	Pos/, 01FEB2021, B.1.2
C4591001 1251 12511065 (USA/FLORIDA/50/F)	Placebo	Dose 2/48	04NOV2020	28NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 12NOV2020, B.1

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased shortness of breath	
C4591001 1251 12511084 (USA/FLORIDA/48/F)	Placebo	Dose 2/55	14NOV2020	17NOV2020	Neg/Neg/Neg	Fever	Pos/, 16NOV2020, B.1.2
						New loss of taste or smell	
C4591001 1251 12511121 (USA/FLORIDA/49/M)	Placebo	Dose 2/81	12DEC2020	30DEC2020	Neg/Neg/Neg	Sore throat	Pos/, 15DEC2020, B.1.2
C4591001 1251 12511159 (USA/FLORIDA/37/F)	Placebo	Dose 2/26	26OCT2020	29OCT2020	Neg/Neg/Neg	New or increased cough	Pos/, 28OCT2020, B.1
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1251 12511160 (USA/FLORIDA/59/F)	Placebo	Dose 2/102	10JAN2021	28JAN2021	Neg/Neg/Neg	Fever	Pos/, 12JAN2021, B.1.2
						Chills	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1251 12511201 (USA/FLORIDA/44/F)	Placebo	Dose 2/24	04NOV2020	23NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 20NOV2020, QNS
						Chills	
						New or increased muscle pain	
						New loss of taste or smell	
						Diarrhea	
						Vomiting	
C4591001 1252 12521018 (USA/SOUTH CAROLINA/74/F)	Placebo	Dose 2/126	13JAN2021	18JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 15JAN2021, B.1.1.207
C4591001 1252 12521026 (USA/SOUTH CAROLINA/72/F)	Placebo	Dose 2/125	13JAN2021	18JAN2021	Neg/Neg/Neg	Diarrhea	Pos/, 15JAN2021, INDETERMINATE
C4591001 1254 12541017 (USA/CALIFORNIA/73/M)	Placebo	Dose 2/96	22DEC2020	27DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 29DEC2020, B.1
C4591001 1254 12541058 (USA/CALIFORNIA/54/M)	Placebo	Dose 2/88	17DEC2020	20DEC2020	Neg/Neg/Neg	Fever	Pos/, 22DEC2020, B.1.1.285
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1254 12541134 (USA/CALIFORNIA/53/M)	Placebo	Dose 2/91	31DEC2020	23JAN2021	Neg/Neg/Neg	Fever	Pos/, 05JAN2021, B.1
						New or increased cough	
						New or increased shortness of breath	
						Sore throat	
						Diarrhea	
C4591001 1254 12541157 (USA/CALIFORNIA/41/M)	Placebo	Dose 2/82	27DEC2020	26JAN2021	Neg/Neg/Neg	Sore throat	Pos/, 29DEC2020, B.1.429
C4591001 1260 12601031 (USA/MASSACHUSETTS/67/F)	Placebo	Dose 2/95	02JAN2021	07JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 02JAN2021, B.1.2
						New or increased muscle pain	
C4591001 1264 12641045 (USA/CALIFORNIA/72/F)	Placebo	Dose 2/94	16DEC2020		Neg/Neg/Neg	New or increased cough	Pos/, 21DEC2020, B.1.2
						New loss of taste or smell	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1264 12641048 (USA/CALIFORNIA/34/M)	Placebo	Dose 2/81	03DEC2020	06DEC2020	Neg/Neg/Neg	Fever	Pos/Pos, 06DEC2020, B.1.234
						Chills	
						New or increased muscle pain	
C4591001 1264 12641056 (USA/CALIFORNIA/47/M)	Placebo	Dose 2/54	09NOV2020	20NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 12NOV2020, B.1.2
						Sore throat	
C4591001 1264 12641090 (USA/CALIFORNIA/34/M)	Placebo	Dose 2/108	06JAN2021	19JAN2021	Neg/Neg/Neg	Fever	Pos/, 06JAN2021, B.1.2
						New or increased cough	
						Chills	
						New loss of taste or smell	
						Sore throat	
C4591001 1264 12641111 (USA/CALIFORNIA/57/M)	Placebo	Dose 2/51	12NOV2020	10DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 13NOV2020, B.1
						Sore throat	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1264 12641182 (USA/CALIFORNIA/70/M)	Placebo	Dose 2/64	14DEC2020	28DEC2020	Neg/Neg/Neg	Fever	Pos/, 15DEC2020, B.1.2
						Chills	
						New or increased muscle pain	
						Sore throat	
C4591001 1264 12641183 (USA/CALIFORNIA/47/F)	Placebo	Dose 2/31	13NOV2020	16NOV2020	Neg/Neg/Neg	Fever	Pos/, 15NOV2020, B.1.404
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1264 12641184 (USA/CALIFORNIA/24/F)	Placebo	Dose 2/33	15NOV2020	18NOV2020	Neg/Neg/Neg	Fever	Pos/, 16NOV2020, B.1.404
						New or increased cough	
						Chills	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
C4591001 1265 12651039 (USA/CALIFORNIA/72/M)	Placebo	Dose 2/105	03JAN2021	03JAN2021	Neg/Neg/Neg	Fever	Pos/, 04JAN2021, B.1.2
						New or increased cough	
						New or increased shortness of breath	
						Chills	
						New or increased muscle pain	
						Sore throat	
						Diarrhea	
						Vomiting	
C4591001 1265 12651152 (USA/CALIFORNIA/70/F)	Placebo	Dose 2/57	07DEC2020	10DEC2020	Neg/Neg/Neg	Fever	Pos/, 09DEC2020, B.1.429
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
						Sore throat	
						Diarrhea	
C4591001 1269 12691061 (USA/CALIFORNIA/60/M)	Placebo	Dose 2/74	28NOV2020	16DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 01DEC2020, B.1.400
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 1270 12701010 (USA/CALIFORNIA/46/F)	Placebo	Dose 2/86	10DEC2020	28DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 14DEC2020, B.1.2
						Sore throat	
C4591001 1270 12701033 (USA/CALIFORNIA/41/M)	Placebo	Dose 2/98	28DEC2020	01JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 29DEC2020, B.1
						Chills	
						New or increased muscle pain	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New loss of taste or smell	
						Sore throat	
C4591001 1270 12701048 (USA/CALIFORNIA/22/F)	Placebo	Dose 2/68	01DEC2020	15DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 03DEC2020, B.1.400
						Chills	
						New loss of taste or smell	
C4591001 1270 12701146 (USA/CALIFORNIA/16/F)	Placebo	Dose 2/39	31DEC2020	11JAN2021	Neg/Neg/Neg	New or increased cough	Pos/, 03JAN2021, B.1.2
						New or increased shortness of breath	
C4591001 4444 44441004 (ARG/23/F)	Placebo	Dose 2/86	06JAN2021	17JAN2021	Neg/Neg/Neg	New or increased muscle pain	Pos/, 07JAN2021, B.1.1.35
						Sore throat	
C4591001 4444 44441046 (ARG/57/F)	Placebo	Dose 2/99	19JAN2021	29JAN2021	Neg/Neg/Neg	Fever	Pos/, 24JAN2021, B.1.1.33
						Chills	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 4444 44441092 (ARG/64/M)	Placebo	Dose 2/23	03NOV2020	16NOV2020	Neg/Neg/Neg	New or increased cough	Pos/, 08NOV2020, B.1.1.33
						New or increased shortness of breath	
						New or increased muscle pain	
						New loss of taste or smell	
						Sore throat	
C4591001 4444 44441144 (ARG/38/M)	Placebo	Dose 2/26	07NOV2020	18NOV2020	Neg/Neg/Neg	Fever	Pos/, 10NOV2020, B.1.1.33
						New or increased muscle pain	
						New loss of taste or smell	
						Diarrhea	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 4444 44441204 (ARG/59/F)	BNT162b2 (30 µg)	Dose 2/21	02NOV2020	14DEC2020	Neg/Neg/Neg	New or increased muscle pain	Pos/, 03NOV2020, B.1.1.33
						New loss of taste or smell	
C4591001 4444 44441211 (ARG/42/M)	Placebo	Dose 2/116	05FEB2021	15FEB2021	Neg/Neg/Neg	Fever	Pos/, 07FEB2021, B.1.1.33
						New or increased cough	
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 4444 44441222 (ARG/59/M)	BNT162b2 (30 µg)	Dose 2/61	12DEC2020	17DEC2020	Neg/Neg/Neg	New or increased cough	Pos/, 15DEC2020, B.1.1.33
						Sore throat	
C4591001 4444 44441224 (ARG/52/M)	Placebo	Dose 2/13	25OCT2020	10NOV2020	Neg/Neg/Neg	Fever	Pos/, 26OCT2020, B.1.1.33
						New or increased	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						shortness of breath	
						New or increased muscle pain	
C4591001 4444 44441563 (ARG/38/M)	Placebo	Dose 2/8	21OCT2020	29OCT2020	Neg/Neg/Neg	New loss of taste or smell	Pos/, 22OCT2020, B.1.1.1
						Diarrhea	
C4591001 4444 44441586 (ARG/45/F)	Placebo	Dose 2/141	03MAR2021	16MAR2021	Neg/Neg/Neg	New or increased cough	Pos/, 05MAR2021, B.1.1.7
						New loss of taste or smell	
C4591001 4444 44441632 (ARG/55/F)	Placebo	Dose 2/112	01FEB2021	18FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 11FEB2021, B.1.1.33
						New loss of taste or smell	
						Diarrhea	
C4591001 4444 44441636 (ARG/48/M)	Placebo	Dose 2/106	26JAN2021	07FEB2021	Neg/Neg/Neg	Fever	Pos/, 29JAN2021, B.1.1.33
						New or increased cough	

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
						New or increased muscle pain	
C4591001 4444 44441735 (ARG/52/M)	Placebo	Dose 2/106	27JAN2021	08FEB2021	Neg/Neg/Neg	New or increased cough	Pos/, 29JAN2021, P.2
						New or increased muscle pain	
C4591001 4444 44441786 (ARG/52/F)	Placebo	Dose 2/85	04JAN2021	26JAN2021	Neg/Neg/Neg	Fever	Pos/, 04JAN2021, B.1.1.33
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 4444 44441985 (ARG/44/F)	Placebo	Dose 2/71	25DEC2020	12JAN2021	Neg/Neg/Neg	Fever	Pos/, 28DEC2020, B.1.499
						New or increased cough	
						Sore throat	
C4591001 4444 44441996 (ARG/32/F)	BNT162b2 (30 µg)	Dose 2/32	14NOV2020	28NOV2020	Neg/Neg/Neg	Diarrhea	Pos/, 19NOV2020, B.1

16.2.8.6 Listing of Subjects and SARS-CoV-2 Variants With First COVID-19 Occurrence From 7 Days After Dose 2 and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Evaluable Efficacy (7 Days) Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 4444 44442167 (ARG/35/F)	BNT162b2 (30 µg)	Dose 2/84	07JAN2021	17JAN2021	Neg/Unk/Neg	New or increased muscle pain Sore throat	Pos/, 09JAN2021, B.1.511

Abbreviations: ARG = Argentina; BRA = Brazil; DEU = Germany; NAAT = nucleic acid amplification test; NS = not sequenced; N-binding = SARS-CoV-2 nucleoprotein–binding; Neg = negative; Pos = positive; QNS = not quantifiable samples; R1 = repeat central swab 1; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; TUR = Turkey; Unk = unknown; ZAF = South Africa.
Note: HIV-positive subjects are included in this listing but not included in the analyses of the overall study objectives.
Note: † = HIV-positive subject.
a. Relative Day (Rel Day) = date of first symptom - date of last dose before first symptom + 1.
b. SARS-CoV-2 NAAT results from the local lab are based on the Cepheid Xpert® Xpress SARS-CoV-2 test, Roche cobas® SARS-CoV-2 real-time RT-PCR test (EUA200009/A001), or Abbott RealTime SARS-CoV-2 assay (EUA200023/A001) only.
PFIZER CONFIDENTIAL SDTM Creation: 01JUN2021 (17:11) Source Data: adsympt Table Generation: 01JUN2021 (22:07)
(Cutoff Date: 13MAR2021, Snapshot Date: 28MAY2021) Output File: ./nda2 unblinded/C4591001 BLA Sequence/adxb l001 seq d2 cov eval

16.2.8.7 Listing of Subjects and SARS-CoV-2 Variants With Multiple COVID-19 Occurrence After Dose 1 – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1116 11161224 (USA/MISSISSIPPI/52/F)	Placebo	Dose 2/46	14NOV2020	20NOV2020	Neg/Neg/Neg	Fever	Pos/, 16NOV2020, B.1.2
						New or increased cough	
						Chills	
						New or increased muscle pain	
						Sore throat	
		Dose 2/82	20DEC2020	15JAN2021	Neg/Neg/Neg	Fever	Pos/, 23DEC2020, B
						New or increased muscle pain	
						New loss of taste or smell	
C4591001 1221 12211002 (USA/MARYLAND/43/M)	Placebo	Dose 1/20	01NOV2020	20NOV2020	Neg/Neg/Unk	Chills	Pos/Pos, 02NOV2020, B.1
						Vomiting	
		Dose 4/5*	26FEB2021	02MAR2021	Neg/Neg/Unk	New or increased cough	Pos/Pos, 27FEB2021, QNS
						Chills	
						New loss of taste or smell	

16.2.8.7 Listing of Subjects and SARS-CoV-2 Variants With Multiple COVID-19 Occurrence After Dose 1 – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
C4591001 1231 12312660 (ARG/35/M)	Placebo	Dose 1/23	11SEP2020	23SEP2020	Neg/Neg/Neg	New or increased cough	Pos/, 11SEP2020, B.1
						New loss of taste or smell	
						Sore throat	
		Dose 1/99	26NOV2020	27NOV2020	Neg/Neg/Neg	Vomiting	Pos/, 26NOV2020, QNS
C4591001 1231 12312679 (ARG/32/M)	Placebo	Dose 2/4	14SEP2020	12NOV2020	Neg/Neg/Neg	Fever	Pos/, 19SEP2020, B.1.499
						New or increased cough	
						New or increased muscle pain	
						Diarrhea	
		Dose 2/151	08FEB2021	17FEB2021	Neg/Neg/Neg	Fever	Pos/, 12FEB2021, B.1.142
						Sore throat	
						Diarrhea	
C4591001 1231 12313510 (ARG/29/F)	Placebo	Dose 1/13	04SEP2020	07SEP2020	Neg/Neg/Pos	Fever	Pos/, 05SEP2020, B.1.499
						New or increased cough	

16.2.8.7 Listing of Subjects and SARS-CoV-2 Variants With Multiple COVID-19 Occurrence After Dose 1 – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day[a]	Start Date of First Symptom	Stop Date of Last Symptom	Visit 1 N-Binding Assay/ Visit 1 NAAT/ Visit 2 NAAT	Signs and Symptoms	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage
		Dose 1/69	30OCT2020	12NOV2020	Neg/Neg/Pos	Diarrhea	Pos/, 14NOV2020, QNS
C4591001 1270 12701237 (USA/CALIFORNIA/13/F)	Placebo	Dose 1/13	19JAN2021	20JAN2021	Neg/Pos/Pos	New or increased shortness of breath	Pos/, 21JAN2021, B.1.1.38
		Dose 1/20	26JAN2021	26JAN2021	Neg/Pos/Pos	Diarrhea	Pos/, 29JAN2021, B.1.1.1

Abbreviations: ARG = Argentina; NAAT = nucleic acid amplification test; NS = not sequenced; N-binding = SARS-CoV-2 nucleoprotein–binding; Neg = negative; Pos = positive; QNS = not quantifiable samples; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; Unk = unknown.
Note: HIV-positive subjects are included in this listing but not included in the analyses of the overall study objectives.
Note: * = COVID-19 occurrence after subject was unblinded.
a. Relative Day (Rel Day) = date of first symptom - date of last dose before first symptom + 1.
b. SARS-CoV-2 NAAT results from the local lab are based on the Cepheid Xpert® Xpress SARS-CoV-2 test, Roche cobas® SARS-CoV-2 real-time RT-PCR test (EUA200009/A001), or Abbott RealTime SARS-CoV-2 assay (EUA200023/A001) only.
PFIZER CONFIDENTIAL SDTM Creation: 01JUN2021 (17:11) Source Data: adsympt Table Generation: 01JUN2021 (22:07)
(Cutoff Date: 13MAR2021, Snapshot Date: 28MAY2021) Output File: ./nda2_unblinded/C4591001_BLA_Sequence/adxb_l001_seq_d1_mul_cov_aai

16.2.8.8 Listing of Subjects and SARS-CoV-2 Variants With First Severe COVID-19 Occurrence Based on CDC-Defined or FDA-Defined Symptoms After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day [a]	Start Date	Stop Date	Visit 1 N-Binding Assay/ Visit 1 NAAT / Visit 2 NAAT	Signs, Symptoms, and Events	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage	FDA-Defined/ CDC-Defined Symptoms
C4591001 1003 10031167 (USA/NEW YORK/57/F)*	Placebo	Dose 2/87	22NOV2020	23DEC2020	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/Pos, 19DEC2020, B.1.404	CDC-defined
		Dose 2/117	22DEC2020	23DEC2020		Hospitalized due to COVID-19 illness		
C4591001 1007 10071306 (USA/OHIO/58/F)*	Placebo	Dose 2/71	11JAN2021		Neg/Neg/Neg	$SpO_2 \leq 93\%$ on room air at sea level	Pos/, 01JAN2021, B.1.2	Both
		Dose 2/71	11JAN2021	12JAN2021		Hospitalized due to COVID-19 illness		
C4591001 1008 10081285 (USA/MISSOURI/60/F)*	Placebo	Dose 2/71	11DEC2020	14DEC2020	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/, 27NOV2020, B.1.2	CDC-defined
C4591001 1009 10091128 (USA/UTAH/51/M)*	Placebo	Dose 2/67	21NOV2020		Neg/Neg/Neg	$SpO_2 \leq 93\%$ on room air at sea level	Pos/, 20OCT2020, B.1.2	Protocol-defined

16.2.8.8 Listing of Subjects and SARS-CoV-2 Variants With First Severe COVID-19 Occurrence Based on CDC-Defined or FDA-Defined Symptoms After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day [a]	Start Date	Stop Date	Visit 1 N-Binding Assay/ Visit 1 NAAT / Visit 2 NAAT	Signs, Symptoms, and Events	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage	FDA-Defined/ CDC-Defined Symptoms
C4591001 1013 10131296 (USA/FLORIDA/44/M)*	Placebo	Dose 2/83	06DEC2020	08DEC2020	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/, 30NOV2020, B.1.1.122	CDC-defined
C4591001 1038 10381051 (USA/TENNESSEE/69/M)*	Placebo	Dose 2/61	17NOV2020	22NOV2020	Neg/Neg/Neg	Admission to an ICU	Pos/, 09NOV2020, B.1.361	Both
C4591001 1047 10471252 (USA/ALABAMA/63/M)	Placebo	Dose 1/26	16OCT2020		Neg/Neg/Pos	$SpO_2 \leq 93\%$ on room air at sea level	Pos/, 14OCT2020, B.1.2	Both
		Dose 1/26	16OCT2020			High-flow oxygen therapy		
		Dose 1/26	16OCT2020	20OCT2020		Hospitalized due to COVID-19 illness		
C4591001 1054 10541202 (USA/CALIFORNIA/57/M)*	Placebo	Dose 2/71	22JAN2021	27JAN2021	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/, 12JAN2021, INDETERMINATE	CDC-defined
C4591001 1072 10721037 (USA/ALABAMA/71/F)	Placebo	Dose 2/82	27DEC2020		Neg/Neg/Neg	High-flow oxygen therapy	Pos/Pos, 21DEC2020, B.1.2	Both
		Dose 2/82	27DEC2020	02JAN2021		Hospitalized due to		

16.2.8.8 Listing of Subjects and SARS-CoV-2 Variants With First Severe COVID-19 Occurrence Based on CDC-Defined or FDA-Defined Symptoms After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day [a]	Start Date	Stop Date	Visit 1 N-Binding Assay/ Visit 1 NAAT / Visit 2 NAAT	Signs, Symptoms, and Events	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage	FDA-Defined/ CDC-Defined Symptoms
						COVID-19 illness		
C4591001 1093 10931050 (USA/IOWA/62/M)	Placebo	Dose 1/33	25SEP2020	27SEP2020	Neg/Neg/Unk	Hospitalized due to COVID-19 illness	Pos/, 21SEP2020, B.1.448	CDC-defined
C4591001 1093 10931122 (USA/IOWA/58/F)*	Placebo	Dose 2/17	16OCT2020	20OCT2020	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/, 09OCT2020, B.1	CDC-defined
C4591001 1109 11091415 (USA/FLORIDA/48/F)*	Placebo	Dose 2/95	29DEC2020		Neg/Neg/Neg	DBP <60 mm Hg	Pos/, 29DEC2020, B.1.2	Both
		Dose 2/95	29DEC2020	31DEC2020		Hospitalized due to COVID-19 illness		
C4591001 1112 11121301 (USA/GEORGIA/47/M)*	Placebo	Dose 2/37	08DEC2020	09DEC2020	Neg/Neg/Neg	High-flow oxygen therapy	Pos/, 29NOV2020, B.1.280	Both
		Dose 2/37	08DEC2020	09DEC2020		Hospitalized due to COVID-19 illness		

16.2.8.8 Listing of Subjects and SARS-CoV-2 Variants With First Severe COVID-19 Occurrence Based on CDC-Defined or FDA-Defined Symptoms After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day [a]	Start Date	Stop Date	Visit 1 N-Binding Assay/ Visit 1 NAAT / Visit 2 NAAT	Signs, Symptoms, and Events	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage	FDA-Defined/ CDC-Defined Symptoms
C4591001 1114 11141075 (USA/KANSAS/40/F)*	Placebo	Dose 2/118	05JAN2021		Neg/Neg/Neg	$SpO_2 \leq 93\%$ on room air at sea level	Pos/, 04JAN2021, QNS	Both
		Dose 2/118	05JAN2021	11JAN2021		High-flow oxygen therapy		
		Dose 2/118	05JAN2021	13JAN2021		Hospitalized due to COVID-19 illness		
C4591001 1116 11161160 (USA/MISSISSIPPI/47/M)*	Placebo	Dose 2/108	13JAN2021		Neg/Neg/Neg	$SpO_2 \leq 93\%$ on room air at sea level	Pos/, 13JAN2021, B.1.2	Protocol-defined
C4591001 1116 11161224 (USA/MISSISSIPPI/52/F)*	Placebo	Dose 2/85	23DEC2020	25DEC2020	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/, 23DEC2020, B	CDC-defined
C4591001 1116 11161253 (USA/MISSISSIPPI/61/M)	Placebo	Dose 1/11	28SEP2020		Neg/Neg/Pos	HR ≥125 beats/minute	Pos/, 28SEP2020, B.1.234	Protocol-defined
C4591001 1120 11201101 (USA/GEORGIA/48/F)*	Placebo	Dose 2/148	19JAN2021	23JAN2021	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/, 06JAN2021, B.1.2	CDC-defined

16.2.8.8 Listing of Subjects and SARS-CoV-2 Variants With First Severe COVID-19 Occurrence Based on CDC-Defined or FDA-Defined Symptoms After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day [a]	Start Date	Stop Date	Visit 1 N-Binding Assay/ Visit 1 NAAT / Visit 2 NAAT	Signs, Symptoms, and Events	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage	FDA-Defined/ CDC-Defined Symptoms
C4591001 1124 11241128 (USA/RHODE ISLAND/67/M)*	Placebo	Dose 2/95	24DEC2020		Neg/Neg/Neg	$SpO_2 \leq 93\%$ on room air at sea level	Pos/, 18JAN2021, B.1.361	Both
		Dose 2/95	24DEC2020	30DEC2020		Hospitalized due to COVID-19 illness		
C4591001 1125 11251014 (USA/NEBRASKA/45/F)*	Placebo	Dose 2/68	08NOV2020		Neg/Neg/Neg	$SpO_2 \leq 93\%$ on room air at sea level	Pos/, 10NOV2020, B.1.413	Protocol-defined
C4591001 1131 11311100 (USA/OHIO/64/M)*	Placebo	Dose 2/67	21NOV2020	30NOV2020	Neg/Neg/Neg	High-flow oxygen therapy	Pos/, 13NOV2020, B.1.2	Both
		Dose 2/67	21NOV2020	24NOV2020		Hospitalized due to COVID-19 illness		
		Dose 2/70	24NOV2020			DBP <60 mm Hg		
C4591001 1134 11341035 (USA/NORTH CAROLINA/59/F)*	Placebo	Dose 2/122	31DEC2020	05JAN2021	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/, 24DEC2020, B.1.2	CDC-defined
C4591001 1146 11461235 (USA/65/M)*	Placebo	Dose 2/60	03DEC2020	07DEC2020	Neg/Neg/Neg	Non-invasive positive	Unk/Pos, 03DEC2020, NS	Both

16.2.8.8 Listing of Subjects and SARS-CoV-2 Variants With First Severe COVID-19 Occurrence Based on CDC-Defined or FDA-Defined Symptoms After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day [a]	Start Date	Stop Date	Visit 1 N-Binding Assay/ Visit 1 NAAT / Visit 2 NAAT	Signs, Symptoms, and Events	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage	FDA-Defined/ CDC-Defined Symptoms
						pressure ventilation		
		Dose 2/60	03DEC2020	07DEC2020		Hospitalized due to COVID-19 illness		
C4591001 1156 11561006 (USA/FLORIDA/45/M)	BNT162b2 (30 µg)	Dose 1/12	31AUG2020	02SEP2020	Neg/Pos/Neg	Hospitalized due to COVID-19 illness	Pos/Pos, 02SEP2020, B.1.306	CDC-defined
C4591001 1156 11561044 (USA/FLORIDA/63/M)	Placebo	Dose 1/8	03SEP2020		Neg/Neg/Neg	Significant acute renal dysfunction	Pos/, 03SEP2020, B.1.2	Both
		Dose 1/8	03SEP2020	09SEP2020		Significant acute hepatic dysfunction		
		Dose 1/10	05SEP2020			$SpO_2 \leq 93\%$ on room air at sea level		
		Dose 1/10	05SEP2020	09SEP2020		High-flow oxygen therapy		
		Dose 1/10	05SEP2020	19SEP2020		Admission to an ICU		

16.2.8.8 Listing of Subjects and SARS-CoV-2 Variants With First Severe COVID-19 Occurrence Based on CDC-Defined or FDA-Defined Symptoms After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day [a]	Start Date	Stop Date	Visit 1 N-Binding Assay/ Visit 1 NAAT / Visit 2 NAAT	Signs, Symptoms, and Events	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage	FDA-Defined/ CDC-Defined Symptoms
		Dose 1/10	05SEP2020	19SEP2020		Hospitalized due to COVID-19 illness		
		Dose 1/19	14SEP2020			$SpO_2 \leq 93\%$ on room air at sea level		
		Dose 1/34	29SEP2020			$SpO_2 \leq 93\%$ on room air at sea level		
		Dose 1/36	01OCT2020			$SpO_2 \leq 93\%$ on room air at sea level		
C4591001 1171 11711212 (USA/TEXAS/33/M)*	Placebo	Dose 2/58	12DEC2020	18DEC2020	Neg/Neg/Neg	Admission to an ICU	Pos/, 07DEC2020, B.1.2	Both
		Dose 2/58	12DEC2020	18DEC2020		Hospitalized due to COVID-19 illness		
C4591001 1205 12051070 (TUR/68/M)*	Placebo	Dose 2/28	28DEC2020	03JAN2021	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/, 30DEC2020, B.1	CDC-defined
C4591001 1205 12051078 (TUR/52/M)	Placebo	Dose 1/10	19NOV2020	20NOV2020	Neg/Pos/Pos	Hospitalized due to	Pos/Pos, 19NOV2020, A	CDC-defined

16.2.8.8 Listing of Subjects and SARS-CoV-2 Variants With First Severe COVID-19 Occurrence Based on CDC-Defined or FDA-Defined Symptoms After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day [a]	Start Date	Stop Date	Visit 1 N-Binding Assay/ Visit 1 NAAT / Visit 2 NAAT	Signs, Symptoms, and Events	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage	FDA-Defined/ CDC-Defined Symptoms
						COVID-19 illness		
C4591001 1217 12171044 (TUR/34/M)	Placebo	Dose 1/8	11NOV2020	16NOV2020	Neg/Neg/Pos	Hospitalized due to COVID-19 illness	Pos/, 12NOV2020, B.1.1.162	Both
		Dose 1/17	20NOV2020			PaO_2/FiO_2 <300 mm Hg		
		Dose 1/17	20NOV2020	21NOV2020		Non-invasive positive pressure ventilation		
		Dose 1/17	20NOV2020	29NOV2020		Hospitalized due to COVID-19 illness		
		Dose 1/19	22NOV2020	28NOV2020		High-flow oxygen therapy		
C4591001 1221 12211002 (USA/MARYLAND/43/M)	Placebo	Dose 2/2	03NOV2020		Neg/Neg/Unk	RR ≥30 breaths/minute	Pos/Pos, 02NOV2020, B.1	Both
		Dose 2/2	03NOV2020	06NOV2020		Hospitalized due to		

16.2.8.8 Listing of Subjects and SARS-CoV-2 Variants With First Severe COVID-19 Occurrence Based on CDC-Defined or FDA-Defined Symptoms After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day [a]	Start Date	Stop Date	Visit 1 N-Binding Assay/ Visit 1 NAAT / Visit 2 NAAT	Signs, Symptoms, and Events	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage	FDA-Defined/ CDC-Defined Symptoms
						COVID-19 illness		
C4591001 1223 12231252 (USA/CONNECTICUT/48/M)*	Placebo	Dose 2/77	19JAN2021		Neg/Neg/Neg	PaO_2/FiO_2 <300 mm Hg	Pos/, 11JAN2021, B.1.409	Both
		Dose 2/77	19JAN2021	21JAN2021		Needs mechanical ventilation		
		Dose 2/77	19JAN2021	26JAN2021		Admission to an ICU		
C4591001 1226 12261599 (BRA/41/F)*	BNT162b2 (30 µg)	Dose 2/37	07NOV2020		Neg/Neg/Neg	$SpO_2 \leq 93\%$ on room air at sea level	Pos/, 07NOV2020, B.1.1.94	Protocol-defined
C4591001 1226 12261624 (BRA/52/M)*	Placebo	Dose 2/37	05NOV2020		Neg/Neg/Neg	$SpO_2 \leq 93\%$ on room air at sea level	Pos/, 05NOV2020, B.1.1.143	Protocol-defined
C4591001 1231 12311014 (ARG/62/F)*	Placebo	Dose 2/136	08JAN2021		Neg/Neg/Neg	$SpO_2 \leq 93\%$ on room air at sea level	Pos/, 08JAN2021, B.1.1.33	Both
		Dose 2/136	08JAN2021	14JAN2021		Hospitalized due to COVID-19 illness		

16.2.8.8 Listing of Subjects and SARS-CoV-2 Variants With First Severe COVID-19 Occurrence Based on CDC-Defined or FDA-Defined Symptoms After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day [a]	Start Date	Stop Date	Visit 1 N-Binding Assay/ Visit 1 NAAT / Visit 2 NAAT	Signs, Symptoms, and Events	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage	FDA-Defined/ CDC-Defined Symptoms
C4591001 1231 12311087 (ARG/44/M)	Placebo	Dose 1/18	29AUG2020	07SEP2020	Neg/Neg/Pos	Hospitalized due to COVID-19 illness	Pos/, 27AUG2020, N.3	CDC-defined
C4591001 1231 12311531 (ARG/35/M)*	Placebo	Dose 2/19	26SEP2020	29SEP2020	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/, 19SEP2020, B.1	CDC-defined
C4591001 1231 12312119 (ARG/32/M)*	Placebo	Dose 2/144	28JAN2021	05FEB2021	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/, 24JAN2021, B.1.1.33	CDC-defined
C4591001 1231 12312130 (ARG/64/F)	Placebo	Dose 1/3	20AUG2020	27AUG2020	Neg/Pos/Neg	Hospitalized due to COVID-19 illness	Pos/, 26AUG2020, B.1.452	CDC-defined
C4591001 1231 12312572 (ARG/46/M)*	Placebo	Dose 2/120	05JAN2021	11JAN2021	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/, 29DEC2020, B.1.1.200	CDC-defined
C4591001 1231 12312635 (ARG/71/M)*	Placebo	Dose 2/40	17OCT2020	20OCT2020	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/, 06OCT2020, B.1.1.33	CDC-defined

16.2.8.8 Listing of Subjects and SARS-CoV-2 Variants With First Severe COVID-19 Occurrence Based on CDC-Defined or FDA-Defined Symptoms After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day [a]	Start Date	Stop Date	Visit 1 N-Binding Assay/ Visit 1 NAAT / Visit 2 NAAT	Signs, Symptoms, and Events	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage	FDA-Defined/ CDC-Defined Symptoms
C4591001 1231 12312914 (ARG/50/M)*	Placebo	Dose 2/54	06NOV2020		Neg/Neg/Neg	$SpO_2 \leq 93\%$ on room air at sea level	Pos/, 29OCT2020, B.1.1.33	Both
		Dose 2/54	06NOV2020	14NOV2020		Hospitalized due to COVID-19 illness		
C4591001 1231 12313090 (ARG/57/M)	Placebo	Dose 1/21	11SEP2020	14SEP2020	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/, 25SEP2020, B.1.241	CDC-defined
C4591001 1231 12313125 (ARG/48/M)	Placebo	Dose 1/77	06NOV2020	09NOV2020	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/, 11NOV2020, B.1.1.33	CDC-defined
C4591001 1231 12313422 (ARG/34/M)*	Placebo	Dose 2/48	01NOV2020	23NOV2020	Neg/Neg/Neg	Admission to an ICU	Pos/, 29OCT2020, B.1.2	Both
		Dose 2/48	01NOV2020	23NOV2020		Hospitalized due to COVID-19 illness		
		Dose 2/53	06NOV2020	16NOV2020		Needs mechanical ventilation		

16.2.8.8 Listing of Subjects and SARS-CoV-2 Variants With First Severe COVID-19 Occurrence Based on CDC-Defined or FDA-Defined Symptoms After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day [a]	Start Date	Stop Date	Visit 1 N-Binding Assay/ Visit 1 NAAT / Visit 2 NAAT	Signs, Symptoms, and Events	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage	FDA-Defined/ CDC-Defined Symptoms
		Dose 2/53	06NOV2020	19NOV2020		Admission to an ICU		
		Dose 2/54	07NOV2020			PaO_2/FiO_2 <300 mm Hg		
C4591001 1231 12313697 (ARG/55/M)*	Placebo	Dose 2/123	15JAN2021	22JAN2021	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/, 14JAN2021, P.2	CDC-defined
C4591001 1231 12313895 (ARG/50/F)*	Placebo	Dose 2/21	03OCT2020	06OCT2020	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/, 07OCT2020, B.1	CDC-defined
C4591001 1231 12314681 (ARG/66/F)*	Placebo	Dose 2/110	03JAN2021	12JAN2021	Neg/Neg/Neg	High-flow oxygen therapy	Pos/, 29DEC2020, B.1.1.33	Both
		Dose 2/110	03JAN2021	13JAN2021		Hospitalized due to COVID-19 illness		
C4591001 1231 12315324 (ARG/58/F)*	Placebo	Dose 2/110	05JAN2021		Neg/Neg/Neg	Admission to an ICU	Pos/, 26DEC2020, B.1.1.291	Both
		Dose 2/110	05JAN2021			Hospitalized due to COVID-19 illness		

16.2.8.8 Listing of Subjects and SARS-CoV-2 Variants With First Severe COVID-19 Occurrence Based on CDC-Defined or FDA-Defined Symptoms After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day [a]	Start Date	Stop Date	Visit 1 N-Binding Assay/ Visit 1 NAAT / Visit 2 NAAT	Signs, Symptoms, and Events	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage	FDA-Defined/ CDC-Defined Symptoms
		Dose 2/119	14JAN2021	31JAN2021		Significant acute renal dysfunction		
		Dose 2/119	14JAN2021	31JAN2021		Admission to an ICU		
		Dose 2/121	16JAN2021			Needs mechanical ventilation		
C4591001 1235 12351071 (USA/LOUISIANA/50/M)	Placebo	Dose 1/9	22SEP2020	26SEP2020	Neg/Neg/Unk	Admission to an ICU	Pos/, 22SEP2020, B.1.2	Both
		Dose 1/11	24SEP2020			$SpO_2 \leq 93\%$ on room air at sea level		
C4591001 1246 12461110 (ZAF/19/M)*	Placebo	Dose 2/71	06JAN2021		Neg/Neg/Neg	DBP <60 mm Hg	Pos/, 06JAN2021, B.1.351	Protocol-defined
C4591001 1247 12471066 (ZAF/58/F)	Placebo	Dose 1/25	23OCT2020	24OCT2020	Neg/Neg/Unk	High-flow oxygen therapy	Pos/, 16OCT2020, B.1.237	Both
		Dose 1/25	23OCT2020	26OCT2020		Hospitalized due to COVID-19 illness		

16.2.8.8 Listing of Subjects and SARS-CoV-2 Variants With First Severe COVID-19 Occurrence Based on CDC-Defined or FDA-Defined Symptoms After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day [a]	Start Date	Stop Date	Visit 1 N-Binding Assay/ Visit 1 NAAT / Visit 2 NAAT	Signs, Symptoms, and Events	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage	FDA-Defined/ CDC-Defined Symptoms
C4591001 1247 12471092 (ZAF/37/M)*	Placebo	Dose 2/65	01JAN2021		Neg/Neg/Neg	RR ≥30 breaths/minute	Pos/, 23DEC2020, B.1.351	Both
		Dose 2/65	01JAN2021	03JAN2021		High-flow oxygen therapy		
		Dose 2/66	02JAN2021			Admission to an ICU		
		Dose 2/66	02JAN2021			Hospitalized due to COVID-19 illness		
C4591001 4444 44441985 (ARG/44/F)*	Placebo	Dose 2/82	05JAN2021	12JAN2021	Neg/Neg/Neg	Hospitalized due to COVID-19 illness	Pos/, 28DEC2020, B.1.499	CDC-defined
C4591001 4444 44442304 (ARG/49/M)	Placebo	Dose 2/13	27OCT2020		Neg/Neg/Neg	HR ≥125 beats/minute	Pos/, 27OCT2020, B.1.1.33	Protocol-defined

Abbreviations: ARG = Argentina; BRA = Brazil; CDC = Centers for Disease Control and Prevention; HR = heart rate; ICU = intensive care unit; FDA = Food and Drug Administration; FiO_2 = fraction of inspired oxygen; NAAT = nucleic acid amplification test; NS = not sequenced; N-binding = SARS-CoV-2 nucleoprotein–binding; Neg = Negative; PaO_2 = partial pressure of oxygen, arterial; Pos = Positive; QNS = not quantifiable samples; RR = respiratory rate; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SpO_2 = oxygen saturation as measured by pulse oximetry; TUR = Turkey; Unk = Unknown; ZAF = South Africa.
Note: * indicates subject in the evaluable efficacy (7 days) population with first severe COVID-19 occurrence from 7 days after Dose 2 and with or without

16.2.8.8 Listing of Subjects and SARS-CoV-2 Variants With First Severe COVID-19 Occurrence Based on CDC-Defined or FDA-Defined Symptoms After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

Subject (Country/Region/Age in Years/Sex)	Vaccine Group (as Randomized)	Dose/Rel Day [a]	Start Date	Stop Date	Visit 1 N-Binding Assay/ Visit 1 NAAT / Visit 2 NAAT	Signs, Symptoms, and Events	SARS-CoV-2 NAAT Result (Central Lab/Local Lab[b]), Swab Date, SARS-CoV-2 Lineage	FDA-Defined/ CDC-Defined Symptoms

evidence of infection prior to 7 days after Dose 2.

Note: HIV-positive subjects are included in this listing but not included in the analyses of the overall study objectives.

a. Relative Day (Rel Day) = date of first symptom - date of last dose before first symptom + 1.

b. SARS-CoV-2 NAAT results from the local lab are based on the Cepheid Xpert® Xpress SARS-CoV-2 test, Roche cobas® SARS-CoV-2 real-time RT-PCR test (EUA200009/A001), or Abbott RealTime SARS-CoV-2 assay (EUA200023/A001) only.

PFIZER CONFIDENTIAL SDTM Creation: 01JUN2021 (17:11) Source Data: adsympt Table Generation: 01JUN2021 (22:07)
(Cutoff Date: 13MAR2021, Snapshot Date: 28MAY2021) Output File: ./nda2_unblinded/C4591001_BLA_Sequence/adxb_l001_seq_d2_cov_cdc_aai

BNT162b2

BLA STN 125842/0

Response to CBER 08 June 2021 Clinical Information Request

June 2021

1. INTRODUCTION

On 08 June 2021, Pfizer/BioNTech received the following Clinical Information Request from the FDA regarding the Study BNT162-01 and Study C4591001 submitted to STN 125742/0 on 18 May 2021 (STN 125742/0/1). Pfizer/BioNTech's response to the Clinical Information Request is provided below.

2. CLINICAL INFORMATION REQUEST

2.1. FDA Information Request Item 1

For Study BNT162-01:

1. *In the IS dataset, there is missing immunogenicity data for at least 12 subjects who received the 30 µg dose of BNT162b2. Please submit all immunogenicity data for participants who received 30 µg dose of BNT162b2 to the BLA.*
2. *Please submit fully functional pdf documents (e.g., that can be searched to locate information) for the following reports that are hyperlinked from the BLA submission (document bnt162-01-interim3-report body):*
    a. *R&D Report R-20-0253 (28 November 2020)*
    b. *R&D Report R-20-0235 (27 Nov 2020)*
    c. *Interim report GA-RB-02201A (19 March 2021)*
    d. *R-20-0244 (19 March 2021)*
    e. *Interim Clinical Study Report R-20-0241 (20 March 2021)*

Response

1. Immunogenicity data for participants who received 30 µg dose of BNT162b2

These data were not available at the time of immunogenicity cut-off for this report because the samples were put on hold due to necessary testing prioritizations at the Pfizer labs (eg C4591001 6-month stability and booster; C4591007). Pfizer has now resumed testing of these samples and an updated BNT162-01 study report will be provided once it is available. Pfizer/BioNTech do not believe these data to be material to the review of the Biologics License Application.

2. Fully functional pdf documents (e.g., that can be searched to locate information) for the following reports

The following pdf documents have been corrected for functionality and can be accessed through the individual links provided below:

a) R&D Report R-20-0253 (28 November 2020)

b) R&D Report R-20-0235 (27 Nov 2020)

c) Interim report GA-RB-02201A (19 March 2021)

d) R-20-0244 (19 March 2021)

e) Interim Clinical Study Report R-20-0241 (20 March 2021)

2.2. FDA Information Request Item 2

For Study C4591001:

1. *Please provide a rationale for the differences in the number of participants described in the reactogenicity subset of the safety population as presented in Tables 1 through 4 in (1) the proposed Prescribing Information (PI), submitted in STN 125742/0/1 (dated May 18, 2021) and (2) the most recent version of the Fact Sheet for Healthcare Providers/Full EUA PI, submitted with EUA 27034/181 (dated May 20, 2021). The descriptions for the safety population in Section 6 of each of the PI documents are similar, with an enrollment by date of October 9, 2020 and differing data cut off dates, as expected. However, we would expect that the entire reactogenicity subset would be included in the BLA submission, without a specified "enrollment by date." If this is the rationale for the differences in the number of participants described in the reactogenicity subset, please provide a revised PI to STN 125742 that accurately describes the safety population in Section 6, in tracked changes.*

Response

The current effective Fact Sheet for Healthcare Providers/Full EUA Prescribing Information (EUA PI) submitted 20 May 2021 does not contain the 6-month post-dose 2 update. This is the rationale for the differences in the number of participants described in the reactogenicity subset of the safety population as presented in Tables 1 through 4 in the proposed BLA PI, submitted 18 May 2021 (STN 125742/0/1) and the most recent version of the EUA PI, submitted 20 May 2021 (EUA 27034/181). Please refer to the EUA PI submitted 14 May 2021, currently under review, which includes the 6-month post-dose 2 update.

QUERY 1

COMIRNATY is supplied in a multiple-dose vial that does not contain a preservative. Our review of the information provided in your BLA STN 125742/0 for COMIRNATY (COVID-19 mRNA Vaccine), for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older, is ongoing. Please note that 21 CFR 610.15(a) requires that "Products in multiple-dose containers shall contain a preservative,…" The regulations in 610.15(d) permit the approval of an exception or alternative to this requirement. Requests for such exceptions or alternatives must be in writing. Your submission does not include a request for an exception or alternative to the requirement of a preservative. Therefore, please submit a request and a justification for an exception or alternative to the requirement under 21 CFR 610.15(a) that products in multiple-dose vials include a preservative.

RESPONSE 1

The Sponsor acknowledges this request to submit a request and justification for an exception or alternative to the requirement under 21 CFR 610.15(a) that products in multiple-dose vials include a preservative. The formal request for an exception is provided in 1.12.5 Request for Exception to the 21 CFR 610.15(a) Requirement for a Preservative.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

1.12.5 Request for Exception to the 21 CFR 610.15(a) Requirement for a Preservative, new

Previously submitted supporting documentation

None

Request for a Waiver

COVID-19 Vaccine
BNT162
(PF-07302048)

Request for Exception
to the
21 CFR 610.15(a)
Requirement for a Preservative

JULY 2021

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INTRODUCTION

This submission is a request for an exception to the regulatory requirement under 21 CFR 610.15(a) that a vaccine product in a multi-dose container should contain a preservative. As discussed more fully below, the requested exception is necessary due to exigent circumstances resulting from the COVID-19 emergency that would otherwise delay production of large quantities of the vaccine necessary for global distribution. The exception is further justified by the favorable post-authorization experience following distribution of more than 871,000,000 doses of vaccine in this multi-dose, non-preserved presentation under the US Emergency Use Authorization (EUA 27034) and other global authorizations from the receipt of the first temporary authorization for emergency supply in the UK on 01 December 2020 through 30 June 2021.

Pfizer and BioNTech have developed a vaccine intended to prevent coronavirus disease 2019 (COVID-19), which is caused by the virus SARS-CoV-2. The vaccine, as authorized under EUA 27034, is a concentrated liquid formulation stored frozen at -90 to -60 °C in a 2 mL Type 1 glass vial, with provisions for short-term storage for up to two weeks at -20 ±5 °C and up to 1 month at 2-8 °C until administration, as described in Module 3.2 of the BLA. Due to the urgency of the COVID-19 pandemic and the immediate and ongoing need to manufacture large numbers of doses for global use throughout 2021 and 2022, a multi-dose, preservative-free vial presentation remains an important tool to enable sufficient global supply, even while a single-dose vial is also under development. Therefore, Pfizer and BioNTech intend to commercialize the current frozen liquid formulation filled into a multidose vial. After dilution with normal saline, six doses would be withdrawn from the multidose vial. The dosage and administration section on the label will include detailed instructions for the health care provider to perform the dilution with 0.9% Sodium Chloride Injection, USP.

Pfizer and BioNTech acknowledge that 21 CFR 610.15(a) requires that

> *Products in multiple-dose containers shall contain a preservative,…*

However, 21 CFR 610.15(d) states that

> *The Director…may approve an exception or alternative to any requirement in this section. Requests for such exceptions or alternatives must be in writing.*

Pfizer and BioNTech are hereby making a written request for an exception to 21 CFR 610.15(a) for the BNT162b2 vaccine as a multi-dose preservative-free presentation.

The justification for this exception request is provided herein including details regarding Pfizer and BioNTech's plans for ensuring that the vaccine will meet the statutory and regulatory requirements for identity, safety, purity, and potency. Please note, this exception has been requested and authorized under Emergency Use Authorization 27034 and is requested to remain in place upon BLA approval.

1. BACKGROUND

1.1. Proposed Multi-dose Vial Design and Proposed User Instructions

The BNT162b2 drug product is frozen at -90 to -60 °C for storage and distribution with provisions for short-term storage for up to two weeks at -20 ±5 °C and up to 1 month at 2-8 °C until administration, as described in Module 3.2 of the BLA. The drug product is provided as a concentrate that is diluted at point of use prior to administration.

On the day of administration, the thawed vaccine vial is prepared for use. 0.9% Sodium Chloride Injection, USP (Normal Saline) is added to the vial to increase the volume of the vaccine solution for dosing to ensure that the injection volumes are appropriate for administration. The vial is labeled with the time of Normal Saline dilution and must be discarded within 6 hours after initial dilution. Dose administration of the BNT162b2 vaccine involves withdrawal of the prescribed dose from the vial into a delivery system such as a syringe.

The dilution scheme for vaccine dosed under the EUA is representative of the proposed dose administration instructions for planned commercial supply under an approved BLA.

1.2. Justification for the Unpreserved Multidose Vial

The BNT162b2 drug product is filled into 2 mL vials at a concentration of 0.5 mg/mL RNA contained in lipid nanoparticles (LNPs). Formulation development studies conducted to date do not support long-term storage of formulations at lower RNA or LNP concentrations without a change to the formulation. A new formulation to enable lower strengths of RNA LNP will require additional time to gain global regulatory authorization and build additional production capacity to supply global demand.

In addition to the formulation limitations, the drug product manufacturing sites have limitations on the lowest volume that can be filled into the vial in a reliable and consistent manner. This has been determined to be 0.3 mL for many of the drug product manufacturing lines that have been qualified for this vaccine drug product. Due to these constraints, the final filled vial will contain enough concentrated active vaccine to supply 6 doses. Normal Saline must be added to the vial in order to achieve an adequate injection volume regardless of whether the vial is used as a single dose or a multi dose vial. If used as a single dose vial, 5 additional doses would be discarded after removal of a single dose. The use of this product as a multi dose vial therefore provides 6 times more doses than if used as a single dose vial and prevents wastage of a critically needed vaccine.

Pfizer and BioNTech have assessed the risks of this approach by taking into consideration formulation factors including, but not limited to, pH, solvent system, osmolality, drug product storage temperature, and solution properties, which may impact the ability of the finished drug product to support or inhibit microbial growth. Additionally, prior knowledge from extensive experience with other products and data from platform formulations and commonly used infusion fluid studies have been used to evaluate dilution and administration risks.

Pfizer performed the microbial challenge assessments based on Dr. Metcalfe's paper[1] which included the panel of microbes in USP <51> and used prepared vaccine dosing solutions. In the study, samples were spiked with a low level inoculum (<100 cfu/mL) of *S.aureus, E. coli, Ps. aeruginosa, A. niger* (name changed to *A. brasiliensis*), and *C. albicans*, held at 20-25 °C, and then assessed for growth at time points up to 16 hours. Testing revealed no significant growth for any of the organisms within 12 hours of inoculation with storage at 20-25 °C which is defined as not more than 0.5 $\log_{10}$ unit higher than the previous value measured cfu. The results of this study are provided in Section 3.2.P.2.6 Compatibility and provide assurance for the microbial integrity of the product over 6 hours. The in-use period of 6 hours is necessary to ensure adequate time is provided to prepare and administer 6 doses and is in alignment with WHO policy on the use of opened multi-dose vaccine vials[2].

The exception is further justified by the favorable post-authorization experience following distribution of more than 871,000,000 doses of vaccine in this multi-dose, non-preserved presentation under the US Emergency Use Authorization (EUA 27034) and other global authorizations from the receipt of the first temporary authorization for emergency supply in the UK on 01 December 2020 through 30 June 2021.

As noted in 21 CFR 610.15, "Any preservative used … shall not denature the specific substances in the product to result in a decrease below the minimum acceptable potency within the dating period when stored at the recommended temperature." Given the lipidic nature of the lipid nanoparticles, compatibility with common preservatives is not expected. As the microbial growth assessment study results support an in-use period of up to 6 hours, the exclusion of a preservative which may otherwise compromise potency is prudent.

2. SUMMARY: REQUEST FOR EXCEPTION

Pfizer and BioNTech hereby request an exception from 21 CFR 610.15(a) regarding the requirement for using a preservative in a Multi-Dose Vial for commercial supply of the candidate vaccine under BLA 125742.

REFERENCES

1 Metcalfe JW. Microbiological quality of drug products after penetration of the container system for dose preparation prior to patient administration. American Pharmaceutical Review 2009;(Jan/Feb):84-9.

2 WHO Policy Statement: Multi-Dose Vial Policy (MDVP) – Handling of Multi-Dose Vaccine Vials After Opening, Revision 2014. WHO/IVB/14.07. Available at https://apps.who.int/iris/bitstream/handle/10665/135972/WHO_IVB_14.07_eng.pdf

Listing of Severe, Serious, Life threatening, or Leading to Withdrawal Adverse Events From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 HIV-Positive Subjects ≥16 Years of Age – Safety Population

Treatment Group/ Age Group (Years)/ Subject	System Organ Class	Preferred Term/ AE Investigator Text	Dose No.	Onset Date	Rel Day[a]/ Dur (Days)[b]	Toxicity Grade	Vax Rel[c]	Cause of AE	Action: Investigational Vaccine Dose/ Subject	Outcome (End Date)	SAE/Imm AE (Yes/No)
BNT162b2 (30 µg)/ 16-55/ C4591001 1226 12262255	MUSC	Myalgia/ muscle pain	1	19OCT2020	4/4	2	Yes		NA/TC	R (22OCT2020)	N/N
	GASTR	Nausea/ Nauseas	2	06NOV2020	1/3	3	Yes		NA	R (08NOV2020)	N/N
		Vomiting/ Vomiting	2	06NOV2020	1/3	3	Yes		NA/TC	R (08NOV2020)	N/N
	GENRL	Chills/ Chills	2	06NOV2020	1/3	3	Yes		NA	R (08NOV2020)	N/N
		Injection site pain/ Pain at the injection site	2	06NOV2020	1/3	3	Yes		NA	R (08NOV2020)	N/N
		Pyrexia/ Fever 39 C	2	06NOV2020	1/3	3	Yes		NA/TC	R (08NOV2020)	N/N
	MUSC	Myalgia/ Muscle pain	2	06NOV2020	1/3	3	Yes		NA/TC	R (08NOV2020)	N/N
BNT162b2 (30 µg)/ 16-55/ C4591001 1230 12301045	INJ&P	Exposure during pregnancy/ Exposure during Pregnancy	1	20OCT2020	22/C		No	O	P	UNK	N/N
Placebo/ 16-55/ C4591001 1229 12291083	METAB	Diabetes mellitus/ Diabetes Mellitus	2	28DEC2020	68/C	4	No	O	NA	N	Y/N
	INFEC	COVID-19 pneumonia/ Covid 19 Pneumonia	2	01JAN2021	72/5	4	No	O	NA/W	F (05JAN2021)	Y/N
BNT162b2 (30 µg)/ >55/ C4591001 1015 10151238	INFEC	Pneumonia/ Pneumonia	2	20JAN2021	86/8	3	No	O	NA/TC	R (27JAN2021)	Y/N

Listing of Severe, Serious, Life threatening, or Leading to Withdrawal Adverse Events From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 HIV-Positive Subjects ≥16 Years of Age – Safety Population

Treatment Group/ Age Group (Years)/ Subject	System Organ Class	Preferred Term/ AE Investigator Text	Dose No.	Onset Date	Rel Day[a]/ Dur (Days)[b]	Toxicity Grade	Vax Rel[c]	Cause of AE	Action: Investigational Vaccine Dose/ Subject	Outcome (End Date)	SAE/Imm AE (Yes/No)
	GENRL	Oedema peripheral/ Peripheral edema	2	03FEB2021	100/31	2	No	O	NA	R (05MAR2021)	N/N
BNT162b2 (30 µg)/ >55/ C4591001 1156 11561160	INJ&P	Road traffic accident/ MOTOR VEHICLE ACCIDENT	2	24DEC2020	74/1	4	No	O	NA/W	F (24DEC2020)	Y/N

Abbreviations: C = continuing; Dur = duration; Imm = immediate. Refer to the AE legend page (Listing 16.2.7.1) for additional definitions.
Note: MedDRA (v23.1) coding dictionary applied.
a. Relative day (Rel Day) = date of AE - date of last vaccination + 1. For an AE that occurred before the date of the first study vaccination, + 1 was not added to compute relative day.
b. Duration (days) was calculated as the difference from the start of the first reported event to resolution of the last reported event, inclusive.
c. Vaccine related (Vax Rel): relationship to investigational vaccine as assessed by the investigator.
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Reason(s) for Narrative: HIV
Unique Subject ID: C4591001 1226 12262255; Country: Brazil
Vaccine Group (as Administered): BNT162b2 (30 µg)
Date of First Dose: 16OCT2020; Date of Last Dose: 06NOV2020
==========

Demography				
Date of Birth	**Age at Enrollment (Years)**	**Race**	**Ethnicity**	**Sex**
(b) (6) 1972	48	White	Hispanic/Latino	M

Vital Signs - Baseline			
Height	**Weight**	**BMI**	**Date Collected (Study Day)**
173.8 cm	95.6 kg	31.6 kg/m2	16OCT2020 (1)

Medical History			
Investigator Text	**MedDRA Preferred Term**	**Start Date**	**Disease Status**
HIV	HIV test positive	2010	Present
Obesity	Obesity	2010	Present
contact dermatitis	Dermatitis contact	2017	Present

Reason(s) for Narrative: HIV
Unique Subject ID: C4591001 1226 12262255; Country: Brazil
Vaccine Group (as Administered): BNT162b2 (30 µg)
Date of First Dose: 16OCT2020; Date of Last Dose: 06NOV2020

==========

Study Vaccination(s)			
Vaccination Number	**Vaccine**	**Vaccination Date (Study Day)**	**Time of Vaccination**
1	BNT162b2	16OCT2020 (1)	14:00
2	BNT162b2	06NOV2020 (22)	12:22

Adverse Events							
AE Number	**MedDRA SOC**	**MedDRA Preferred Term**	**Investigator Text**	**Start Date (Study Day)**	**Start Time**	**Stop Date (Study Day)**	**Stop Time**
1	GENRL	Chills	Chills	06NOV2020 (22)	23:00	08NOV2020 (24)	
2	GENRL	Injection site pain	Pain at the injection site	06NOV2020 (22)	23:00	08NOV2020 (24)	
3	MUSC	Myalgia	Muscle pain	06NOV2020 (22)	23:00	08NOV2020 (24)	
4	MUSC	Myalgia	muscle pain	19OCT2020 (4)		22OCT2020 (7)	
5	GASTR	Nausea	Nauseas	06NOV2020 (22)	23:00	08NOV2020 (24)	
6	GENRL	Pyrexia	Fever 39 C	06NOV2020 (22)	23:00	08NOV2020 (24)	
7	GASTR	Vomiting	Vomiting	06NOV2020 (22)	23:00	08NOV2020 (24)	

Adverse Events									
AE Number	**Duration (Days)**	**Toxicity Grade**	**Action to Subject**	**SAE**	**AE Still Present?**	**AE Related To:**	**Prior Vaccination Number**	**Relative Day From Prior Vaccination**	**Narrative Event**
1	3	3	N	N	Resolved (08NOV2020)	Study Treatment	2	1	N
2	3	3	N	N	Resolved (08NOV2020)	Study Treatment	2	1	N

Reason(s) for Narrative: HIV
Unique Subject ID: C4591001 1226 12262255; Country: Brazil
Vaccine Group (as Administered): BNT162b2 (30 µg)
Date of First Dose: 16OCT2020; Date of Last Dose: 06NOV2020
==========

Adverse Events

AE Number	Duration (Days)	Toxicity Grade	Action to Subject	SAE	AE Still Present?	AE Related To:	Prior Vaccination Number	Relative Day From Prior Vaccination	Narrative Event
3	3	3	TC	N	Resolved (08NOV2020)	Study Treatment	2	1	N
4	4	2	TC	N	Resolved (22OCT2020)	Study Treatment	1	4	N
5	3	3	N	N	Resolved (08NOV2020)	Study Treatment	2	1	N
6	3	3	TC	N	Resolved (08NOV2020)	Study Treatment	2	1	N
7	3	3	TC	N	Resolved (08NOV2020)	Study Treatment	2	1	N

Prohibited Concomitant Medications

No Prohibited Concomitant Medications

Nonstudy Vaccines

No Nonstudy Vaccines

Subject Summary			
Status	**Study Phase**	**Withdrawal/Completion Date**	**Reason for Withdrawal**
Completed	SCREENING	16OCT2020	
Completed	VACCINATION	06JAN2021	
	REPEAT SCREENING 1		
	OPEN LABEL TREATMENT		
	FOLLOW-UP		

ATTACHMENT A — DEFERRAL REQUEST

Product Name	COVID-19 Vaccine (BNT162, PF-07302048)
IND number	019736
Applicant	BioNTech
Proposed Initial Indication	Active immunization against COVID-19 in individuals ≥16 years of age
Future Supplemental Indications	Active immunization against COVID-19 in children and adolescents 12 through 15 years of age; Active immunization against COVID-19 in children and infants <12 years of age.
1. Pediatric age groups for whom deferrals are requested	Adolescents, children, and infants 15 years of age and younger
2. Reason for requesting deferral of pediatric studies (address each age group separately and for each group choose all that apply):	A deferral of the evaluation of the COVID-19 vaccine in individuals ≤15 years of age is requested based on the following Criteria for Deferral (Section 505B(a)(4)(A)(i)(I) of the Act): "Pediatric studies should be delayed until additional safety or effectiveness data have been collected" and "The drug or biological product will be ready for approval for use in adults before pediatric studies are complete." Adequate evidence of safety and efficacy has been established in the pivotal study C4591001 in individuals ≥16 years of age to allow Emergency Use Authorization in that age group. Study C4591001 includes subjects 12 through 17 years of age. It was~~is~~ appropriate to defer studies in children 6 months~~5~~ to <12~~11~~ years of age until adequate safety and immunogenicity information was~~is~~ available in 12- through 15-year-old children and adolescents. It would then be appropriate to defer further age-de-escalation to <6 months until adequate safety data is available in 6 month~~5~~ through 11-year-old children.

3. Pediatric age group(s) not included in the deferral request	Children and adolescents 16 through 17 years of age
4. Reason for not including the pediatric age group(s) listed in number 3 in the deferral request	Study C4591001 includes subjects 16 through 17 years of age
5. Has a pediatric plan been submitted to the Agency.	Yes
6. Suggested deferred date for initiation and submission of studies	The ~~estimated~~ initiation date for Study C4591007, a safety and effectiveness study in children ~~<11~~<12 years of age, was 24 March~~is no later than April~~ 2021. The estimated initiation date for Study C4591023, a dose-finding safety and effectiveness study in infants less than 6 months of age, is 31 January 2022.

AGREED ~~INITIAL~~ PEDIATRIC STUDY PLAN (~~i~~PSP)

Product: COVID-19 Vaccine (BNT162, PF-07302048)

Dosage Form: Liquid formulation for intramuscular injection

IND #: 019736

Drug Class: Vaccine

Approved Indication: Not applicable

Proposed Initial Indication: Active immunization against COVID-19 in individuals ≥16 years of age

Proposed Supplemental Indications: Active immunization against COVID-19 in children and adolescents 12 through 15 years of age; Active immunization against COVID-19 in children and infants <12 years of age

Proposed General Plan:

- Deferral of assessment in adolescents, children, and infants 15 years of age and younger

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LIST OF ABBREVIATIONS

Abbreviation	Definition
ACE2	angiotensin-converting enzyme 2
A:G	Albumin: Globulin ratio
CAS	Chemical Abstracts Service
CBER	Center for Biologics Evaluation and Research
COVID-19	coronavirus disease 2019
DART	developmental and reproductive toxicity
DSPC	1,2-distearoyl-sn-glycero-3-phosphocholine
EUA	Emergency Use Authorization
FDA	US Food and Drug Administration
GLP	Good Laboratory Practice
HCoV-229E	human coronavirus 229E
HCoV-NL63	human coronavirus NL63
ICU	intensive care unit
IFNγ	interferon-gamma
IgG	immunoglobulin G
IgM	immunoglobulin M
IM	intramuscular
IND	investigational new drug
~~i~~PSP	~~initial~~ pediatric study plan
LNP	lipid nanoparticles
MIS-C	multisystem inflammatory syndrome in children
modRNA	nucleoside-modified RNA
NAAT	nucleic acid amplification test
NaCl	sodium chloride
P2 S	prefusion spike glycoprotein
PCR	polymerase chain reaction
PLT	platelet
RBC	red blood cell
RDW	red cell distribution width
RETIC	reticulocyte
RNA	ribonucleic acid
S	spike protein
S1	spike protein S1 subunit
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
Th1	Type 1 T helper cells
UK	United Kingdom
US	United States
VAED	vaccine-associated enhanced disease
VE	vaccine efficacy
WBC	white blood cell
WHO	World Health Organization

1. OVERVIEW OF THE DISEASE IN THE PEDIATRIC POPULATION

1.1. Pathophysiology of the Disease

SARS-CoV-2 is the causative agent of COVID-19. There are several other coronaviruses already circulating in humans, such as HCoV-229E or HCoV-NL63, very often as asymptomatic infections or infections causing mild respiratory symptoms.[1]

SARS-CoV-2 uses a densely glycosylated S to bind to the angiotensin-converting enzyme 2 (ACE2) receptor of the human host cell, as found previously in SARS-CoV, to fuse the viral and host cell membranes.[2] The distribution of the ACE2 receptor in pulmonary tissues underlies the predominantly respiratory nature of COVID-19.[3]

1.2. Clinical Presentation of SARS-CoV-2–Associated Disease in Adults and in the Pediatric Population

COVID-19 is generally milder in children than adults, possibly because common risk factors for severe COVID-19 in adults are generally less prevalent in pediatric age groups. Like adults, over half of children present with fever and dry cough.[4] Gastrointestinal symptoms, including diarrhea and vomiting, which occur rarely in adults, occur more commonly in children and may, in some cases, be the only presenting features.[5] Rhinorrhea and sore throat may also be more prominent in children with SARS-CoV-2 infection, although this picture is likely confounded by coinfection with other respiratory pathogens common in children.[5,6] Pulmonary involvement in symptomatic children is generally mild.[7] In a systematic review of the clinical characteristics and outcomes of SARS-CoV-2 infections in 7480 children from around the world, mild (42.5%; 608/1432) or moderate (39.6%; 567/1432) signs of infection were reported, and approximately 2% were admitted to pediatric intensive care.[8]

Nevertheless, severe cases, including those requiring intensive care support, have been reported.[9] In a nationwide case series of 2135 pediatric patients with COVID-19 reported to the Chinese Center for Disease Control and Prevention,[10] severe/critical disease defined by a combination of clinical, radiographic, and laboratory criteria was identified in 10.6%, 7.3%, and 3.9% of patients within the <1, 1 to 5, and 6 to 18 years of age groups, respectively, compared with 18.5% in adults.[11,12] In a retrospective review of 341 pediatric patients with a definite diagnosis of COVID-19 reported to health authorities in China, severe or critical disease was reported in 0.6% and 0.3%, respectively.[13] In an analysis of pediatric COVID-19 hospitalization data from 14 states in the US, although the cumulative rate of COVID-19-associated hospitalization was lower among children (8.0 per 100,000 population) compared with that in adults (164.5), 33.2% were admitted to an intensive care unit.[14] Common radiographic findings in severe disease are similar to those in adults and include the presence of ground-glass opacities and segmental consolidation in bilateral lung fields,[7,15] especially in the peripheral zones.[15]

In addition to the above, children may acquire multisystem inflammatory syndrome in children (MIS-C), an emerging condition that appears to be temporally related to recent exposure to SARS-CoV-2, frequently requires intensive care admission, and may have a fatal outcome.[16,17] MIS-C is a febrile hyperinflammatory condition with frequent evidence of cardiac damage and dermatological, mucocutaneous, and gastrointestinal features.[17] MIS-C

can lead to shock and multiple organ failure requiring admission to an intensive care unit (ICU).[18] The syndrome appears to have some overlap with Kawasaki disease shock syndrome.[19,20] Compared with Kawasaki disease, patients with MIS-C are older, have more cardiac injury, and are more likely to be black, Hispanic, or of South Asian descent.[21] As of 30 June 2020, over 1000 cases have been reported.[21] As of 29 July 2020, a total of 570 cases were reported in the US to the CDC. Of these, 86.0% involved four or more organ systems, 63.9% of patients required ICU admission, and severe complications included cardiac dysfunction (40.6%), shock (35.4%), myocarditis (22.8%), coronary artery dilation or aneurysm (18.6%), and acute kidney injury (18.4%).[22] Death rates of 2% to 4% have been reported.[21] MIS-C has been reported in many countries throughout North America, Europe, Asia, and Latin America,[18] including the US,[16,17] Italy,[23] and France.[24]

COVID-19 has been reported in neonates born to infected mothers.[25,26] There is limited evidence that neonates acquire infection through intrauterine vertical transmission; thus, neonatal infection likely mostly occurs from postnatal contact.[26] Outcomes were generally good in neonates, though assessment may be complex in neonates where other conditions may be relevant.[25,26]

1.3. Incidence and Prevalence Overall and in the Pediatric Population

In general, COVID-19 affects pediatric populations less frequently as compared with other age groups.[11,27,28] In the US, ~~subjects~~ individuals <17 years of age represent 10.9% of reported cases with 1.9% of cases reported in children~~subjects~~ 0-4 years of age, and 9.0% reported in ~~subjects~~ children and adolescents 5-17 years of age.[29] The hospitalization rate as of 16 January 2021 in the US was 36.9/100,000 in children 0 to 4 years of age and 22/100,000 in children and adolescents 5 to 17 years of age, compared with 380.3/100,000 of the overall population.[30]

Between March 1–December 12, 2020, a total of 2,871,828 laboratory-confirmed cases of COVID-19 were reported in children, adolescents, and young adults aged 0–24 years in the United States. Among these cases, 16.3% were reported in children and adolescents aged 14–17 years old, 7.9% were reported in children 11–13 years old, 10.9% were reported in children 5–10 years old, and 7.4% were reported in those 0–4 years old. Hospitalizations, ICU admission, and death were available for 41.9%, 8.9%, and 49.1% of the cases (respectively) and among children, adolescents, and young adults, 30,229 (2.5%) were hospitalized, 1,973 (0.8%) required ICU admission, and 654 (<0.1%) died. Children 0-4 years of age accounted for the largest percentage of hospitalizations (4.6%), and ICU admissions (1.8%).[31]

In China, out of a series of 72,314 cases, children 0 to 9 years of age represented only 0.9% of COVID-19 cases, while children and adolescents 10 to 19 years of age represented 1.2% of cases.[32] In the United Kingdom (UK), children and adolescents accounted for 9,944 out of a total of 257,029 confirmed COVID-19 cases (3.87%) (0.62% [0-4 years of age], 0.70% [5-9 years of age], 0.81% [10-14 years of age], to a maximum of 1.74% [15-19 years of age]) as of 30 July 2020.[33] However, these figures may be related to pediatric and adolescent SARS-CoV-2 infections generally being asymptomatic or mild, limiting

presentation to hospital or other medical care, as well as reduced diagnostic testing.[1,9,10,34,35] An analysis conducted in the province of Shenzhen, China, examined household contacts of infected cases as well as primary subjects presenting with symptoms.[36] Children 0 to 9 years of age represented 14.9% of cases identified as household contacts but only 2.1% of those presenting with symptoms.[36] Children were as likely to be infected through household exposure as any other age group.[36]

1.4. Methods of Diagnosis

As in adults, the primary diagnostic method for children presenting with symptoms suggestive of COVID-19 is by polymerase chain reaction (PCR), also termed nucleic acid amplification test (NAAT), on respiratory tract secretions, typically nasopharyngeal or midturbinate nasal swabs, although the virus can be detected in other samples.[1,34,35,37] Serological methods rely on the development of immunoglobulin G (IgG) and/or immunoglobulin M (IgM) to SARS-CoV-2 antigens following infection. Serological methods are not useful diagnostics in acute disease but are useful for diagnosing prior infection.[38]

1.5. Currently Available Treatments and/or Prevention Strategies in the Pediatric Population, Including Neonates

Currently, there are no FDA-approved vaccines for prevention of COVID-19 in pediatric populations. BNT162b2 has Emergency Use Authorization (EUA) in the United States for individuals 16 years of age and older. The Moderna COVID-19 vaccine has an EUA in the United States for individuals 18 years of age and older.

For pediatric subjects with COVID-19, the standard of care is generally supportive therapy, as indicated for children infected with other known respiratory viruses.[1]

Remdesivir is approved for the treatment of children ≥12 years of age and ≥40 kg (as well as adults) requiring hospitalization for COVID-19, and can be used under FDA EUA for hospitalized pediatric patients weighing 3.5 kg to less than 40 kg or hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg.[39]

A combination of two monoclonal antibodies, casirivimab and imdevimab administered together, are authorized for emergency use for the treatment of mild to moderate COVID-19 in adults, as well as in pediatric patients at least 12 years of age and weighing at least 40 kg, who have received positive results of direct SARS-CoV-2 viral testing and are at high risk for progressing to severe COVID-19 and/or hospitalization.[40]

Baricitinib in combination with remdesivir is authorized for emergency use for the treatment of suspected or laboratory-confirmed COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or extracorporeal membrane oxygenation.[40]

Bamlanivimab is authorized for emergency use for the treatment of mild-to-moderate COVID-19 in adult and pediatric patients with positive results of direct SARS-CoV-2 viral

testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.[40]

1.6. Summary

SARS-CoV-2 infection may be common in children and adolescents, but compared to adults, severe disease and hospitalizations are rare. Nevertheless, severe disease may occur at any age, and there is a unique severe pediatric manifestation of SARS-CoV-2 infection termed MIS-C. These data indicate a need for a pediatric immunization strategy.

2. OVERVIEW OF THE DRUG OR BIOLOGICAL PRODUCT

BioNTech has developed RNA-based vaccine candidates using a platform approach that enables the rapid development of vaccines against emerging viral diseases, including COVID-19. BNT162b2 is based on a platform of nucleoside--modified messenger RNA (modRNA) that expresses the SARS–CoV-2 full-length, P2 mutant, prefusion spike glycoprotein (P2 S) (version 9). The RNA is encapsulated in lipid nanoparticles, which enable entry of the RNA into host cells. The stabilized S antigen is expressed from the RNA in the host cells and elicits virus neutralizing antibody and cell mediated immune responses.

BNT162b2 is currently authorized for Emergency Use.

Emergency Use Authorized Indication: Active immunization against COVID-19 in individuals ≥16 years of age.

Proposed Initial Indication: Active immunization against COVID-19 in individuals ≥16 years of age.

Proposed Supplemental Indications: Active immunization against COVID-19 in children and adolescents 12 through 15 years of age; Active immunization against COVID-19 in children and infants <12 years of age.

Planned Pediatric Clinical Studies are discussed in Table 1.

3. OVERVIEW OF PLANNED EXTRAPOLATION OF EFFECTIVENESS TO SPECIFIC PEDIATRIC POPULATIONS

No extrapolation is planned.

4. PLAN TO REQUEST DRUG-SPECIFIC WAIVER(S)

Not applicable.

5. PLAN TO REQUEST DEFERRAL OF PEDIATRIC STUDIES

Pfizer and BioNTech propose to request a deferral of the evaluation of the COVID-19 vaccine in individuals ≤15 years of age (Attachment A) based on the following Criteria for Deferral (Section 505B(a)(4)(A)(i)(I) of the Act): "*Pediatric studies should be delayed until additional safety or effectiveness data have been collected" and "The drug or biological product will be ready for approval for use in adults before pediatric studies are complete*."

Adequate evidence of safety and efficacy has been established in the pivotal study C4591001 in individuals ≥16 years of age to allow Emergency Use Authorization in that age group. Study C4591001 includes subjects 12 through 17 years of age. It was~~is~~ appropriate to defer studies in children ~~5~~6 months to ~~≥11 years~~ <12 years of age until adequate safety and immunogenicity information ~~is~~was available in 12- through 15-year-old children and adolescents. It would then be appropriate to defer further age-de-escalation to <6 months until adequate safety data is available in ~~5~~6 month through 11-year-old children.

6. TABULAR SUMMARY OF PLANNED NONCLINICAL AND CLINICAL STUDIES

6.1. Planned Nonclinical Studies

No juvenile toxicity studies are planned because the current nonclinical and clinical data are sufficient to support pediatric clinical studies in children.

6.2. Planned Clinical Studies

Pfizer and BioNTech request a deferral for a planned pediatric evaluation of the COVID-19 vaccine in adolescents, children, and infants ≤15 years of age (Table 1). Details for this planned pediatric study can be found in Section 10.

Table 1. Table of Clinical Studies for COVID-19 Vaccine

PLANNED PEDIATRIC CLINICAL STUDIES			
Pediatric Pharmacokinetic Studies			
Age Group	**Type of Study**	**Comments**	**Deferral Request Planned for the Study (Y/N)**
Not applicable			
Clinical Studies Including Safety, and Effectiveness			
Age Group	**Type of Study**	**Comments**	**Deferral Request Planned for the Study (Y/N)**
16 through 17 years	Safety and effectiveness	Study C4591001	N
12 through 15 years	Safety and effectiveness	Study C4591001	Y
5 through 11 years	Dose finding followed by safety and effectiveness	Study C4591007	Y
6 months to <5 years	Age de-escalating dose finding followed by safety and effectiveness	Study C4591007	Y
< 6 months	D~~d~~ose finding followed by safety and effectiveness	Study C4591023	Y

7. AGE-APPROPRIATE FORMULATION DEVELOPMENT

No formulation changes are planned for the pediatric development.

7.1. Description of the drug product

The drug product is a preservative-free, sterile dispersion of RNA formulated in LNP in aqueous cryoprotectant buffer for intramuscular (IM) administration. The RNA drug substance is the only active ingredient in the drug product. The product is a concentrate for solution at 0.5 mg/mL drug product.

The composition of RNA drug products for use in the planned clinical trials and the function of the respective components are given in Table 2.

Table 2. Composition of Drug Products

Component	Quality Standard	Function
Drug substance	In-house	Active
ALC-0315[a]	In-house	Functional lipid
ALC-0159[b]	In-house	Functional lipid
DSPC[c]	In-house	Structural lipid
Cholesterol	Ph. Eur.	Structural lipid
Sucrose	NF/Ph. Eur.	Cryoprotectant
NaCl	USP/Ph. Eur.	Buffer
KCl	USP/Ph. Eur.	Buffer
Na2HPO4	USP/Ph. Eur.	Buffer
KH2PO4	NF/Ph. Eur.	Buffer
Water for injection	Ph. Eur.	Solvent/Vehicle

[a] ALC-0315 = ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate).
[b] ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide.
[c] DSPC = 1,2-distearoyl-sn-glycero-3-phosphocholine.

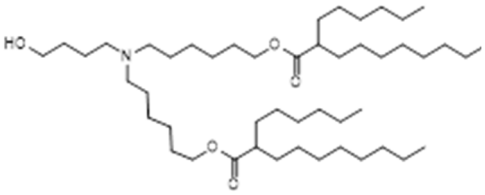
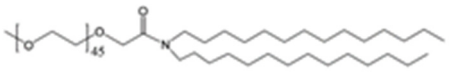
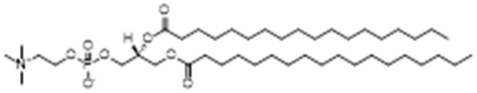
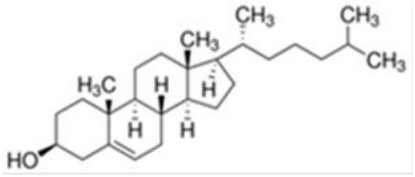
7.2. Description of the excipients

All excipients used in the formulation of the drug product are listed in Table 3.

The drug product contains the 2 functional lipids ALC-0315 and ALC-0159 and the 2 structural lipids DSPC (1,2-distearoyl-sn-glycero-3-phosphocholine) and cholesterol.

Physicochemical properties and the structures of the 4 lipids are shown in Table 3.

Table 3. Lipid Excipients in the Drug Product

Lipid (CAS Number)	Molecular Weight [Da]	Molecular Formula	Physical State and Storage Condition	Chemical Name (Synonyms) and Structure
ALC-0315 (not applicable)	766	$C_{48}H_{95}NO_5$	Liquid (oil) -20ºC	(4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) 
ALC-0159 (1849616-42-7)	~2400-2600	$C_{30}H_{60}NO(C_2H_4O)_nOCH_3$ n=45-50	Solid -20ºC	2-[(polyethylene glycol)-2000]-N,N-ditetradecyclacetamide 
DSPC (816-94-4)	790	$C_{44}H_{88}NO_8P$	Solid -20ºC	1,2-Distearoyl-*sn*-glycero-3-phosphocholine 
Cholesterol (57-88-5)	387	$C_{27}H_{46}O$	Solid -20ºC	

7.3. Description of the diluent

For the dilution of drug products for IM injection, isotonic NaCl solution (0.9%) is sourced as an approved medicinal product. The composition is according to the supplier's specifications.

8. NONCLINICAL STUDIES

8.1. Nonclinical Pharmacology

Nonclinical studies in mice and nonhuman primates for BNT162b2 (V9), a nucleoside-modified mRNA (modRNA) vaccine that encodes the SARS-CoV-2 full-length spike glycoprotein (S), demonstrated a strong neutralizing antibody response, Th1-type $CD4^+$ T-cell response, and a $CD8^+$ IFNγ response. Antigen-binding IgG and neutralizing antibody responses were detectable as early as 14 d post-immunization, with substantial increases observed in nonhuman primates after the second dose. BNT162b2 (V9) provided complete protection from the presence of detectable viral RNA in the lungs compared to the saline control with no clinical, radiological or histopathological evidence of vaccine-elicited disease

enhancement. A strong humoral response was also observed in an accessory study to the GLP-compliant repeat-dose toxicology study with BNT162b2 (V8) in rats (Study 38166). Nonclinical development is further described in Module 2.4 of BB-IND 019736 (Nonclinical Overview).

For nonclinical mouse immunogenicity studies, a pseudotype neutralization assay has been used as a surrogate of virus neutralization. For nonhuman primate nonclinical studies and for clinical testing was performed using, qualified SARS-CoV-2 neutralization and SARS-CoV-2 S1-binding IgG Luminex assays (VR-MQR-10214 and VR-MQR-10211).

8.2. Nonclinical Safety Data

The nonclinical toxicity assessment of BNT162b2 (BioNTech code number BNT162, Pfizer code number PF-07302048) includes 2 GLP-compliant repeat-dose toxicity studies and a developmental and reproductive toxicity (DART) study in Wistar Han rats outlined below in Table 4. The nonclinical safety evaluation included 2 variants of BNT162b2: V8 and V9. BNT162b2 (V9), the candidate granted EUA approval, differs from BNT162b2 (V8) only in the presence of optimized codons to improve antigen expression, but the amino acid sequences of the encoded antigens are identical. Two GLP repeat-dose toxicity studies for BNT162b2 (V8) and BNT162b2 (V9), one study for each variant, have been completed. In both studies, the nonclinical toxicology findings were similar between BNT162b2 (V9) and BNT162b2 (V8). BNT162b2 (V9) was assessed for development and reproductive toxicity in rats.

The IM route of exposure was selected as it is the intended route of clinical administration. The selection of rats as the toxicology test species is consistent with the WHO guidance documents on nonclinical evaluation of vaccines,[44] which recommend that vaccine toxicity studies be conducted in a species in which an immune response is induced by the vaccine. Generation of an immune response to BNT162b2 has been confirmed in rats in both repeat-dose toxicity and DART studies. The Wistar Han rat is used routinely for regulatory toxicity studies, and there is an extensive historical safety database on this strain of rat.

Table 4. Overview of Toxicity Testing Program

Study[a]	Study (Sponsor) No.	Group/ Dose, µg RNA	Total Volume (µL)[b]	No. of Animals/ Group	Study Status
Repeat-Dose Toxicity					
17-Day, 2 or 3 Dose (1 Dose/Week) IM Toxicity With a 3 Week Recovery Phase in Rats[c,d]	38166	Control[e], 0	200[f]	15/sex	Completed
		BNT162b2 (V8)[i], 100	200[f]	15/sex	
17-Day, 3 Dose (1 Dose/Week) IM Toxicity With a 3 Week Recovery Phase in Rats[g]	20GR142	Saline[h], 0	60	15/sex	Completed
		BNT162b2 (V9)[i], 30	60	15/sex	
Developmental and Reproductive Toxicity					
Combined Fertility and Developmental Study (Including Teratogenicity and Postnatal Investigations) of BNT162b1, BNT162b2 and BNT162b3 by the IM route in Rats	20256434 (RN9391 R58)	Saline[h], 0	60	44 F	Completed
		BNT162b2 (V9)[i], 30	60	44 F	

a. All studies are GLP-compliant and were conducted in an OECD mutual acceptance of data-compliant member state.
b. Doses were administered as 1 application at 1 site unless otherwise indicated.
c. Study also evaluated the BNT162a1, BNT162b1 and BNT162c1 vaccine candidates.
d. QW x 3 (Days 1, 8, 15) for BNT162a1, BNT162b1, and BNT162b2 (V8); QW x 2 (Days 1, 8) for BNT162c1.
e. Phosphate buffered saline, 300 mM sucrose.
f. One application (100 µL) at 2 sites for a total dose volume of 200 µL.
g. Study also evaluated BNT162b3.
h. Sterile saline (0.9% NaCl).
i. BNT162b2 (V8) and BNT162b2 (V9) both encode the same amino acid sequence of the spike protein antigen with two prefusion conformation-stabilizing amino acids in the stalk.

In both repeat dose toxicity studies, administration of BNT162b2 by IM injection to male and female Wistar Han rats once every week for a total of 3 doses was tolerated without evidence of systemic toxicity. Expected immune responses to the vaccine were evident such as edema and erythema at the injection sites, transient elevation in body temperature, elevations in WBCs and acute phase reactants, and decreased A:G ratios. Injection site reactions were common in all vaccine-administered animals and were greater after boost immunizations. Changes secondary to inflammation included slight and transient reductions in body weights and transient reductions in RETIC, PLT, and RBC mass parameters.[41,42,43] All changes in hematology parameters and acute phase proteins were similar to control at the end of the

recovery phase for BNT162b2 with the exception of higher RDW and lower A:G ratios in animals administered BNT162b2 (V9). Macroscopic pathology and organ weight changes were also consistent with immune activation and inflammatory response and included increased size of draining iliac lymph nodes and increased size and weight of spleen. Vaccine-related microscopic findings at the end of dosing for BNT162b2 were evident in injection sites and surrounding tissues, in the draining iliac lymph nodes, bone marrow, spleen, and liver. Microscopic findings at the end of the dosing phase were partially (recovery in progress) or completely recovered in all animals at the end of the recovery phase for BNT162b2. A robust immune response was elicited to the BNT162b2 vaccine antigen.

In the DART study, administration of BNT162b2 to female rats twice before the start of mating and twice during gestation at the human clinical dose (30 µg RNA/dosing day) was associated with non-adverse effects (body weight, food consumption and effects localized to the injection site) after each dose administration. However, there were no effects of BNT162b2 administration on mating performance, fertility, or any ovarian or uterine parameters in the F0 female rats nor on embryo-fetal or postnatal survival, growth, or development in the F1 offspring through the end of lactation. An immune response to the vaccine was confirmed in F0 female rats prior to mating, at the end of gestation and at the end of lactation and these responses were also detectable in the F1 offspring (fetuses and pups).

Stand-alone safety pharmacology, genotoxicity, and carcinogenicity studies have not been performed with the COVID-19 vaccine. This is consistent with the World Health Organization guidance on the nonclinical safety assessment of vaccines.[44]

No nonclinical studies have been conducted in juvenile animals.

9. CLINICAL DATA TO SUPPORT DESIGN AND/OR INITIATION OF STUDIES IN PEDIATRIC PATIENTS

BNT162b2 has been studied in three clinical trials in adults. These are BNT162-01, a phase 1/2 study in Germany, C4591001 (BNT162-02), and C4591005 (BNT162-05), a phase 1/2 safety and immunogenicity study in Japan. Study C4591001 included a phase 1 component for candidate and dose selection, allowing progression to a large placebo-controlled phase 2/3 safety, immunogenicity and efficacy study conducted in the US, Argentina, Brazil, South Africa, Turkey and Germany. While these studies continue, the available clinical evidence demonstrates induction of strong immune responses and high VE, suggesting the vaccine confers protection against COVID-19 in individuals ≥16 years of age. This evidence supported the granting of an EUA.

The observed safety profile in clinical trials to date shows mostly mild reactogenicity, low incidence of severe or serious events, and no clinically concerning safety observations. The vaccine appears to be safe and well-tolerated across the safety population and within demographic subgroups based on age, sex, race/ethnicity, country, and baseline SARS-CoV-2 status. The preponderance of severe cases of COVID-19 in the placebo group relative to the BNT162b2 group (9 of 10) suggests no evidence of vaccine-associated enhanced disease (VAED).

Vaccine efficacy was high, ≥95% for participants without prior evidence of SARS-CoV-2 infection and >94% for those with and without prior infection, in the planned interim and final analyses. Observed VE was >93% across subgroups identified by age, sex, race/ethnicity, and country with the exception of "all others" race group (89.3% VE) and Brazil (87.7% VE).

10. PLANNED PEDIATRIC CLINICAL STUDIES

10.1. Pediatric Pharmacokinetic Studies

Not applicable.

10.2. Clinical Effectiveness and Safety Studies Planned

10.2.1. Ongoing Pediatric Clinical Study

10.2.1.1. Study C4591001: Ages 12 Through 17 Years

Approximately 600 individuals 16 through 17 years of age have been enrolled within the Phase 3 C4591001 study. Data analyses to be submitted will examine safety and effectiveness endpoints.

Approximately 2000 individuals 12 through 15 years of age have been enrolled in the Phase 3 C4591001 study. Data analyses to be submitted will examine safety and effectiveness endpoints to support an indication for use in individuals 12 through 15 years of age.

10.2.2. Proposed Pediatric Clinical Studies

10.2.2.1. Study C4591007: 6 months to ~~≤~~11~~<~~12 years of age ~~and younger~~

Study C4591007 is a dose-finding, age de-escalating safety and effectiveness study in children 6 months to ~~≤~~11~~<~~12 years of age ~~and younger~~.

10.2.2.2. Study C4591023: Less than 6 months of age

Study C4591023 is a dose-finding safety and effectiveness study in infants less than 6 months of age

11. TIMELINE OF THE PEDIATRIC DEVELOPMENT PLAN

1. Formulation Development: Not applicable.

2. Nonclinical Studies: None.

3. Clinical Studies:

   PK Study: Not applicable.

   Safety and Effectiveness Study: C4591007 (6 months to ~~≤11~~<12 years of age)

~~Estimated~~ Pprotocol submission date:	8 February 2021~~No later than March 2021~~
~~Estimated~~ Sstudy initiation date:	~~No later than April 2021~~24 March 2021
Estimated study completion date:	~~To be determined~~31 October 2023
Estimated final report submission date:	~~To be determined~~31 March 2024

   Safety and Effectiveness Study: C4591023 (< 6 months)

Estimated protocol submission date:	31 January 2022
Estimated study initiation date:	31 April 2022
Estimated study completion date:	31 July 2024
Estimated final report submission date:	31 October 2024

4. Target Date for submission of supplemental BLA is October 2021.

   Target Date for submission of supplemental BLA for <12 years of age is to be determined.

12. AGREEMENTS FOR PEDIATRIC STUDIES WITH OTHER REGULATORY AUTHORITIES

BioNTech received approval from the European Medicines Agency for the Paediatric Investigation Plan on 27 November 2020 (EMA Decision P/0480/2020). A deferral is granted for studies from birth to less than 18 years of age.

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PHARMACOVIGILANCE PLAN FOR

BIOLOGIC LICENSE APPLICATION #125742

OF

COVID-19 mRNA vaccine (nucleoside modified) (BNT162b2, PF-07302048)

Date of Report: 28 JULY 2021

Version 1.1

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LIST OF ABBREVIATIONS

Abbreviation	Definition of Term
AE	adverse event
AESI	adverse event of special interest
A:G	albumin:globulin
ARDS	acute respiratory distress syndrome
BALB/c	bagg albino
BC	Brighton Collaboration
BEST	biologics effectiveness and safety
BLA	biologics license application
BMI	body mass index
BP	blood pressure
CD4, CD8	cluster of differentiation-4, 8
CDC	Centers for Disease Control and Prevention
CI	confidence interval
COPD	chronic obstructive pulmonary disease
COVID-19	coronavirus disease 2019
CSR	clinical study report
CT	clinical trial
DART	developmental and reproductive toxicology
DCA	data capture aid
DLP	data-lock point
DoD	Department of Defense
ECDC	European Center for Disease Control
EEA	European Economic Area
eGFR	estimated glomerular filtration rate
EU	European Union
EUA	emergency use authorization
FDA	(US) Food and Drug Administration
GLP	good laboratory practice
HbA1c	glycated hemoglobin
HBV	hepatitis b virus
HCV	hepatitis c virus
HIV	human immunodeficiency virus
IA	interim analysis
ICU	intensive care unit
IFN	interferon
IL-4	interleukin-4
IM	intramuscular(ly)
IMD	index of multiple deprivation
IND	investigational new drug
LNP	lipid nanoparticle
MAA	marketing authorization applicant
MedDRA	Medical Dictionary for Regulatory Activities

Abbreviation	Definition of Term
MERS-CoV	Middle East respiratory syndrome–coronavirus
MHS	Military Health System
MIS-C	multisystem inflammatory syndrome in children
MOA	mechanism of action
modRNA	nucleoside-modified messenger ribonucleic acid
mRNA	messenger ribonucleic acid
NDA	new drug application
NHP	nonhuman primate
NICE	National Institute for Health and Care Excellence
OCS	oral corticosteroids
PK	pharmacokinetic
PT	Preferred Term
PVP	pharmacovigilance plan
RBC	red blood cell
RNA	ribonucleic acid
RR	relative risk
SAE	serious adverse event
SARS	severe acute respiratory syndrome
SARS-CoV-1	severe acute respiratory syndrome coronavirus 1
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
siRNA	small-interfering RNA
SMQ	standardised MedDRA query
Tdap	tetanus, diphtheria, and acellular pertussis
TESSy	The European Surveillance System
Th1	T helper cell type 1
Th2	T helper cell type 2
UK	United Kingdom
US	United States
USP	United States pharmacopeia
V8	variant 8
V9	variant 9
VAED	vaccine-associated enhanced disease
VAERD	vaccine-associated enhanced respiratory disease
WBC	white blood cells
WHO	World Health Organization
WOCBP	women of childbearing potential

1. INTRODUCTION

1.1. Product Details

Table 1. Product Details[a]

Product	COVID-19 mRNA Vaccine (nucleoside modified), herein after referred to as BNT162b2 is a nucleoside-modified messenger RNA –(modRNA) encoding the viral spike (S) glycoprotein of severe acute respiratory syndrome coronavirus (SARS-CoV-2).
Brief description of the product	Chemical class: Nucleoside-modRNA formulated in lipid particles. Mechanism of Action: The modRNA in the BNT162b2 is formulated in lipid particles, which enable delivery of the RNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19. Important information about its composition: • The BNT162b2 is supplied as a frozen suspension in multiple dose vials. • Each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. • Each dose of the BNT162b2 contains 30 mcg of a nucleoside-modified messenger RNA (modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2. • Each dose of the BNT162b2 also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose. • The BNT162b2 does not contain preservative. • The vial stoppers are not made with natural rubber latex.
Indication	Proposed: Active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older.
Dosage and route of administration	Proposed: Series of two doses (0.3 mL each) 3 weeks apart, intramuscularly.

a. COVID-19 mRNA vaccine (nucleoside-modified) US Prescribing Information

Data Lock Point / Data cut-off:	16 years and older	13 March 2021 (Pfizer Clinical Database)
		23 October 2020 (BioNTech Clinical Database)
		28 February 2021 (Pfizer Safety Database)
	12 to 15 years older	13 March 2021 (Pfizer Clinical Database)
		28 February 2021 (Pfizer Safety Database)
	Important Identified Risk "Myocarditis and pericarditis"	18 June 2021 (Pfizer Safety Database)

2. SAFETY SPECIFICATION

2.1. Elements of the Safety Specification

2.1.1. Non-Clinical

Nonclinical evaluation of BNT162b2 included pharmacology (mouse immunogenicity and NHP immunogenicity and challenge studies), pharmacokinetic (series of biodistribution, metabolism and pharmacokinetic studies), and toxicity (2 GLP rat repeat-dose toxicity and a GLP DART) studies in vitro and in vivo. No additional toxicity studies are planned for BNT162b2.

Nonclinical studies in mice and NHP for BNT162b2 demonstrated both a strong neutralizing antibody response and a Th1-type $CD4^+$ and an $IFN\gamma^+$ $CD8^+$ T-cell response. The Th1 profile is characterized by a strong IFNγ, but not IL-4, response indicating the absence of a potentially deleterious Th2 immune response and is a pattern favored for vaccine safety and efficacy.[1] Rhesus macaques (Study VR-VRT-10671) that had received two IM immunizations with 100 µg BNT162b2 or saline 21 days apart were challenged with 1.05×10^6 plaque forming units of SARS-CoV-2 (strain USA-WA1/2020), split equally between the intranasal and intratracheal routes.[2] BNT162b2 provided complete protection from the presence of detectable viral RNA in the lungs compared to the saline control with no clinical, radiological or histopathological evidence of vaccine-elicited disease enhancement.

An intravenous rat PK study, using an LNP with the identical lipid composition asBNT162b2, demonstrated that the novel lipid excipients in the LNP formulation, ALC-0315 and ALC-0159, distribute from the plasma to the liver. While there was no detectable excretion of either lipid in the urine, the percent of dose excreted unchanged in feces was ~1% for ALC-0315 and ~50% for ALC-0159. Further studies indicated metabolism played a role in the elimination of ALC-0315. Biodistribution was assessed using luciferase expression as a surrogate reporter formulated likeBNT162b2, with the identical lipid composition. After IM injection of the LNP-formulated RNA encoding luciferase in BALB/c mice, luciferase protein expression was demonstrated at the site of injection 6 hours post dose and expression decreased over time to almost reach background levels after 9 days. Luciferase was detected to a lesser extent in the liver; expression was present at 6 hours after injection and was not detected by 48 hours after injection. After IM administration of a radiolabeled LNP-mRNA formulation containing ALC-0315 and ALC-0159 to rats, the percent of administered dose was also greatest at the injection site. Outside of the injection site, total recovery of radioactivity was greatest in the liver and much lower in the spleen, with very little recovery in the adrenal glands and ovaries. The metabolism of ALC-0315 and ALC-0159 was evaluated in blood, liver microsomes, S9 fractions, and hepatocytes from mice, rats, monkeys, and humans. The in vivo metabolism was examined in rat plasma, urine, feces, and liver samples from the PK study. ALC-0315 and ALC-0159 are metabolized by hydrolytic metabolism of the ester and amide functionalities, respectively, and this hydrolytic metabolism is observed across the species evaluated.

In GLP toxicity studies, two variants of the BNT162b2 candidate were tested, designated "variant 8" and "variant 9" (V8 and V9, respectively). The variants differ only in their codon optimization sequences which are designed to improve antigen expression, otherwise the

amino acid sequences of the encoded antigens are identical. BNT162b2 (V9) was evaluated clinically and submitted for application. Two GLP-compliant repeat-dose toxicity studies were performed in Wistar Han rats; one with each variant. Both studies were 17 days in duration with a 3-week recovery period. A GLP-compliant DART study in Wistar Han rats has also been completed. Safety pharmacology, genotoxicity and carcinogenicity studies have not been conducted, in accordance with the 2005 WHO vaccine guideline.[3]

The IM route of exposure was selected for nonclinical investigations as it is the clinical route of administration. Rats were selected as the toxicology test species as they demonstrated an antigen-specific immune response to the vaccine and are routinely used for regulatory toxicity studies with an extensive historical safety database.

Administration of up to 100 µg BNT162b2 by IM injection to male and female Wistar Han rats once every week, for a total of 3 doses, was tolerated without evidence of systemic toxicity. Expected inflammatory responses to the vaccine were evident such as edema and erythema at the injection sites, transient elevation in body temperature, elevations in WBC count and acute phase reactants, and lower A:G ratios. Injection site reactions were common in all vaccine-administered animals and were greater after boost immunizations. Changes secondary to inflammation included slight and transient reduction in body weights and transient reduction in reticulocytes, platelets and RBC mass parameters. Decreased reticulocytes were reported in rats treated with the licensed LNP-siRNA pharmaceutical Onpattro™ (NDA # 210922) but have not been observed in humans treated with this biotherapeutic[4] suggesting this is a species-specific effect. Decreased platelet counts were noted after repeat administration, but were small in magnitude of change, likely related to inflammation-related platelet activation and consumption, and unassociated with other alterations in hemostasis. Elevated levels of gamma-glutamyl transferase were observed in the first repeat-dose toxicity study with BNT162b2 (V8) without evidence of cholestasis or hepatobiliary injury but was not recapitulated in the second repeat dose-toxicity study with BNT162b2 (V9), the final clinical candidate. All changes in clinical pathology parameters and acute phase proteins were reversed at the end of the recovery phase for BNT162b2, with the exception of low magnitude higher red cell distribution width (consistent with a regenerative erythroid response) and lower A:G ratios (resulting from acute phase response) in animals administered BNT162b2. Macroscopic pathology and organ weight changes were also consistent with immune activation and inflammatory response and included increased size and/or weight of draining iliac lymph nodes and spleen. Vaccine-related microscopic findings at the end of the dosing phase consisted of edema and inflammation in injection sites and surrounding tissues, increased cellularity in the draining iliac lymph nodes, bone marrow and spleen and hepatocyte vacuolation in the liver. Vacuolation of periportal hepatocytes, the only test article-related liver microscopic finding, was not associated with any microscopic evidence of hepatic injury or hepatic functional effects (i.e., liver functional enzymes were not elevated) and may be associated with hepatocyte uptake of the LNP lipids.[5] Microscopic findings at the end of the dosing phase were partially or completely recovered in all animals at the end of the 3-week recovery period for BNT162b2. A robust immune response was elicited to the BNT162b2 antigen.

Administration of BNT162b2 to female rats twice before the start of mating and twice during gestation at the human clinical dose (30 µg) was associated with non-adverse effects (body

weight, food consumption and effects localized to the injection site) after each dose administration. However, there were no effects of BNT162b2 administration on mating performance, fertility, or any ovarian or uterine parameters in the F0 female rats nor on embryo-fetal or postnatal survival, growth, or development in the F1 offspring. An immune response was confirmed in F0 female rats following administration of each vaccine candidate and these responses were also detectable in the F1 offspring (fetuses and pups).

In summary, the nonclinical safety findings related to BNT162b2 administration primarily represent an expected immune reaction to vaccine administration and are clinically manageable or acceptable risks in the intended population. The key safety findings regarding BNT162b2 from nonclinical studies and their relevance to human usage are presented in Table 2. There was no evidence of vaccine-elicited disease enhancement.

Table 2. Key Safety Findings and Relevance to Human Usage

Key Safety findings from Nonclinical Studies[a]	Relevance to Human Usage
Pharmacology	
NHP Challenge Model • No evidence of vaccine-elicited disease enhancement.	• Suggests low risk of vaccine-enhanced disease in humans; being investigated in CTs.
Toxicity	
Injection site reactions: • Injection site reactions were common and reversible or showed signs of reversibility at the end of the 3-week recovery period in nonclinical studies.	• In common with other vaccines, BNT162b2 administration has the potential to generate injection site reactions such as edema and erythema at the injection sites.
Inflammation and immune activation: • Evidence of inflammation or immune activation was common, reversible, and included transiently higher body temperature, higher circulating WBCs, and higher acute phase reactants. Secondarily, transiently lower body weights, reticulocytes, platelets, and RBC mass parameters were observed.	• In common with all vaccines, BNT162b2 administration has the potential to generate inflammation which can lead to increased body temperature, higher circulating WBCs and higher acute phase proteins. • Decreased reticulocytes have not been observed in humans treated with the LNP-siRNA pharmaceutical Onpattro[4], suggesting this finding in rats is a species-specific effect. • BNT162b2 administration has the potential to transiently decrease platelets and RBC mass parameters. These slight decreases are not likely to be clinically meaningful due to their small magnitude.
Developmental and Reproductive Toxicity • No vaccine-related effects on female fertility or the development of fetuses or offspring were observed in a DART study of BNT162b2 in rats.	• No effects are anticipated in WOCBP, pregnant women or their offspring.

a. Safety pharmacology, genotoxicity, and carcinogenicity studies were not conducted, in accordance with 2005 WHO vaccine guideline, as they are generally not considered necessary to support development and licensure of vaccines for infectious diseases.[3] In addition, the components of the vaccine construct are lipids and RNA and are not expected to have carcinogenic or genotoxic potential.

2.1.2. Clinical

2.1.2.a. Limitations of the Human Safety Database

The pivotal study was initially planned to enroll approximately 30,000 participants, which would have a probability of 78% of detecting an AE with a frequency of 0.01% (1/1000) and a probability of 95% of detecting an AE with a frequency of 0.02% (1/500). The protocol was amended to enroll approximately 46,000 participants, which would slightly enhance the ability to detect AEs. However, rarer events might not be detected.

Participants in the pivotal study were initially planned to be followed for up to 24 months in order to assess the potential for late-occurring adverse reactions, such as the theoretical risk of VAED. After completing the final efficacy analysis with vaccine efficacy shown to be 95%, and obtaining regulatory authorization to vaccinate in many countries, Pfizer-BioNTech started to unblind all participants to determine those randomized to placebo so that they could be offered vaccine in accordance with local authorization. To date, most placebo subjects have been unblinded to receive active vaccine at or prior to 6 months after the second dose, therefore, a placebo group for comparison of safety data is only available for up to 6 months post Dose 2.

2.1.2.a.1. Clinical Trial Exposure

Brief Overview of Development

BioNTech is conducting a first-in-human dose level–finding Phase 1/2 study (BNT162-01) in Germany to gather safety and immunogenicity data to enable evaluation of 4 vaccines candidates individually to inform the overall clinical development of a BNT162b2.

BNT162-01 is not conducted under the US IND application but is being conducted under a German Clinical Trial Application.

Four vaccine candidates were evaluated in Study BNT162-01. Based on safety and immunogenicity results from this study, 2 vaccine candidates, BNT162b1 and BNT162b2, were selected for evaluation in Study C4591001, which is a Phase 1/2/3 randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection, and efficacy study in healthy adults (conducted under IND 019736).

Phase 1 of Study C4591001 comprised dose-level–finding evaluations of the 2 selected vaccine candidates; multiple dose levels (some corresponding to those evaluated in Study BNT162-01) were evaluated. Study vaccine was administered using the same 2-dose schedule as in Study BNT162-01 (21 days apart). Dose levels were administered first to an 18- to 55-year age cohort, then to a 65- to 85-year age cohort.

Both vaccine candidate constructs were safe and well tolerated. BNT162b2 at the 30-µg dose level was selected and advanced to the Phase 2/3 expanded cohort and efficacy evaluation primarily because:

- the reactogenicity profile for BNT162b2 was more favorable than BNT162b1 in both younger and older adults with similar immunogenicity results;
- in the NHP challenge study (VR-VTR-10671, see Section 2.1.1), a trend toward earlier clearance of BNT162b2 was observed in the nose.

Phase 2 of the study (for which enrollment has completed) comprised the evaluation of safety and immunogenicity data for the first 360 participants (180 from the active vaccine group and 180 from the placebo group, with each group divided between the younger and older age cohorts) entering the study after completion of Phase 1.

The Phase 3 part of the study (which is ongoing) evaluates the efficacy and safety in all participants (including the first 360 participants from Phase 2). Phase 3 introduced:

- enrollment of participants 16 to 17 years of age to be evaluated with the 18- to 55-year-old cohort,
- enrollment of a 12- to 15-year-old cohort,
- immunogenicity data from the 12- to 15-year-old cohort (Table 3, Table 5, Table 11, Table 13, Table 15, and Table 17),anticipated to bridge to the 16- to 25-year-old cohort.

Participants in the pivotal study were initially planned to be followed for up to 24 months in order to assess the potential for late-occurring adverse reactions, such as the theoretical risk of VAED including VAERD. After completing the final efficacy analysis with vaccine efficacy shown to be 95%, and obtaining regulatory authorisation to vaccinate in many countries, Pfizer-BioNTech started to unblind all participants to determine those participants randomised to placebo so that they could be offered vaccine in accordance with local authorisation. To date, most placebo subjects have been unblinded to receive active vaccine at or prior to 6 months after the second dose, therefore, a placebo group for comparison of safety data is only available for up to 6 months post Dose 2.

The initial efficacy analysis on the 16 years and older population was event-driven, with prespecified interim analyses after accrual of at least 62, 92, and 120 cases and a final analysis at 164 cases.

A further efficacy analysis has been conducted on 12- to ≤15-year-old cohort participants and on 16 years and older participants cohort participants reported by 13 March 2021.

Ongoing BNT162b2 studies at the cut-off of the clinical database (13 March 2021) also include:

- C4591005: *A phase 1/2 study to evaluate the safety, tolerability, and immunogenicity of an RNA vaccine candidate against COVID-19 in healthy Japanese adults.*
  One hundred sixty participants were randomly assigned in a 3:1 ratio to study intervention (candidate vaccine: 120, placebo: 40).

- C4591015: *A phase 2/3 study to evaluate the safety, tolerability, and immunogenicity of SARS-CoV-2 RNA vaccine candidate (BNT162b2) against COVID-19 in healthy pregnant women 18 years of age and older.*
  Approximately 4000 pregnant women at 24 to 34 weeks gestation are being randomized in a 1:1 ratio to vaccine or placebo.

- C4591017: *A phase 3 study to evaluate the safety, tolerability, and immunogenicity of multiple production lots and dose levels of BNT162b2 against COVID-19 in healthy participants.*
  Approximately 340 participants were randomly assigned to each of 3 US lots and to a 20-µg arm and approximately 170 participants were randomly assigned an EU lot, for a total of approximately 1530 randomized participants in 5 study arms.

Clinical Trial Exposure

Population for analysis of CTs data in this US Pharmacovigilance Plan includes the following 2 studies:

- C4591001: *Phase 1/2/3, placebo-controlled, randomized, observer-blind, dose finding, study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals*.

- BNT162-01: *A multi-site, phase I/II, 2-part, dose-escalation trial investigating the safety and immunogenicity of four prophylactic SARS-CoV-2 RNA vaccines against COVID-19 using different dosing regimens in healthy adults.*

Participants 16 years of age and older

At the cut-off date of 13 March 2021, a total of 46,505 participants were vaccinated in the BNT162b2 clinical development program:

- 21,745 participants received 2 doses and 360 received 1 dose of BNT162b2 during the blinded follow-up period; 96 participants from study BNT162-01 received 2 doses of the vaccine.

- 19,647 participants, who originally received placebo, then received 1 dose of BNT162b2 in the Open-Label Follow-up period after unblinding. (none from study BNT162-01).

Exposure to BNT162b2 for participants aged 16 years and older in the 2 ongoing studies by number of doses, and demographic characteristics is shown in Table 3 through Table 21.

In addition, exposure in clinical studies in special populations is provided in Table 22 and Table 23.

Participants 12 to 15 years of age

At the cut-off date of 13 March 2021, a total of 2260 participants were vaccinated in the BNT162b2 clinical development program:

Clinical study exposure data for the 12- to 15 years of age are provided for the ongoing study C4591001 at the cut-off date of 13 March 2021.

In this study

- 1124 participants received 2 doses and 7 received 1 dose of BNT162b2 in the Blinded-Placebo Controlled Follow-up period.

- 49 participants who originally received placebo, then received 1 dose of BNT162b2 in the Open-Label Follow-up period after unblinding.

Exposure to BNT162b2 for participants aged 12- to 15 years of age by number of doses and demographic characteristics is shown in Table 3,Table 5, Table 11, Table 13, Table 15, Table 17. In addition, exposure in clinical studies in special populations is provided in Table 22 and Table 23.

Table 3. Exposure to BNT162b2 by Age Group and Dose (C4591001) – Blinded Placebo-Controlled Follow-up Period

Age Group Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
≥12 years to ≤15 years		
Vaccine 30 µg		
1 Dose	7	7
2 Doses	1124	2248
Total	1131	2255
≥16 years to ≤17 years		
Vaccine 30 µg		
1 Dose	4	4
2 Doses	374	748
Total	378	752
≥18 years to ≤55 years		
Vaccine 10 µg		
2 Doses	12	24
Total	12	24
Vaccine 20 µg		
2 Doses	12	24
Total	12	24
Vaccine 30 µg		
1 Dose	267	267
2 Doses	12438	24876
Total	12705	25143
>55 years to ≤64 years		
Vaccine 30 µg		
1 Dose	67	67
2 Doses	4341	8682
Total	4408	8749
≥65 years to ≤74 years		
Vaccine 10 µg		
2 Doses	12	24
Total	12	24
Vaccine 20 µg		
2 Doses	9	18
Total	9	18
Vaccine 30 µg		
1 Dose	17	17
2 Doses	3624	7248
Total	3641	7265
≥75 years to ≤84 years		

Table 3. Exposure to BNT162b2 by Age Group and Dose (C4591001) – Blinded Placebo-Controlled Follow-up Period

Age Group Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Vaccine 20 µg		
2 Doses	3	6
Total	3	6
Vaccine 30 µg		
1 Dose	3	3
2 Doses	899	1798
Total	902	1801
≥85 years		
Vaccine 30 µg		
1 Dose	2	2
2 Doses	21	42
Total	23	44

Note: 30 µg includes data from phase 1 and phase 2/3.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:42)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s912

Table 4. Exposure to BNT162b2 by Age Group and Dose (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

Age Group Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
≥16 years to ≤17 years		
Vaccine 30 µg		
1 Dose	3	3
≥18 years to ≤55 years		
Vaccine 30 µg		
1 Dose	58	58
>55 years to ≤64 years		
Vaccine 30 µg		
1 Dose	17	17
≥65 years to ≤74 years		
Vaccine 30 µg		
1 Dose	8	8
≥75 years to ≤84 years		
Vaccine 30 µg		
1 Dose	1	1

Table 4. Exposure to BNT162b2 by Age Group and Dose (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

Age Group Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
≥85 years		
Vaccine 30 µg		
1 Dose	2	2

Note: 30 µg includes data from phase 1 and phase 2/3.
Note: Subjects who received 2nd Dose of BNT162b2 after unblinding.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s9123

Table 5. Exposure to BNT162b2 by Age Group and Dose (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Age Group Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
≥12 years to ≤15 years[a]		
Vaccine 30 µg		
1 Dose	30	30
2 Doses	19	38
Total	49	68
≥16 years to ≤17 years		
Vaccine 30 µg		
1 Dose	107	107
2 Doses	186	372
Total	293	479
≥18 years to ≤55 years		
Vaccine 30 µg		
1 Dose	2713	2713
2 Doses	8419	16838
Total	11132	19551
>55 years to ≤64 years		
Vaccine 30 µg		
1 Dose	655	655
2 Doses	3330	6660
Total	3985	7315
≥65 years to ≤74 years		
Vaccine 30 µg		

Table 5. Exposure to BNT162b2 by Age Group and Dose (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Age Group Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
1 Dose	128	128
2 Doses	3286	6572
Total	3414	6700
≥75 years to ≤84 years		
Vaccine 30 µg		
1 Dose	23	23
2 Doses	783	1566
Total	806	1589
≥85 years		
Vaccine 30 µg		
1 Dose	1	1
2 Doses	16	32
Total	17	33

Note: 30 µg includes data from phase 1 and phase 2/3.
a. Includes subjects who became eligible for unblinding at 16 years of age, confirmed to have received placebo originally and then received BNT162b2 post unblinding.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:
./nda2 unblinded/C4591001 PVP BLA/adsl s9122

Table 6. Exposure to BNT162b2 by Age Group and Dose (BNT162-01)

Age Group Dose Exposure (Number of Doses Received)	No. of Subjects Exposed to BNT162b2	Total No. of Vaccine Doses
≥18 years to ≤64 years		
Vaccine 1 µg		
1 Dose	1	1
2 Doses	11	22
Total	12	23
Vaccine 3 µg		
1 Dose	0	0
2 Doses	12	24
Total	12	24

Table 6. Exposure to BNT162b2 by Age Group and Dose (BNT162-01)

Age Group Dose Exposure (Number of Doses Received)	No. of Subjects Exposed to BNT162b2	Total No. of Vaccine Doses
Vaccine 10 µg		
1 Dose	1	1
2 Doses	11	22
Total	12	23
Vaccine 20 µg		
1 Dose	0	0
2 Doses	17	34
Total	17	34
Vaccine 30 µg		
1 Dose	0	0
2 Doses	18	36
Total	18	36
≥65 years to ≤74 years		
Vaccine 1 µg		
1 Dose	0	0
2 Doses	0	0
Total	0	0
Vaccine 3 µg		
1 Dose	0	0
2 Doses	0	0
Total	0	0
Vaccine 10 µg		
1 Dose	0	0
2 Doses	5	10
Total	5	10
Vaccine 20 µg		
1 Dose	0	0

Table 6. Exposure to BNT162b2 by Age Group and Dose (BNT162-01)

Age Group Dose Exposure (Number of Doses Received)	No. of Subjects Exposed to BNT162b2	Total No. of Vaccine Doses
2 Doses	6	12
Total	6	12
Vaccine 30 µg		
1 Dose	0	0
2 Doses	6	12
Total	6	12
≥75 years to ≤84 years		
Vaccine 1 µg		
1 Dose	0	0
2 Doses	0	0
Total	0	0
Vaccine 3 µg		
1 Dose	0	0
2 Doses	0	0
Total	0	0
Vaccine 10 µg		
1 Dose	0	0
2 Doses	1	2
Total	1	2
Vaccine 20 µg		
1 Dose	0	0
2 Doses	1	2
Total	1	2
Vaccine 30 µg		
1 Dose	0	0
2 Doses	0	0
Total	0	0

PFIZER CONFIDENTIAL SDTM Creation: 24NOV2020 (15:06) Source Data: adsl Table Generation: 10MAR2021 (11:32) (Cutoff date:23OCT2020, Snapshot Date: 23OCT2020)
Output File: ex_b2_age_dose2 rtf

Table 7. Exposure to BNT162b2 by Dose (Totals) (C4591001) – Blinded Placebo-Controlled Follow-up Period

Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Vaccine 10 µg		
2 Doses	24	48
Total	24	48
Vaccine 20 µg		
2 Doses	24	48
Total	24	48
Vaccine 30 µg		
1 Dose	367	367
2 Doses	22821	45642
Total	23188	46009

Note: 30 µg includes data from phase 1 and phase 2/3.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s922

Table 8. Exposure to BNT162b2 by Dose (Totals) (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Vaccine 30 µg		
1 Dose	89	89

Note: 30 µg includes data from phase 1 and phase 2/3.
Note: Subjects who received 2nd Dose of BNT162b2 after unblinding.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2 unblinded/C4591001 PVP BLA/adsl s9223

Table 9. Exposure to BNT162b2 by Dose (Totals) (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Vaccine 30 µg		
1 Dose	3657	3657
2 Doses	16039	32078
Total	19696	35735

Table 9. Exposure to BNT162b2 by Dose (Totals) (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses

Note: 30 µg includes data from phase 1 and phase 2/3.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2 unblinded/C4591001 PVP BLA/adsl s9222

Table 10. Exposure to BNT162b2 by Dose (Totals) (BNT162-01)

Dose Exposure (Number of Doses Received)	No. of Subjects Exposed to BNT162b2	Total No. of Vaccine Doses
Vaccine 1 µg		
1 Dose	1	1
2 Doses	11	22
Total	12	23
Vaccine 3 µg		
1 Dose	0	0
2 Doses	12	24
Total	12	24
Vaccine 10 µg		
1 Dose	1	1
2 Doses	23	46
Total	24	47
Vaccine 20 µg		
1 Dose	0	0
2 Doses	24	48
Total	24	48
Vaccine 30 µg		
1 Dose	0	0
2 Doses	24	48
Total	24	48

PFIZER CONFIDENTIAL SDTM Creation: 24NOV2020 (15:06) Source Data: adsl Table Generation: 10MAR2021 (11:49) (Cutoff date:23OCT2020, Snapshot Date: 23OCT2020)
Output File: ex_b2_dose.rtf

Table 11. Exposure to BNT162b2 by Dose, Age Group, and Gender (C4591001) – Blinded Placebo-Controlled Follow-up Period

Dose Age Group	Number of Subjects Exposed to BNT162b2		Total Number of Vaccine Doses	
	Male	Female	Male	Female
Vaccine 10 µg				
≥18 years to ≤55 years	5	7	10	14
≥65 years to ≤74 years	2	10	4	20
Total	7	17	14	34
Vaccine 20 µg				
≥18 years to ≤55 years	6	6	12	12
≥65 years to ≤74 years	4	5	8	10
≥75 years to ≤84 years	1	2	2	4
Total	11	13	22	26
Vaccine 30 µg				
≥12 years to ≤15 years	567	564	1128	1127
≥16 years to ≤17 years	187	191	373	379
≥18 years to ≤55 years	6456	6249	12770	12373
>55 years to ≤64 years	2231	2177	4421	4328
≥65 years to ≤74 years	1934	1707	3858	3407
≥75 years to ≤84 years	511	391	1020	781
≥85 years	12	11	23	21
Total	11898	11290	23593	22416

Note: 30 µg includes data from phase 1 and phase 2/3.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s932

Table 12. Exposure to BNT162b2 by Dose, Age Group, and Gender (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

Dose Age Group	Number of Subjects Exposed to BNT162b2		Total Number of Vaccine Doses	
	Male	Female	Male	Female
Vaccine 30 µg				
≥16 years to ≤17 years	0	3	0	3
≥18 years to ≤55 years	24	34	24	34
>55 years to ≤64 years	12	5	12	5
≥65 years to ≤74 years	4	4	4	4

Table 12. Exposure to BNT162b2 by Dose, Age Group, and Gender (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

	Number of Subjects Exposed to BNT162b2		Total Number of Vaccine Doses	
Dose Age Group	**Male**	**Female**	**Male**	**Female**
≥75 years to ≤84 years	0	1	0	1
≥85 years	1	1	1	1
Total	41	48	41	48

Note: 30 µg includes data from phase 1 and phase 2/3.
Note: Subjects who received 2nd Dose of BNT162b2 after unblinding.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s9323

Table 13. Exposure to BNT162b2 by Dose, Age Group, and Gender (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

	Number of Subjects Exposed to BNT162b2		Total Number of Vaccine Doses	
Dose Age Group	**Male**	**Female**	**Male**	**Female**
Vaccine 30 µg				
≥12 years to ≤15 years[a]	26	23	36	32
≥16 years to ≤17 years	152	141	250	229
≥18 years to ≤55 years	5424	5708	9450	10101
>55 years to ≤64 years	1973	2012	3602	3713
≥65 years to ≤74 years	1801	1613	3530	3170
≥75 years to ≤84 years	495	311	976	613
≥85 years	13	4	25	8
Total	9884	9812	17869	17866

Note: 30 µg includes data from phase 1 and phase 2/3.
a. Includes subjects who became eligible for unblinding at 16 years of age, confirmed to have received placebo originally and then received BNT162b2 post unblinding.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s932_open

Table 14. Exposure to BNT162b2 by Dose, Age Group, and Gender (BNT162-01)

	No. of Subjects Exposed to BNT162b2		Total No. of Vaccine Doses	
Dose Age Group	**Male**	**Female**	**Male**	**Female**
Vaccine 1 µg				
≥18 years to ≤64 years	7	5	14	9
≥65 years to ≤74 years	0	0	0	0
≥75 years to ≤84 years	0	0	0	0
Total	7	5	14	9
Vaccine 3 µg				
≥18 years to ≤64 years	5	7	10	14
≥65 years to ≤74 years	0	0	0	0
≥75 years to ≤84 years	0	0	0	0
Total	5	7	10	14
Vaccine 10 µg				
≥18 years to ≤64 years	8	10	16	19
≥65 years to ≤74 years	3	2	6	4
≥75 years to ≤84 years	1	0	2	0
Total	12	12	24	23
Vaccine 20 µg				
≥18 years to ≤64 years	7	10	14	20
≥65 years to ≤74 years	1	5	2	10
≥75 years to ≤84 years	0	1	0	2
Total	8	16	16	32
Vaccine 30 µg				
≥18 years to ≤64 years	10	8	20	16
≥65 years to ≤74 years	2	4	4	8
≥75 years to ≤84 years	0	0	0	0
Total	12	12	24	24

PFIZER CONFIDENTIAL SDTM Creation: 24NOV2020 (15:06) Source Data: adsl Table Generation: 10MAR2021 (11:53) (Cutoff date:23OCT2020, Snapshot Date: 23OCT2020)
Output File: ex_b2_age_dose_sex rtf

Table 15. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Blinded Placebo-Controlled Follow-up Period

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
≥12 years to ≤15 years		
Vaccine 30 µg		
Racial origin		
White	971	1937
Black or African American	52	103
Asian	72	143
American Indian or Alaska Native	4	8
Native Hawaiian or other Pacific Islander	3	6
Multiracial	23	46
Not reported	6	12
Total	1131	2255
Ethnic origin		
Hispanic/Latino	132	263
Non-Hispanic/non-Latino	997	1988
Not reported	2	4
Total	1131	2255
≥16 years to ≤17 years		
Vaccine 30 µg		
Racial origin		
White	309	614
Black or African American	30	60
Asian	22	44
American Indian or Alaska Native	4	8
Native Hawaiian or other Pacific Islander	3	6
Multiracial	10	20
Total	378	752
Ethnic origin		
Hispanic/Latino	49	98
Non-Hispanic/non-Latino	329	654
Total	378	752
≥18 years to ≤55 years		
Vaccine 10 µg		
Racial origin		
White	11	22
Asian	1	2
Total	12	24
Ethnic origin		
Hispanic/Latino	1	2
Non-Hispanic/non-Latino	11	22

Table 15. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Blinded Placebo-Controlled Follow-up Period

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Total	12	24
Vaccine 20 µg		
Racial origin		
White	10	20
Black or African American	2	4
Total	12	24
Ethnic origin		
Hispanic/Latino	1	2
Non-Hispanic/non-Latino	11	22
Total	12	24
Vaccine 30 µg		
Racial origin		
White	9923	19637
Black or African American	1400	2764
Asian	683	1358
American Indian or Alaska Native	161	311
Native Hawaiian or other Pacific Islander	40	80
Multiracial	427	851
Not reported	71	142
Total	12705	25143
Ethnic origin		
Hispanic/Latino	4000	7874
Non-Hispanic/non-Latino	8650	17160
Not reported	55	109
Total	12705	25143
>55 years to ≤64 years		
Vaccine 30 µg		
Racial origin		
White	3719	7388
Black or African American	430	849
Asian	135	267
American Indian or Alaska Native	30	58
Native Hawaiian or other Pacific Islander	8	15
Multiracial	76	152
Not reported	10	20
Total	4408	8749
Ethnic origin		
Hispanic/Latino	965	1903
Non-Hispanic/non-Latino	3413	6786

Table 15. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Blinded Placebo-Controlled Follow-up Period

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Not reported	30	60
Total	4408	8749
≥65 years to ≤74 years		
Vaccine 10 µg		
Racial origin		
White	12	24
Total	12	24
Ethnic origin		
Non-Hispanic/non-Latino	12	24
Total	12	24
Vaccine 20 µg		
Racial origin		
White	9	18
Total	9	18
Ethnic origin		
Non-Hispanic/non-Latino	9	18
Total	9	18
Vaccine 30 µg		
Racial origin		
White	3272	6528
Black or African American	219	437
Asian	82	164
American Indian or Alaska Native	22	44
Native Hawaiian or other Pacific Islander	6	12
Multiracial	30	60
Not reported	10	20
Total	3641	7265
Ethnic origin		
Hispanic/Latino	583	1158
Non-Hispanic/non-Latino	3038	6067
Not reported	20	40
Total	3641	7265
≥75 years to ≤84 years		
Vaccine 20 µg		
Racial origin		
White	3	6
Total	3	6
Ethnic origin		
Non-Hispanic/non-Latino	3	6

Table 15. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Blinded Placebo-Controlled Follow-up Period

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Total	3	6
Vaccine 30 µg		
Racial origin		
White	838	1673
Black or African American	22	44
Asian	31	62
American Indian or Alaska Native	3	6
Native Hawaiian or other Pacific Islander	1	2
Multiracial	7	14
Total	902	1801
Ethnic origin		
Hispanic/Latino	107	213
Non-Hispanic/non-Latino	789	1576
Not reported	6	12
Total	902	1801
≥85 years		
Vaccine 30 µg		
Racial origin		
White	20	38
Asian	1	2
American Indian or Alaska Native	1	2
Multiracial	1	2
Total	23	44
Ethnic origin		
Hispanic/Latino	2	4
Non-Hispanic/non-Latino	21	40
Total	23	44

Note: 30 µg includes data from phase 1 and phase 2/3.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s942

Table 16. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
≥16 years to ≤17 years		
Vaccine 30 µg		
Racial origin		
White	3	3
Total	3	3
Ethnic origin		
Non-Hispanic/non-Latino	3	3
Total	3	3
≥18 years to ≤55 years		
Vaccine 30 µg		
Racial origin		
White	46	46
Black or African American	2	2
Asian	2	2
American Indian or Alaska Native	8	8
Total	58	58
Ethnic origin		
Hispanic/Latino	31	31
Non-Hispanic/non-Latino	27	27
Total	58	58
>55 years to ≤64 years		
Vaccine 30 µg		
Racial origin		
White	14	14
Asian	1	1
American Indian or Alaska Native	2	2
Total	17	17
Ethnic origin		
Hispanic/Latino	10	10
Non-Hispanic/non-Latino	7	7
Total	17	17
≥65 years to ≤74 years		
Vaccine 30 µg		
Racial origin		
White	8	8
Total	8	8
Ethnic origin		
Hispanic/Latino	5	5

Table 16. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Non-Hispanic/non-Latino	3	3
Total	8	8
≥75 years to ≤84 years		
Vaccine 30 µg		
Racial origin		
White	1	1
Total	1	1
Ethnic origin		
Non-Hispanic/non-Latino	1	1
Total	1	1
≥85 years		
Vaccine 30 µg		
Racial origin		
White	2	2
Total	2	2
Ethnic origin		
Non-Hispanic/non-Latino	2	2
Total	2	2

Note: 30 µg includes data from phase 1 and phase 2/3.
Note: Subjects who received 2nd Dose of BNT162b2 after unblinding.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s9423

Table 17. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
≥12 years to ≤15 years[a]		
Vaccine 30 µg		
Racial origin		
White	45	62
Asian	3	5
Multiracial	1	1
Total	49	68

Table 17. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Ethnic origin		
Hispanic/Latino	2	4
Non-Hispanic/non-Latino	47	64
Total	49	68
≥16 years to ≤17 years		
Vaccine 30 µg		
Racial origin		
White	251	410
Black or African American	11	19
Asian	14	25
American Indian or Alaska Native	2	4
Native Hawaiian or other Pacific Islander	1	2
Multiracial	12	16
Not reported	2	3
Total	293	479
Ethnic origin		
Hispanic/Latino	26	43
Non-Hispanic/non-Latino	266	434
Not reported	1	2
Total	293	479
≥18 years to ≤55 years		
Vaccine 30 µg		
Racial origin		
White	8806	15340
Black or African American	1087	1899
Asian	619	1136
American Indian or Alaska Native	128	236
Native Hawaiian or other Pacific Islander	17	32
Multiracial	405	781
Not reported	70	127
Total	11132	19551
Ethnic origin		
Hispanic/Latino	3441	5300
Non-Hispanic/non-Latino	7635	14157
Not reported	56	94
Total	11132	19551
>55 years to ≤64 years		
Vaccine 30 µg		

Table 17. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Racial origin		
White	3416	6271
Black or African American	331	592
Asian	120	227
American Indian or Alaska Native	35	67
Native Hawaiian or other Pacific Islander	4	7
Multiracial	63	120
Not reported	16	31
Total	3985	7315
Ethnic origin		
Hispanic/Latino	901	1560
Non-Hispanic/non-Latino	3067	5724
Not reported	17	31
Total	3985	7315
≥65 years to ≤74 years		
Vaccine 30 µg		
Racial origin		
White	3093	6076
Black or African American	187	360
Asian	78	154
American Indian or Alaska Native	20	39
Native Hawaiian or other Pacific Islander	6	12
Multiracial	22	43
Not reported	8	16
Total	3414	6700
Ethnic origin		
Hispanic/Latino	547	1060
Non-Hispanic/non-Latino	2842	5590
Not reported	25	50
Total	3414	6700
≥75 years to ≤84 years		
Vaccine 30 µg		
Racial origin		
White	752	1483
Black or African American	22	42
Asian	17	34
American Indian or Alaska Native	4	8
Multiracial	6	12
Not reported	5	10

Table 17. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Total	806	1589
Ethnic origin		
Hispanic/Latino	89	174
Non-Hispanic/non-Latino	706	1393
Not reported	11	22
Total	806	1589
≥85 years		
Vaccine 30 µg		
Racial origin		
White	15	29
Asian	1	2
Multiracial	1	2
Total	17	33
Ethnic origin		
Non-Hispanic/non-Latino	17	33
Total	17	33

Note: 30 µg includes data from phase 1 and phase 2/3.
a. Includes subjects who became eligible for unblinding at 16 years of age, confirmed to have received placebo originally and then received BNT162b2 post unblinding.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s942_open

Table 18. Exposure to BNT162b2 by Dose and Race/Ethnic Origin (C4591001) – Blinded Placebo-Controlled Follow-up Period

Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Vaccine 10 µg		
Racial origin		
White	23	46
Asian	1	2
Total	24	48
Ethnic origin		
Hispanic/Latino	1	2
Non-Hispanic/non-Latino	23	46
Total	24	48
Vaccine 20 µg		

Table 18. Exposure to BNT162b2 by Dose and Race/Ethnic Origin (C4591001) – Blinded Placebo-Controlled Follow-up Period

Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Racial origin		
White	22	44
Black or African American	2	4
Total	24	48
Ethnic origin		
Hispanic/Latino	1	2
Non-Hispanic/non-Latino	23	46
Total	24	48
Vaccine 30 µg		
Racial origin		
White	19052	37815
Black or African American	2153	4257
Asian	1026	2040
American Indian or Alaska Native	225	437
Native Hawaiian or other Pacific Islander	61	121
Multiracial	574	1145
Not reported	97	194
Total	23188	46009
Ethnic origin		
Hispanic/Latino	5838	11513
Non-Hispanic/non-Latino	17237	34271
Not reported	113	225
Total	23188	46009

Note: 30 µg includes data from phase 1 and phase 2/3.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:47)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s952

Table 19. Exposure to BNT162b2 by Dose and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Vaccine 30 µg		
Racial origin		
White	74	74
Black or African American	2	2
Asian	3	3
American Indian or Alaska Native	10	10

Table 19. Exposure to BNT162b2 by Dose and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Total	89	89
Ethnic origin		
Hispanic/Latino	46	46
Non-Hispanic/non-Latino	43	43
Total	89	89

Note: 30 µg includes data from phase 1 and phase 2/3.
Note: Subjects who received 2nd Dose of BNT162b2 after unblinding.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:47)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2 unblinded/C4591001 PVP BLA/adsl s9523

Table 20. Exposure to BNT162b2 by Dose and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Vaccine 30 µg		
Racial origin		
White	16378	29671
Black or African American	1638	2912
Asian	852	1583
American Indian or Alaska Native	189	354
Native Hawaiian or other Pacific Islander	28	53
Multiracial	510	975
Not reported	101	187
Total	19696	35735
Ethnic origin		
Hispanic/Latino	5006	8141
Non-Hispanic/non-Latino	14580	27395
Not reported	110	199
Total	19696	35735

Note: 30 µg includes data from phase 1 and phase 2/3.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:47)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s952_open

Table 21. Exposure to BNT162b2 by Dose and Race/Ethnic Origin (BNT162-01)

Dose Race/Ethnic Origin	No. of Subjects Exposed to BNT162b2	Total No. of Vaccine Doses
Vaccine 1 µg		
Racial Origin		
White	12	23
Total	12	23
Ethnic Origin		
Non-Hispanic/non-Latino	12	23
Total	12	23
Vaccine 3 µg		
Racial Origin		
White	12	24
Total	12	24
Ethnic Origin		
Non-Hispanic/non-Latino	12	24
Total	12	24
Vaccine 10 µg		
Racial Origin		
White	24	47
Total	24	47
Ethnic Origin		
Non-Hispanic/non-Latino	24	47
Total	24	47
Vaccine 20 µg		
Racial Origin		
White	24	48
Total	24	48
Ethnic Origin		
Non-Hispanic/non-Latino	24	48
Total	24	48
Vaccine 30 µg		
Racial Origin		
White	24	48
Total	24	48
Ethnic Origin		
Non-Hispanic/non-Latino	24	48
Total	24	48

Table 21. Exposure to BNT162b2 by Dose and Race/Ethnic Origin (BNT162-01)

Dose Race/Ethnic Origin	No. of Subjects Exposed to BNT162b2	Total No. of Vaccine Doses

Only race, ethnic origins collected on the case report form with a count of at least one in either column are displayed.
PFIZER CONFIDENTIAL SDTM Creation: 24NOV2020 (15:06) Source Data: adsl Table Generation: 10MAR2021 (12:27) (Cutoff date:23OCT2020, Snapshot Date: 23OCT2020)
Output File: ex_b2_dose_race rtf

Table 22. Exposure to BNT162b2 (30 µg) by Special Population (C4591001) – Blinded Placebo-Controlled Follow-up Period

Population	Number of Subjects Exposed to BNT162b2 (30 µg) (N[a]=23188) n[b]	Total Number of Vaccine Doses
Subjects with any baseline comorbidity	10371	26487
AIDS/HIV	100	196
Any Malignancy + Metastatic Solid Tumor + Leukemia + Lymphoma	852	1696
Chronic Pulmonary Disease	1901	3774
Renal Disease	140	279
Rheumatic Disease	75	147
Mild Liver Disease + Moderate or Severe Liver Disease	154	302
Cerebrovascular Disease + Peripheral Vascular Disease + Myocardial Infarction + Congestive Heart Failure	651	1298
Dementia	7	14
Diabetes With/Without Chronic Complication	1706	3385
Hemiplegia or Paraplegia	4	8
Peptic Ulcer Disease	63	126
Obese	7689	15262

Note: Comorbidity is based on Charlson Comorbidity Index categories. Participants identified as belonging to these categories were identified by medical history data collected during the study.
Note: 30 µg includes data from phase 1 and phase 2/3.
Note: Hemiplegia or Paraplegia only includes preferred terms Hemiplegia and Paraplegia.
a. N = number of subjects in the specified group.
b. n = Number of subjects reporting at least 1 occurrence of any comorbidity or obese (BMI ≥30 kg/m^2 [≥16 Years of age] or BMI ≥95th percentile [12-15 Years of age]).
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:25) Source Data: admh Table Generation: 27MAR2021 (12:47)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/admh_s953

Table 23. Exposure to BNT162b2 (30 µg) by Special Population (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Population	Number of Subjects Exposed to BNT162b2 (30 µg) (N[a]=19696) n[b]	Total Number of Vaccine Doses
Subjects with any baseline comorbidity	8981	21590
AIDS/HIV	86	161
Any Malignancy + Metastatic Solid Tumor + Leukemia + Lymphoma	734	1406
Chronic Pulmonary Disease	1590	2953
Renal Disease	139	262
Rheumatic Disease	66	122
Mild Liver Disease + Moderate or Severe Liver Disease	102	193
Cerebrovascular Disease + Peripheral Vascular Disease + Myocardial Infarction + Congestive Heart Failure	567	1075
Dementia	9	17
Diabetes With/Without Chronic Complication	1555	2928
Hemiplegia or Paraplegia	4	8
Peptic Ulcer Disease	76	145
Obese	6760	12320

Note: Comorbidity is based on Charlson Comorbidity Index categories. Participants identified as belonging to these categories were identified by medical history data collected during the study.
Note: 30 µg includes data from phase 1 and phase 2/3.
Note: Hemiplegia or Paraplegia only includes preferred terms Hemiplegia and Paraplegia.
a. N = number of subjects in the specified group.
b. n = Number of subjects reporting at least 1 occurrence of any comorbidity or obese (BMI ≥30 kg/m^2 [≥16 Years of age] or BMI ≥95th percentile [12-15 Years of age]).
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:25) Source Data: admh Table Generation: 27MAR2021 (12:47)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/admh_s953_open

2.1.2.a.2. Inclusion and Exclusion Criteria

Detailed descriptions of all inclusion and exclusion criteria for clinical studies are provided in the individual CSRs which were filed to IND 019736.

Inclusion criteria

- Healthy participants who are determined by medical history, physical examination (if required), and clinical judgment of the investigator to be eligible for inclusion in the study.

- Healthy participants with pre-existing stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, can be included. In order for the overall Phase 3 study population to be as representative and diverse as possible, the inclusion of participants with known chronic stable infection with HIV, HCV, or HBV was permitted as the study progressed. Specific criteria for these Phase 3 participants can be found in the C4591001 protocol, Section 10.8.

- Phase 2/3 only: Participants who, in the judgment of the investigator, are at higher risk for acquiring COVID-19 (including, but not limited to, use of mass transportation, relevant demographics, front-line essential workers, and others).

- The participants enrolled were 12 years of age and older; the 12- to 15-year-old cohort was included in the protocol in October 2020.

Exclusion criteria

Phase 1 exclusion criteria were stricter than criteria in Phases 2 and 3 of the study. Participants were excluded from the studies according to the general criteria listed below:

- **Previous vaccination with any coronavirus vaccine**

  Reason for exclusion: To avoid confounding the assessment of serological or clinical immune response in the study population.

  Is it considered to be included as missing information? No.

  Rationale: Minimal potential clinical impact on the target population.

- **Previous clinical or microbiological diagnosis of COVID-19**

  Reason for exclusion: Phase 1 excluded participants with a previous clinical or microbiological diagnosis of COVID-19 because these participants may have some degree of protection from subsequent infection by SARS-CoV-2 and therefore would confound the pivotal efficacy endpoint. During Phase 2/3, participants with prior undiagnosed infection were allowed to be enrolled. Screening for SARS-CoV-2 with nucleic acid amplification test by nasal swab or antibodies to non-vaccine SARS-CoV-2

antigen by serology was not conducted before vaccine administration in Phase 2/3, but samples were taken to run these assays after vaccination, thus identifying participants with unidentified prior infection. This group will be assessed to identify whether prior infection affects safety.

Is it considered to be included as missing information? No.

Rationale: Safety in study participants with prior infection will be assessed in the pivotal study.

- **Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination.**

  Reason for exclusion: Immunocompromised participants may have impaired immune responses to vaccines and would therefore limit the ability to demonstrate efficacy, which is the primary pivotal endpoint.

  Is it considered to be included as missing information? No.

  Rationale: Participants with potential immunodeficient status were not specifically included in the study population. However, since the study population is intended to be as representative as possible of the vulnerable population to COVID-19 illness, sub-analyses of immunogenicity data in future studies may provide further understanding of immune responses in this population.

- **Receipt of blood/plasma products or immunoglobulin, from 60 days before study intervention administration or planned receipt throughout the study**

  Reason for exclusion: To avoid confounding the assessment of serological or clinical immune response in the study population.

  Is it considered to be included as missing information? No.

  Rationale: No impact on the safety of the target population.

- **Women who are pregnant or breastfeeding**

  Reason for exclusion: To avoid use in a vulnerable population.

  Is it considered to be included as missing information? Yes.

  Rationale: It is not known if maternal vaccination with BNT162b2 would have unexpected negative consequences to the embryo or fetus.

- **Other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation or, in the investigator's judgment, make the participant inappropriate for the study**

  Reason for exclusion: To avoid misleading results deriving from non-compliance to study procedures.

  Is it considered to be included as missing information? No.

  Rationale: Safety profile of BNT162b2 is not expected to differ in these subjects when properly administered.

2.1.2.a.2.1. Non-Study Post-Authorization Exposure

It is not possible to determine with certainty the number of individuals who received BNT162b2 since it was first authorized for emergency use on 01 December 2020. Estimated worldwide shipped doses may serve as a reasonable indicator of subject exposure by region and countries; the estimated exposure by gender and age group is not available. Cumulatively, through the DLP (28 February 2021) approximately 126,212,580 doses of BNT162b2 were shipped worldwide. The estimated cumulative number of shipped doses of BNT162b2 by region, are summarized in Table 24.

Table 24. Cumulative Estimated Shipped Doses[a] of BNT162b2 by Region Worldwide

Region/Country	Total Number of Shipped Doses	% of Doses
Europe	**51,545,325**	**40.8%**
European Union (27)	36340590	28.8%
European Free Trade Association (3)	513825	0.4%
Switzerland	767520	0.6%
UK	13643175	10.8%
Other Countries	280215	0.2%
Commonwealth of Independent States[b]	0	**0.0%**
North America	**56577885**	**44.8%**
US	54326415	43.0%
Canada	2251470	1.8%
Central and South America	**2965170**	**2.3%**
Asia	**14467830**	**11.5%**
Oceania	**656370**	**0.5%**
Africa	**0**	**0.0%**
Total	**126,212,580**	**100.0%**

a. Data for US are based on Order Management Dashboard, while for the remaining Regions and Countries are based on the Order Book which is the most accurate tracker of shipment data.
b. Includes: Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russia, Tajikistan, Turkmenistan, Ukraine, Uzbekistan;

Method Used to Calculate Exposure

Not applicable.

Exposure

Not applicable.

2.1.2.a.3. Regulatory Actions Related to Safety

There were no withdrawals for safety reasons up to 28 February 2021.

2.1.2.b. Populations Not Studied in the Pre-Approval Phase

There has been limited exposure to BNT162b2 in some special populations and no epidemiologic studies have been conducted in pregnant/lactating women, pediatric participants (<12 years of age), and specific subpopulations that were initially excluded from the BNT162b2 program.

Table 25. Exposure of Special Populations Included or not in Clinical Trial Development Programs

Type of special population	Exposure
Pregnant women	Available data on BNT162b2 administered to pregnant women are insufficient to inform on vaccine-associated risks in pregnancy. In a reproductive and developmental toxicity study, no vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported. Through the cut-off date of 13 March 2021, there were 50 cases (52 events) originating from Study C4591001 in participant 16 years of age and older, and all were unique pregnancies.
Breastfeeding women	Breastfeeding women were not initially included in the BNT162b2 clinical development program. Data are not available to assess the effects of BNT162b2 on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for BNT162b2 and any potential adverse effects on the breastfed child from BNT162b2 or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptible to disease prevented by the vaccine. Through the cut-off date of 13 March 2021, there were no CT cases indicative of exposure during breastfeeding from study C4591001 in participants 16 years of age and older.
Participants with relevant comorbidities: • Participants with hepatic impairment • Participants with renal impairment • Participants with cardiovascular disease • Immunocompromised participants • Participants with a disease severity different from inclusion criteria in CTs	Healthy participants with pre-existing stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included. This allowed enrollment of a proportion of participants with common comorbidities such as cardiovascular diseases including hypertension, chronic pulmonary diseases, asthma, chronic liver disease, BMI >30 kg/m^2, participants with stage 3 or worse chronic kidney disease, and participants with varying disease severity. Participants with potential immunodeficient status were not specifically included in the study population. Please refer to Table 22 and Table 23 for the exposure of special populations.

Table 25. Exposure of Special Populations Included or not in Clinical Trial Development Programs

Type of special population	Exposure
Participants of different racial and/or ethnic origin	Please refer to Table 21 for exposure information by ethnic origin from the studies.
Subpopulations carrying known and relevant polymorphisms	No data available.
Pediatric participants	The safety and effectiveness of BNT162b2 in individuals younger than 16 years of age have not been established. **Participants 16 years of age and older** A total of 671 pediatric participants 16 to 17 years of age received BNT162b2 through the DLP of 13 March 2021: • 378 participants in the blinded-placebo controlled follow-up period (Table 3). • 293 participants in the open-label follow-up period after the unblinding (Table 5). **Participants 12 to 15 years of age** One thousand and hundred eighty (1180) pediatric participants 12 to 15 years of age received BNT162b2 through the cut-off date of 13 March 2021 (Table 3 and Table 5).
Elderly (≥65 years old)	The safety and effectiveness of BNT162b2 in elderly participants was consistent with that seen in younger adult participants. Clinical studies of BNT162b2 included a total of 8846 participants 65 years of age and over; of these, 8827 were from study C4591001, through the cut-off date of 13 March 2021: • 4590 participants in the blinded-placebo controlled follow-up period (Table 3) • 4237 participants in the open-label follow-up period after unblinding (Table 5). Nineteen (19) participants 65 years of age and over were from study BNT162-01 study through the cut-off date of 23 October 2020 (Table 6).

Abbreviations: EUA = emergency use authorization; BMI = body mass index; COVID-19 = coronavirus disease 2019; CT = clinical trial

2.1.2.c. Adverse Events / Adverse Reactions

2.1.2.c.1. Identification of Safety Concern in the Initial PVP Submission

2.1.2.c.1.1. Risks not Considered Important for Inclusion in the List of Safety Concerns in the PVP

Not all potential or identified risks for the vaccine are considered to meet the level of importance necessitating inclusion in the list of safety concerns in the PVP:

- Risks with minimal and temporary clinical impact on patients (in relation to the severity of the disease prevented).

- The following reactogenicity events are identified risks not included in the list of safety concerns in the PVP: Injection site pain, Fever, Chills, Fatigue, Headache, Muscle pain, and Joint pain.

- Very rare potential risks for any medicinal treatment, including vaccines which are well known to healthcare professionals are not included in the list of safety concerns.

2.1.2.c.2. Important Identified and Potential Risks and Missing Information

2.1.2.c.2.1. Presentation of Important Identified Risks and Important Potential Risks

Important Identified Risks

Table 26. Myocarditis and Pericarditis

Potential mechanisms, evidence source and strength of evidence	A mechanism of action (MOA) by which the vaccine could cause myocarditis and pericarditis has not been established. Nonclinical studies, protein sequence analyses and animal studies in rats and non-human primates have not identified a MOA. Hypotheses for MOA include an immune stimulated response (including the possibility of molecular mimicry), a general systemic inflammatory response from vaccination or a hypersensitivity response.
Characterisation of the risk	***Participants 16 years of age and older*** Data from the CT dataset Two cases were retrieved with the myocarditis and pericarditis search strategy[a] in the clinical trial dataset through the cut-off date of 18 June 2021. These cases originated from Phase 3 clinical study C4591001 and are summarized below: Myocarditis: There were no cases reporting myocarditis as SAE. Pericarditis (2 cases): Two (2) serious adverse events [PT Pericarditis] were reported, both deemed not related to study treatment by the Investigator. Data from the safety database: Since the first temporary authorization for emergency supply under Regulation 174 in the UK (01 December 2020) and through 18 June 2021, 823 potentially relevant cases (0.3% of the total post-authorization dataset) were retrieved from the Myocarditis and Pericarditis search strategy:[a] 490 cases reported events related to myocarditis and 371 cases reported events related to pericarditis (in 38 of these 823 cases, the subjects developed both myocarditis and pericarditis related events). Myocarditis (490 cases): These 490 cases were individually reviewed and assessed according to Brighton Collaboration (BC) Myocarditis Case Definition and Level of Certainty Classification (version 1.4.2, 30 May 2021), as shown in the Table below:

Brighton Collaboration Level	Number of cases
BC 1	41
BC 2	44

Table 26. Myocarditis and Pericarditis

BC 3	42
BC 4	337
BC 5	26
Total	490

Level 1 indicates a definitive case with the highest level of diagnostic certainty of myocarditis, level 2 indicates a probable case, and level 3 indicates a possible case. Level 4 is defined as "reported event of myocarditis with insufficient evidence to meet the case definition" and Level 5 as not a case of myocarditis.

There were 464 cases meeting BC Level 1 to 4, which are presented below:

Country of incidence: Israel (135), US (78), Germany (76), UK (55), France (21), Italy, Japan (13 each), Austria (10), Greece, Spain (8 each), Sweden (7), Canada, Norway (6 each), Ireland (5); the remaining 23 cases originated from 17 different countries.

Gender: Females (133), Males (325), Unknown (6).

Age (n=443) ranged from 16 to 97 years (mean = 37.2 years, median = 32.0 years).

Reported relevant PTs: Myocarditis (463) and Autoimmune myocarditis (1).

Overall event seriousness and outcome of these 464 cases are summarized below.

	Total Events N = 464 (%)
Serious events	459 (98.9)
Events with Criterion of Hospitalization	337 (72.6)
Distribution of events by Outcome	
Outcome: Death	14 (3.0)
Outcome: Resolved/Resolving	149 (32.1)
Outcome: Not resolved	106 (22.8)
Outcome: Resolved with sequelae	10 (2.2)
Outcome: Unknown/No data	185 (39.9)

Pericarditis (371 cases)

Country of incidence: US (68), France (62), Israel (50), UK (38), Italy (33), Norway, Spain (24 each), Canada (10), Australia (9), Greece (7), Germany (6), Belgium, Denmark, Netherlands, Switzerland (5 each); the remaining 20 cases originated from 11 different countries.

Gender: Females (185), Males (181), Unknown (5).

Age (n=335) ranged from 16 to 92 years (mean = 51.5 years, median = 51.0 years).

Reported relevant PTs: Pericarditis (360) and Pleuropericarditis (12).

Overall event seriousness and outcome of these 371 cases are summarized below.

	Total Events N = 372 (%)
Serious events	370 (99.5)
Events with Criterion of Hospitalization	206 (55.4)
Distribution of events by Outcome	

Table 26. Myocarditis and Pericarditis

Outcome: Death	3 (0.8)
Outcome: Resolved/Resolving	213 (57.3)
Outcome: Not resolved	63 (16.9)
Outcome: Resolved with sequelae	7 (1.9)
Outcome: Unknown/No data	86 (23.1)

Participants 12 to 15 years of age

Data from the CT dataset:
No cases were retrieved reporting Myocarditis and Pericarditis as SAE in the clinical trial dataset through the cut-off date of 18 June 2021.

Data from the safety database:
Through 18 June 2021, 15 potentially relevant cases were retrieved from the Myocarditis and Pericarditis search strategy:[a] 13 cases reported myocarditis and 4 cases reported pericarditis (in 2 of these 15 cases, the subjects developed both myocarditis and pericarditis).

Myocarditis (13 cases)

These 13 cases were individually reviewed and assessed according to Brighton Collaboration (BC) Myocarditis Case Definition and Level of Certainty Classification, as shown in the Table below:

Brighton Collaboration Level	Number of cases
BC 1	0
BC 2	0
BC 3	0
BC 4	11
BC 5	2
Total	13

Level 1 indicates a definitive case with the highest level of diagnostic certainty of myocarditis, level 2 indicates a probable case, and level 3 indicates a possible case. Level 4 is defined as "reported event of myocarditis with insufficient evidence to meet the case definition" and Level 5 as not a case of myocarditis.

No cases met BC levels 1 to 3. There were 11 cases meeting BC Level 4, which are presented below:

Country of incidence: US (10) and Bahrain (1).
Gender: Female (1), Males (10).

Age (n=11) ranged from 12 to 15 years (mean = 13.8 years, median = 14.0 years).

Reported relevant PT: Myocarditis (11).

Overall event seriousness and outcome of these 11 cases are summarized below.

	Total Events N = 11
Serious events	10
Events with Criterion of Hospitalization	9

Table 26. Myocarditis and Pericarditis

<table>
<tr><td></td><td>
<table>
<tr><td colspan="2">Distribution of events by Outcome</td></tr>
<tr><td>Outcome: Death</td><td>0</td></tr>
<tr><td>Outcome: Resolved/Resolving</td><td>3</td></tr>
<tr><td>Outcome: Not resolved</td><td>4</td></tr>
<tr><td>Outcome: Resolved with sequelae</td><td>0</td></tr>
<tr><td>Outcome: Unknown/No data</td><td>4</td></tr>
</table>

<u>Pericarditis (4 cases)</u>
Country of incidence: US (4).
Gender: Males (4).
Age (n=4) ranged from 12 to 15 years (mean = 13.5 years, median = 13.5 years).
Reported relevant PT: Pericarditis (4).

Overall event seriousness and outcome of these 4 cases are summarized below.

<table>
<tr><td></td><td>Total Events
N = 4</td></tr>
<tr><td>Serious events</td><td>3</td></tr>
<tr><td>Events with Criterion of Hospitalization</td><td>1</td></tr>
<tr><td colspan="2">Distribution of events by Outcome</td></tr>
<tr><td>Outcome: Death</td><td>0</td></tr>
<tr><td>Outcome: Resolved/Resolving</td><td>1</td></tr>
<tr><td>Outcome: Not resolved</td><td>1</td></tr>
<tr><td>Outcome: Resolved with sequelae</td><td>0</td></tr>
<tr><td>Outcome: Unknown/No data</td><td>2</td></tr>
</table>
</td></tr>
<tr><td>Risk factors and risk groups</td><td>Post-authorization reports have been received for more males than females, over a wide age range and following dose 1 and dose 2 of the vaccine. Evaluation by the US CDC has found reports to be most frequent in adolescent and young adult male patients following the second dose of vaccine.</td></tr>
<tr><td>Preventability</td><td>Due to an unknown MOA, preventative measures are not clear for individuals with or without a personal history of myocarditis or pericarditis.</td></tr>
<tr><td>Impact on the risk-benefit balance of the biologic product</td><td>The vaccine continues to have a favorable risk benefit balance</td></tr>
<tr><td>Public health impact</td><td>Considering the low rates of myocarditis and pericarditis reported following vaccination, balanced with the risk of death and illness (including myocarditis) caused by SARS-CoV-2, the public health impact of post-vaccination myocarditis and pericarditis is minimal.</td></tr>
</table>

a. Search criteria: the following PTs were used to retrieve cases of Myocarditis and Pericarditis: Autoimmune myocarditis; Eosinophilic myocarditis; Giant cell myocarditis; Hypersensitivity myocarditis; Immune-mediated myocarditis; Myocarditis; Autoimmune pericarditis, Pericarditis; Pericarditis adhesive; Pericarditis constrictive; Pleuropericarditis.
Please note that CT dataset from the safety dabase includes only cases reporting SAEs.

Table 27. Anaphylaxis

<table>
<tr><td>Potential mechanisms, evidence source and strength of evidence</td><td>Interaction of an allergen with IgE on basophils and mast cells triggers release of histamine, leukotrienes and other mediators that cause diffuse smooth muscle contraction and vasodilation with plasma leakage. This can manifest clinically with dyspnea, hypotension, swelling (sometimes leading to airway compromise), and rash (including hives).</td></tr>
<tr><td>Characterisation of the risk</td><td>
<u>Data from the CT database</u>

Information pertinent to the anaphylactic reactions observed participants 16 years and older in the ongoing Phase 3 clinical study C4591001 through the cut-off date of 13 March 2021, are summarized below:

Five (5) serious events [Acute respiratory failure, Cardiac arrest, Anaphylactic reaction, Anaphylactoid reaction (post bee sting), and Anaphylactic shock] were reported. The Anaphylactoid reaction, occurred to a participant in the age group 16-55 years, was assessed as related to study treatment by the Investigator. The remaining 4 events were deemed not related to study treatment by the Investigator.

<u>Data from the safety database:</u>

Since the first temporary authorization for emergency supply under Regulation 174 in the UK (01 December 2020) and through 28 February 2021, 1833 potentially relevant cases[b], were retrieved from the Anaphylactic reaction SMQ (Narrow and Broad) search strategy, applying the MedDRA algorithm. These 1833 cases were individually reviewed and assessed according to Brighton Collaboration (BC) definition and level of diagnostic certainty as shown in the Table below:
<table>
<tr><th>Brighton Collaboration Level</th><th>Number of cases</th></tr>
<tr><td>BC 1</td><td>290</td></tr>
<tr><td>BC 2</td><td>311</td></tr>
<tr><td>BC 3</td><td>10</td></tr>
<tr><td>BC 4</td><td>391</td></tr>
<tr><td>BC 5</td><td>831</td></tr>
<tr><td>Total</td><td>1833</td></tr>
</table>
Level 1 indicates a case with the highest level of diagnostic certainty of anaphylaxis, whereas the diagnostic certainty is lowest for Level 3. Level 4 is defined as “reported event of anaphylaxis with insufficient evidence to meet the case definition” and Level 5 as not a case of anaphylaxis.

There were 1002 cases (54.0% of the potentially relevant cases retrieved), 2958 potentially relevant events, from the Anaphylactic reaction SMQ (Broad and Narrow) search strategy, meeting BC Level 1 to 4. Country of incidence: UK (261), US (184), Mexico (99), Italy (82), Germany (67), Spain (38), France (36), Portugal (22), Denmark (20), Finland, Greece (19 each), Sweden (17), Czech Republic, Netherlands (16 each), Belgium, Ireland (13 each), Poland (12), Austria (11); the remaining 57 cases originated from 15 different countries.
Gender: Females (876), Males (106), Unknown (20);
Age (n=961) ranged from 16 to 98 years (mean = 54.8 years, median = 42.5 years);

Overall event seriousness and outcome of these 1002 cases are summarized below.
<table>
<tr><th></th><th>Total Events
N = 2958 (%)</th></tr>
<tr><td>Serious events</td><td>2341 (79.1)</td></tr>
<tr><td>Events with Criterion of Hospitalization</td><td>752 (25.4)</td></tr>
<tr><td colspan="2">Distribution of events by Outcome*</td></tr>
</table>
</td></tr>
</table>

Table 27. Anaphylaxis

	Outcome∞: Death§ 9 (0.3) Outcome: Resolved/Resolving 1922 (65.0) Outcome: Not resolved 229 (7.7) Outcome: Resolved with sequelae 48 (1.6) Outcome: Unknown/No data 754 (25.5) * For the outcome count, the multiple Lowest Level Terms that code to the same PT within a case are counted and presented individually. Therefore, for selected PTs the total count of the event outcome may exceed the total number of events. ∞ Different clinical outcomes may be reported for an event occurred more than once to the same individual. § There were 4 individuals in the anaphylaxis evaluation who died on the same day they were vaccinated. Although these patients experienced adverse events (9) that are potential symptoms of anaphylaxis, they all had serious underlying medical conditions, and one individual appeared to also have COVID-19 pneumonia, that likely contributed to their deaths. The most frequently reported relevant PTs (≥2%), from the Anaphylactic reaction SMQ (Broad and Narrow) search strategy were: Anaphylactic reaction (435), Dyspnoea (356), Rash (190), Pruritus (175), Erythema (159), Urticaria (133), Cough (115), Respiratory distress, Throat tightness (97 each), Swollen tongue (93), Anaphylactic shock (80), Hypotension (72), Chest discomfort (71), Swelling face (70), Pharyngeal swelling (68), and Lip swelling (64). Conclusion: Evaluation of BC cases Level 1 – 4 did not reveal any significant new safety information. Anaphylaxis is appropriately described in the product labeling as are non-anaphylactic hypersensitivity events. Surveillance will continue.
Risk factors and risk groups	Known hypersensitivity to any components of the vaccine.
Preventability	Prevention of anaphylaxis may not be possible, particularly with the 1st dose of a vaccine; therefore, healthcare professionals administering the vaccine must be vigilant for early signs and symptoms.
Impact on the risk-benefit balance of the biologic product	Anaphylactic reaction in an individual can be impactful (medically important) because it is a potentially life-threatening event requiring medical intervention.
Public health impact	Minimal due to rarity of the event. Although the potential clinical consequences of an anaphylactic reaction are severe, this is a known risk of vaccines to healthcare professionals with negligible public health impact.

b. Search criteria Anaphylactic reaction SMQ (Narrow and Broad, with the MedDRA algorithm applied), with relevant cases assessed according to Brighton Collaboration (BC) criteria.

Important Potential Risks

Table 28. Vaccine-Associated Enhanced Disease (VAED), including Vaccine-Associated Enhanced Respiratory Disease (VAERD)

<table>
<tr><td>Potential mechanisms, evidence source and strength of evidence</td><td>This potential risk is theoretical because it has not been described in association with the BNT162b2 or it has not been reported from any other late phase clinical trial of other human vaccine. Animal models of SARS-CoV-2 infection have not shown evidence of VAED after immunization, whereas cellular immunopathology has been demonstrated after viral challenge in some animal models administered SARS-CoV-1 (murine, ferret and non-human primate models) or MERS-CoV (mice model) vaccines.[1,6] This potential risk has been included based on these animal data with these related betacoronaviruses. Historically, disease enhancement in vaccinated children following infection with natural virus has been observed with an inactivated respiratory syncytial virus vaccine.[7]
Potential mechanisms of enhanced disease may include both T cell-mediated [an immunopathological response favoring T helper cell type 2 (T_H2) over T helper cell type 1 (T_H1)] and antibody-mediated activity (antibody responses with insufficient neutralizing activity leading to formation of immune complexes and activation of complement or allowing for Fc-mediated increase in viral entry to cells).[8]</td></tr>
<tr><td>Characterization of the risk</td><td>Data from the CT database (Participant 16 years and older)
Confirmed Case of Postvaccination Severe COVID-19 – Blinded Placebo-Controlled Follow-up Period - Safety Population (C4591001)
<table><tr><th></th><th colspan="2">BNT162b2 (30 µg) (N[a]=23164)</th><th colspan="2">Placebo (N[a]=23155)</th></tr><tr><th>Timing</th><th>n[b] (%)</th><th>(95% CI[c])</th><th>n[b] (%)</th><th>(95% CI[c])</th></tr><tr><td>PD1 Before Dose 2</td><td>0</td><td>(0.0, 0.0)</td><td>6 (0.0)</td><td>(0.0, 0.0)</td></tr><tr><td>Within 7 days PD1</td><td>0</td><td>(0.0, 0.0)</td><td>0</td><td>(0.0, 0.0)</td></tr><tr><td>PD2</td><td>1 (0.0)</td><td>(0.0, 0.0)</td><td>25 (0.1)</td><td>(0.1, 0.2)</td></tr><tr><td>Within 7 days PD2</td><td>0</td><td>(0.0, 0.0)</td><td>2 (0.0)</td><td>(0.0, 0.0)</td></tr><tr><td>Total[d]</td><td>1 (0.0)</td><td>(0.0, 0.0)</td><td>31 (0.1)</td><td>(0.1, 0.2)</td></tr></table>Note: This table includes subjects from Phase 2/3 only.
Abbreviations: PD1 = post-dose 1; PD2 = post-dose 2.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the specified event.
c. Exact 2-sided CI based on the Clopper and Pearson method.
d. Total is the sum of PD1 and PD2.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adc19ef Table Generation: 27MAR2021 (12:47) (Cutoff date: 13MAR2021, Snapshot Date: 25MAR2021)
Output File: /nda2_unblinded/C4591001_PVP_BLA/adeff_s901

If VAED/VAERD were to occur in vaccinated individuals, it may manifest as a modified and/or more severe clinical presentation of SARS-CoV-2 viral infection upon subsequent natural infection. This may result in individuals assumed to be at lower risk for severe COVID-19 having more severe disease, for individuals at known risk for severe COVID-19 (e.g. older or immunocompromised) having higher rates of fatal outcomes, or for observation of an unfavorable imbalance in severe COVID-19</td></tr>
</table>

Table 28. Vaccine-Associated Enhanced Disease (VAED), including Vaccine-Associated Enhanced Respiratory Disease (VAERD)

cases in vaccinated individuals when compared to those not vaccinated. It is challenging to assess for VAED/VAERD on an individual case basis, given the lack of specific clinical or laboratory markers at this time, rather surveillance for this theoretical risk is best performed at a population level,[9] as noted above. The table above shows a favorable balance of severe COVID-19 cases in participants receiving BNT162b2 versus those receiving placebo, providing reassurance against the potential risk of VAED/VAERD at this time.

Data from the safety database

No post-authorized AE reports have been identified as cases of VAED/VAERD, therefore, there is no observed data at this time. An expected rate of VAED is difficult to establish so a meaningful observed/expected analysis cannot be conducted at this point based on available data. The feasibility of conducting such an analysis will be re-evaluated on an ongoing basis as data on the virus grows and the vaccine safety data continues to accrue.

The search criteria utilised to identify potential cases of VAED for this report includes PTs indicating a lack of effect of the vaccine and PTs potentially indicative of severe or atypical COVID-19[a].

Since the first temporary authorization for emergency supply under Regulation 174 in the UK (01 December 2020) and through 28 February 2021, the following numbers of potentially relevant cases were retrieved:

138 cases [0.25% of the total post-authorization dataset], reporting 317 potentially relevant events.
Seriousness criteria for the total 138 cases: Medically significant (71, of which 8 also serious for disability), Hospitalization required (non-fatal/non-life threatening) (16, of which 1 also serious for disability), Life threatening (13, of which 7 were also serious for hospitalization), Death (38).
Gender: Females (73), Males (57), Unknown (8).
Age (n=132) ranged from 21 to 100 years (mean = 57.2 years, median = 59.5).

Overall event seriousness and outcome are summarized below.

	Total Events N = 317 (%)
Serious events	279 (88.0)
Events with Criterion of Hospitalization	91 (28.7)
Distribution of events by Outcome[a]	
Outcome: Death	62 (19.6)
Outcome: Resolved/Resolving	61 (19.2)
Outcome: Not resolved	90 (28.4)
Outcome: Resolved with sequelae	1 (0.3)
Outcome: Unknown/No data	106 (33.4)

a. For the outcome count, the multiple Lowest Level Terms that code to the same PT within a case are counted and presented individually. Therefore, for selected PTs the total count of the event outcome may exceed the total number of events.

The most frequently reported relevant PTs (≥5 events) were: Drug ineffective (135), Dyspnoea (53), Diarrhoea (30), COVID-19 pneumonia (23), Vomiting (20), Respiratory failure (8), Seizure (7), Hypoxia (6), Abdominal pain, and Pulmonary embolism (5 each).

Table 28. Vaccine-Associated Enhanced Disease (VAED), including Vaccine-Associated Enhanced Respiratory Disease (VAERD)

	Conclusion: VAED may present as severe or unusual clinical manifestations of COVID-19. Overall, there were 37 subjects with suspected COVID-19 and 101 subjects with confirmed COVID 19 following one or both doses of the vaccine; 75 of the 101 cases were severe, resulting in hospitalisation, disability, life threatening consequences or death. None of the 75 cases could be definitively considered as VAED/VAERD. In this review of subjects with COVID-19 following vaccination, based on the current evidence, VAED/VAERVAED remains a theoretical risk for the vaccine. Surveillance will continue.
Risk factors and risk groups	It is postulated that the potential risk may be increased in individuals producing lower neutralizing antibody titers or in those demonstrating waning immunity.[8,9]
Preventability	An effective vaccine against COVID-19 that produces high neutralizing titers and a T_H1 predominant $CD4^+$ T cell response and strong $CD8^+$ T cell response, is expected to mitigate the risk of VAED/VAERD;[1,8] that immune profile is elicited by BNT162b2 in clinical and preclinical studies.[10,11]
Impact on the risk-benefit balance of the biologic product	If there were an unfavorable balance in COVID-19 cases, including severe cases, in the pivotal clinical study between the vaccine and placebo groups, that may signal VAED/VAERD.
Public health impact	The potential risk of VAED/VAERD could have a public health impact if large populations of individuals are affected.

a. Standard Decreased Therapeutic Response Search AND at least 1 of the following PTs Dyspnoea; Tachypnoea; Hypoxia; COVID 19 pneumonia; Respiratory Failure; Acute Respiratory Distress Syndrome; Cardiac Failure; Cardiogenic shock; Acute myocardial infarction; Arrhythmia; Myocarditis; Vomiting; Diarrhoea; Abdominal pain; Jaundice; Acute hepatic failure; Deep vein thrombosis; Pulmonary embolism; Peripheral Ischaemia; Vasculitis; Shock; Acute kidney injury; Renal failure; Altered state of consciousness; Seizure; Encephalopathy; Meningitis; Cerebrovascular accident; Thrombocytopenia; Disseminated intravascular coagulation; Chillblains; Erythema multiforme; Multiple organ dysfunction syndrome; Multisystem inflammatory syndrome in children.
Note: the "Standard Decreased Therapeutic Response" search includes the Lack of efficacy PTs (Drug ineffective/Vaccination failure).

2.1.2.c.2.2. Presentation of Missing Information

Table 29. Use in Pregnancy and Lactation

Evidence source:
The safety profile of the vaccine is not known in pregnant or lactating women due to their exclusion from the pivotal clinical study. There may be pregnant women who choose to be vaccinated despite the lack of safety data. It will be important to follow these women for pregnancy and birth outcomes. The timing of vaccination in a pregnant woman and the subsequent immune response may have varying favorable or unfavorable impacts on the embryo/fetus. The clinical consequences of SARS-CoV-2 infection to the woman and fetus during pregnancy is not yet fully understood and the pregnant woman's baseline health status may affect both the clinical course of her pregnancy and the severity of COVID-19 disease. These factors and the extent to which the pregnant woman may be at risk of exposure to SARS-CoV-2 will influence the benefit risk considerations for use of the vaccine.

Population in need of further characterization:
The lack of data will be communicated in product labeling; one clinical study of the safety and immunogenicity of the BNT162b2 in pregnant women is ongoing (C4591015); 2 non-interventional studies (C4591009 and C4591011) to assess whether sub-cohorts of interest, such as pregnant women, experience increased risk of safety events of interest following receipt of the BNT162b2 are planned (see 3.1.3 – *Action plan for safety issues*).

Data from the Safety Database[a]
Since the first temporary authorization for emergency supply under Regulation 174 in the UK (01 December 2020) and through 28 February 2021, there were 413 cases (1.0 % of the total Post-authorization dataset) reporting use during pregnancy or lactation.

Overall event seriousness and outcome are summarized below:

	Total Events N = 1122 (%)
Serious events	270 (24.1)
Events with Criterion of Hospitalization	14 (1.2)
Distribution of events by Outcome*	
Outcome: Death§	5 (0.4)
Outcome: Resolved/Resolving	205 (18.3)
Outcome: Not resolved	64 (5.7)
Outcome: Resolved with sequelae	4 (0.4)
Outcome: Unknown/No data	849 (75.7)

* For the outcome count, the multiple Lowest Level Terms that code to the same PT within a case are counted and presented individually. Therefore, for selected PTs the total count of the event outcome may exceed the total number of events.
§ Two babies whose mothers were vaccinated during their second trimester of gestation, were pre-maturely delivered 5 days after vaccination and died on their second day of life.

The most frequently reported relevant PTs (≥2%) were: Maternal exposure during pregnancy (187), Product use issue (148), Off label use (147), Exposure via breast milk (133), Exposure during pregnancy (55), Headache (33), Abortion spontaneous (25), Vaccination site pain (24), Pain in extremity, Pyrexia (23 each) and Fatigue (22).

a. Cumulative RMP tables on Missing information are provided as per FDA's request to include a cumulative analysis, from post-authorization experience, of the Important Missing Information identified in the Pharmacovigilance Plan. More detailed information is available in the cumulative analysis of post-authorization data provided as a standalone document with the BLA submission.

Table 30. Vaccine Effectiveness

Evidence source:

Although vaccine efficacy in a controlled clinical study is the objective of the pivotal study, real-world vaccine effectiveness when the BNT162b2 is used in a large and more diverse population is unknown.

Anticipated risk/consequence of missing information:

Efficacy information obtained from clinical study data will be communicated in the product labeling. Three post-authorization effectiveness studies in real-world use are planned: 1 non-interventional study (C4591014) and 2 low-interventional studies (WI235284 and WI255886) to determine the effectiveness of BNT162b2 when administered outside of the clinical setting (see 3.1.3 – *Action plan for safety issues*).

Data from the Safety Database[a]

Since the first temporary authorization for emergency supply under Regulation 174 in the UK (01 December 2020) and through 28 February 2021, there were 1665 cases (3.9% of the total Post-authorization dataset) reporting lack of efficacy.

Overall event seriousness and outcome are summarized below:

	Total Events N = 1665 (%)
Serious events	1644 (98.7)
Events with Criterion of Hospitalization	65 (3.9)
Distribution of events by Outcome*	
Outcome: Death	65 (4.0)
Outcome: Resolved/Resolving	164 (9.8)
Outcome: Not resolved	205 (12.3)
Outcome: Resolved with sequelae	0 (0)
Outcome: Unknown/No data	1231 (73.9)

* For the outcome count, the multiple Lowest Level Terms that code to the same PT within a case are counted and presented individually. Therefore, for selected PTs the total count of the event outcome may exceed the total number of events.

The PT Drug ineffective was reported in 1646 cases, Vaccination failure was reported in 19 cases; the most frequently co-reported PTs (≥2%) were: COVID 19 (1244), SARS-CoV-2 test positive(219), Suspected COVID-19 (161), Pyrexia (134), and Headache (110).

a. Cumulative RMP tables on Missing information are provided as per FDA's request to include a cumulative analysis, from post-authorization experience, of the Important Missing Information identified in the Pharmacovigilance Plan. More detailed information is available in the cumulative analysis of post-authorization data provided as a standalone document with the BLA submission.

Table 31. Use in Paediatric Individuals <12 Years of Age

Evidence source:
BNT162b2 has not been initially studied in pediatric individuals younger than 12 years of age due to their exclusion from the pivotal clinical study.

Paediatric individuals may display different reactogenicity and safety profiles compared to adults, due to lower body mass and differently matured immunological responses.

Population in need of further characterization:
The are no data in individuals less than 12 years of age; a clinical study of the safety, tolerability, immunogenicity and efficacy of BNT162b2 in individuals younger than 12 years [C4591007 (< 12 years of age)][a] is ongoing (see 3.1.3 – *Action plan for safety issues*); a non-interventional study (C4591009) is planned to assess the occurrence of safety events of interest in a general US population (< 12 and ≥ 12 to ≤15 years of age) (see 3.1.3 – *Action plan for safety issues*).

Data from the Safety Database[b]
Since the first temporary authorization for emergency supply under Regulation 174 in the UK (01 December 2020) and through 28 February 2021, there were 34 cases (0.08% of the total Post-authorization dataset) involving individuals below 12 years of age.
Overall event seriousness and outcome are summarized below:

	Total Events N = 132 (%)
Serious events	66 (50)
Events with Criterion of Hospitalization	19 (14.4)
Distribution of events by Outcome*	
Outcome: Death	0
Outcome: Resolved/Resolving	25 (18.9)
Outcome: Not resolved	42 (31.8)
Outcome: Resolved with sequelae	0
Outcome: Unknown/No data	65 (49.2)

* For the outcome count, the multiple Lowest Level Terms that code to the same PT within a case are counted and presented individually. Therefore, for selected PTs the total count of the event outcome may exceed the total number of events.

The most frequently reported PTs (≥2%) were: Product administered to patient of inappropriate age (27), Off label use (11), Pyrexia (6), Product use issue (5), Fatigue, Headache, Nausea (4 each) and Vaccination site pain (3).

a. Phase 1 open label dose-finding study to evaluate safety, tolerability, and immunogenicity and phase 2/3 placebo-controlled, observer blinded safety, tolerability, and immunogenicity, study of a SARS-CoV-2 RNA vaccine candidate against COVID 19 in healthy children <12 years of age.
b. Cumulative RMP tables on Missing information are provided as per FDA's request to include a cumulative analysis, from post-authorization experience, of the Important Missing Information identified in the Pharmacovigilance Plan. More detailed information is available in the cumulative analysis of post-authorization data provided as a standalone document with the BLA submission.

2.1.2.d. Identified and Potential Interactions, Including Food-Biologic Product and Drug-Biologic Product Interactions

As noted in the WHO Guidelines on Nonclinical Evaluation of Vaccines,[3] pharmacokinetics testing is not required for final formulation. No interaction linked to metabolism is expected with vaccines. The only potential for interaction is with other vaccines administered concomitantly and with immunosuppressive drugs.

Co-administration studies with BNT162b2 have not been done, therefore there is not sufficient data to understand the effect on vaccine effectiveness of BNT162b2 or co-administered vaccines. A co-administration study with seasonal influenza vaccine is planned. If BNT162b2 is given at the same time as other injectable vaccine(s), the vaccine(s) should be administered at different injection sites.

2.1.2.e. Epidemiology of Indication and Target Population

Indication

Active immunization against COVID-19 disease caused by SARS-CoV-2 virus in individuals ≥ 16 years of age.

Incidence:

The COVID-19 is caused by a novel coronavirus labeled as SARS-CoV-2. The disease first emerged in December 2019, when a cluster of patients with pneumonia of unknown cause was recognized in Wuhan City, Hubei Province, China.[12] The number of infected cases rapidly increased and spread beyond China throughout the world. On 30 January 2020, the WHO declared COVID-19 a Public Health Emergency of International Concern and thus a pandemic.[13]

Estimates of SARS-CoV-2 incidence change rapidly. We obtained incidence and prevalence estimates using data from Worldometer, a trusted independent organization that collects COVID-19 data from official reports and publishes current global and country-specific statistics online.[14]

As of 03 March 2021, the overall number of people who had been infected with SARS-CoV-2 was over 115 million worldwide,[15] an increase of nearly 100 million in the 7 months since 28 July 2020.[16] Table 32 shows the incidence and prevalence as of 03 March 2021 for the US, UK, and EU-27 countries. In the EU and the UK, by 03 March 2021 the total number of confirmed cases had accumulated to almost 27 million people, or 5,226 per 100,000 people (from 1.7 million, or 337 per 100,000 by 28 July 2020). Across countries in the EU, the number of confirmed cases ranged from 1,072 to 11,836 cases per 100,000 people. Finland and Greece reported the lowest incidence rates while Czech Republic, Slovenia, and Luxembourg reported the highest.[15]

In the US, the number of confirmed cases had reached over 29 million (8,864 per 100,000 people) by 03 March 2021.[15] This is an increase from 4.5 million (1,357 per 100,000) by 28 July 2020.[17]

Table 32. Incidence, Prevalence, and Mortality of COVID-19 as of 03 March 2021 [15]

	Total Cases	Incidence: Total Cases/ 100,000	Active Cases[a]	Prevalence: Active Cases/ 100,000	Total Deaths	Mortality: Deaths / 100,000	Population
Global	115,760,943	1,485	21,707,680	278	2,571,518	33	7,794,824,793
EU-27	22,642,536	5,083	6,113,464	1,462	553,363	124	445,424,167
UK	4,194,785	6,157	1,065,282	1,564	123,783	182	68,125,249
EU-27 + UK	26,837,321	5,226	7,178,746	1,398	677,146	132	513,549,416
US	29,456,377	8,864	8,921,400	2,685	531,652	160	332,304,437
EU-27 Countries							
Austria	465,322	5,147	21,028	233	8,625	95	9,040,866
Belgium	774,344	6,662	699,566	6,019	22,141	191	11,623,476
Bulgaria	253,183	3,662	33,770	488	10,413	151	6,913,156
Croatia	244,205	5,973	3,322	81	5,555	136	4,088,197
Cyprus	35,620	2,936	33,331	2,747	232	19	1,213,250
Czech Republic	1,269,058	11,836	154,580	1,442	20,941	195	10,722,330
Denmark	212,798	3,665	6,995	120	2,370	41	5,805,897
Estonia	69,193	5,214	17,938	1,352	615	46	1,327,135
Finland	59,442	1,072	12,683	229	759	14	5,546,504
France	3,810,316	5,829	3,461,485	5,295	87,542	134	65,370,546
Germany	2,472,896	2,945	126,785	151	71,711	85	83,963,843
Greece	197,279	1,899	21,157	204	6,597	64	10,388,744
Hungary	439,900	4,561	98,361	1,020	15,324	159	9,643,837
Ireland	221,189	4,446	193,468	3,889	4,357	88	4,974,683
Italy	2,976,274	4,927	437,421	724	98,635	163	60,401,999
Latvia	88,022	4,702	9,233	493	1,654	88	1,872,109
Lithuania	200,349	7,430	10,859	403	3,281	122	2,696,596
Luxembourg	55,902	8,834	3,074	486	643	102	632,773
Malta	23,226	5,251	3,000	678	321	73	442,333
Netherlands	1,101,430	6,418	-	-	15,697	92	17,160,343
Poland	1,735,406	4,589	249,567	660	44,360	117	37,818,722
Portugal	806,626	7,926	64,797	637	16,430	161	10,176,690
Romania	812,318	4,242	44,953	235	20,586	108	19,151,141
Slovakia	314,359	5,756	51,570	944	7,489	137	5,461,420
Slovenia	192,266	9,247	10,751	517	3,874	186	2,079,130
Spain	3,136,321	6,706	343,770	735	70,247	150	46,766,954
Sweden	675,292	6,659	-	-	12,964	128	10,141,493

a. Active case counts were not available for Netherlands and Sweden; therefore, those two countries are excluded from the overall prevalence calculations for EU-27 and EU-27 + UK.

The reported numbers refer only to cases that have been tested and confirmed to be carrying the virus. There are large geographic variations in the proportion of the population tested as well as in the quality of reporting across countries. People who carry the virus but remain

asymptomatic are less likely to be tested and therefore mild cases are likely underreported. The numbers should therefore be interpreted with caution.[18]

Prevalence:

The prevalence of SARS-CoV-2 infection is defined as active cases per 100,000 people including confirmed cases in people who have not recovered or died. On 03 March 2021, the overall prevalence for the EU and UK (though not available for Sweden and the Netherlands) was 1,398 active cases per 100,000,[15] compared to 51 per 100,000 on 28 July 2020.[16] The range of reported prevalence was 81 to 6,019 per 100,000: Croatia, Denmark, and Germany reported the lowest prevalence while Belgium, France and Ireland reported the highest (Table 32).

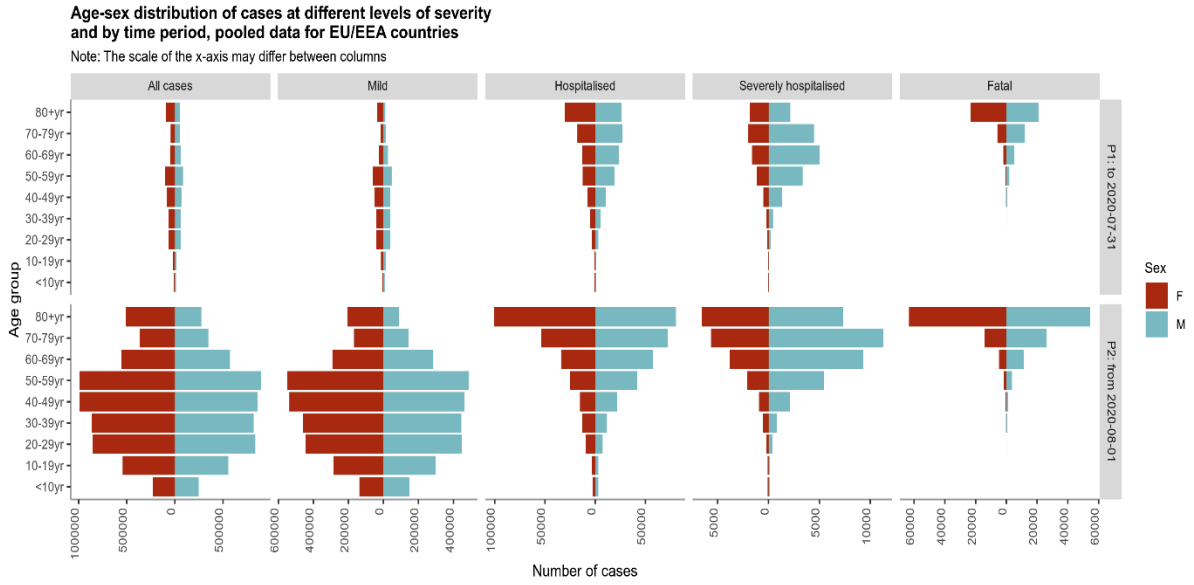
In the US, the prevalence on 03 March 2021 was nearly twice as high as the combined EU+UK estimates, with 2,685 active cases per 100,000.[15] The prevalence in the US was 653 per 100,000 on 28 July 2020.[16]

Demographics of the population in the proposed indication and risk factors for the disease:

Since the beginning of the pandemic, the ECDC has continuously collected COVID-19 information from all countries who are members of EU/EEA and the UK. In the ECDC's TESSy database, COVID-19 case-based data, including age and gender, are available for over 80% of the official number of cases reported by ECDC epidemic intelligence,[19] enabling estimates of age and gender distribution representative of the European population. TESSy data on age and sex distributions by severity of symptoms as posted on 04 March 2021 are shown in Figure 1.[20]

The top half of the figure represents data ending on 31 July 2020 and the bottom half presents data from 01 August 2020 to 04 March 2021 (Figure 1). In general, the age-sex patterns before 01 August 2020 have remained the same since then. The gender distribution of persons testing positive for SARS-CoV-2 in the European population is similar for most age groups. Cases reported in TESSy have been older than the general population throughout the pandemic, with few cases observed in people aged younger than 20 years. This likely reflects the age distribution of people who met the requirements for being tested and is unlikely to reflect the actual distribution of infections in the population. Those with severe outcomes (hospitalized, severely hospitalized, or fatal) have been disproportionately older and male compared to COVID-19 cases overall. While age-sex patterns have remained consistent throughout the pandemic, a notable difference between the periods before and since 01 August 2020 is that the absolute numbers of cases have increased dramatically in the latter period compared to the earlier one.

Figure 1. Age-Sex distribution of COVID-19 Cases as Different Levels of Severity, EU/EEA and UK. Case-based Data from TESSy produced on 04 March 2021[a]



Note: "mild"= a case that has not been reported as hospitalized or a case that resulted in death.

a. Data from ECDC. COVID-19 Surveillance report. Week 8, 2021. 4 March 2021. "2.2 Age-sex pyramids" Accessed 6 March 2021[20]

US distributions of COVID cases and deaths by age, sex, and race, as well as the cross-tabulation of age and sex, are shown in Table 33.[21] Those under age 50 account for 65% of cases but less than 5% of deaths. For ages 18-74, males account for less than half of cases but over 60% of deaths.

Table 33. Distributions of Cases (n=21,895,936) and Deaths (n=382,009) by Age, Sex, Race, and Cross-Tabulated Age and Sex – United States as of 08 March 2021[21,a]

Event	Age Group	Age %	Sex	Sex %	Race[b]	Race %	Age Group	Age x Sex %	
								Males	Females
Cases	**0-4**	2	**Males**	47.8	**H/L**	20.7	**0-4**	51.7	48.3
	5-17	9.5	**Females**	52.2	**AI/AN**	1.2	**5-17**	49.8	50.2
	18-29	22.4			**Asian**	3.6	**18-29**	47.1	52.9
	30-39	16.3			**Black**	12.2	**30-39**	48.2	51.8
	40-49	14.9			**NH/PI**	0.4	**40-49**	47.7	52.3
	50-64	20.5			**White**	56	**50-64**	48.5	51.5
	65-74	7.8			**M/O**	6	**65-74**	49	51
	75-84	4.1					**75-84**	45.7	54.3
	85+	2.4					**85+**	33.9	66.1
Deaths	**0-4**	<0.1	**Males**	54.3	**H/L**	12.2	**0-4**	47.6	52.4
	5-17	0.1	**Females**	45.7	**AI/AN**	1	**5-17**	57.7	42.3
	18-29	0.5			**Asian**	4.3	**18-29**	63	37
	30-39	1.1			**Black**	14.7	**30-39**	66	34
	40-49	2.8			**NH/PI**	0.2	**40-49**	66.5	33.5

Table 33. Distributions of Cases (n=21,895,936) and Deaths (n=382,009) by Age, Sex, Race, and Cross-Tabulated Age and Sex – United States as of 08 March 2021[21,a]

Event	Age Group	Age %	Sex	Sex %	Race[b]	Race %	Age Group	Age x Sex %	
								Males	Females
	50-64	14.5			**White**	63.1	**50-64**	65	35
	65-74	21.3			**M/O**	4.4	**65-74**	61.4	38.6
	75-84	27.7					**75-84**	55.8	44.2
	85+	32.1					**85+**	41.8	58.2

a. Percentage of missing demographic data varied by types of event and demographic.
b. Except for Hispanics/Latinos, all categories refer to non-Hispanics
Abbreviations: AI/AN=American Indian/Alaska Native, H/L=Hispanic/Latino, M/O=Multiple/Other, NH/PI=Native Hawaiian/Other Pacific Islander

In general, disease has been much less severe among ages 0-24 compared to ages ≥25 years, with 2.5% hospitalized, 0.8% admitted to an intensive care unit, and <0.1% dying among ages 0-24, versus 16.6% hospitalized, 8.6% intensive care, and 5% dying among ages ≥25 years.[22] Among hospitalized cases with COVID-19 in the US, approximately 90% are over 40 years old, and between 58% to 66% are at least 60 years old.[23] The majority (approximately 60%) of COVID-19 patients admitted to hospitals in the US have been male.[23,24,25,26,27]

African American COVID-19 patients have been reported to have an increased risk of hospitalization[24,28] and mortality,[29] compared to white patients in the United States. A CDC report examined demographic trends among US COVID-19 deaths from May to August of 2020.[30] During the observation period, the percentage of US COVID-19 deaths that were Hispanic increased from 16.3% in May to 26.4% in August, the only racial or ethnic group among whom the percentage of deaths increased during that time. In terms of setting, 64.3% of deaths occurred in inpatient hospitals and 21.5% in nursing homes or long-term care facilities.

As of 08 March 2021, the CDC estimated that the total number of *excess* deaths (as opposed to overall deaths in the preceding paragraph) across the US from 01 February 2020 to the present from all causes (COVID-19 and otherwise) ranged from 509,890-624,307.[31] A CDC report examining US excess deaths associated with race and age, restricted to the period 26 January 2020 to 03 October 2020, estimated that 66% of US excess deaths during that period were attributable to COVID-19.[32] By age, the largest increase in deaths compared to average expected deaths occurred among adults aged 25-44 (26.5% increase). By race, increases in deaths compared to expectation were largest among Hispanics (53.6% increase), Asian Americans (36.6% increase), African Americans (32.9% increase), and Native Americans and Native Alaskans (28.9% increase), all compared to an excess 11.9% deaths among non-Hispanic whites.

Risk Factors

While anyone can become infected with SARS-CoV-2, symptoms of COVID-19 disease can range from very mild (or no symptoms) to severe or fatal. A person's risk of initial infection

increases through spending time in close physical proximity to others, especially in indoor spaces with poor ventilation.[33] People living in long-term care facilities or high-density apartment homes, or working in occupations with close proximity to others (e.g. healthcare, transportation), have a higher risk of infection.[33,34,35] According to the CDC, people ages 18-29 have the highest risk of initial infection, while children age 4 and under have the lowest rate (Table 34).[36] Risk of infection is also higher among some ethnic minority groups.[37,38]

Table 34. Risk for COVID-19 Infection, Hospitalization, and Death by Age Group [36] and by Race/Ethnicity [37]

	Rate ratios		
Age Group (years)	**Cases**	**Hospitalization**	**Death**
0-4	<1	2	2
5-17 [a]	1	1	1
18-29	3	7	15
30-39	2	10	45
40-49	2	15	130
50-64	2	25	400
65-74	2	35	1100
75-84	2	55	2800
85+	2	80	7900
Race/Ethnicity			
Non-Hispanic White [b]	1	1	1
American Indian or Alaska Native, non-Hispanic	1.9	3.7	2.4
Asian, non-Hispanic	0.7	1.1	1.0
Black or African American, non-Hispanic	1.1	2.9	1.9
Hispanic or Latino	1.3	3.2	2.3

a. Rate ratios for each age group are relative to the 5—17-year age category.
b. Rate ratios for each race/ethnicity group are relative to the Non-Hispanic White category.

Risk for severe or fatal COVID-19 disease has been shown to increase with older age, male sex, or ethnic minority status.[36,37,38,39,40,41] Risks of hospitalization and death increase dramatically for every 10-year age group above age 17 (Table 34).[36,41] Table 34 also gives estimated rate ratios for COVID-19 hospitalization and death by race/ethnicity relative to white, non-Hispanic persons in the US. The highest risks of hospitalization and death were observed among American Indian or Alaska native persons (RR = 3.7 for hospitalization and 2.4 for death) and Hispanic or Latino persons (RR = 3.2 for hospitalization and 2.3 for death). These differences in risk among ethnic groups may be attributed to differences in underlying factors that are correlated with race/ethnicity including socioeconomic status, access to health care, and occupation-related virus exposure.[37]

Risk of severe or fatal COVID-19 disease is higher among persons who are current or former smokers, have lower socioeconomic status, have no or public insurance, or live in neighborhoods with higher rates of limited English proficiency.[38,40,41,42] The CDC has also recognized other socio-demographic groups who may need to take extra precautions against COVID-19 due to increased risk for severe illness: pregnant women; breastfeeding mothers; people with disabilities or developmental/behavioral disorders; people living in rural

communities, nursing homes, long-term care facilities, or prisons; people experiencing homelessness; and newly resettled refugee populations.[43]

Risk for severe or fatal COVID-19 disease also increases with the presence of chronic medical conditions, including obesity, respiratory diseases (e.g., COPD or asthma), cardiovascular disease, diabetes, cancer, liver disease, neurological diseases (e.g., stroke or dementia), chronic kidney disease, sickle cell disease, autoimmune conditions and immunosuppression, or higher scores on the WHO Clinical Progression Scale and Charlson Comorbidity Index.[38,39,40,41,42] Table 35 shows the estimated hazard ratios of COVID-19 mortality associated with these chronic conditions and socio-demographics from a cohort study of 17 million adults in England.[41]

Table 35. Hazard Ratios and 95% Confidence Intervals for COVID-19-related Death[41]

		COVID-19 death Hazard Ratio	
Characteristic	**Category**	**Adjusted for age and sex**	**Fully adjusted**
Age	18-39	0.05 (0.04-0.07)	0.06 (0.04-0.08)
	40-49	0.28 (0.23-0.33)	0.30 (0.25 - 0.36)
	50-59	1.00 (ref)	1.00 (ref)
	60-69	2.79 (2.52-3.10)	2.40 (2.16-2.66)
	70-79	8.62 (7.84-9.46)	6.07 (5.51-6.69)
	80+	38.29 (35.02-41.87)	20.60 (18.70-22.68)
Sex	Female	1.00 (ref)	1.00 (ref)
	Male	1.78 (1.71-1.85)	1.59 (1.53-1.65)
BMI (kg/m^2)	Not obese	1.00 (ref)	1.00 (ref)
	30-34.9 (obese class I)	1.23 (1.17–1.30)	1.05 (1.00–1.11)
	35-39.9 (obese class II)	1.81 (1.68–1.95)	1.40 (1.30–1.52)
	40+ (obese class III)	2.66 (2.39–2.95)	1.92 (1.72–2.13)
Smoking	Never	1.00 (ref)	1.00 (ref)
	Former	1.43 (1.37–1.49)	1.19 (1.14–1.24)
	Current	1.14 (1.05–1.23)	0.89 (0.82–0.97)
Ethnicity[a]	White	1.00 (ref)	1.00 (ref)
	Mixed	1.62 (1.26–2.08)	1.43 (1.11–1.84)
	South Asian	1.69 (1.54–1.84)	1.45 (1.32–1.58)
	Black	1.88 (1.65–2.14)	1.48 (1.29–1.69)
	Other	1.37 (1.13–1.65)	1.33 (1.10–1.61)
IMD quintile[e]	1 (least deprived)	1.00 (ref)	1.00 (ref)
	2	1.16 (1.08-1.23)	1.12 (1.05–1.19)
	3	1.31 (1.23–1.40)	1.22 (1.15–1.30)
	4	1.69 (1.59–1.79)	1.51 (1.42–1.61)
	5 (most deprived)	2.11 (1.98–2.25)	1.79 (1.68–1.91)
Blood pressure	Normal	1.00 (ref)	1.00 (ref)
	High BP or diagnosed hypertension	1.09 (1.05–1.14)	0.89 (0.85–0.93)
Respiratory disease excluding asthma		1.95 (1.86–2.04)	1.63 (1.55–1.71)
Asthma[b] (vs. none)	With no recent OCS use	1.13 (1.07–1.20)	0.99 (0.93–1.05)
	With recent OCS use	1.55 (1.39–1.73)	1.13 (1.01–1.26)

Table 35. Hazard Ratios and 95% Confidence Intervals for COVID-19-related Death[41]

		COVID-19 death Hazard Ratio	
Characteristic	**Category**	**Adjusted for age and sex**	**Fully adjusted**
Chronic heart disease		1.57 (1.51–1.64)	1.17 (1.12–1.22)
Diabetes[c] (vs. none)	With HbA1c < 58 mmol/mol	1.58 (1.51–1.66)	1.31 (1.24–1.37)
	With HbA1c ≥ 58 mmol/mol	2.61 (2.46–2.77)	1.95 (1.83–2.08)
	With no recent HbA1c measure	2.27 (2.06–2.50)	1.90 (1.72–2.09)
Cancer (non-hematological, vs. none)	Diagnosed <1 year ago	1.81 (1.58–2.07)	1.72 (1.50–1.96)
	Diagnosed 1-4.9 years ago	1.20 (1.10–1.32)	1.15 (1.05–1.27)
	Diagnosed ≥ 5 years ago	0.99 (0.93–1.06)	0.96 (0.91–1.03)
Hematological malignancy (vs. none)	Diagnosed <1 year ago	3.02 (2.24–4.08)	2.80 (2.08–3.78)
	Diagnosed 1-4.9 years ago	2.56 (2.14–3.06)	2.46 (2.06–2.95)
	Diagnosed ≥ 5 years ago	1.70 (1.46–1.98)	1.61 (1.39–1.87)
Reduced kidney function[d] (vs. none)	eGFR 30-60	1.56 (1.49–1.63)	1.33 (1.28–1.40)
	eGFR < 30	3.48 (3.23–3.75)	2.52 (2.33–2.72)
Liver disease		2.39 (2.06–2.77)	1.75 (1.51–2.03)
Stroke or dementia		2.57 (2.46–2.70)	2.16 (2.06–2.27)
Other neurological disease		3.08 (2.85–3.33)	2.58 (2.38–2.79)
Organ transplant		6.00 (4.73–7.61)	3.53 (2.77–4.49)
Asplenia		1.62 (1.19–2.21)	1.34 (0.98–1.83)
Rheumatoid arthritis, lupus, or psoriasis		1.30 (1.21–1.38)	1.19 (1.11–1.27)
Other immunosuppressive condition		2.75 (2.10–3.62)	2.21 (1.68–2.90)

a. Ethnicity hazard ratios were estimated from a model restricted to those with recorded ethnicity.
b. For OCS use, 'recent' refers to during the year before baseline.
c. Classification by HbA1c is based on measurements within 15 months of baseline.
d. eGFR is measured in ml min−1 per 1.73 m^2 and taken from the most recent serum creatinine measurement.
e. Index of Multiple Deprivation
Models were adjusted for age using a four-knot cubic spline for age, except for estimation of age-group hazard ratios. Ref, reference group; 95% CI, 95% confidence interval.

The main existing treatment options:

Through 28 February 2021, other COVID-19 vaccines were authorized and recommended for use in the United States including vaccines from Moderna (NCT04470427), and Johnson & Johnson/Janssen (NCT04505722). Others may subsequently be approved.

Natural history of the indicated condition in the untreated population, including mortality and morbidity:

Symptoms of COVID-19

The clinical manifestations of COVID-19 vary widely, from asymptomatic infection in 17-20%,[44,45] to critical illness and death. The most common symptoms of COVID-19 are fever, cough, and shortness of breath (Table 36).[46]

Table 36. Signs and symptoms among 291 pediatric (age <18 years) and 10,944 adult (age 18–64 years) patients[a] with laboratory confirmed COVID-19 — United States, 12 February– 2April 2020[46]

	No. (%) with sign/symptom	
Sign/Symptom	**Pediatric**	**Adult**
Fever, cough, or shortness of breath[b]	213 (73)	10,167 (93)
Fever[d]	163 (56)	7,794 (71)
Cough	158 (54)	8,775 (80)
Shortness of breath	39 (13)	4,674 (43)
Myalgia	66 (23)	6,713 (61)
Runny nose[c]	21 (7.2)	757 (6.9)
Sore throat	71 (24)	3,795 (35)
Headache	81 (28)	6,335 (58)
Nausea/Vomiting	31 (11)	1,746 (16)
Abdominal pain[d]	17 (5.8)	1,329 (12)
Diarrhea	37 (13)	3,353 (31)

a. Cases were included in the denominator if they had a known symptom status for fever, cough, shortness of breath, nausea/vomiting, and diarrhea. Total number of patients by age group: <18 years (N = 2,572), 18–64 years (N = 113,985).
b. Includes all cases with one or more of these symptoms.
c. Runny nose and abdominal pain were less frequently completed than other symptoms; therefore, percentages with these symptoms are likely underestimates.
d. Patients were included if they had information for either measured or subjective fever variables and were considered to have a fever if "yes" was indicated for either variable.

Progression and Timeline of Mild to Moderate Disease

Mild to moderate disease is defined as the absence of viral pneumonia and hypoxia. For those who develop symptoms, the incubation period is usually 4 to 5 days, with 97.5% experiencing symptoms within 11 days of exposure.[47,48] Those with mild COVID-19 recover at home with supportive care and guidance to self-isolate. Those with moderate disease are monitored at home and are sometimes recommended to be hospitalized if conditions worsen.[48] Data on rates of re-infection are limited but variants that are not neutralized by immune antisera, such as the recent South African variant, may lead to increased risk of re-infection in the future.[47]

Progression and Timeline of Severe Disease Requiring Hospitalization

Those with severe disease will require hospitalization to manage their illness. Based on data that have been systematically collected for the US by the CDC between 01 August 2020 and 02 March 2021, there were 1,814,606 new hospital admissions for patients with confirmed COVID-19 in the US.[49] For the week ending 28 February 2021, 10 patients per 100,000 population were hospitalized due to COVID-19 in 22 countries of the EU/EEA with available data.[50]

The most common symptoms in patients are fever (42-80%), shortness of breath (35-71%), fatigue (33-62%), cough (77-84%), chills (63%), myalgias (63%), headache (59%), and diarrhea (33%).[51,52,53,54] Approximately 17% to 40% of those hospitalized with COVID-19

experience severe symptoms necessitating intensive care.[23,28,51] More than 75% of patients hospitalized with COVID-19 require supplemental- oxygen.[55]

Studies early in the pandemic demonstrated that time from onset of illness to ARDS was 8-12 -days and time from onset of illness to ICU admission was 9.5–12 days.[47] In 17 countries of the EU/EEA with available data, 1.8 patients per 100,000 population were in the ICU due to COVID-19 for the week ending 28 February 2021.[50] A recent meta-analysis found that, of patients <19 years of age, 11% went to the ICU, non-invasive ventilation was administered among 12%, and 4% required mechanical ventilation.[45]

Mortality

As of 07 March 2021, there were 522,973 deaths reported in the US for all age groups among 28,771,749 cases (1.8% of cases).[49] As of 28 February 2021 there were 547,267 deaths reported for all age groups in the EU/EEA among 22,527,370 cases (2.4% of cases).[56] As of 7 March 2021, the UK has seen 124,736 deaths from COVID-19 in all age groups among 4,231,166 cases (2.9% of cases).[57] According to a recent meta-analysis of pediatric studies published through October 2020, the mortality for patients <19 years of age is 2%.[45]

Mortality data are also presented from Worldometer, an independent organization that publishes current, reliable COVID-19 statistics online.[17] The mortality of SARS-CoV-2 infection is defined as the cumulative number of deaths among detected cases.

As of 03 March 2021, the overall SARS-CoV-2 mortality for the EU + UK was 677,146 deaths, or 132 per 100,000 people. Reported mortality among EU countries and the UK ranged from 14 to 195 deaths per 100,000 (Table 32). Finland and Cyprus reported the lowest mortality; Czech Republic, Belgium and Slovenia reported the highest.[15]

In the US, as of 03 March 2021, the mortality was 531,652 deaths (160 per 100,000 people). Mortality in the US was similar to that of EU countries Hungary, Portugal, and Italy. [15]

Overall reported mortality among hospitalized COVID-19 patients varies from 12.8% to 26% in the EU and UK. [28,30,58,59] Mortality rates are declining over time, presumably due to an improved understanding of COVID-19 and its management.[58,60]

Complications of COVID-19 and Long-COVID

Complications of COVID-19 include impaired function of the heart, brain, lung, liver, kidney, and coagulation system.[23,25,54] Based on a meta-analysis of 42 studies, the risk of thromboembolism was 21% overall and 31% in the ICU, with the pooled odds of mortality being 74% higher among those who experienced thromboembolism compared to those who did not.[61]

COVID-19 symptoms can persist weeks or months beyond the acute infection.[62,63] The NICE guideline scope published on 30 October 2020 defined “Long COVID” signs and symptoms that continue or develop after acute COVID-19. It includes both ongoing symptomatic COVID-19 (from 4 to 12 weeks) and post-COVID-19 syndrome (12 weeks or more and for which signs and symptoms are not explained by an alternative diagnosis).[64]

A meta analysis of 31 studies among patients between 18 to 49 years of age found that COVID-19 symptoms were experienced for 14 days to 3 months post-infection, including persistent fatigue (39–73%), breathlessness (39–74%), decrease in quality of life (44–69%), impaired pulmonary function, abnormal CT findings including pulmonary fibrosis (39–83%), evidence of peri-/perimyo-/myocarditis (3–26%), changes in microstructural and functional brain integrity with persistent neurological symptoms (55%), increased incidence of psychiatric diagnoses (5.8% versus 2.5–3.4% in controls), and incomplete recovery of olfactory and gustatory dysfunction (33–36%).[65] Children who are infected with COVID-19 are at risk of subsequent multisystem inflammatory syndrome (MIS-C) and often develop a rash following resolution of COVID-19.[66,67,45]

Important co-morbidities:

Important comorbidities in hospitalized COVID-19 patients include hypertension, diabetes, obesity, cardiovascular disease, chronic pulmonary disease or asthma, chronic kidney disease, cancer, and chronic liver disease.[24,25,26,51,54] Prevalence of these conditions have been reported to be lower in mild cases and higher among fatal cases, as shown as shown for European countries in Table 37 below.

Table 37. Preconditions among COVID-19 Patients in EU/EEA and UK, by Severity of Disease. Case-based Data from TESSy Produced 04 March 2021

	EU/EEA, produced on 04 March 2021			
	Mild	**Hosp**	**Severe**	**Fatal**
Total N	1,155,969	214,784	35,468	67,011
Asplenia (%)	0	0	0	0
Asthma (%)	0.5	1.6	1.7	1.6
Cancer, malignancy (%)	2.1	7.2	9.7	9.3
Cardiac disorder, excluding hypertension (%)	6.2	18.4	20.7	24.7
Chronic lung disease, excluding asthma (%)	1.8	4.7	5.3	5.3
Current smoking (%)	0.9	0.3	0.4	0.1
Diabetes (%)	3.3	13.9	18.9	15.6
Haematological disorders (%)	0	0.3	0.1	0.2
HIV/other immune deficiency (%)	0.1	0.9	1	0.8
Hypertension (%)	0.7	3.9	4.4	6.3
Kidney-related condition, renal disease (%)	0.3	2.3	2.2	3.7
Liver-related condition, liver disease (%)	0.2	0.7	0.7	0.6
Neuromuscular disorder, chronic neurological (%)	0.6	2.4	1.6	4.2
Obesity (%)	0.2	0.2	0.4	0.2
Other endocrine disorder, excluding diabetes (%)	0.4	0.2	0.1	0.1
Rheumatic diseases including arthritis (%)	0	0	0	0
Tuberculosis (%)	0	0	0	0
None (%)	82.5	42.8	32.7	27.3

Abbreviation: Hosp = Hospitalized

Table 38 below summarizes comorbidities among US COVID-19 patients in a retrospective cohort study conducted among 629,953 individuals tested for COVID-19 in a large health system in the US Northwest between 01 March and 31 December 2020.[38] The most common comorbidities were similar in the full cohort and among those who tested positive: obesity, hypertension, diabetes, and asthma. Among those hospitalized for COVID-19, a large

number of comorbidities had elevated prevalence compared to the full cohort and those who tested positive: obesity, hypertension, diabetes, kidney disease, congestive heart failure, coronary artery disease, and chronic obstructive pulmonary disease.

Table 38. Comorbidities in individuals tested for COVID-19 in the Providence St. Joseph Health System – States of California, Oregon, and Washington, 01 March–31 December 2020[38]

Comorbidity	Tested (N= 629,953) %	Positive (N= 54,645) %	Hospitalized (N= 8,536) %
Hypertension	23.3	19.8	40.2
Diabetes	9.4	10.9	28.3
Weight			
Underweight	2.1	1.7	3.1
Normal	29.0	23.9	24.3
Overweight	31.7	32.6	30.3
Class 1 Obesity	19.8	22.3	21.2
Class 2 Obesity	9.6	11.1	10.9
Class 3 Obesity	7.7	8.6	10.3
Asthma	6.5	5.3	6.7
Chronic Obstructive Pulmonary Disease	4.0	2.6	8.3
Coronary Artery Disease	5.5	3.6	9.7
Myocardial Infarction	2.2	1.6	5.5
Congestive Heart Failure	5.3	3.9	13.2
Kidney Disease	5.6	5.3	17.2
Liver Disease	3.1	2.5	4.0
Cancer	6.1	3.0	6.3

2.1.2.f. Pharmacological Class Effects

There are 2 vaccines (including BNT162b2) with a mRNA platform authorized for emergency use in multiple US jurisdictions since 11 December 2020. Theoretical concerns in mRNA vaccines have included the risk of the presence of naked extracellular RNA in the body which may lead to edema or coagulation and concerns about aberrant immune responses to the RNA or lipid particles. The immunogenicity and efficacy data from study C4591001 are indicative of the vaccine delivery system's success in transfecting the RNA into the appropriate target cells to stimulate an immune response. The RNA itself cannot integrate into the DNA genome.[68,69] The probability of any sequences from the vaccine RNA being integrated into the human genome by a reverse transcription mediated mechanism is considered remote, no higher than the probability of host RNA sequences being re-inserted into the genome, especially given the small quantity of RNA in the vaccine, the barriers to transfected RNA reaching the nucleus, the non-replicating nature of the vaccine RNA, the limited stability of RNA in a cellular context, and the expected targeting of transfected cells for elimination by T cells elicited by the vaccine antigen expressed from the RNA.

3. PHARMACOVIGILANCE PLAN

3.1. Structure of the Pharmacovigilance Plan

3.1.1. Summary of Ongoing Safety Concerns

Table 39. Ongoing Safety Concerns

Important Identified Risks	Anaphylaxis
	Myocarditis and Pericarditis
Important Potential Risks	Vaccine-associated enhanced disease (VAED) including Vaccine-associated enhanced respiratory disease (VAERD)
Missing Information	Use in pregnancy and lactation
	Vaccine effectiveness
	Use in pediatric individuals <12 years of age

3.1.2. Routine Pharmacovigilance Practices

- Routine pharmacovigilance activities is a critical component of activities relating to the detection, assessment, understanding and prevention of risks. The objective of routine pharmacovigilance is to have processes in place to assure the ongoing and timely collection, processing, follow-up, and analysis of individual AE reports globally, following global safety Standard Operating Procedures and regulatory guidance.

- Pfizer, on behalf of the marketing authorization applicant (MAA), monitors the safety profile of its products, evaluates issues potentially impacting product benefit-risk profiles in a timely manner, and ensures that appropriate communication of relevant information is conveyed in a timely manner to regulatory authorities and other interested parties as appropriate and in accordance with international principles and prevailing regulations.

- Pfizer, on behalf of the MAA, conducts scientific data gathering activities for the detection and evaluation of AEs in order to ensure safety monitoring, which is commensurate with product characteristics.

- Signal detection activities include periodic literature review for the life cycle of the product. This includes reviewing the medical literature for individual case reports that should be entered into the safety database as well as periodic aggregate literature review for broader signal detection.

- Safety signal evaluation requires the collection, analysis and assessment of information to evaluate whether there is a potential causal association between an event and the administration of the product and includes subsequent qualitative or quantitative characterization of the relevant safety risk to determine appropriate pharmacovigilance and risk mitigation actions.

- Routine pharmacovigilance activities will include the use of DCAs. They are intended to facilitate the capture of clinical details about:
  - the nature and severity of COVID-19 illness in individuals who have received the COVID-19 vaccine and is anticipated to provide insight into potential cases of vaccine lack of effect or VAED.
  - potential anaphylactic reactions in individuals who have received the COVID-19 vaccine.
- A web-based AE reporting portal will be available for vaccine providers and recipients, to assist with anticipated high volume of reports (based on expected large target population). The portal will capture key adverse event data in the initial interaction and will provide automated intake into the Pfizer safety database via E2B for safety review.
- At the country level, the Drug Safety Unit performs routine pharmacovigilance activities including the collection of AEs from various sources and the reporting of AEs to the regulatory authority as per local regulatory guidelines.

3.1.3. Action Plan for Safety Issues

Action Plan for Important Identified Risks

Table 40. Action Plan for Important Identified Risk "Myocarditis and Pericarditis"

Actions proposed	• C4591009: A non-interventional post-approval safety study of the Pfizer--BioNTech COVID-19 mRNA vaccine in the United States. • C4591011: Active safety surveillance of the Pfizer-BioNTech COVID-19 vaccine in the US Department of Defense population following Emergency Use Authorization. • C4591012: Post-emergency use authorization active safety surveillance study among individuals in the Veteran's Affairs Health System receiving Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) vaccine.
Objective of proposed actions	• C4591009: To assess the occurrence of safety events of interest, including myocarditis and pericarditis, in the general US population, pregnant women, the immunocompromised and persons with a prior history of COVID-19 within selected data sources participating in the US Sentinel System. • C4591011: To assess whether individuals in the US DoD Military Health System (MHS) experience increased risk of safety events of interest, including myocarditis and pericarditis, following receipt of the Pfizer-BioNTech COVID-19 Vaccine. • C4591012: To assess whether individuals in the US Veteran's Affairs Health System experience increased risk of safety events of interest, including myocarditis and pericarditis, following receipt of the Pfizer-BioNTech COVID-19 Vaccine.
Rationale for proposed actions	• C4591009: Robust surveillance is needed to ensure comprehensive understanding of real-world safety of the Pfizer-BioNTech COVID-19 Vaccine in the general US population and in subcohorts of interest, including pregnant women, immunocompromised individuals and persons with a prior history of COVID-19 infection. • C4591011 and C4591012: Robust surveillance is needed to ensure comprehensive understanding of real-world safety. This surveillance strategy consists of complementary approaches to ensure timely signal identification and evaluation in populations who have received the Pfizer-BioNTech COVID-19 Vaccine under an Emergency Use Authorization (EUA).
Monitoring by the sponsor for safety issue and proposed actions	• C4591009: Post-approval observational studies using real-world data are needed to assess the association between Pfizer-BioNTech COVID-19 Vaccine and safety events of interest, among persons administered the vaccine in both the overall US population and in populations of interest (e.g., pregnant women, the immunocompromised and persons with a prior history of COVID-19 infection). This observational study will capture safety events (based on AESI) including myocarditis and pericarditis, in individuals of any age who received the Pfizer-BioNTech COVID-19 Vaccine since its availability under an EUA using electronic health records and claims data from data partners participating in the Sentinel System. This study, will capture hospitalizations, deaths and serious safety events of interest, including myocarditis and pericarditis, as well as selected pregnancy-related and birth outcomes. • C4591011 and C4591012: 1. The collection of safety data in vaccine recipients is critical to our understanding of the vaccine safety profile and to enable safety signal

Table 40. Action Plan for Important Identified Risk "Myocarditis and Pericarditis"

	detection and, if needed, further risk mitigation during the EUA. In addition to the collection and monitoring of AEs reported voluntarily by healthcare professionals providing the vaccine and by individuals receiving the vaccine, active surveillance studies of the Pfizer-BioNTech COVID-19 Vaccine under EUA are also planned. 2. Active surveillance of large numbers of individuals vaccinated with the Pfizer-BioNTech COVID-19 Vaccine is necessary to confirm the safety profile demonstrated in the clinical study in a broader population under real-world conditions. Pfizer-BioNTech is conducting active surveillance studies of individuals vaccinated with the Pfizer--BioNTech COVID-19 Vaccine under an EUA in populations prioritized in the early stages of the EUA, e.g., active military and elderly, as described in the study protocols C4591011 (study planned) and C4591012 (study ongoing) submitted to FDA on 29 January 2021. The study period is/will be approximately 30 months following availability of vaccine under EUA. The studies capture hospitalizations, deaths and serious safety events of interest, including myocarditis and pericarditis.

Milestones for evaluation and reporting	• C4591009:
	  • Protocol submission: 31 August 2021
	  • Monitoring report submission: 31 October 2022
	  • Interim Analysis submission: 31 October 2023
	  • Final study report submission: 31 October 2025.
	• C4591011:
	  • Interim study reports[a] will be submitted on the following dates based on data collected post-EUA in target populations:
	  – 31 December 2021
	  – 30 June 2022
	  – 31 December 2022
	  • Final study reports submission: 31 December 2023.
	• C4591012
	  • Interim study reports will be submitted on the following dates based on data collected post-EUA in target populations:
	  – 30 June 2021
	  – 31 December 2021
	  – 30 June 2022
	  – 31 December 2022
	  • Final study reports submission: 31 December 2023.

a. FDA was informed (Response to FDA 12 May 2021 - Information Request Regarding Active Surveillance Studies) that the first milestone (Interim Report submission due 30 June 2021) is delayed due to a change in study collaboration; therefore it has been removed from this table.

Table 41. Action Plan for Important Identified Risk "Anaphylaxis"

Actions proposed	• Communication of this important identified risk via label (Sections 4 - *Contraindications*, 5.1 - *Management of Acute Allergic Reactions,* Section 6 - *Adverse reactions* - and 6.2 - *Post Authorization Experience*). • C4591001: Phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals. • C4591009: A non-interventional post-approval safety study of the Pfizer--BioNTech COVID-19 mRNA vaccine in the United States. • C4591011: Active safety surveillance of the Pfizer-BioNTech COVID-19 vaccine in the US Department of Defense population following Emergency Use Authorization. • C4591012: Post-emergency use authorization active safety surveillance study among individuals in the Veteran's Affairs Health System receiving Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) vaccine.
Objective of proposed actions	• Labelling communicates the risk of anaphylaxis. • C4591001: To evaluate the safety, tolerability, immunogenicity, and efficacy of BNT162b2. Further, an unfavorable imbalance between the vaccine and control groups in the frequency of COVID-19 disease, in particular for severe COVID-19 disease, may indicate the occurrence of VAED/VAERD. Surveillance is planned for 2 years following Dose 2. • C4591009: To assess the occurrence of safety events of interest in the general US population, pregnant women, the immunocompromised and persons with a prior history of COVID-19 within selected data sources participating in the US Sentinel System. • C4591011: To assess whether individuals in the US DoD Military Health System (MHS) experience increased risk of safety events of interest, following receipt of the BNT162b2. • C4591012: To assess whether individuals in the US Veteran's Affairs Health System experience increased risk of safety events of interest, following receipt of the BNT162b2.
Rationale for proposed actions	• Labeling communicates to health care provider the risk of anaphylaxis. • C4591001: Long-term monitoring throughout the clinical study for up to 2 years to assess the risk for vaccine-associated enhanced disease. • C4591009: Robust surveillance is needed to ensure comprehensive understanding of real-world safety of the BNT162b2 in the general US population and in subcohorts of interest, including pregnant women, immunocompromised individuals and persons with a prior history of COVID-19 infection. • C4591011 and C4591012: Robust surveillance is needed to ensure comprehensive understanding of real-world safety. This surveillance strategy consists of complementary approaches to ensure timely signal identification and evaluation in populations expected to receive the BNT162b2 under an Emergency Use Authorization (EUA).
Monitoring by the sponsor for safety issue and proposed actions	• C4591001: Safety evaluations will include AESI, including anaphylaxis; these will be collected systemically and monitored throughout the Phase 3 study. • C4591009: Post-approval observational studies using real-world data are needed to assess the association between BNT162b2 and safety events of

Table 41. Action Plan for Important Identified Risk "Anaphylaxis"

	interest, among persons administered the vaccine in both the overall US population and in populations of interest (e.g., pregnant women, the immunocompromised and persons with a prior history of COVID-19 infection). This observational study will capture safety events (based on AESI) including anaphylaxis, in individuals of any age who received the BNT162b2 since its availability under an EUA using electronic health records and claims data from data partners participating in the Sentinel System. This study, will capture hospitalizations, deaths and serious safety events of interest, including anaphylaxis, as well as selected pregnancy-related and birth outcomes. • C4591011 and C4591012: 1. The collection of safety data in vaccine recipients is critical to our understanding of the vaccine safety profile and to enable safety signal detection and, if needed, further risk mitigation during the EUA. In addition to the collection and monitoring of AEs reported voluntarily by healthcare professionals providing the vaccine and by individuals receiving the vaccine, active surveillance studies of the BNT162b2 under EUA are also planned. 2. Active surveillance of large numbers of individuals vaccinated with the BNT162b2 is necessary to confirm the safety profile demonstrated in the clinical study in a broader population under real-world conditions. Pfizer-BioNTech plans to conduct active surveillance studies of individuals vaccinated with the BNT162b2 under an EUA in populations prioritized in the early stages of the EUA, e.g., active military and elderly, as described in the study protocols C4591011 and C4591012 submitted to FDA on 29 January 2021. The study period will be approximately 30 months following availability of vaccine under EUA. The studies will capture hospitalizations, deaths and serious safety events of interest, including anaphylaxis.
Milestones for evaluation and reporting	• C4591001 (ongoing Study): • CSR submission upon regulatory request: at any time • CSR submission 6 months post Dose 2: 31 May 2021 • Final CSR submission with supplemental follow-up: 31 August 2023. • C4591009: • Protocol submission: 31 August 2021 • Monitoring report submission: 31 October 2022 • Interim Analysis submission: 31 October 2023 • Final study report submission: 31 October 2025. • C4591011 • Interim study reports[a] will be submitted on the following dates based on data collected post-EUA in target populations: – 31 December 2021 – 30 June 2022 – 31 December 2022 • Final study reports submission: 31 December 2023. • C4591012 • Interim study reports will be submitted on the following dates based on data collected post-EUA in target populations:

Table 41. Action Plan for Important Identified Risk "Anaphylaxis"

	– 30 June 2021 – 31 December 2021 – 30 June 2022 – 31 December 2022 • Final study reports submission: 31 December 2023.

a. FDA was informed (Response to FDA 12 May 2021 - Information Request Regarding Active Surveillance Studies) that the first milestone (Interim Report submission due 30 June 2021) is delayed due to a change in study collaboration;, therefore, it has been removed from in this table.

Action Plan for Important Potential Risks

Table 42. Action Plan for Important Potential Risk "Vaccine-associated enhanced disease (VAED) including Vaccine-associated enhanced respiratory disease (VAERD)"

Actions proposed	• C4591001: Phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals. • C4591008: HERO Together: A post-Emergency Use Authorization observational cohort study to evaluate the safety of the Pfizer-BioNTech COVID-19 Vaccine in US healthcare workers, their families, and their communities. • C4591009: A non-interventional post-approval safety study of the Pfizer--BioNTech COVID-19 mRNA vaccine in the United States. • C4591011: Active safety surveillance of the Pfizer--BioNTech COVID-19 vaccine in the US Department of Defense population following Emergency Use Authorization. • C4591012: Post-emergency use authorization active safety surveillance study among individuals in the Veteran's Affairs Health System receiving Pfizer--BioNTech Coronavirus Disease 2019 (COVID-19) vaccine.
Objective of proposed actions	• C4591001: to evaluate the safety, tolerability, immunogenicity, and efficacy of BNT162b2. An unfavorable imbalance between the vaccine and control groups in the frequency of COVID-19 disease, in particular for severe COVID-19 disease, may indicate the occurrence of VAED/VAERD. Surveillance is planned for 2 years following Dose 2. • C4591008, C4591009, C4591011, and C4591012: to characterize the real-world incidence of safety events of interest, including events indicative of severe or atypical COVID-19 disease, among individuals vaccinated with the BNT162b2 since EUA.
Rationale for proposed actions	• C4591001: Robust and long-term monitoring throughout the clinical study for up to 2 years to assess the risk for vaccine-associated enhanced disease. • C4591008, C4591009, C4591011 and C4591012: Robust surveillance is needed to ensure comprehensive understanding of real-world safety. This surveillance strategy consists of complementary approaches to ensure timely signal identification and evaluation in populations expected to receive the vaccine in the early stages of an EUA as well as with broader vaccination roll-out.
Monitoring by the sponsor for safety	• C4591001: Protocol prespecified stopping and alert rules were set for detecting enhanced COVID-19.

Table 42. Action Plan for Important Potential Risk "Vaccine-associated enhanced disease (VAED) including Vaccine-associated enhanced respiratory disease (VAERD)"

issue and proposed actions Monitoring by the sponsor for safety issue and proposed actions *(Cont'd)*	Participants in all stages of the study will be monitored for COVID-19 illness including severe COVID-19 from Visit 1 onward. Cases will undergo blinded review to identify whether any features of each case appear unusual, in particular greater severity. Indicators of severity may include accelerated deterioration, need for hospitalization, need for ventilation, or death. The Data Monitoring Committee, supported by an unblinded medical monitor, will look for adverse imbalances between vaccine and control groups in COVID-19 disease outcomes, in particular for cases of severe COVID-19, that may be a signal for vaccine-associated enhanced disease on an ongoing basis and at interim analyses. Stopping rules were set so that enrollment could be paused in the event of an adverse imbalance. Additional safety evaluations will include AESI that could represent symptoms of severe COVID-19 disease; these will be collected systemically and monitored throughout the Phase 3 study. • C4591008, C4591011, C4591012: The collection of safety data in vaccine recipients is critical to our understanding of the vaccine safety profile and to enable efficient safety signal detection and, if needed, further risk mitigation during the EUA. In addition to the collection and monitoring of AEs reported voluntarily by healthcare professionals providing the vaccine and by individuals receiving the vaccine, active surveillance studies of the BNT162b2 under EUA are also planned. Active surveillance of large numbers of individuals vaccinated with the BNT162b2 is necessary to confirm the safety profile demonstrated in the clinical study in a broader population under real-world conditions. Pfizer-BioNTech plans to conduct active surveillance studies of vaccinated individuals in populations prioritized in the early stages of the EUA, e.g., healthcare workers, active military, and elderly, as described in C4591008 protocol submitted to FDA on 28 January 2021; C4591011 protocol submitted to FDA on 29 January 2021 and C4591012 protocol submitted to FDA on 29 January 2021. The study period will be approximately 30 months following availability of vaccine under EUA. The studies will capture hospitalizations, deaths and serious safety events of interest, including severe COVID-19 (which, if associated with vaccination, may indicate VAED/VAERD). • C4591009: Surveillance of large numbers of individuals vaccinated with the BNT162b2 is necessary to confirm the safety profile demonstrated in the clinical study in a broader population under real-world conditions. This study is intended to capture a broader sample of vaccinated individuals of any age in the general US population using large scale data sources.
Milestones for evaluation and reporting	• C4591001 (ongoing Study): • CSR submission upon regulatory request: at any time • CSR submission 6 months post Dose 2: 31 May 2021 • Final CSR submission with supplemental follow-up: 31 August 2023. • Three observational post-authorization safety studies for EUA (C4591008, C4591011, and C4591012): • C4591008 and C4591012: Interim study reports will be submitted on the following dates based on data collected post-EUA in target populations: o 30 June 2021 o 31 December 2021 o 30 June 2022

Table 42. Action Plan for Important Potential Risk "Vaccine-associated enhanced disease (VAED) including Vaccine-associated enhanced respiratory disease (VAERD)"

	○ 31 December 2022 • Final study reports submission: 31 December 2023. • C4591011: Interim study reports[a] will be submitted on the following dates based on data collected post-EUA in target populations: ○ 31 December 2021 ○ 30 June 2022 ○ 31 December 2022 • Final study reports submission: 31 December 2023. • C4591009: • Protocol submission: 31 August 2021 • Monitoring report submission: 31 October 2022 • Interim Analysis submission: 31 October 2023 • Final study report submission: 31 October 2025.

a. FDA was informed (Response to FDA 12 May 2021 - Information Request Regarding Active Surveillance Studies) that the first milestone (Interim Report submission due 30 June 2021) is delayed due to a change in study collaboration;, therefore, it has been removed from in this table.

Action Plan for Missing Information

Table 43. Action Plan for Missing Information "Use in Pregnancy and Lactation"

Actions proposed	• C4591015: A phase 2/3, placebo-controlled, randomized, observer blind study to evaluate the safety, tolerability, and immunogenicity of a SARS-CoV-2 RNA vaccine candidate (BNT162b2) against COVID-19 in healthy pregnant women 18 years of age and older. • C4591009: A non-interventional post-approval safety study of the Pfizer--BioNTech COVID-19 mRNA vaccine in the United States. • C4591011: Active safety surveillance of the Pfizer-BioNTech COVID-19 Vaccine in the US Department of Defense population following Emergency Use Authorization. • C4591022: Pfizer-BioNTech COVID-19 Vaccine exposure during pregnancy: A non-interventional post-approval safety study of pregnancy and infant outcomes in the Organization of Teratology Information Specialists (OTIS)/MotherToBaby Pregnancy Registry.
Objective of proposed actions	• C4591015: To assess safety and immunogenicity of BNT162b2 in pregnant women. In addition, exploratory objectives include: To describe the immune response in infants born to breastfeeding maternal participants vaccinated with prophylactic BNT162b2 during pregnancy. To describe the safety of maternal immunization in infants born to breastfeeding maternal participants vaccinated with prophylactic BNT162b2 during pregnancy. • C4591009[a]: To assess whether pregnant women experience increased risk of safety events of interest following receipt of the BNT162b2. • C4591011[a]: To assess whether sub-cohorts of interest, such as pregnant women, in the MHS experience increased risk of safety events of interest following receipt of the BNT162b2.

Table 43. Action Plan for Missing Information "Use in Pregnancy and Lactation"

	• C4591022[a]: To assess whether pregnant women receiving BNT162b2 experience increased risk of pregnancy and infant safety outcomes, including major congenital malformations, spontaneous abortion, stillbirth, preterm delivery, small for gestational age, and small for age postnatal growth to one year of age.
Rationale for proposed actions	Acquisition of data in an unstudied population with potentially different safety considerations from the time vaccine is available.
Monitoring by the sponsor for safety issue and proposed actions	• C4591015: Monitoring via ongoing clinical study. • C4591009: The collection of safety data in vaccine recipients, including pregnant women, is critical to our understanding of the vaccine safety profile and to enable robust safety signal detection and evaluation and, if needed, further risk mitigation under BLA. • C4591011: 1. The collection of safety data in vaccine recipients is critical to our understanding of the vaccine safety profile and to enable efficient safety signal detection and, if needed, further risk mitigation. Active surveillance studies of the BNT162b2 under EUA are also planned. 2. Active surveillance of large numbers of individuals vaccinated with the BNT162b2 is necessary to confirm the safety profile demonstrated in the clinical study in a broader population under real-world conditions. Pfizer-BioNTech plans to conduct active surveillance studies of individuals vaccinated with the BNT162b2 under an EUA in populations prioritized in the early stages of the EUA, e.g., active military and their family members, as described in C4591011 (protocol submitted to FDA on 29 January 2021). The study period will be approximately 30 months following availability of vaccine under EUA. The study will capture hospitalizations, deaths and serious safety events of interest, including anaphylaxis. • C4591022: This study will monitor rates of pregnancy and infant outcomes in planned and unplanned pregnancies exposed to BNT162b2 using an established pregnancy registry. Women receiving BNT162b2 during pregnancy will be followed from exposure to one-year post-partum. Analyses will be conducted to evaluate if the pregnant women receiving the vaccine during pregnancy experience increased risk of pregnancy and infant outcomes compared with 1) pregnant women who are unvaccinated and 2) pregnant women who have received an influenza or tetanus, diphtheria, and acellular pertussis (Tdap) vaccine during pregnancy.
Milestones for evaluation and reporting	• C4591015: Primary endpoints completion: 30 April 2023. • C4591009: • Protocol submission: 31 August 2021 • Monitoring report submission: 31 October 2022 • Interim Analysis submission: 31 October 2023 • Final study report submission: 31 October 2025. • C4591011: • Interim study reports[b] will be submitted on the following dates based on data collected post-EUA in target populations: o 31 December 2021 o 30 June 2022 o 31 December 2022

Table 43. Action Plan for Missing Information "Use in Pregnancy and Lactation"

	• Final study report submission: 31 December 2023. • C4591022: • Protocol submission: 01 July 2021 • Interim reports submission: o 31 January 2022 o 31 January 2023 o 31 January 2024 o 31 January 2025 • Final study report submission: 01 December 2025

a. Study assesses pregnancy only.
b. FDA was informed (Response to FDA 12 May 2021 - Information Request Regarding Active Surveillance Studies) that the first milestone (Interim Report submission due 30 June 2021) is delayed due to a change in study collaboration; therefore, it has been removed from in this table.

Table 44. Action Plan for Missing Information "Vaccine Effectiveness"

Action proposed	• C4591014: Pfizer-BioNTech COVID-19 BNT162b2 Vaccine Effectiveness Study - Kaiser Permanente Southern California. • WI235284: Determining RSV Burden and Outcomes in Pregnant Women and Older Adults Requiring Hospitalization. COVID-19 Amendment for COVID VE/ Sub-study 6. • WI255886: Avon Community Acquired Pneumonia Surveillance Study: A Pan-pandemic Acute Lower Respiratory Tract Disease Surveillance Study. • BNT162-01 cohort 13: Immunogenicity of Pfizer-BioNTech COVID-19 Vaccine in immunocompromised subjects, including assessment of antibody responses and cell-mediated responses.
Objective of proposed actions	• C4591014: To estimate the effectiveness of 2 doses of BNT162b2 against hospitalization and emergency department admission for acute respiratory illness due to SARS-CoV-2 infection. • WI235284: To estimate the effectiveness of 2 doses of BNT162b2 against hospitalization for acute respiratory illness due to SARS-CoV-2 infection. • WI255886: To estimate the effectiveness of 2 doses of BNT162b2 against hospitalization for acute respiratory illness due to SARS-CoV-2 infection. • BNT-162-01 cohort 13: To assess potentially protective immune responses in immunocompromised adults.
Rationale for proposed actions	• C4591014: To determine the effectiveness of BNT162b2 when administered outside of the clinical setting. • WI235284: To determine the effectiveness of BNT162b2 when administered outside of the clinical setting. • WI255886: To determine the effectiveness of BNT162b2 when administered outside of the clinical setting. • BNT-162-01 cohort 13: To determine whether the BNT162b2 has potential to protect immunocompromised adults.

Table 44. Action Plan for Missing Information "Vaccine Effectiveness"

Monitoring by the sponsor for safety issue and proposed actions	• C4591014: Use of primary and secondary data sources to monitor COVID-19 infection in vaccinated individuals. • WI235284: Use of primary and secondary data sources to monitor COVID-19 infection in vaccinated individuals. • WI255886: Use of primary and secondary data sources to monitor COVID-19 infection in vaccinated individuals. • BNT-162-01 cohort 13: Reactogenicity, AE and SAE assessment.
Milestones for evaluation and reporting	• C4591014: Final CSR submission: 30 June 2023. • WI235284: Final CSR submission: 30 June 2023. • WI255886: Final CSR submission: 30 June 2023. • BNT-162-01 cohort 13: First IA submission: 30 September 2021.

Table 45. Action Plan for Missing Information "Use in Paediatric Individuals <12 Years of Age"

Actions proposed	• C4591001 ≥12 to ≤15 years of age: Phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals[a]. Randomised placebo-controlled study in 2000 participants (1000 active recipients) of 2 doses of BNT162b2 at a 21-day interval. • C4591007 <12 years of age: Phase 1 open label dose-finding study to evaluate safety, tolerability, and immunogenicity and phase 2/3 placebo-controlled, observer- blinded safety, tolerability, and immunogenicity study of a SARS-CoV-2 RNA vaccine candidate against COVID-19 in healthy children <12 years of age. Phase 1: open-label dose finding portion up to 3 age groups (participants ≥5 to <12 years, ≥2 to <5 years, and ≥6 months to <2 years of age) with 16 participants per dose level. Dose finding is being initiated in this study in participants ≥5 to <12 years of age based on the acceptable blinded safety assessment of the 30-µg dose in 12- to 15-year-olds in the C4591001 study. The purpose of Phase 1 is to identify preferred dose level(s) of BNT162b2 from up to 3 different dose levels in each age group. Phase 2/3: Children ≥5 to <12 years of age are randomized 2:1 at selected dose level of BNT162b2 at a 21-day interval (2250 total subjects; 1500 active vaccine). Children 2 to < 5 years and 6 to 23 months of age randomized 2:1 placebo controlled at selected dose level of BNT162b2 at a 21-day interval (1125 total subjects per age group; 750 active vaccine per age group). • C4591009: A non-interventional post-approval safety study of the Pfizer-BioNTech COVID-19 mRNA vaccine in the United States.

Table 45. Action Plan for Missing Information "Use in Paediatric Individuals <12 Years of Age"

Objective of proposed actions	• C4591001 ≥12 to ≤15 years of age: Safety compared to placebo and immune-non-inferiority of neutralizing antibody immune response compared to subjects 16-25 years of age. • C4591007 <12 years of age: Dose selection. Safety compared to placebo and immune-non-inferiority by 3 age cohorts of neutralizing antibody immune response compared to subjects 16-25 years of age. Efficacy if sufficient cases accrue. • C4591009: To assess the occurrence of safety events of interest in a general US population (<12 and ≥12 to ≤15 years of age) within selected data sources participating in the Sentinel System.
Rationale for proposed actions	• C4591001 ≥12 to ≤15 years of age: Need to collect evidence of safety and effectiveness to support immunization in this age group. • C4591007 <12 years of age: Need to collect evidence of safety and effectiveness to support immunization in this age group. • C4591009: Long-term surveillance of large numbers of individuals (<12 and ≥12 to ≤15 years of age) vaccinated with the BNT162b2 is necessary to confirm the safety profile demonstrated in the clinical study in a broader population under real-world conditions.

Monitoring by the sponsor for safety issue and proposed actions	• C4591001 ≥12 to ≤15 years of age:
	  • Electronic diary for reactogenicity 7 days following each dose of vaccine.
	  • Adverse events for one month after second dose.
	  • Serious Adverse Events for 6 months after the second dose.
	  • Related SAEs and related deaths for 24 months after the second dose.
	  • Collection of COVID-19 and MIS-C cases up to 24 months after the second dose.
	• C4591007 <12 years of age:
	  • Electronic diary for reactogenicity 7 days following each dose of vaccine.
	  • Adverse events for one month after second dose.
	  • Serious Adverse Events for 6 months after the second dose.
	  • Related SAEs and related deaths for 24 months after the second dose.
	  • Collection of COVID-19 and MIS-C cases up to 24 months after the second dose.
	• C4591009: < 12 and ≥12 to ≤15 years of age
	  • Longitudinal medical care information on outpatient medication dispensing, vaccine administrations, and inpatient and outpatient diagnoses and procedures in addition to adjudication of select events via medical records.
	  • Incidence rates and comparative incidence rate ratios of safety events of interest (AESIs from FDA's BEST System[70] and CDC's Vaccine Safety Datalink[71] in addition to vaccine-associated enhanced respirator disease).
	  • Study period to start on date that BNT162b2 became available under EUA (December 11, 2020) and will end a minimum of 3 years after this date.
	  • Risk windows will be defined for safety events of interest that have a hypothesized increased risk during specific time periods following vaccination. For other safety events of interest, patients will be followed for a maximum of 1 year.

Table 45. Action Plan for Missing Information "Use in Paediatric Individuals <12 Years of Age"

Milestones for evaluation and reporting	• C4591001 ≥12 to ≤15 years of age:
	  • First report with up to 1-month post dose 2 (safety): 30 April 2021
	  • Further reports:
	  – 6-month post dose 2 (safety): 31 October 2021[b]
	  – 24-month post dose 2 (safety): 30 April 2023[c].
	• C4591007 <12 years of age:
	  • First report with up to 1-month post dose 2 in ≥5 to <12 years of age (safety): 30 September 2021
	  • Further reports:
	  – 6-month post dose 2 (safety): 31 March 2022
	  – 24-month post dose 2 (safety): 30 September 2023.
	• C4591009:
	  • Protocol submission: 31 August 2021
	  • Monitoring report submission: 31 October 2022
	  • Interim Analysis submission: 31 October 2023
	  • Final study report submission: 31 October 2025.

a. Study originally included in the PVP to address the Missing Information "Use in pediatric individuals < 16 years of age".
b. Due date updated from 31 July 2021 because the last subject visit for this group will not be until September 2021.
c. Due updated from 31 January 2023 for the same reason above..

3.1.4. Summary of Actions to be Completed, Including Milestones

Table 46. Summary of Safety Concerns and Action Plans

Safety Concerns	Ongoing/Planned Action	Summary of Objectives	Milestones	Due dates
Myocarditis and Pericarditis	C4591009: A non-interventional post-approval safety study of the Pfizer-BioNTech COVID-19 mRNA vaccine in the United States. *Planned*	To assess the occurrence of safety events of interest, including myocarditis and pericarditis, in the general US population, pregnant women, the immunocompromised and persons with a prior history of COVID-19 within selected data sources participating in the US Sentinel System	• Protocol submission: • Monitoring report submission: • Interim analysis submission: • Final study report submission:	• 31 August 2021 • 31 October 2022 • 31 October 2023 • 31 October 2025
	C4591011: Active safety surveillance of the Pfizer-BioNTech COVID-19 Vaccine in the US Department of Defense population following Emergency Use Authorization *Planned*	To assess whether individuals in the US DoD Military Health System (MHS) experience increased risk of safety events of interest, including myocarditis and pericarditis, following receipt of the Pfizer-BioNTech COVID-19 Vaccine.	• Interim reports submission:[a] • Final study report submission:	• 31 December 2021 30 June 2022 31 December 2022 • 31 December 2023
	C4591012: Post-emergency use authorization active safety surveillance study among individuals in the Veteran's Affairs Health System receiving Pfizer-BioNTech COVID-19 Vaccine. *Ongoing*	To assess whether individuals in the US Veteran's Affairs Health System experience increased risk of safety events of interest, including myocarditis and pericarditis, following receipt of the Pfizer-BioNTech COVID-19 Vaccine	• Interim reports submission: • Final study report submission:	• 30 June 2021 31 December 2021 30 June 2022 31 December 2022 • 31 December 2023
Anaphylaxis	C4591001: Phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals.	To evaluate the safety, tolerability, immunogenicity, and efficacy of BNT162b2. An unfavorable imbalance between the vaccine and control groups in the frequency of COVID-19 disease, in particular for severe COVID-19 disease, may indicate the occurrence	• CSR submission upon regulatory request: • CSR submission 6-month post Dose 2: • Final CSR submission with supplemental follow-up:	• At any time • 31 May 2021 • 31 August 2023

Table 46. Summary of Safety Concerns and Action Plans

Safety Concerns	Ongoing/Planned Action	Summary of Objectives	Milestones	Due dates
	Ongoing	of VAED/VAERD. Surveillance is planned for 2 years following Dose 2.		
	C4591009: A non-interventional post-approval safety study of the Pfizer-BioNTech COVID-19 mRNA Vaccine in the United States. *Planned*	To assess the occurrence of safety events of interest in the general US population, pregnant women, the immunocompromised and persons with a prior history of COVID-19 within selected data sources participating in the US Sentinel System.	• Protocol submission: • Monitoring report submission: • Interim analysis submission: • Final study report submission:	• 31 August 2021 • 31 October 2022 • 31 October 2023 • 31 October 2025
	C4591011: Active safety surveillance of the Pfizer-BioNTech COVID-19 Vaccine in the US Department of Defense population following Emergency Use Authorization. *Planned*	To assess whether individuals in the US DoD Military Health System (MHS) experience increased risk of safety events of interest, following receipt of the BNT162b2.	• Interim reports submission[a]: • Final study report submission:	• 31 December 2021 30 June 2022 31 December 2022 • 31 December 2023
Anaphylaxis *(Cont'd)*	C4591012: Post-emergency use authorization active safety surveillance study among individuals in the Veteran's Affairs Health System receiving Pfizer-BioNTech COVID-19 Vaccine. Ongoing	To assess whether individuals in the US Veteran's Affairs Health System experience increased risk of safety events of interest, following receipt of the BNT162b2.	• Interim reports submission: • Final study report submission:	• 30 June 2021 31 December 2021 30 June 2022 31 December 2022 • 31 December 2023

Table 46. Summary of Safety Concerns and Action Plans

Safety Concerns	Ongoing/Planned Action	Summary of Objectives	Milestones	Due dates
Vaccine-associated enhanced disease (VAED) including vaccine-associated enhanced respiratory disease (VAERD)	C4591001: Phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals. *Ongoing*	To evaluate the safety, tolerability, immunogenicity, and efficacy of BNT162b2. An unfavorable imbalance between the vaccine and control groups in the frequency of COVID-19 disease, in particular for severe COVID-19 disease, may suggest the occurrence of VAED/VAERD. Surveillance is planned for 2 years following Dose 2	• CSR submission upon regulatory request: • CSR submission 6-month post Dose 2: • Final CSR submission with supplemental follow-up:	• Any time • 31 May 2021 • 31 August 2023
	C4591008/C4591012: Post-authorization epidemiological safety studies using active and passive surveillance strategies for safety events, including severe or atypical COVID-19, among individuals receiving Pfizer-BioNTech COVID-19 Vaccine C4591008: *Ongoing* C4591012: *Ongoing*	To characterize the real-world incidence of safety events of interest, including events indicative of severe or atypical COVID-19 disease, among individuals vaccinated with the BNT162b2 since EUA	• Interim reports submission: • Final study report submission:	• 30 June 2021 31 December 2021 30 June 2022 31 December 2022 • 31 December 2023
	C4591011: Active safety surveillance of the Pfizer-BioNTech COVID-19 Vaccine in the US Department of Defense population following Emergency Use Authorization *Planned*	To characterize the real-world incidence of safety events of interest, including events indicative of severe or atypical COVID-19 disease, among individuals vaccinated with the BNT162b2 since EUA	• Interim reports submission[a] • Final study report submission	• 31 December 2021 30 June 2022 31 December 2022 • 31 December 2023
Vaccine-associated enhanced disease (VAED)	C4591009: A non-interventional post-approval safety study of the Pfizer-BioNTech COVID-19 mRNA Vaccine in the United States	To characterize the real-world incidence of safety events of interest, including events indicative of severe or atypical COVID-19 disease,	• Protocol submission: • Monitoring report submission:	• 31 August 2021 • 31 October 2022 • 31 October 2023

Table 46. Summary of Safety Concerns and Action Plans

Safety Concerns	Ongoing/Planned Action	Summary of Objectives	Milestones	Due dates
including vaccine-associated enhanced respiratory disease (VAERD) *(Cont'd)*	*Planned*	among individuals vaccinated with the BNT162b2	• Interim analysis submission: • Final study report submission:	• 31 October 2025
Use in pregnancy and lactation	C4591015: A phase 2/3, placebo-controlled, randomized, observer-blind study to evaluate the safety, tolerability, and immunogenicity of a SARS-CoV-2 RNA vaccine candidate (BNT162b2) against COVID-19 in healthy pregnant women 18 years of age and older. *Ongoing*	To assess safety and immunogenicity of BNT162b2 in pregnant women. Exploratory objectives include: To describe the immune response in infants born to breastfeeding maternal participants vaccinated with prophylactic BNT162b2 during pregnancy. To describe the safety of maternal immunization in infants born to breastfeeding maternal participants vaccinated with prophylactic BNT162b2 during pregnancy.	• Primary endpoints completion:	• 30 April 2023
Use in pregnancy and lactation *(Cont'd)*	C4591011: Active safety surveillance of the Pfizer-BioNTech COVID-19 Vaccine in the United States Department of Defense population following Emergency Use Authorization *Planned*	To assess whether sub-cohorts of interest, such as pregnant women, in the MHS experience increased risk of safety events of interest following receipt of the BNT162b2.	• Interim reports submission:[a] • Final study report submission:	• 31 December 2021 30 June 2022 31 December 2022 • 31 December 2023
	C4591009: A non-interventional post-approval safety study of the Pfizer-BioNTech COVID-19 mRNA Vaccine in the United States. *Planned*	To assess whether pregnant women, experience increased risk of safety events of interest following receipt of the BNT162b2.	• Protocol submission: • Monitoring report submission: • Interim analysis submission: • Final study report submission:	• 31 August 2021 • 31 October 2022 • 31 October 2023 • 31 October 2025

Table 46. Summary of Safety Concerns and Action Plans

Safety Concerns	Ongoing/Planned Action	Summary of Objectives	Milestones	Due dates
	C4591022: Pfizer-BioNTech COVID-19 Vaccine exposure during pregnancy: A non-interventional post-approval safety study of pregnancy and infant outcomes in the Organization of Teratology Information Specialists (OTIS)/MotherToBaby Pregnancy Registry	To assess whether pregnant women receiving BNT162b2 experience increased risk of pregnancy and infant safety outcomes, including major congenital malformations, spontaneous abortion, stillbirth, preterm delivery, small for gestational age, and small for age postnatal growth to one year of age.	• Protocol submission: • Interim reports submission: Final study report submission:	• 01 July 2021 • 31 January 2022 31 January 2023 31 January 2024 31 January 2025 01 December 2025
Vaccine effectiveness	C4591014: Pfizer-BioNTech COVID-19 BNT162b2 Vaccine Effectiveness Study - Kaiser Permanente Southern California. *Planned*	To estimate the effectiveness of 2 doses of BNT162b2 against hospitalization and emergency department admission for acute respiratory illness due to SARS-CoV-2 infection.	• Final CSR submission:	• 30 June 2023
Vaccine effectiveness *(Cont'd)*	WI235284: Determining RSV Burden and Outcomes in Pregnant Women and Older Adults Requiring Hospitalization. Amendment for COVID VE/ Sub-study 6. *Planned*	To estimate the effectiveness of 2 dosed of BNT162b2 against hospitalization for acute respiratory illness due to SARS-CoV-2 infection.	• Final CSR submission:	• 30 June 2023

Table 46. Summary of Safety Concerns and Action Plans

Safety Concerns	Ongoing/Planned Action	Summary of Objectives	Milestones	Due dates
	WI255886: Avon Community Acquired Pneumonia Surveillance Study: A Pan-pandemic Acute Lower Respiratory Tract Disease Surveillance. *Planned*	To estimate the effectiveness of 2 doses of BNT162b2 against hospitalization for acute respiratory illness due to SARS-CoV-2 infection.	• Final CSR submission:	• 30 June 2023
	BNT162-01 cohort 13: Immunogenicity of Pfizer-BioNTech COVID-19 Vaccine in immunocompromised subjects, including assessment of antibody responses and cell-mediated responses. *Ongoing*	To assess potentially protective immune responses in immunocompromised adults.	• First IA submission:	• 30 September 2021

Table 46. Summary of Safety Concerns and Action Plans

Safety Concerns	Ongoing/Planned Action	Summary of Objectives	Milestones	Due dates
Use in pediatric individuals <12 years of age	C4591001 ≥12 to ≤15 years of age: Phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals[b]. *Ongoing*	Safety compared to placebo and immune-non-inferiority of neutralizing antibody immune response compared to subjects 16-25 years of age.	• First report with up to 1-month post dose 2 (safety): • Report 6-month post dose 2 (safety): • Report 24-month post dose 2 (safety):	• 30 April 2021 • 31 October 2021[c] • 30 April 2023[d]
	C4591007 <12 years of age: Phase 1 open label dose-finding study to evaluate safety, tolerability, and immunogenicity and phase 2/3 placebo-controlled, observer blinded safety, tolerability, and immunogenicity, study of a SARS-CoV-2 RNA vaccine candidate against COVID-19 in healthy children <12 years of age. *Ongoing (started in March)*	Dose selection. Safety compared to placebo and immune-non-inferiority by 3 age cohorts of neutralizing antibody immune response compared to subjects 16-25 years of age. Efficacy if sufficient cases accrue.	• First report with up to 1-month post dose 2 (safety) in ≥5 to <12 years of age: • Report 6-month post dose 2 (safety) in ≥5 to <12 years of age: • Report 24-month post dose 2 (safety) in ≥5 to <12 years of age:	• 30 September 2021 • 31 March 2022 • 30 September 2023
	C4591009: A non-interventional post-approval safety study of the Pfizer-BioNTech COVID-19 mRNA vaccine in the United States. *Planned*	To assess the occurrence of safety events of interest in a general US population (< 12 and ≥ 12 to ≤15 years of age) within selected data sources participating in the Sentinel System.	• Protocol submission: • Monitoring report submission: • Interim analysis submission: • Final study report submission:	• 31 August 2021 • 31 October 2022 • 31 October 2023 • 31 October 2025

a. FDA was informed (Response to FDA – 12 May 2021 – Information Request Regarding Active Surveillance Studies) that the first milestone (Interim Report submission due 30 June 2021) is delayed due to a change in study collaboration; therefore, it has been removed from this table.
b. Study originally included in the PVP to address the Missing Information "Use in pediatric individuals < 16 years of age.
c. Due date updated from 31 July 2021 because the last subject visit for this group will not be until September 2021.
d. Due updated from 31 January 2023 for the same reason above.

ANNEX

3.2. Pharmacovigilance Methods

- BNT162b2 Vaccine: BNT162b2 Data Capture Aids:
    - Pfizer-BioNTech COVID-19 Vaccine VAED Data Capture Aid.
    - Pfizer-BioNTech COVID-19 Vaccine Anaphylactic Reaction Data Capture Aid.

3.2.1. List of Studies Included in the Pharmacovigilance Plan

C4591001

C4591007

C4591008

C4591009

C4591011

C4591012

C4591014

C4591015

C4591022

BNT162-01 cohort 13

WI235284

WI255886

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PHARMACOVIGILANCE PLAN FOR

BIOLOGIC LICENSE APPLICATION #125742

OF

COVID-19 mRNA vaccine (nucleoside modified) (BNT162b2, PF-07302048)

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LIST OF ABBREVIATIONS

Abbreviation	Definition of Term
AE	adverse event
AESI	adverse event of special interest
A:G	albumin:globulin
ARDS	acute respiratory distress syndrome
BALB/c	bagg albino
BC	Brighton Collaboration
BEST	biologics effectiveness and safety
BLA	biologics license application
BMI	body mass index
BP	blood pressure
CD4, CD8	cluster of differentiation-4, 8
CDC	Centers for Disease Control and Prevention
CI	confidence interval
COPD	chronic obstructive pulmonary disease
COVID-19	coronavirus disease 2019
CSR	clinical study report
CT	clinical trial
DART	developmental and reproductive toxicology
DCA	data capture aid
DLP	data-lock point
DoD	Department of Defense
ECDC	European Center for Disease Control
EEA	European Economic Area
eGFR	estimated glomerular filtration rate
EU	European Union
EUA	emergency use authorization
FDA	(US) Food and Drug Administration
GLP	good laboratory practice
HbA1c	glycated hemoglobin
HBV	hepatitis b virus
HCV	hepatitis c virus
HIV	human immunodeficiency virus
IA	interim analysis
ICU	intensive care unit
IFN	interferon
IL-4	interleukin-4
IM	intramuscular(ly)
IMD	index of multiple deprivation
IND	investigational new drug
LNP	lipid nanoparticle
MAA	marketing authorization applicant
MedDRA	Medical Dictionary for Regulatory Activities

Abbreviation	Definition of Term
MERS-CoV	Middle East respiratory syndrome–coronavirus
MHS	Military Health System
MIS-C	multisystem inflammatory syndrome in children
MOA	mechanism of action
modRNA	nucleoside-modified messenger ribonucleic acid
mRNA	messenger ribonucleic acid
NDA	new drug application
NHP	nonhuman primate
NICE	National Institute for Health and Care Excellence
OCS	oral corticosteroids
PK	pharmacokinetic
PT	Preferred Term
PVP	pharmacovigilance plan
RBC	red blood cell
RNA	ribonucleic acid
RR	relative risk
SAE	serious adverse event
SARS	severe acute respiratory syndrome
SARS-CoV-1	severe acute respiratory syndrome coronavirus 1
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
siRNA	small-interfering RNA
SMQ	standardised MedDRA query
Tdap	tetanus, diphtheria, and acellular pertussis
TESSy	The European Surveillance System
Th1	T helper cell type 1
Th2	T helper cell type 2
UK	United Kingdom
US	United States
USP	United States pharmacopeia
V8	variant 8
V9	variant 9
VAED	vaccine-associated enhanced disease
VAERD	vaccine-associated enhanced respiratory disease
WBC	white blood cells
WHO	World Health Organization
WOCBP	women of childbearing potential

1. INTRODUCTION

1.1. Product Details

Table 1. Product Details[a]

Product	COVID-19 mRNA Vaccine (nucleoside modified), herein after referred to as BNT162b2 is a nucleoside-modified messenger RNA –(modRNA) encoding the viral spike (S) glycoprotein of severe acute respiratory syndrome coronavirus (SARS-CoV-2).
Brief description of the product	Chemical class: Nucleoside-modRNA formulated in lipid particles. Mechanism of Action: The modRNA in the BNT162b2 is formulated in lipid particles, which enable delivery of the RNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19. Important information about its composition: • The BNT162b2 is supplied as a frozen suspension in multiple dose vials. • Each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. • Each dose of the BNT162b2 contains 30 mcg of a nucleoside-modified messenger RNA (modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2. • Each dose of the BNT162b2 also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose. • The BNT162b2 does not contain preservative. • The vial stoppers are not made with natural rubber latex.
Indication	Proposed: Active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older.
Dosage and route of administration	Proposed: Series of two doses (0.3 mL each) 3 weeks apart, intramuscularly.

a. COVID-19 mRNA vaccine (nucleoside-modified) US Prescribing Information

Data Lock Point / Data cut-off:	16 years and older	13 March 2021 (Pfizer Clinical Database)
		23 October 2020 (BioNTech Clinical Database)
		28 February 2021 (Pfizer Safety Database)
	12 to 15 years older	13 March 2021 (Pfizer Clinical Database)
		28 February 2021 (Pfizer Safety Database)
	Important Identified Risk "Myocarditis and pericarditis"	18 June 2021 (Pfizer Safety Database)

2. SAFETY SPECIFICATION

2.1. Elements of the Safety Specification

2.1.1. Non-Clinical

Nonclinical evaluation of BNT162b2 included pharmacology (mouse immunogenicity and NHP immunogenicity and challenge studies), pharmacokinetic (series of biodistribution, metabolism and pharmacokinetic studies), and toxicity (2 GLP rat repeat-dose toxicity and a GLP DART) studies in vitro and in vivo. No additional toxicity studies are planned for BNT162b2.

Nonclinical studies in mice and NHP for BNT162b2 demonstrated both a strong neutralizing antibody response and a Th1-type $CD4^+$ and an $IFN\gamma^+$ $CD8^+$ T-cell response. The Th1 profile is characterized by a strong IFNγ, but not IL-4, response indicating the absence of a potentially deleterious Th2 immune response and is a pattern favored for vaccine safety and efficacy.[1] Rhesus macaques (Study VR-VRT-10671) that had received two IM immunizations with 100 µg BNT162b2 or saline 21 days apart were challenged with 1.05×10^6 plaque forming units of SARS-CoV-2 (strain USA-WA1/2020), split equally between the intranasal and intratracheal routes.[2] BNT162b2 provided complete protection from the presence of detectable viral RNA in the lungs compared to the saline control with no clinical, radiological or histopathological evidence of vaccine-elicited disease enhancement.

An intravenous rat PK study, using an LNP with the identical lipid composition asBNT162b2, demonstrated that the novel lipid excipients in the LNP formulation, ALC-0315 and ALC-0159, distribute from the plasma to the liver. While there was no detectable excretion of either lipid in the urine, the percent of dose excreted unchanged in feces was ~1% for ALC-0315 and ~50% for ALC-0159. Further studies indicated metabolism played a role in the elimination of ALC-0315. Biodistribution was assessed using luciferase expression as a surrogate reporter formulated likeBNT162b2, with the identical lipid composition. After IM injection of the LNP-formulated RNA encoding luciferase in BALB/c mice, luciferase protein expression was demonstrated at the site of injection 6 hours post dose and expression decreased over time to almost reach background levels after 9 days. Luciferase was detected to a lesser extent in the liver; expression was present at 6 hours after injection and was not detected by 48 hours after injection. After IM administration of a radiolabeled LNP-mRNA formulation containing ALC-0315 and ALC-0159 to rats, the percent of administered dose was also greatest at the injection site. Outside of the injection site, total recovery of radioactivity was greatest in the liver and much lower in the spleen, with very little recovery in the adrenal glands and ovaries. The metabolism of ALC-0315 and ALC-0159 was evaluated in blood, liver microsomes, S9 fractions, and hepatocytes from mice, rats, monkeys, and humans. The in vivo metabolism was examined in rat plasma, urine, feces, and liver samples from the PK study. ALC-0315 and ALC-0159 are metabolized by hydrolytic metabolism of the ester and amide functionalities, respectively, and this hydrolytic metabolism is observed across the species evaluated.

In GLP toxicity studies, two variants of the BNT162b2 candidate were tested, designated "variant 8" and "variant 9" (V8 and V9, respectively). The variants differ only in their codon optimization sequences which are designed to improve antigen expression, otherwise the

amino acid sequences of the encoded antigens are identical. BNT162b2 (V9) was evaluated clinically and submitted for application. Two GLP-compliant repeat-dose toxicity studies were performed in Wistar Han rats; one with each variant. Both studies were 17 days in duration with a 3-week recovery period. A GLP-compliant DART study in Wistar Han rats has also been completed. Safety pharmacology, genotoxicity and carcinogenicity studies have not been conducted, in accordance with the 2005 WHO vaccine guideline.[3]

The IM route of exposure was selected for nonclinical investigations as it is the clinical route of administration. Rats were selected as the toxicology test species as they demonstrated an antigen-specific immune response to the vaccine and are routinely used for regulatory toxicity studies with an extensive historical safety database.

Administration of up to 100 µg BNT162b2 by IM injection to male and female Wistar Han rats once every week, for a total of 3 doses, was tolerated without evidence of systemic toxicity. Expected inflammatory responses to the vaccine were evident such as edema and erythema at the injection sites, transient elevation in body temperature, elevations in WBC count and acute phase reactants, and lower A:G ratios. Injection site reactions were common in all vaccine-administered animals and were greater after boost immunizations. Changes secondary to inflammation included slight and transient reduction in body weights and transient reduction in reticulocytes, platelets and RBC mass parameters. Decreased reticulocytes were reported in rats treated with the licensed LNP-siRNA pharmaceutical Onpattro™ (NDA # 210922) but have not been observed in humans treated with this biotherapeutic[4] suggesting this is a species-specific effect. Decreased platelet counts were noted after repeat administration, but were small in magnitude of change, likely related to inflammation-related platelet activation and consumption, and unassociated with other alterations in hemostasis. Elevated levels of gamma-glutamyl transferase were observed in the first repeat-dose toxicity study with BNT162b2 (V8) without evidence of cholestasis or hepatobiliary injury but was not recapitulated in the second repeat dose-toxicity study with BNT162b2 (V9), the final clinical candidate. All changes in clinical pathology parameters and acute phase proteins were reversed at the end of the recovery phase for BNT162b2, with the exception of low magnitude higher red cell distribution width (consistent with a regenerative erythroid response) and lower A:G ratios (resulting from acute phase response) in animals administered BNT162b2. Macroscopic pathology and organ weight changes were also consistent with immune activation and inflammatory response and included increased size and/or weight of draining iliac lymph nodes and spleen. Vaccine-related microscopic findings at the end of the dosing phase consisted of edema and inflammation in injection sites and surrounding tissues, increased cellularity in the draining iliac lymph nodes, bone marrow and spleen and hepatocyte vacuolation in the liver. Vacuolation of periportal hepatocytes, the only test article-related liver microscopic finding, was not associated with any microscopic evidence of hepatic injury or hepatic functional effects (i.e., liver functional enzymes were not elevated) and may be associated with hepatocyte uptake of the LNP lipids.[5] Microscopic findings at the end of the dosing phase were partially or completely recovered in all animals at the end of the 3-week recovery period for BNT162b2. A robust immune response was elicited to the BNT162b2 antigen.

Administration of BNT162b2 to female rats twice before the start of mating and twice during gestation at the human clinical dose (30 µg) was associated with non-adverse effects (body

weight, food consumption and effects localized to the injection site) after each dose administration. However, there were no effects of BNT162b2 administration on mating performance, fertility, or any ovarian or uterine parameters in the F0 female rats nor on embryo-fetal or postnatal survival, growth, or development in the F1 offspring. An immune response was confirmed in F0 female rats following administration of each vaccine candidate and these responses were also detectable in the F1 offspring (fetuses and pups).

In summary, the nonclinical safety findings related to BNT162b2 administration primarily represent an expected immune reaction to vaccine administration and are clinically manageable or acceptable risks in the intended population. The key safety findings regarding BNT162b2 from nonclinical studies and their relevance to human usage are presented in Table 2. There was no evidence of vaccine-elicited disease enhancement.

Table 2. Key Safety Findings and Relevance to Human Usage

Key Safety findings from Nonclinical Studies[a]	Relevance to Human Usage
Pharmacology	
NHP Challenge Model • No evidence of vaccine-elicited disease enhancement.	• Suggests low risk of vaccine-enhanced disease in humans; being investigated in CTs.
Toxicity	
Injection site reactions: • Injection site reactions were common and reversible or showed signs of reversibility at the end of the 3-week recovery period in nonclinical studies.	• In common with other vaccines, BNT162b2 administration has the potential to generate injection site reactions such as edema and erythema at the injection sites.
Inflammation and immune activation: • Evidence of inflammation or immune activation was common, reversible, and included transiently higher body temperature, higher circulating WBCs, and higher acute phase reactants. Secondarily, transiently lower body weights, reticulocytes, platelets, and RBC mass parameters were observed.	• In common with all vaccines, BNT162b2 administration has the potential to generate inflammation which can lead to increased body temperature, higher circulating WBCs and higher acute phase proteins. • Decreased reticulocytes have not been observed in humans treated with the LNP-siRNA pharmaceutical Onpattro[4], suggesting this finding in rats is a species-specific effect. • BNT162b2 administration has the potential to transiently decrease platelets and RBC mass parameters. These slight decreases are not likely to be clinically meaningful due to their small magnitude.
Developmental and Reproductive Toxicity • No vaccine-related effects on female fertility or the development of fetuses or offspring were observed in a DART study of BNT162b2 in rats.	• No effects are anticipated in WOCBP, pregnant women or their offspring.

a. Safety pharmacology, genotoxicity, and carcinogenicity studies were not conducted, in accordance with 2005 WHO vaccine guideline, as they are generally not considered necessary to support development and licensure of vaccines for infectious diseases.[3] In addition, the components of the vaccine construct are lipids and RNA and are not expected to have carcinogenic or genotoxic potential.

2.1.2. Clinical

2.1.2.a. Limitations of the Human Safety Database

The pivotal study was initially planned to enroll approximately 30,000 participants, which would have a probability of 78% of detecting an AE with a frequency of 0.01% (1/1000) and a probability of 95% of detecting an AE with a frequency of 0.02% (1/500). The protocol was amended to enroll approximately 46,000 participants, which would slightly enhance the ability to detect AEs. However, rarer events might not be detected.

Participants in the pivotal study were initially planned to be followed for up to 24 months in order to assess the potential for late-occurring adverse reactions, such as the theoretical risk of VAED. After completing the final efficacy analysis with vaccine efficacy shown to be 95%, and obtaining regulatory authorization to vaccinate in many countries, Pfizer-BioNTech started to unblind all participants to determine those randomized to placebo so that they could be offered vaccine in accordance with local authorization. To date, most placebo subjects have been unblinded to receive active vaccine at or prior to 6 months after the second dose, therefore, a placebo group for comparison of safety data is only available for up to 6 months post Dose 2.

2.1.2.a.1. Clinical Trial Exposure

Brief Overview of Development

BioNTech is conducting a first-in-human dose level–finding Phase 1/2 study (BNT162-01) in Germany to gather safety and immunogenicity data to enable evaluation of 4 vaccines candidates individually to inform the overall clinical development of a BNT162b2.

BNT162-01 is not conducted under the US IND application but is being conducted under a German Clinical Trial Application.

Four vaccine candidates were evaluated in Study BNT162-01. Based on safety and immunogenicity results from this study, 2 vaccine candidates, BNT162b1 and BNT162b2, were selected for evaluation in Study C4591001, which is a Phase 1/2/3 randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection, and efficacy study in healthy adults (conducted under IND 019736).

Phase 1 of Study C4591001 comprised dose-level–finding evaluations of the 2 selected vaccine candidates; multiple dose levels (some corresponding to those evaluated in Study BNT162-01) were evaluated. Study vaccine was administered using the same 2-dose schedule as in Study BNT162-01 (21 days apart). Dose levels were administered first to an 18- to 55-year age cohort, then to a 65- to 85-year age cohort.

Both vaccine candidate constructs were safe and well tolerated. BNT162b2 at the 30-µg dose level was selected and advanced to the Phase 2/3 expanded cohort and efficacy evaluation primarily because:

- the reactogenicity profile for BNT162b2 was more favorable than BNT162b1 in both younger and older adults with similar immunogenicity results;
- in the NHP challenge study (VR-VTR-10671, see Section 2.1.1), a trend toward earlier clearance of BNT162b2 was observed in the nose.

Phase 2 of the study (for which enrollment has completed) comprised the evaluation of safety and immunogenicity data for the first 360 participants (180 from the active vaccine group and 180 from the placebo group, with each group divided between the younger and older age cohorts) entering the study after completion of Phase 1.

The Phase 3 part of the study (which is ongoing) evaluates the efficacy and safety in all participants (including the first 360 participants from Phase 2). Phase 3 introduced:

- enrollment of participants 16 to 17 years of age to be evaluated with the 18- to 55-year-old cohort,
- enrollment of a 12- to 15-year-old cohort,
- immunogenicity data from the 12- to 15-year-old cohort (Table 3, Table 5, Table 11, Table 13, Table 15, and Table 17),anticipated to bridge to the 16- to 25-year-old cohort.

Participants in the pivotal study were initially planned to be followed for up to 24 months in order to assess the potential for late-occurring adverse reactions, such as the theoretical risk of VAED including VAERD. After completing the final efficacy analysis with vaccine efficacy shown to be 95%, and obtaining regulatory authorisation to vaccinate in many countries, Pfizer-BioNTech started to unblind all participants to determine those participants randomised to placebo so that they could be offered vaccine in accordance with local authorisation. To date, most placebo subjects have been unblinded to receive active vaccine at or prior to 6 months after the second dose, therefore, a placebo group for comparison of safety data is only available for up to 6 months post Dose 2.

The initial efficacy analysis on the 16 years and older population was event-driven, with prespecified interim analyses after accrual of at least 62, 92, and 120 cases and a final analysis at 164 cases.

A further efficacy analysis has been conducted on 12- to ≤15-year-old cohort participants and on 16 years and older participants cohort participants reported by 13 March 2021.

Ongoing BNT162b2 studies at the cut-off of the clinical database (13 March 2021) also include:

- C4591005: *A phase 1/2 study to evaluate the safety, tolerability, and immunogenicity of an RNA vaccine candidate against COVID-19 in healthy Japanese adults.*
  One hundred sixty participants were randomly assigned in a 3:1 ratio to study intervention (candidate vaccine: 120, placebo: 40).

- C4591015: *A phase 2/3 study to evaluate the safety, tolerability, and immunogenicity of SARS-CoV-2 RNA vaccine candidate (BNT162b2) against COVID-19 in healthy pregnant women 18 years of age and older.*
  Approximately 4000 pregnant women at 24 to 34 weeks gestation are being randomized in a 1:1 ratio to vaccine or placebo.

- C4591017: *A phase 3 study to evaluate the safety, tolerability, and immunogenicity of multiple production lots and dose levels of BNT162b2 against COVID-19 in healthy participants.*
  Approximately 340 participants were randomly assigned to each of 3 US lots and to a 20-µg arm and approximately 170 participants were randomly assigned an EU lot, for a total of approximately 1530 randomized participants in 5 study arms.

Clinical Trial Exposure

Population for analysis of CTs data in this US Pharmacovigilance Plan includes the following 2 studies:

- C4591001: *Phase 1/2/3, placebo-controlled, randomized, observer-blind, dose finding, study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals*.

- BNT162-01: *A multi-site, phase I/II, 2-part, dose-escalation trial investigating the safety and immunogenicity of four prophylactic SARS-CoV-2 RNA vaccines against COVID-19 using different dosing regimens in healthy adults.*

Participants 16 years of age and older

At the cut-off date of 13 March 2021, a total of 46,505 participants were vaccinated in the BNT162b2 clinical development program:

- 21,745 participants received 2 doses and 360 received 1 dose of BNT162b2 during the blinded follow-up period; 96 participants from study BNT162-01 received 2 doses of the vaccine.

- 19,647 participants, who originally received placebo, then received 1 dose of BNT162b2 in the Open-Label Follow-up period after unblinding. (none from study BNT162-01).

Exposure to BNT162b2 for participants aged 16 years and older in the 2 ongoing studies by number of doses, and demographic characteristics is shown in Table 3 through Table 21.

In addition, exposure in clinical studies in special populations is provided in Table 22 and Table 23.

Participants 12 to 15 years of age

At the cut-off date of 13 March 2021, a total of 2260 participants were vaccinated in the BNT162b2 clinical development program:

Clinical study exposure data for the 12- to 15 years of age are provided for the ongoing study C4591001 at the cut-off date of 13 March 2021.

In this study

- 1124 participants received 2 doses and 7 received 1 dose of BNT162b2 in the Blinded-Placebo Controlled Follow-up period.

- 49 participants who originally received placebo, then received 1 dose of BNT162b2 in the Open-Label Follow-up period after unblinding.

Exposure to BNT162b2 for participants aged 12- to 15 years of age by number of doses and demographic characteristics is shown in Table 3,Table 5, Table 11, Table 13, Table 15, Table 17. In addition, exposure in clinical studies in special populations is provided in Table 22 and Table 23.

Table 3. Exposure to BNT162b2 by Age Group and Dose (C4591001) – Blinded Placebo-Controlled Follow-up Period

Age Group Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
≥12 years to ≤15 years		
Vaccine 30 µg		
1 Dose	7	7
2 Doses	1124	2248
Total	1131	2255
≥16 years to ≤17 years		
Vaccine 30 µg		
1 Dose	4	4
2 Doses	374	748
Total	378	752
≥18 years to ≤55 years		
Vaccine 10 µg		
2 Doses	12	24
Total	12	24
Vaccine 20 µg		
2 Doses	12	24
Total	12	24
Vaccine 30 µg		
1 Dose	267	267
2 Doses	12438	24876
Total	12705	25143
>55 years to ≤64 years		
Vaccine 30 µg		
1 Dose	67	67
2 Doses	4341	8682
Total	4408	8749
≥65 years to ≤74 years		
Vaccine 10 µg		
2 Doses	12	24
Total	12	24
Vaccine 20 µg		
2 Doses	9	18
Total	9	18
Vaccine 30 µg		
1 Dose	17	17
2 Doses	3624	7248
Total	3641	7265
≥75 years to ≤84 years		

Table 3. Exposure to BNT162b2 by Age Group and Dose (C4591001) – Blinded Placebo-Controlled Follow-up Period

Age Group Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Vaccine 20 µg		
2 Doses	3	6
Total	3	6
Vaccine 30 µg		
1 Dose	3	3
2 Doses	899	1798
Total	902	1801
≥85 years		
Vaccine 30 µg		
1 Dose	2	2
2 Doses	21	42
Total	23	44

Note: 30 µg includes data from phase 1 and phase 2/3.
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(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s912

Table 4. Exposure to BNT162b2 by Age Group and Dose (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

Age Group Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
≥16 years to ≤17 years		
Vaccine 30 µg		
1 Dose	3	3
≥18 years to ≤55 years		
Vaccine 30 µg		
1 Dose	58	58
>55 years to ≤64 years		
Vaccine 30 µg		
1 Dose	17	17
≥65 years to ≤74 years		
Vaccine 30 µg		
1 Dose	8	8
≥75 years to ≤84 years		
Vaccine 30 µg		
1 Dose	1	1

Table 4. Exposure to BNT162b2 by Age Group and Dose (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

Age Group Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
≥85 years		
Vaccine 30 µg		
1 Dose	2	2

Note: 30 µg includes data from phase 1 and phase 2/3.
Note: Subjects who received 2nd Dose of BNT162b2 after unblinding.
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Table 5. Exposure to BNT162b2 by Age Group and Dose (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Age Group Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
≥12 years to ≤15 years[aa]		
Vaccine 30 µg		
1 Dose	30	30
2 Doses	19	38
Total	49	68
≥16 years to ≤17 years		
Vaccine 30 µg		
1 Dose	107	107
2 Doses	186	372
Total	293	479
≥18 years to ≤55 years		
Vaccine 30 µg		
1 Dose	2713	2713
2 Doses	8419	16838
Total	11132	19551
>55 years to ≤64 years		
Vaccine 30 µg		
1 Dose	655	655
2 Doses	3330	6660
Total	3985	7315
≥65 years to ≤74 years		
Vaccine 30 µg		

Table 5. Exposure to BNT162b2 by Age Group and Dose (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Age Group Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
1 Dose	128	128
2 Doses	3286	6572
Total	3414	6700
≥75 years to ≤84 years		
Vaccine 30 µg		
1 Dose	23	23
2 Doses	783	1566
Total	806	1589
≥85 years		
Vaccine 30 µg		
1 Dose	1	1
2 Doses	16	32
Total	17	33

Note: 30 µg includes data from phase 1 and phase 2/3.
a. Includes subjects who became eligible for unblinding at 16 years of age, confirmed to have received placebo originally and then received BNT162b2 post unblinding.
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(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:
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Table 6. Exposure to BNT162b2 by Age Group and Dose (BNT162-01)

Age Group Dose Exposure (Number of Doses Received)	No. of Subjects Exposed to BNT162b2	Total No. of Vaccine Doses
≥18 years to ≤64 years		
Vaccine 1 µg		
1 Dose	1	1
2 Doses	11	22
Total	12	23
Vaccine 3 µg		
1 Dose	0	0
2 Doses	12	24
Total	12	24

Table 6. Exposure to BNT162b2 by Age Group and Dose (BNT162-01)

Age Group Dose Exposure (Number of Doses Received)	No. of Subjects Exposed to BNT162b2	Total No. of Vaccine Doses
Vaccine 10 µg		
1 Dose	1	1
2 Doses	11	22
Total	12	23
Vaccine 20 µg		
1 Dose	0	0
2 Doses	17	34
Total	17	34
Vaccine 30 µg		
1 Dose	0	0
2 Doses	18	36
Total	18	36
≥65 years to ≤74 years		
Vaccine 1 µg		
1 Dose	0	0
2 Doses	0	0
Total	0	0
Vaccine 3 µg		
1 Dose	0	0
2 Doses	0	0
Total	0	0
Vaccine 10 µg		
1 Dose	0	0
2 Doses	5	10
Total	5	10
Vaccine 20 µg		
1 Dose	0	0

Table 6. Exposure to BNT162b2 by Age Group and Dose (BNT162-01)

Age Group Dose Exposure (Number of Doses Received)	No. of Subjects Exposed to BNT162b2	Total No. of Vaccine Doses
2 Doses	6	12
Total	6	12
Vaccine 30 µg		
1 Dose	0	0
2 Doses	6	12
Total	6	12
≥75 years to ≤84 years		
Vaccine 1 µg		
1 Dose	0	0
2 Doses	0	0
Total	0	0
Vaccine 3 µg		
1 Dose	0	0
2 Doses	0	0
Total	0	0
Vaccine 10 µg		
1 Dose	0	0
2 Doses	1	2
Total	1	2
Vaccine 20 µg		
1 Dose	0	0
2 Doses	1	2
Total	1	2
Vaccine 30 µg		
1 Dose	0	0
2 Doses	0	0
Total	0	0

PFIZER CONFIDENTIAL SDTM Creation: 24NOV2020 (15:06) Source Data: adsl Table Generation: 10MAR2021 (11:32) (Cutoff date:23OCT2020, Snapshot Date: 23OCT2020)
Output File: ex_b2_age_dose2 rtf

Table 7. Exposure to BNT162b2 by Dose (Totals) (C4591001) – Blinded Placebo-Controlled Follow-up Period

Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Vaccine 10 µg		
2 Doses	24	48
Total	24	48
Vaccine 20 µg		
2 Doses	24	48
Total	24	48
Vaccine 30 µg		
1 Dose	367	367
2 Doses	22821	45642
Total	23188	46009

Note: 30 µg includes data from phase 1 and phase 2/3.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s922

Table 8. Exposure to BNT162b2 by Dose (Totals) (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Vaccine 30 µg		
1 Dose	89	89

Note: 30 µg includes data from phase 1 and phase 2/3.
Note: Subjects who received 2nd Dose of BNT162b2 after unblinding.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s9223

Table 9. Exposure to BNT162b2 by Dose (Totals) (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Vaccine 30 µg		
1 Dose	3657	3657
2 Doses	16039	32078
Total	19696	35735

Table 9. Exposure to BNT162b2 by Dose (Totals) (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Dose Exposure (Number of Doses Received)	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses

Note: 30 µg includes data from phase 1 and phase 2/3.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2 unblinded/C4591001 PVP BLA/adsl s9222

Table 10. Exposure to BNT162b2 by Dose (Totals) (BNT162-01)

Dose Exposure (Number of Doses Received)	No. of Subjects Exposed to BNT162b2	Total No. of Vaccine Doses
Vaccine 1 µg		
1 Dose	1	1
2 Doses	11	22
Total	12	23
Vaccine 3 µg		
1 Dose	0	0
2 Doses	12	24
Total	12	24
Vaccine 10 µg		
1 Dose	1	1
2 Doses	23	46
Total	24	47
Vaccine 20 µg		
1 Dose	0	0
2 Doses	24	48
Total	24	48
Vaccine 30 µg		
1 Dose	0	0
2 Doses	24	48
Total	24	48

PFIZER CONFIDENTIAL SDTM Creation: 24NOV2020 (15:06) Source Data: adsl Table Generation: 10MAR2021 (11:49) (Cutoff date:23OCT2020, Snapshot Date: 23OCT2020)
Output File: ex_b2_dose.rtf

Table 11. Exposure to BNT162b2 by Dose, Age Group, and Gender (C4591001) – Blinded Placebo-Controlled Follow-up Period

Dose Age Group	Number of Subjects Exposed to BNT162b2		Total Number of Vaccine Doses	
	Male	Female	Male	Female
Vaccine 10 µg				
≥18 years to ≤55 years	5	7	10	14
≥65 years to ≤74 years	2	10	4	20
Total	7	17	14	34
Vaccine 20 µg				
≥18 years to ≤55 years	6	6	12	12
≥65 years to ≤74 years	4	5	8	10
≥75 years to ≤84 years	1	2	2	4
Total	11	13	22	26
Vaccine 30 µg				
≥12 years to ≤15 years	567	564	1128	1127
≥16 years to ≤17 years	187	191	373	379
≥18 years to ≤55 years	6456	6249	12770	12373
>55 years to ≤64 years	2231	2177	4421	4328
≥65 years to ≤74 years	1934	1707	3858	3407
≥75 years to ≤84 years	511	391	1020	781
≥85 years	12	11	23	21
Total	11898	11290	23593	22416

Note: 30 µg includes data from phase 1 and phase 2/3.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s932

Table 12. Exposure to BNT162b2 by Dose, Age Group, and Gender (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

Dose Age Group	Number of Subjects Exposed to BNT162b2		Total Number of Vaccine Doses	
	Male	Female	Male	Female
Vaccine 30 µg				
≥16 years to ≤17 years	0	3	0	3
≥18 years to ≤55 years	24	34	24	34
>55 years to ≤64 years	12	5	12	5
≥65 years to ≤74 years	4	4	4	4

Table 12. Exposure to BNT162b2 by Dose, Age Group, and Gender (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

	Number of Subjects Exposed to BNT162b2		Total Number of Vaccine Doses	
Dose Age Group	Male	Female	Male	Female
≥75 years to ≤84 years	0	1	0	1
≥85 years	1	1	1	1
Total	41	48	41	48

Note: 30 µg includes data from phase 1 and phase 2/3.
Note: Subjects who received 2nd Dose of BNT162b2 after unblinding.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s9323

Table 13. Exposure to BNT162b2 by Dose, Age Group, and Gender (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

	Number of Subjects Exposed to BNT162b2		Total Number of Vaccine Doses	
Dose Age Group	Male	Female	Male	Female
Vaccine 30 µg				
≥12 years to ≤15 years[a]	26	23	36	32
≥16 years to ≤17 years	152	141	250	229
≥18 years to ≤55 years	5424	5708	9450	10101
>55 years to ≤64 years	1973	2012	3602	3713
≥65 years to ≤74 years	1801	1613	3530	3170
≥75 years to ≤84 years	495	311	976	613
≥85 years	13	4	25	8
Total	9884	9812	17869	17866

Note: 30 µg includes data from phase 1 and phase 2/3.
a. Includes subjects who became eligible for unblinding at 16 years of age, confirmed to have received placebo originally and then received BNT162b2 post unblinding.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s932_open

Table 14. Exposure to BNT162b2 by Dose, Age Group, and Gender (BNT162-01)

	No. of Subjects Exposed to BNT162b2		Total No. of Vaccine Doses	
Dose Age Group	**Male**	**Female**	**Male**	**Female**
Vaccine 1 µg				
≥18 years to ≤64 years	7	5	14	9
≥65 years to ≤74 years	0	0	0	0
≥75 years to ≤84 years	0	0	0	0
Total	7	5	14	9
Vaccine 3 µg				
≥18 years to ≤64 years	5	7	10	14
≥65 years to ≤74 years	0	0	0	0
≥75 years to ≤84 years	0	0	0	0
Total	5	7	10	14
Vaccine 10 µg				
≥18 years to ≤64 years	8	10	16	19
≥65 years to ≤74 years	3	2	6	4
≥75 years to ≤84 years	1	0	2	0
Total	12	12	24	23
Vaccine 20 µg				
≥18 years to ≤64 years	7	10	14	20
≥65 years to ≤74 years	1	5	2	10
≥75 years to ≤84 years	0	1	0	2
Total	8	16	16	32
Vaccine 30 µg				
≥18 years to ≤64 years	10	8	20	16
≥65 years to ≤74 years	2	4	4	8
≥75 years to ≤84 years	0	0	0	0
Total	12	12	24	24

PFIZER CONFIDENTIAL SDTM Creation: 24NOV2020 (15:06) Source Data: adsl Table Generation: 10MAR2021 (11:53) (Cutoff date:23OCT2020, Snapshot Date: 23OCT2020)
Output File: ex_b2_age_dose_sex rtf

Table 15. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Blinded Placebo-Controlled Follow-up Period

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
≥12 years to ≤15 years		
Vaccine 30 µg		
Racial origin		
White	971	1937
Black or African American	52	103
Asian	72	143
American Indian or Alaska Native	4	8
Native Hawaiian or other Pacific Islander	3	6
Multiracial	23	46
Not reported	6	12
Total	1131	2255
Ethnic origin		
Hispanic/Latino	132	263
Non-Hispanic/non-Latino	997	1988
Not reported	2	4
Total	1131	2255
≥16 years to ≤17 years		
Vaccine 30 µg		
Racial origin		
White	309	614
Black or African American	30	60
Asian	22	44
American Indian or Alaska Native	4	8
Native Hawaiian or other Pacific Islander	3	6
Multiracial	10	20
Total	378	752
Ethnic origin		
Hispanic/Latino	49	98
Non-Hispanic/non-Latino	329	654
Total	378	752
≥18 years to ≤55 years		
Vaccine 10 µg		
Racial origin		
White	11	22
Asian	1	2
Total	12	24
Ethnic origin		
Hispanic/Latino	1	2
Non-Hispanic/non-Latino	11	22

Table 15. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Blinded Placebo-Controlled Follow-up Period

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Total	12	24
Vaccine 20 µg		
Racial origin		
White	10	20
Black or African American	2	4
Total	12	24
Ethnic origin		
Hispanic/Latino	1	2
Non-Hispanic/non-Latino	11	22
Total	12	24
Vaccine 30 µg		
Racial origin		
White	9923	19637
Black or African American	1400	2764
Asian	683	1358
American Indian or Alaska Native	161	311
Native Hawaiian or other Pacific Islander	40	80
Multiracial	427	851
Not reported	71	142
Total	12705	25143
Ethnic origin		
Hispanic/Latino	4000	7874
Non-Hispanic/non-Latino	8650	17160
Not reported	55	109
Total	12705	25143
>55 years to ≤64 years		
Vaccine 30 µg		
Racial origin		
White	3719	7388
Black or African American	430	849
Asian	135	267
American Indian or Alaska Native	30	58
Native Hawaiian or other Pacific Islander	8	15
Multiracial	76	152
Not reported	10	20
Total	4408	8749
Ethnic origin		
Hispanic/Latino	965	1903
Non-Hispanic/non-Latino	3413	6786

Table 15. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Blinded Placebo-Controlled Follow-up Period

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Not reported	30	60
Total	4408	8749
≥65 years to ≤74 years		
Vaccine 10 µg		
Racial origin		
White	12	24
Total	12	24
Ethnic origin		
Non-Hispanic/non-Latino	12	24
Total	12	24
Vaccine 20 µg		
Racial origin		
White	9	18
Total	9	18
Ethnic origin		
Non-Hispanic/non-Latino	9	18
Total	9	18
Vaccine 30 µg		
Racial origin		
White	3272	6528
Black or African American	219	437
Asian	82	164
American Indian or Alaska Native	22	44
Native Hawaiian or other Pacific Islander	6	12
Multiracial	30	60
Not reported	10	20
Total	3641	7265
Ethnic origin		
Hispanic/Latino	583	1158
Non-Hispanic/non-Latino	3038	6067
Not reported	20	40
Total	3641	7265
≥75 years to ≤84 years		
Vaccine 20 µg		
Racial origin		
White	3	6
Total	3	6
Ethnic origin		
Non-Hispanic/non-Latino	3	6

Table 15. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Blinded Placebo-Controlled Follow-up Period

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Total	3	6
Vaccine 30 µg		
Racial origin		
White	838	1673
Black or African American	22	44
Asian	31	62
American Indian or Alaska Native	3	6
Native Hawaiian or other Pacific Islander	1	2
Multiracial	7	14
Total	902	1801
Ethnic origin		
Hispanic/Latino	107	213
Non-Hispanic/non-Latino	789	1576
Not reported	6	12
Total	902	1801
≥85 years		
Vaccine 30 µg		
Racial origin		
White	20	38
Asian	1	2
American Indian or Alaska Native	1	2
Multiracial	1	2
Total	23	44
Ethnic origin		
Hispanic/Latino	2	4
Non-Hispanic/non-Latino	21	40
Total	23	44

Note: 30 µg includes data from phase 1 and phase 2/3.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s942

Table 16. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
≥16 years to ≤17 years		
Vaccine 30 µg		
Racial origin		
White	3	3
Total	3	3
Ethnic origin		
Non-Hispanic/non-Latino	3	3
Total	3	3
≥18 years to ≤55 years		
Vaccine 30 µg		
Racial origin		
White	46	46
Black or African American	2	2
Asian	2	2
American Indian or Alaska Native	8	8
Total	58	58
Ethnic origin		
Hispanic/Latino	31	31
Non-Hispanic/non-Latino	27	27
Total	58	58
>55 years to ≤64 years		
Vaccine 30 µg		
Racial origin		
White	14	14
Asian	1	1
American Indian or Alaska Native	2	2
Total	17	17
Ethnic origin		
Hispanic/Latino	10	10
Non-Hispanic/non-Latino	7	7
Total	17	17
≥65 years to ≤74 years		
Vaccine 30 µg		
Racial origin		
White	8	8
Total	8	8
Ethnic origin		
Hispanic/Latino	5	5

Table 16. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Non-Hispanic/non-Latino	3	3
Total	8	8
≥75 years to ≤84 years		
Vaccine 30 µg		
Racial origin		
White	1	1
Total	1	1
Ethnic origin		
Non-Hispanic/non-Latino	1	1
Total	1	1
≥85 years		
Vaccine 30 µg		
Racial origin		
White	2	2
Total	2	2
Ethnic origin		
Non-Hispanic/non-Latino	2	2
Total	2	2

Note: 30 µg includes data from phase 1 and phase 2/3.
Note: Subjects who received 2nd Dose of BNT162b2 after unblinding.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s9423

Table 17. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
≥12 years to ≤15 years[aa]		
Vaccine 30 µg		
Racial origin		
White	45	62
Asian	3	5
Multiracial	1	1
Total	49	68

Table 17. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Ethnic origin		
Hispanic/Latino	2	4
Non-Hispanic/non-Latino	47	64
Total	49	68
≥16 years to ≤17 years		
Vaccine 30 µg		
Racial origin		
White	251	410
Black or African American	11	19
Asian	14	25
American Indian or Alaska Native	2	4
Native Hawaiian or other Pacific Islander	1	2
Multiracial	12	16
Not reported	2	3
Total	293	479
Ethnic origin		
Hispanic/Latino	26	43
Non-Hispanic/non-Latino	266	434
Not reported	1	2
Total	293	479
≥18 years to ≤55 years		
Vaccine 30 µg		
Racial origin		
White	8806	15340
Black or African American	1087	1899
Asian	619	1136
American Indian or Alaska Native	128	236
Native Hawaiian or other Pacific Islander	17	32
Multiracial	405	781
Not reported	70	127
Total	11132	19551
Ethnic origin		
Hispanic/Latino	3441	5300
Non-Hispanic/non-Latino	7635	14157
Not reported	56	94
Total	11132	19551
>55 years to ≤64 years		
Vaccine 30 µg		

Table 17. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Racial origin		
White	3416	6271
Black or African American	331	592
Asian	120	227
American Indian or Alaska Native	35	67
Native Hawaiian or other Pacific Islander	4	7
Multiracial	63	120
Not reported	16	31
Total	3985	7315
Ethnic origin		
Hispanic/Latino	901	1560
Non-Hispanic/non-Latino	3067	5724
Not reported	17	31
Total	3985	7315
≥65 years to ≤74 years		
Vaccine 30 µg		
Racial origin		
White	3093	6076
Black or African American	187	360
Asian	78	154
American Indian or Alaska Native	20	39
Native Hawaiian or other Pacific Islander	6	12
Multiracial	22	43
Not reported	8	16
Total	3414	6700
Ethnic origin		
Hispanic/Latino	547	1060
Non-Hispanic/non-Latino	2842	5590
Not reported	25	50
Total	3414	6700
≥75 years to ≤84 years		
Vaccine 30 µg		
Racial origin		
White	752	1483
Black or African American	22	42
Asian	17	34
American Indian or Alaska Native	4	8
Multiracial	6	12
Not reported	5	10

Table 17. Exposure to BNT162b2 by Age Group, Dose, and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Age Group Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Total	806	1589
Ethnic origin		
Hispanic/Latino	89	174
Non-Hispanic/non-Latino	706	1393
Not reported	11	22
Total	806	1589
≥85 years		
Vaccine 30 µg		
Racial origin		
White	15	29
Asian	1	2
Multiracial	1	2
Total	17	33
Ethnic origin		
Non-Hispanic/non-Latino	17	33
Total	17	33

Note: 30 µg includes data from phase 1 and phase 2/3.
a. Includes subjects who became eligible for unblinding at 16 years of age, confirmed to have received placebo originally and then received BNT162b2 post unblinding.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s942_open

Table 18. Exposure to BNT162b2 by Dose and Race/Ethnic Origin (C4591001) – Blinded Placebo-Controlled Follow-up Period

Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Vaccine 10 µg		
Racial origin		
White	23	46
Asian	1	2
Total	24	48
Ethnic origin		
Hispanic/Latino	1	2
Non-Hispanic/non-Latino	23	46
Total	24	48
Vaccine 20 µg		

Table 18. Exposure to BNT162b2 by Dose and Race/Ethnic Origin (C4591001) – Blinded Placebo-Controlled Follow-up Period

Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Racial origin		
White	22	44
Black or African American	2	4
Total	24	48
Ethnic origin		
Hispanic/Latino	1	2
Non-Hispanic/non-Latino	23	46
Total	24	48
Vaccine 30 µg		
Racial origin		
White	19052	37815
Black or African American	2153	4257
Asian	1026	2040
American Indian or Alaska Native	225	437
Native Hawaiian or other Pacific Islander	61	121
Multiracial	574	1145
Not reported	97	194
Total	23188	46009
Ethnic origin		
Hispanic/Latino	5838	11513
Non-Hispanic/non-Latino	17237	34271
Not reported	113	225
Total	23188	46009

Note: 30 µg includes data from phase 1 and phase 2/3.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:47)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s952

Table 19. Exposure to BNT162b2 by Dose and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Vaccine 30 µg		
Racial origin		
White	74	74
Black or African American	2	2
Asian	3	3
American Indian or Alaska Native	10	10

Table 19. Exposure to BNT162b2 by Dose and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2

Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Total	89	89
Ethnic origin		
Hispanic/Latino	46	46
Non-Hispanic/non-Latino	43	43
Total	89	89

Note: 30 µg includes data from phase 1 and phase 2/3.
Note: Subjects who received 2nd Dose of BNT162b2 after unblinding.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:47)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2 unblinded/C4591001 PVP BLA/adsl s9523

Table 20. Exposure to BNT162b2 by Dose and Race/Ethnic Origin (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Dose Race/Ethnic Origin	Number of Subjects Exposed to BNT162b2	Total Number of Vaccine Doses
Vaccine 30 µg		
Racial origin		
White	16378	29671
Black or African American	1638	2912
Asian	852	1583
American Indian or Alaska Native	189	354
Native Hawaiian or other Pacific Islander	28	53
Multiracial	510	975
Not reported	101	187
Total	19696	35735
Ethnic origin		
Hispanic/Latino	5006	8141
Non-Hispanic/non-Latino	14580	27395
Not reported	110	199
Total	19696	35735

Note: 30 µg includes data from phase 1 and phase 2/3.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (12:47)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/adsl_s952_open

Table 21. Exposure to BNT162b2 by Dose and Race/Ethnic Origin (BNT162-01)

Dose Race/Ethnic Origin	No. of Subjects Exposed to BNT162b2	Total No. of Vaccine Doses
Vaccine 1 µg		
Racial Origin		
White	12	23
Total	12	23
Ethnic Origin		
Non-Hispanic/non-Latino	12	23
Total	12	23
Vaccine 3 µg		
Racial Origin		
White	12	24
Total	12	24
Ethnic Origin		
Non-Hispanic/non-Latino	12	24
Total	12	24
Vaccine 10 µg		
Racial Origin		
White	24	47
Total	24	47
Ethnic Origin		
Non-Hispanic/non-Latino	24	47
Total	24	47
Vaccine 20 µg		
Racial Origin		
White	24	48
Total	24	48
Ethnic Origin		
Non-Hispanic/non-Latino	24	48
Total	24	48
Vaccine 30 µg		
Racial Origin		
White	24	48
Total	24	48
Ethnic Origin		
Non-Hispanic/non-Latino	24	48
Total	24	48

Table 21. Exposure to BNT162b2 by Dose and Race/Ethnic Origin (BNT162-01)

Dose Race/Ethnic Origin	No. of Subjects Exposed to BNT162b2	Total No. of Vaccine Doses

Only race, ethnic origins collected on the case report form with a count of at least one in either column are displayed.
PFIZER CONFIDENTIAL SDTM Creation: 24NOV2020 (15:06) Source Data: adsl Table Generation: 10MAR2021 (12:27) (Cutoff date:23OCT2020, Snapshot Date: 23OCT2020)
Output File: ex_b2_dose_race rtf

Table 22. Exposure to BNT162b2 (30 µg) by Special Population (C4591001) – Blinded Placebo-Controlled Follow-up Period

Population	Number of Subjects Exposed to BNT162b2 (30 µg) (N[aa]=23188) n[bb]	Total Number of Vaccine Doses
Subjects with any baseline comorbidity	10371	26487
AIDS/HIV	100	196
Any Malignancy + Metastatic Solid Tumor + Leukemia + Lymphoma	852	1696
Chronic Pulmonary Disease	1901	3774
Renal Disease	140	279
Rheumatic Disease	75	147
Mild Liver Disease + Moderate or Severe Liver Disease	154	302
Cerebrovascular Disease + Peripheral Vascular Disease + Myocardial Infarction + Congestive Heart Failure	651	1298
Dementia	7	14
Diabetes With/Without Chronic Complication	1706	3385
Hemiplegia or Paraplegia	4	8
Peptic Ulcer Disease	63	126
Obese	7689	15262

Note: Comorbidity is based on Charlson Comorbidity Index categories. Participants identified as belonging to these categories were identified by medical history data collected during the study.
Note: 30 µg includes data from phase 1 and phase 2/3.
Note: Hemiplegia or Paraplegia only includes preferred terms Hemiplegia and Paraplegia.
a. N = number of subjects in the specified group.
b. n = Number of subjects reporting at least 1 occurrence of any comorbidity or obese (BMI ≥30 kg/m^2 [≥16 Years of age] or BMI ≥95th percentile [12-15 Years of age]).
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:25) Source Data: admh Table Generation: 27MAR2021 (12:47)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/admh_s953

Table 23. Exposure to BNT162b2 (30 µg) by Special Population (C4591001) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding

Population	Number of Subjects Exposed to BNT162b2 (30 µg) (N[aa]=19696) n[bb]	Total Number of Vaccine Doses
Subjects with any baseline comorbidity	8981	21590
AIDS/HIV	86	161
Any Malignancy + Metastatic Solid Tumor + Leukemia + Lymphoma	734	1406
Chronic Pulmonary Disease	1590	2953
Renal Disease	139	262
Rheumatic Disease	66	122
Mild Liver Disease + Moderate or Severe Liver Disease	102	193
Cerebrovascular Disease + Peripheral Vascular Disease + Myocardial Infarction + Congestive Heart Failure	567	1075
Dementia	9	17
Diabetes With/Without Chronic Complication	1555	2928
Hemiplegia or Paraplegia	4	8
Peptic Ulcer Disease	76	145
Obese	6760	12320

Note: Comorbidity is based on Charlson Comorbidity Index categories. Participants identified as belonging to these categories were identified by medical history data collected during the study.
Note: 30 µg includes data from phase 1 and phase 2/3.
Note: Hemiplegia or Paraplegia only includes preferred terms Hemiplegia and Paraplegia.
a. N = number of subjects in the specified group.
b. n = Number of subjects reporting at least 1 occurrence of any comorbidity or obese (BMI ≥30 kg/m^2 [≥16 Years of age] or BMI ≥95th percentile [12-15 Years of age]).
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:25) Source Data: admh Table Generation: 27MAR2021 (12:47)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_PVP_BLA/admh_s953_open

2.1.2.a.2. Inclusion and Exclusion Criteria

Detailed descriptions of all inclusion and exclusion criteria for clinical studies are provided in the individual CSRs which were filed to IND 019736.

Inclusion criteria

- Healthy participants who are determined by medical history, physical examination (if required), and clinical judgment of the investigator to be eligible for inclusion in the study.

- Healthy participants with pre-existing stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, can be included. In order for the overall Phase 3 study population to be as representative and diverse as possible, the inclusion of participants with known chronic stable infection with HIV, HCV, or HBV was permitted as the study progressed. Specific criteria for these Phase 3 participants can be found in the C4591001 protocol, Section 10.8.

- Phase 2/3 only: Participants who, in the judgment of the investigator, are at higher risk for acquiring COVID-19 (including, but not limited to, use of mass transportation, relevant demographics, front-line essential workers, and others).

- The participants enrolled were 12 years of age and older; the 12- to 15-year-old cohort was included in the protocol in October 2020.

Exclusion criteria

Phase 1 exclusion criteria were stricter than criteria in Phases 2 and 3 of the study. Participants were excluded from the studies according to the general criteria listed below:

- **Previous vaccination with any coronavirus vaccine**

  Reason for exclusion: To avoid confounding the assessment of serological or clinical immune response in the study population.

  Is it considered to be included as missing information? No.

  Rationale: Minimal potential clinical impact on the target population.

- **Previous clinical or microbiological diagnosis of COVID-19**

  Reason for exclusion: Phase 1 excluded participants with a previous clinical or microbiological diagnosis of COVID-19 because these participants may have some degree of protection from subsequent infection by SARS-CoV-2 and therefore would confound the pivotal efficacy endpoint. During Phase 2/3, participants with prior undiagnosed infection were allowed to be enrolled. Screening for SARS-CoV-2 with nucleic acid amplification test by nasal swab or antibodies to non-vaccine SARS-CoV-2

antigen by serology was not conducted before vaccine administration in Phase 2/3, but samples were taken to run these assays after vaccination, thus identifying participants with unidentified prior infection. This group will be assessed to identify whether prior infection affects safety.

Is it considered to be included as missing information? No.

Rationale: Safety in study participants with prior infection will be assessed in the pivotal study.

- **Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination.**

  Reason for exclusion: Immunocompromised participants may have impaired immune responses to vaccines and would therefore limit the ability to demonstrate efficacy, which is the primary pivotal endpoint.

  Is it considered to be included as missing information? No.

  Rationale: Participants with potential immunodeficient status were not specifically included in the study population. However, since the study population is intended to be as representative as possible of the vulnerable population to COVID-19 illness, sub-analyses of immunogenicity data in future studies may provide further understanding of immune responses in this population.

- **Receipt of blood/plasma products or immunoglobulin, from 60 days before study intervention administration or planned receipt throughout the study**

  Reason for exclusion: To avoid confounding the assessment of serological or clinical immune response in the study population.

  Is it considered to be included as missing information? No.

  Rationale: No impact on the safety of the target population.

- **Women who are pregnant or breastfeeding**

  Reason for exclusion: To avoid use in a vulnerable population.

  Is it considered to be included as missing information? Yes.

  Rationale: It is not known if maternal vaccination with BNT162b2 would have unexpected negative consequences to the embryo or fetus.

- **Other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation or, in the investigator's judgment, make the participant inappropriate for the study**

  Reason for exclusion: To avoid misleading results deriving from non-compliance to study procedures.

  Is it considered to be included as missing information? No.

  Rationale: Safety profile of BNT162b2 is not expected to differ in these subjects when properly administered.

2.1.2.a.2.1. Non-Study Post-Authorization Exposure

It is not possible to determine with certainty the number of individuals who received BNT162b2 since it was first authorized for emergency use on 01 December 2020. Estimated worldwide shipped doses may serve as a reasonable indicator of subject exposure by region and countries; the estimated exposure by gender and age group is not available. Cumulatively, through the DLP (28 February 2021) approximately 126,212,580 doses of BNT162b2 were shipped worldwide. The estimated cumulative number of shipped doses of BNT162b2 by region, are summarized in Table 24.

Table 24. Cumulative Estimated Shipped Doses[a] of BNT162b2 by Region Worldwide

Region/Country	Total Number of Shipped Doses	% of Doses
Europe	**51,545,325**	**40.8%**
European Union (27)	36340590	28.8%
European Free Trade Association (3)	513825	0.4%
Switzerland	767520	0.6%
UK	13643175	10.8%
Other Countries	280215	0.2%
Commonwealth of Independent States[b]	0	**0.0%**
North America	**56577885**	**44.8%**
US	54326415	43.0%
Canada	2251470	1.8%
Central and South America	**2965170**	**2.3%**
Asia	**14467830**	**11.5%**
Oceania	**656370**	**0.5%**
Africa	**0**	**0.0%**
Total	**126,212,580**	**100.0%**

a. Data for US are based on Order Management Dashboard, while for the remaining Regions and Countries are based on the Order Book which is the most accurate tracker of shipment data.
b. Includes: Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russia, Tajikistan, Turkmenistan, Ukraine, Uzbekistan;

Method Used to Calculate Exposure

Not applicable.

Exposure

Not applicable.

2.1.2.a.3. Regulatory Actions Related to Safety

There were no withdrawals for safety reasons up to 28 February 2021.

2.1.2.b. Populations Not Studied in the Pre-Approval Phase

There has been limited exposure to BNT162b2 in some special populations and no epidemiologic studies have been conducted in pregnant/lactating women, pediatric participants (<12 years of age), and specific subpopulations that were initially excluded from the BNT162b2 program.

Table 25. Exposure of Special Populations Included or not in Clinical Trial Development Programs

Type of special population	Exposure
Pregnant women	Available data on BNT162b2 administered to pregnant women are insufficient to inform on vaccine-associated risks in pregnancy. In a reproductive and developmental toxicity study, no vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported. Through the cut-off date of 13 March 2021, there were 50 cases (52 events) originating from Study C4591001 in participant 16 years of age and older, and all were unique pregnancies.
Breastfeeding women	Breastfeeding women were not initially included in the BNT162b2 clinical development program. Data are not available to assess the effects of BNT162b2 on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for BNT162b2 and any potential adverse effects on the breastfed child from BNT162b2 or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptible to disease prevented by the vaccine. Through the cut-off date of 13 March 2021, there were no CT cases indicative of exposure during breastfeeding from study C4591001 in participants 16 years of age and older.
Participants with relevant comorbidities: • Participants with hepatic impairment • Participants with renal impairment • Participants with cardiovascular disease • Immunocompromised participants • Participants with a disease severity different from inclusion criteria in CTs	Healthy participants with pre-existing stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included. This allowed enrollment of a proportion of participants with common comorbidities such as cardiovascular diseases including hypertension, chronic pulmonary diseases, asthma, chronic liver disease, BMI >30 kg/m^2, participants with stage 3 or worse chronic kidney disease, and participants with varying disease severity. Participants with potential immunodeficient status were not specifically included in the study population. Please refer to Table 22 and Table 23 for the exposure of special populations.

Table 25. Exposure of Special Populations Included or not in Clinical Trial Development Programs

Type of special population	Exposure
Participants of different racial and/or ethnic origin	Please refer to Table 21 for exposure information by ethnic origin from the studies.
Subpopulations carrying known and relevant polymorphisms	No data available.
Pediatric participants	The safety and effectiveness of BNT162b2 in individuals younger than 16 years of age have not been established. **Participants 16 years of age and older** A total of 671 pediatric participants 16 to 17 years of age received BNT162b2 through the DLP of 13 March 2021: • 378 participants in the blinded-placebo controlled follow-up period (Table 3). • 293 participants in the open-label follow-up period after the unblinding (Table 5). **Participants 12 to 15 years of age** One thousand and hundred eighty (1180) pediatric participants 12 to 15 years of age received BNT162b2 through the cut-off date of 13 March 2021 (Table 3 and Table 5).
Elderly (≥65 years old)	The safety and effectiveness of BNT162b2 in elderly participants was consistent with that seen in younger adult participants. Clinical studies of BNT162b2 included a total of 8846 participants 65 years of age and over; of these, 8827 were from study C4591001, through the cut-off date of 13 March 2021: • 4590 participants in the blinded-placebo controlled follow-up period (Table 3) • 4237 participants in the open-label follow-up period after unblinding (Table 5). Nineteen (19) participants 65 years of age and over were from study BNT162-01 study through the cut-off date of 23 October 2020 (Table 6).

Abbreviations: EUA = emergency use authorization; BMI = body mass index; COVID-19 = coronavirus disease 2019; CT = clinical trial

2.1.2.c. Adverse Events / Adverse Reactions

2.1.2.c.1. Identification of Safety Concern in the Initial PVP Submission

2.1.2.c.1.1. Risks not Considered Important for Inclusion in the List of Safety Concerns in the PVP

Not all potential or identified risks for the vaccine are considered to meet the level of importance necessitating inclusion in the list of safety concerns in the PVP:

- Risks with minimal and temporary clinical impact on patients (in relation to the severity of the disease prevented).

- The following reactogenicity events are identified risks not included in the list of safety concerns in the PVP: Injection site pain, Fever, Chills, Fatigue, Headache, Muscle pain, and Joint pain.

- Very rare potential risks for any medicinal treatment, including vaccines which are well known to healthcare professionals are not included in the list of safety concerns.

2.1.2.c.2. Important Identified and Potential Risks and Missing Information

2.1.2.c.2.1. Presentation of Important Identified Risks and Important Potential Risks

Important Identified Risks

Table 26. Myocarditis and Pericarditis

Potential mechanisms, evidence source and strength of evidence	A mechanism of action (MOA) by which the vaccine could cause myocarditis and pericarditis has not been established. Nonclinical studies, protein sequence analyses and animal studies in rats and non-human primates have not identified a MOA. Hypotheses for MOA include an immune stimulated response (including the possibility of molecular mimicry), a general systemic inflammatory response from vaccination or a hypersensitivity response.
Characterisation of the risk	***Participants 16 years of age and older*** Data from the CT dataset Two cases were retrieved with the myocarditis and pericarditis search strategy[a] in the clinical trial dataset through the cut-off date of 18 June 2021. These cases originated from Phase 3 clinical study C4591001 and are summarized below: Myocarditis: There were no cases reporting myocarditis as SAE. Pericarditis (2 cases): Two (2) serious adverse events [PT Pericarditis] were reported, both deemed not related to study treatment by the Investigator. Data from the safety database: Since the first temporary authorization for emergency supply under Regulation 174 in the UK (01 December 2020) and through 18 June 2021, 823 potentially relevant cases (0.3% of the total post-authorization dataset) were retrieved from the Myocarditis and Pericarditis search strategy:[a] 490 cases reported events related to myocarditis and 371 cases reported events related to pericarditis (in 38 of these 823 cases, the subjects developed both myocarditis and pericarditis related events). Myocarditis (490 cases): These 490 cases were individually reviewed and assessed according to Brighton Collaboration (BC) Myocarditis Case Definition and Level of Certainty Classification (version 1.4.2, 30 May 2021), as shown in the Table below:

Brighton Collaboration Level	Number of cases
BC 1	41
BC 2	44

Table 26. Myocarditis and Pericarditis

BC 3	42
BC 4	337
BC 5	26
Total	490

Level 1 indicates a definitive case with the highest level of diagnostic certainty of myocarditis, level 2 indicates a probable case, and level 3 indicates a possible case. Level 4 is defined as "reported event of myocarditis with insufficient evidence to meet the case definition" and Level 5 as not a case of myocarditis.

There were 464 cases meeting BC Level 1 to 4, which are presented below:

Country of incidence: Israel (135), US (78), Germany (76), UK (55), France (21), Italy, Japan (13 each), Austria (10), Greece, Spain (8 each), Sweden (7), Canada, Norway (6 each), Ireland (5); the remaining 23 cases originated from 17 different countries.

Gender: Females (133), Males (325), Unknown (6).

Age (n=443) ranged from 16 to 97 years (mean = 37.2 years, median = 32.0 years).

Reported relevant PTs: Myocarditis (463) and Autoimmune myocarditis (1).

Overall event seriousness and outcome of these 464 cases are summarized below.

	Total Events N = 464 (%)
Serious events	459 (98.9)
Events with Criterion of Hospitalization	337 (72.6)
Distribution of events by Outcome	
Outcome: Death	14 (3.0)
Outcome: Resolved/Resolving	149 (32.1)
Outcome: Not resolved	106 (22.8)
Outcome: Resolved with sequelae	10 (2.2)
Outcome: Unknown/No data	185 (39.9)

Pericarditis (371 cases)

Country of incidence: US (68), France (62), Israel (50), UK (38), Italy (33), Norway, Spain (24 each), Canada (10), Australia (9), Greece (7), Germany (6), Belgium, Denmark, Netherlands, Switzerland (5 each); the remaining 20 cases originated from 11 different countries.

Gender: Females (185), Males (181), Unknown (5).

Age (n=335) ranged from 16 to 92 years (mean = 51.5 years, median = 51.0 years).

Reported relevant PTs: Pericarditis (360) and Pleuropericarditis (12).

Overall event seriousness and outcome of these 371 cases are summarized below.

	Total Events N = 372 (%)
Serious events	370 (99.5)
Events with Criterion of Hospitalization	206 (55.4)
Distribution of events by Outcome	

Table 26. Myocarditis and Pericarditis

Outcome: Death	3 (0.8)
Outcome: Resolved/Resolving	213 (57.3)
Outcome: Not resolved	63 (16.9)
Outcome: Resolved with sequelae	7 (1.9)
Outcome: Unknown/No data	86 (23.1)

Participants 12 to 15 years of age

Data from the CT dataset:
No cases were retrieved reporting Myocarditis and Pericarditis as SAE in the clinical trial dataset through the cut-off date of 18 June 2021.

Data from the safety database:
Through 18 June 2021, 15 potentially relevant cases were retrieved from the Myocarditis and Pericarditis search strategy:[a] 13 cases reported myocarditis and 4 cases reported pericarditis (in 2 of these 15 cases, the subjects developed both myocarditis and pericarditis).

Myocarditis (13 cases)

These 13 cases were individually reviewed and assessed according to Brighton Collaboration (BC) Myocarditis Case Definition and Level of Certainty Classification, as shown in the Table below:

Brighton Collaboration Level	Number of cases
BC 1	0
BC 2	0
BC 3	0
BC 4	11
BC 5	2
Total	13

Level 1 indicates a definitive case with the highest level of diagnostic certainty of myocarditis, level 2 indicates a probable case, and level 3 indicates a possible case. Level 4 is defined as "reported event of myocarditis with insufficient evidence to meet the case definition" and Level 5 as not a case of myocarditis.

No cases met BC levels 1 to 3. There were 11 cases meeting BC Level 4, which are presented below:

Country of incidence: US (10) and Bahrain (1).
Gender: Female (1), Males (10).
Age (n=11) ranged from 12 to 15 years (mean = 13.8 years, median = 14.0 years).
Reported relevant PT: Myocarditis (11).

Overall event seriousness and outcome of these 11 cases are summarized below.

	Total Events N = 11
Serious events	10
Events with Criterion of Hospitalization	9

Table 26. Myocarditis and Pericarditis

	Distribution of events by Outcome
	Outcome: Death: 0
	Outcome: Resolved/Resolving: 3
	Outcome: Not resolved: 4
	Outcome: Resolved with sequelae: 0
	Outcome: Unknown/No data: 4
	Pericarditis (4 cases) Country of incidence: US (4). Gender: Males (4). Age (n=4) ranged from 12 to 15 years (mean = 13.5 years, median = 13.5 years). Reported relevant PT: Pericarditis (4). Overall event seriousness and outcome of these 4 cases are summarized below.
	Total Events N = 4
	Serious events: 3
	Events with Criterion of Hospitalization: 1
	Distribution of events by Outcome
	Outcome: Death: 0
	Outcome: Resolved/Resolving: 1
	Outcome: Not resolved: 1
	Outcome: Resolved with sequelae: 0
	Outcome: Unknown/No data: 2
Risk factors and risk groups	Post-authorization reports have been received for more males than females, over a wide age range and following dose 1 and dose 2 of the vaccine. Evaluation by the US CDC has found reports to be most frequent in adolescent and young adult male patients following the second dose of vaccine.
Preventability	Due to an unknown MOA, preventative measures are not clear for individuals with or without a personal history of myocarditis or pericarditis.
Impact on the risk-benefit balance of the biologic product	The vaccine continues to have a favorable risk benefit balance
Public health impact	Considering the low rates of myocarditis and pericarditis reported following vaccination, balanced with the risk of death and illness (including myocarditis) caused by SARS-CoV-2, the public health impact of post-vaccination myocarditis and pericarditis is minimal.

a. Search criteria: the following PTs were used to retrieve cases of Myocarditis and Pericarditis: Autoimmune myocarditis; Eosinophilic myocarditis; Giant cell myocarditis; Hypersensitivity myocarditis; Immune-mediated myocarditis; Myocarditis; Autoimmune pericarditis, Pericarditis; Pericarditis adhesive; Pericarditis constrictive; Pleuropericarditis.
Please note that CT dataset from the safety dabase includes only cases reporting SAEs.

Table 27. Anaphylaxis

Potential mechanisms, evidence source and strength of evidence	Interaction of an allergen with IgE on basophils and mast cells triggers release of histamine, leukotrienes and other mediators that cause diffuse smooth muscle contraction and vasodilation with plasma leakage. This can manifest clinically with dyspnea, hypotension, swelling (sometimes leading to airway compromise), and rash (including hives).
Characterisation of the risk	Data from the CT database Information pertinent to the anaphylactic reactions observed participants 16 years and older in the ongoing Phase 3 clinical study C4591001 through the cut-off date of 13 March 2021, are summarized below: Five (5) serious events [Acute respiratory failure, Cardiac arrest, Anaphylactic reaction, Anaphylactoid reaction (post bee sting), and Anaphylactic shock] were reported. The Anaphylactoid reaction, occurred to a participant in the age group 16-55 years, was assessed as related to study treatment by the Investigator. The remaining 4 events were deemed not related to study treatment by the Investigator. Data from the safety database: Since the first temporary authorization for emergency supply under Regulation 174 in the UK (01 December 2020) and through 28 February 2021, 1833 potentially relevant cases[b], were retrieved from the Anaphylactic reaction SMQ (Narrow and Broad) search strategy, applying the MedDRA algorithm. These 1833 cases were individually reviewed and assessed according to Brighton Collaboration (BC) definition and level of diagnostic certainty as shown in the Table below:

Brighton Collaboration Level	Number of cases
BC 1	290
BC 2	311
BC 3	10
BC 4	391
BC 5	831
Total	1833

Level 1 indicates a case with the highest level of diagnostic certainty of anaphylaxis, whereas the diagnostic certainty is lowest for Level 3. Level 4 is defined as "reported event of anaphylaxis with insufficient evidence to meet the case definition" and Level 5 as not a case of anaphylaxis.

There were 1002 cases (54.0% of the potentially relevant cases retrieved), 2958 potentially relevant events, from the Anaphylactic reaction SMQ (Broad and Narrow) search strategy, meeting BC Level 1 to 4. Country of incidence: UK (261), US (184), Mexico (99), Italy (82), Germany (67), Spain (38), France (36), Portugal (22), Denmark (20), Finland, Greece (19 each), Sweden (17), Czech Republic, Netherlands (16 each), Belgium, Ireland (13 each), Poland (12), Austria (11); the remaining 57 cases originated from 15 different countries.
Gender: Females (876), Males (106), Unknown (20);
Age (n=961) ranged from 16 to 98 years (mean = 54.8 years, median = 42.5 years);

Overall event seriousness and outcome of these 1002 cases are summarized below.

	Total Events N = 2958 (%)
Serious events	2341 (79.1)
Events with Criterion of Hospitalization	752 (25.4)
Distribution of events by Outcome**	

Table 27. Anaphylaxis

	Outcome[∞]: Death[§] 9 (0.3) Outcome: Resolved/Resolving 1922 (65.0) Outcome: Not resolved 229 (7.7) Outcome: Resolved with sequelae 48 (1.6) Outcome: Unknown/No data 754 (25.5) * For the outcome count, the multiple Lowest Level Terms that code to the same PT within a case are counted and presented individually. Therefore, for selected PTs the total count of the event outcome may exceed the total number of events. ∞ Different clinical outcomes may be reported for an event occurred more than once to the same individual. § There were 4 individuals in the anaphylaxis evaluation who died on the same day they were vaccinated. Although these patients experienced adverse events (9) that are potential symptoms of anaphylaxis, they all had serious underlying medical conditions, and one individual appeared to also have COVID-19 pneumonia, that likely contributed to their deaths. The most frequently reported relevant PTs (≥2%), from the Anaphylactic reaction SMQ (Broad and Narrow) search strategy were: Anaphylactic reaction (435), Dyspnoea (356), Rash (190), Pruritus (175), Erythema (159), Urticaria (133), Cough (115), Respiratory distress, Throat tightness (97 each), Swollen tongue (93), Anaphylactic shock (80), Hypotension (72), Chest discomfort (71), Swelling face (70), Pharyngeal swelling (68), and Lip swelling (64). Conclusion: Evaluation of BC cases Level 1 – 4 did not reveal any significant new safety information. Anaphylaxis is appropriately described in the product labeling as are non-anaphylactic hypersensitivity events. Surveillance will continue.
Risk factors and risk groups	Known hypersensitivity to any components of the vaccine.
Preventability	Prevention of anaphylaxis may not be possible, particularly with the 1st dose of a vaccine; therefore, healthcare professionals administering the vaccine must be vigilant for early signs and symptoms.
Impact on the risk-benefit balance of the biologic product	Anaphylactic reaction in an individual can be impactful (medically important) because it is a potentially life-threatening event requiring medical intervention.
Public health impact	Minimal due to rarity of the event. Although the potential clinical consequences of an anaphylactic reaction are severe, this is a known risk of vaccines to healthcare professionals with negligible public health impact.

b. Search criteria Anaphylactic reaction SMQ (Narrow and Broad, with the MedDRA algorithm applied), with relevant cases assessed according to Brighton Collaboration (BC) criteria.

Important Potential Risks

Table 28. Vaccine-Associated Enhanced Disease (VAED), including Vaccine-Associated Enhanced Respiratory Disease (VAERD)

<table>
<tr><td>Potential mechanisms, evidence source and strength of evidence</td><td>This potential risk is theoretical because it has not been described in association with the BNT162b2 or it has not been reported from any other late phase clinical trial of other human vaccine. Animal models of SARS-CoV-2 infection have not shown evidence of VAED after immunization, whereas cellular immunopathology has been demonstrated after viral challenge in some animal models administered SARS-CoV-1 (murine, ferret and non-human primate models) or MERS-CoV (mice model) vaccines.[1,6] This potential risk has been included based on these animal data with these related betacoronaviruses. Historically, disease enhancement in vaccinated children following infection with natural virus has been observed with an inactivated respiratory syncytial virus vaccine.[7]
Potential mechanisms of enhanced disease may include both T cell-mediated [an immunopathological response favoring T helper cell type 2 (T_H2) over T helper cell type 1 (T_H1)] and antibody-mediated activity (antibody responses with insufficient neutralizing activity leading to formation of immune complexes and activation of complement or allowing for Fc-mediated increase in viral entry to cells).[8]</td></tr>
<tr><td>Characterization of the risk</td><td>Data from the CT database (Participant 16 years and older)

Confirmed Case of Postvaccination Severe COVID-19 – Blinded Placebo-Controlled Follow-up Period - Safety Population (C4591001)
<table><tr><th></th><th colspan="2">BNT162b2 (30 µg) (N[a]=23164)</th><th colspan="2">Placebo (N[a]=23155)</th></tr><tr><th>Timing</th><th>n[b] (%)</th><th>(95% CI[c])</th><th>n[b] (%)</th><th>(95% CI[c])</th></tr><tr><td>PD1 Before Dose 2</td><td>0</td><td>(0.0, 0.0)</td><td>6 (0.0)</td><td>(0.0, 0.0)</td></tr><tr><td>Within 7 days PD1</td><td>0</td><td>(0.0, 0.0)</td><td>0</td><td>(0.0, 0.0)</td></tr><tr><td>PD2</td><td>1 (0.0)</td><td>(0.0, 0.0)</td><td>25 (0.1)</td><td>(0.1, 0.2)</td></tr><tr><td>Within 7 days PD2</td><td>0</td><td>(0.0, 0.0)</td><td>2 (0.0)</td><td>(0.0, 0.0)</td></tr><tr><td>Total[d]</td><td>1 (0.0)</td><td>(0.0, 0.0)</td><td>31 (0.1)</td><td>(0.1, 0.2)</td></tr></table>Note: This table includes subjects from Phase 2/3 only.
Abbreviations: PD1 = post-dose 1; PD2 = post-dose 2.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the specified event.
c. Exact 2-sided CI based on the Clopper and Pearson method.
d. Total is the sum of PD1 and PD2.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adc19ef Table Generation: 27MAR2021 (12:47) (Cutoff date: 13MAR2021, Snapshot Date: 25MAR2021)
Output File: /nda2_unblinded/C4591001_PVP_BLA/adeff_s901

If VAED/VAERD were to occur in vaccinated individuals, it may manifest as a modified and/or more severe clinical presentation of SARS-CoV-2 viral infection upon subsequent natural infection. This may result in individuals assumed to be at lower risk for severe COVID-19 having more severe disease, for individuals at known risk for severe COVID-19 (e.g. older or immunocompromised) having higher rates of fatal outcomes, or for observation of an unfavorable imbalance in severe COVID-19</td></tr>
</table>

Table 28. Vaccine-Associated Enhanced Disease (VAED), including Vaccine-Associated Enhanced Respiratory Disease (VAERD)

cases in vaccinated individuals when compared to those not vaccinated. It is challenging to assess for VAED/VAERD on an individual case basis, given the lack of specific clinical or laboratory markers at this time, rather surveillance for this theoretical risk is best performed at a population level,[9] as noted above. The table above shows a favorable balance of severe COVID-19 cases in participants receiving BNT162b2 versus those receiving placebo, providing reassurance against the potential risk of VAED/VAERD at this time.

Data from the safety database

No post-authorized AE reports have been identified as cases of VAED/VAERD, therefore, there is no observed data at this time. An expected rate of VAED is difficult to establish so a meaningful observed/expected analysis cannot be conducted at this point based on available data. The feasibility of conducting such an analysis will be re-evaluated on an ongoing basis as data on the virus grows and the vaccine safety data continues to accrue.

The search criteria utilised to identify potential cases of VAED for this report includes PTs indicating a lack of effect of the vaccine and PTs potentially indicative of severe or atypical COVID-19[a].

Since the first temporary authorization for emergency supply under Regulation 174 in the UK (01 December 2020) and through 28 February 2021, the following numbers of potentially relevant cases were retrieved:

138 cases [0.25% of the total post-authorization dataset], reporting 317 potentially relevant events.
Seriousness criteria for the total 138 cases: Medically significant (71, of which 8 also serious for disability), Hospitalization required (non-fatal/non-life threatening) (16, of which 1 also serious for disability), Life threatening (13, of which 7 were also serious for hospitalization), Death (38).
Gender: Females (73), Males (57), Unknown (8).
Age (n=132) ranged from 21 to 100 years (mean = 57.2 years, median = 59.5).

Overall event seriousness and outcome are summarized below.

	Total Events N = 317 (%)
Serious events	279 (88.0)
Events with Criterion of Hospitalization	91 (28.7)
Distribution of events by Outcome[a]	
Outcome: Death	62 (19.6)
Outcome: Resolved/Resolving	61 (19.2)
Outcome: Not resolved	90 (28.4)
Outcome: Resolved with sequelae	1 (0.3)
Outcome: Unknown/No data	106 (33.4)

a. For the outcome count, the multiple Lowest Level Terms that code to the same PT within a case are counted and presented individually. Therefore, for selected PTs the total count of the event outcome may exceed the total number of events.

The most frequently reported relevant PTs (≥5 events) were: Drug ineffective (135), Dyspnoea (53), Diarrhoea (30), COVID-19 pneumonia (23), Vomiting (20), Respiratory failure (8), Seizure (7), Hypoxia (6), Abdominal pain, and Pulmonary embolism (5 each).

Table 28. Vaccine-Associated Enhanced Disease (VAED), including Vaccine-Associated Enhanced Respiratory Disease (VAERD)

	Conclusion: VAED may present as severe or unusual clinical manifestations of COVID-19. Overall, there were 37 subjects with suspected COVID-19 and 101 subjects with confirmed COVID 19 following one or both doses of the vaccine; 75 of the 101 cases were severe, resulting in hospitalisation, disability, life threatening consequences or death. None of the 75 cases could be definitively considered as VAED/VAERD. In this review of subjects with COVID-19 following vaccination, based on the current evidence, VAED/VAERVAED remains a theoretical risk for the vaccine. Surveillance will continue.
Risk factors and risk groups	It is postulated that the potential risk may be increased in individuals producing lower neutralizing antibody titers or in those demonstrating waning immunity.[8,9]
Preventability	An effective vaccine against COVID-19 that produces high neutralizing titers and a T_H1 predominant $CD4^+$ T cell response and strong $CD8^+$ T cell response, is expected to mitigate the risk of VAED/VAERD;[1,8] that immune profile is elicited by BNT162b2 in clinical and preclinical studies.[10,11]
Impact on the risk-benefit balance of the biologic product	If there were an unfavorable balance in COVID-19 cases, including severe cases, in the pivotal clinical study between the vaccine and placebo groups, that may signal VAED/VAERD.
Public health impact	The potential risk of VAED/VAERD could have a public health impact if large populations of individuals are affected.

a. Standard Decreased Therapeutic Response Search AND at least 1 of the following PTs Dyspnoea; Tachypnoea; Hypoxia; COVID 19 pneumonia; Respiratory Failure; Acute Respiratory Distress Syndrome; Cardiac Failure; Cardiogenic shock; Acute myocardial infarction; Arrhythmia; Myocarditis; Vomiting; Diarrhoea; Abdominal pain; Jaundice; Acute hepatic failure; Deep vein thrombosis; Pulmonary embolism; Peripheral Ischaemia; Vasculitis; Shock; Acute kidney injury; Renal failure; Altered state of consciousness; Seizure; Encephalopathy; Meningitis; Cerebrovascular accident; Thrombocytopenia; Disseminated intravascular coagulation; Chillblains; Erythema multiforme; Multiple organ dysfunction syndrome; Multisystem inflammatory syndrome in children.
Note: the "Standard Decreased Therapeutic Response" search includes the Lack of efficacy PTs (Drug ineffective/Vaccination failure).

2.1.2.c.2.2. Presentation of Missing Information

Table 29. Use in Pregnancy and Lactation

Evidence source:
The safety profile of the vaccine is not known in pregnant or lactating women due to their exclusion from the pivotal clinical study. There may be pregnant women who choose to be vaccinated despite the lack of safety data. It will be important to follow these women for pregnancy and birth outcomes. The timing of vaccination in a pregnant woman and the subsequent immune response may have varying favorable or unfavorable impacts on the embryo/fetus. The clinical consequences of SARS-CoV-2 infection to the woman and fetus during pregnancy is not yet fully understood and the pregnant woman's baseline health status may affect both the clinical course of her pregnancy and the severity of COVID-19 disease. These factors and the extent to which the pregnant woman may be at risk of exposure to SARS-CoV-2 will influence the benefit risk considerations for use of the vaccine.

Population in need of further characterization:
The lack of data will be communicated in product labeling; one clinical study of the safety and immunogenicity of the BNT162b2 in pregnant women is ongoing (C4591015); 2 non-interventional studies (C4591009 and C4591011) to assess whether sub-cohorts of interest, such as pregnant women, experience increased risk of safety events of interest following receipt of the BNT162b2 are planned (see 3.1.3 – *Action plan for safety issues*).

Data from the Safety Database[a]
Since the first temporary authorization for emergency supply under Regulation 174 in the UK (01 December 2020) and through 28 February 2021, there were 413 cases (1.0 % of the total Post-authorization dataset) reporting use during pregnancy or lactation.

Overall event seriousness and outcome are summarized below:

	Total Events N = 1122 (%)
Serious events	270 (24.1)
Events with Criterion of Hospitalization	14 (1.2)
Distribution of events by Outcome*	
Outcome: Death§	5 (0.4)
Outcome: Resolved/Resolving	205 (18.3)
Outcome: Not resolved	64 (5.7)
Outcome: Resolved with sequelae	4 (0.4)
Outcome: Unknown/No data	849 (75.7)

* For the outcome count, the multiple Lowest Level Terms that code to the same PT within a case are counted and presented individually. Therefore, for selected PTs the total count of the event outcome may exceed the total number of events.
§ Two babies whose mothers were vaccinated during their second trimester of gestation, were pre-maturely delivered 5 days after vaccination and died on their second day of life.

The most frequently reported relevant PTs (≥2%) were: Maternal exposure during pregnancy (187), Product use issue (148), Off label use (147), Exposure via breast milk (133), Exposure during pregnancy (55), Headache (33), Abortion spontaneous (25), Vaccination site pain (24), Pain in extremity, Pyrexia (23 each) and Fatigue (22).

a. Cumulative RMP tables on Missing information are provided as per FDA's request to include a cumulative analysis, from post-authorization experience, of the Important Missing Information identified in the Pharmacovigilance Plan. More detailed information is available in the cumulative analysis of post-authorization data provided as a standalone document with the BLA submission.

Table 30. Vaccine Effectiveness

Evidence source:

Although vaccine efficacy in a controlled clinical study is the objective of the pivotal study, real-world vaccine effectiveness when the BNT162b2 is used in a large and more diverse population is unknown.

Anticipated risk/consequence of missing information:

Efficacy information obtained from clinical study data will be communicated in the product labeling. Three post-authorization effectiveness studies in real-world use are planned: 1 non-interventional study (C4591014) and 2 low-interventional studies (WI235284 and WI255886) to determine the effectiveness of BNT162b2 when administered outside of the clinical setting (see 3.1.3 – *Action plan for safety issues*).

Data from the Safety Database[a]

Since the first temporary authorization for emergency supply under Regulation 174 in the UK (01 December 2020) and through 28 February 2021, there were 1665 cases (3.9% of the total Post-authorization dataset) reporting lack of efficacy.

Overall event seriousness and outcome are summarized below:

	Total Events N = 1665 (%)
Serious events	1644 (98.7)
Events with Criterion of Hospitalization	65 (3.9)
Distribution of events by Outcome*	
Outcome: Death	65 (4.0)
Outcome: Resolved/Resolving	164 (9.8)
Outcome: Not resolved	205 (12.3)
Outcome: Resolved with sequelae	0 (0)
Outcome: Unknown/No data	1231 (73.9)

* For the outcome count, the multiple Lowest Level Terms that code to the same PT within a case are counted and presented individually. Therefore, for selected PTs the total count of the event outcome may exceed the total number of events.

The PT Drug ineffective was reported in 1646 cases, Vaccination failure was reported in 19 cases; the most frequently co-reported PTs (≥2%) were: COVID 19 (1244), SARS-CoV-2 test positive(219), Suspected COVID-19 (161), Pyrexia (134), and Headache (110).

a. Cumulative RMP tables on Missing information are provided as per FDA's request to include a cumulative analysis, from post-authorization experience, of the Important Missing Information identified in the Pharmacovigilance Plan. More detailed information is available in the cumulative analysis of post-authorization data provided as a standalone document with the BLA submission.

Table 31. Use in Paediatric Individuals <12 Years of Age

Evidence source:
BNT162b2 has not been initially studied in pediatric individuals younger than 12 years of age due to their exclusion from the pivotal clinical study.

Paediatric individuals may display different reactogenicity and safety profiles compared to adults, due to lower body mass and differently matured immunological responses.

Population in need of further characterization:
The are no data in individuals less than 12 years of age; a clinical study of the safety, tolerability, immunogenicity and efficacy of BNT162b2 in individuals younger than 12 years [C4591007 (< 12 years of age)][a] is ongoing (see 3.1.3 – *Action plan for safety issues*); a non-interventional study (C4591009) is planned to assess the occurrence of safety events of interest in a general US population (< 12 and ≥ 12 to ≤15 years of age) (see 3.1.3 – *Action plan for safety issues*).

Data from the Safety Database[b]
Since the first temporary authorization for emergency supply under Regulation 174 in the UK (01 December 2020) and through 28 February 2021, there were 34 cases (0.08% of the total Post-authorization dataset) involving individuals below 12 years of age.
Overall event seriousness and outcome are summarized below:

	Total Events N = 132 (%)
Serious events	66 (50)
Events with Criterion of Hospitalization	19 (14.4)
Distribution of events by Outcome*	
Outcome: Death	0
Outcome: Resolved/Resolving	25 (18.9)
Outcome: Not resolved	42 (31.8)
Outcome: Resolved with sequelae	0
Outcome: Unknown/No data	65 (49.2)

* For the outcome count, the multiple Lowest Level Terms that code to the same PT within a case are counted and presented individually. Therefore, for selected PTs the total count of the event outcome may exceed the total number of events.

The most frequently reported PTs (≥2%) were: Product administered to patient of inappropriate age (27), Off label use (11), Pyrexia (6), Product use issue (5), Fatigue, Headache, Nausea (4 each) and Vaccination site pain (3).

a. Phase 1 open label dose-finding study to evaluate safety, tolerability, and immunogenicity and phase 2/3 placebo-controlled, observer blinded safety, tolerability, and immunogenicity, study of a SARS-CoV-2 RNA vaccine candidate against COVID 19 in healthy children <12 years of age.
b. Cumulative RMP tables on Missing information are provided as per FDA's request to include a cumulative analysis, from post-authorization experience, of the Important Missing Information identified in the Pharmacovigilance Plan. More detailed information is available in the cumulative analysis of post-authorization data provided as a standalone document with the BLA submission.

2.1.2.d. Identified and Potential Interactions, Including Food-Biologic Product and Drug-Biologic Product Interactions

As noted in the WHO Guidelines on Nonclinical Evaluation of Vaccines,[3] pharmacokinetics testing is not required for final formulation. No interaction linked to metabolism is expected with vaccines. The only potential for interaction is with other vaccines administered concomitantly and with immunosuppressive drugs.

Co-administration studies with BNT162b2 have not been done, therefore there is not sufficient data to understand the effect on vaccine effectiveness of BNT162b2 or co-administered vaccines. A co-administration study with seasonal influenza vaccine is planned. If BNT162b2 is given at the same time as other injectable vaccine(s), the vaccine(s) should be administered at different injection sites.

2.1.2.e. Epidemiology of Indication and Target Population

Indication

Active immunization against COVID-19 disease caused by SARS-CoV-2 virus in individuals ≥ 16 years of age.

Incidence:

The COVID-19 is caused by a novel coronavirus labeled as SARS-CoV-2. The disease first emerged in December 2019, when a cluster of patients with pneumonia of unknown cause was recognized in Wuhan City, Hubei Province, China.[12] The number of infected cases rapidly increased and spread beyond China throughout the world. On 30 January 2020, the WHO declared COVID-19 a Public Health Emergency of International Concern and thus a pandemic.[13]

Estimates of SARS-CoV-2 incidence change rapidly. We obtained incidence and prevalence estimates using data from Worldometer, a trusted independent organization that collects COVID-19 data from official reports and publishes current global and country-specific statistics online.[14]

As of 03 March 2021, the overall number of people who had been infected with SARS-CoV-2 was over 115 million worldwide,[15] an increase of nearly 100 million in the 7 months since 28 July 2020.[16] Table 32 shows the incidence and prevalence as of 03 March 2021 for the US, UK, and EU-27 countries. In the EU and the UK, by 03 March 2021 the total number of confirmed cases had accumulated to almost 27 million people, or 5,226 per 100,000 people (from 1.7 million, or 337 per 100,000 by 28 July 2020). Across countries in the EU, the number of confirmed cases ranged from 1,072 to 11,836 cases per 100,000 people. Finland and Greece reported the lowest incidence rates while Czech Republic, Slovenia, and Luxembourg reported the highest.[15]

In the US, the number of confirmed cases had reached over 29 million (8,864 per 100,000 people) by 03 March 2021.[15] This is an increase from 4.5 million (1,357 per 100,000) by 28 July 2020.[17]

Table 32. Incidence, Prevalence, and Mortality of COVID-19 as of 03 March 2021 [15]

	Total Cases	Incidence: Total Cases/ 100,000	Active Cases[a]	Prevalence: Active Cases/ 100,000	Total Deaths	Mortality: Deaths / 100,000	Population
Global	115,760,943	1,485	21,707,680	278	2,571,518	33	7,794,824,793
EU-27	22,642,536	5,083	6,113,464	1,462	553,363	124	445,424,167
UK	4,194,785	6,157	1,065,282	1,564	123,783	182	68,125,249
EU-27 + UK	26,837,321	5,226	7,178,746	1,398	677,146	132	513,549,416
US	29,456,377	8,864	8,921,400	2,685	531,652	160	332,304,437
EU-27 Countries							
Austria	465,322	5,147	21,028	233	8,625	95	9,040,866
Belgium	774,344	6,662	699,566	6,019	22,141	191	11,623,476
Bulgaria	253,183	3,662	33,770	488	10,413	151	6,913,156
Croatia	244,205	5,973	3,322	81	5,555	136	4,088,197
Cyprus	35,620	2,936	33,331	2,747	232	19	1,213,250
Czech Republic	1,269,058	11,836	154,580	1,442	20,941	195	10,722,330
Denmark	212,798	3,665	6,995	120	2,370	41	5,805,897
Estonia	69,193	5,214	17,938	1,352	615	46	1,327,135
Finland	59,442	1,072	12,683	229	759	14	5,546,504
France	3,810,316	5,829	3,461,485	5,295	87,542	134	65,370,546
Germany	2,472,896	2,945	126,785	151	71,711	85	83,963,843
Greece	197,279	1,899	21,157	204	6,597	64	10,388,744
Hungary	439,900	4,561	98,361	1,020	15,324	159	9,643,837
Ireland	221,189	4,446	193,468	3,889	4,357	88	4,974,683
Italy	2,976,274	4,927	437,421	724	98,635	163	60,401,999
Latvia	88,022	4,702	9,233	493	1,654	88	1,872,109
Lithuania	200,349	7,430	10,859	403	3,281	122	2,696,596
Luxembourg	55,902	8,834	3,074	486	643	102	632,773
Malta	23,226	5,251	3,000	678	321	73	442,333
Netherlands	1,101,430	6,418	-	-	15,697	92	17,160,343
Poland	1,735,406	4,589	249,567	660	44,360	117	37,818,722
Portugal	806,626	7,926	64,797	637	16,430	161	10,176,690
Romania	812,318	4,242	44,953	235	20,586	108	19,151,141
Slovakia	314,359	5,756	51,570	944	7,489	137	5,461,420
Slovenia	192,266	9,247	10,751	517	3,874	186	2,079,130
Spain	3,136,321	6,706	343,770	735	70,247	150	46,766,954
Sweden	675,292	6,659	-	-	12,964	128	10,141,493

a. Active case counts were not available for Netherlands and Sweden; therefore, those two countries are excluded from the overall prevalence calculations for EU-27 and EU-27 + UK.

The reported numbers refer only to cases that have been tested and confirmed to be carrying the virus. There are large geographic variations in the proportion of the population tested as well as in the quality of reporting across countries. People who carry the virus but remain

asymptomatic are less likely to be tested and therefore mild cases are likely underreported. The numbers should therefore be interpreted with caution.[18]

Prevalence:

The prevalence of SARS-CoV-2 infection is defined as active cases per 100,000 people including confirmed cases in people who have not recovered or died. On 03 March 2021, the overall prevalence for the EU and UK (though not available for Sweden and the Netherlands) was 1,398 active cases per 100,000,[15] compared to 51 per 100,000 on 28 July 2020.[16] The range of reported prevalence was 81 to 6,019 per 100,000: Croatia, Denmark, and Germany reported the lowest prevalence while Belgium, France and Ireland reported the highest (Table 32).

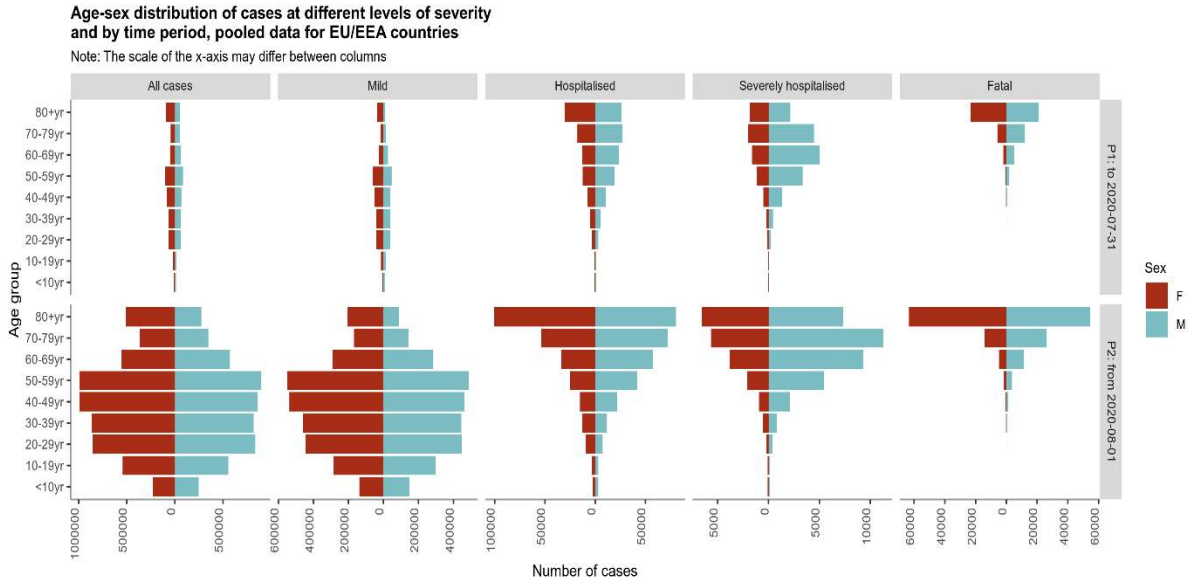
In the US, the prevalence on 03 March 2021 was nearly twice as high as the combined EU+UK estimates, with 2,685 active cases per 100,000.[15] The prevalence in the US was 653 per 100,000 on 28 July 2020.[16]

Demographics of the population in the proposed indication and risk factors for the disease:

Since the beginning of the pandemic, the ECDC has continuously collected COVID-19 information from all countries who are members of EU/EEA and the UK. In the ECDC's TESSy database, COVID-19 case-based data, including age and gender, are available for over 80% of the official number of cases reported by ECDC epidemic intelligence,[19] enabling estimates of age and gender distribution representative of the European population. TESSy data on age and sex distributions by severity of symptoms as posted on 04 March 2021 are shown in Figure 1.[20]

The top half of the figure represents data ending on 31 July 2020 and the bottom half presents data from 01 August 2020 to 04 March 2021 (Figure 1). In general, the age-sex patterns before 01 August 2020 have remained the same since then. The gender distribution of persons testing positive for SARS-CoV-2 in the European population is similar for most age groups. Cases reported in TESSy have been older than the general population throughout the pandemic, with few cases observed in people aged younger than 20 years. This likely reflects the age distribution of people who met the requirements for being tested and is unlikely to reflect the actual distribution of infections in the population. Those with severe outcomes (hospitalized, severely hospitalized, or fatal) have been disproportionately older and male compared to COVID-19 cases overall. While age-sex patterns have remained consistent throughout the pandemic, a notable difference between the periods before and since 01 August 2020 is that the absolute numbers of cases have increased dramatically in the latter period compared to the earlier one.

Figure 1. Age-Sex distribution of COVID-19 Cases as Different Levels of Severity, EU/EEA and UK. Case-based Data from TESSy produced on 04 March 2021[a]



Note: "mild"= a case that has not been reported as hospitalized or a case that resulted in death.

a. Data from ECDC. COVID-19 Surveillance report. Week 8, 2021. 4 March 2021. "2.2 Age-sex pyramids" Accessed 6 March 2021[20]

US distributions of COVID cases and deaths by age, sex, and race, as well as the cross-tabulation of age and sex, are shown in Table 33.[21] Those under age 50 account for 65% of cases but less than 5% of deaths. For ages 18-74, males account for less than half of cases but over 60% of deaths.

Table 33. Distributions of Cases (n=21,895,936) and Deaths (n=382,009) by Age, Sex, Race, and Cross-Tabulated Age and Sex – United States as of 08 March 2021[21,a]

Event	Age Group	Age %	Sex	Sex %	Race[b]	Race %	Age Group	Age x Sex %	
								Males	Females
Cases	**0-4**	2	**Males**	47.8	**H/L**	20.7	**0-4**	51.7	48.3
	5-17	9.5	**Females**	52.2	**AI/AN**	1.2	**5-17**	49.8	50.2
	18-29	22.4			**Asian**	3.6	**18-29**	47.1	52.9
	30-39	16.3			**Black**	12.2	**30-39**	48.2	51.8
	40-49	14.9			**NH/PI**	0.4	**40-49**	47.7	52.3
	50-64	20.5			**White**	56	**50-64**	48.5	51.5
	65-74	7.8			**M/O**	6	**65-74**	49	51
	75-84	4.1					**75-84**	45.7	54.3
	85+	2.4					**85+**	33.9	66.1
Deaths	**0-4**	<0.1	**Males**	54.3	**H/L**	12.2	**0-4**	47.6	52.4
	5-17	0.1	**Females**	45.7	**AI/AN**	1	**5-17**	57.7	42.3
	18-29	0.5			**Asian**	4.3	**18-29**	63	37
	30-39	1.1			**Black**	14.7	**30-39**	66	34
	40-49	2.8			**NH/PI**	0.2	**40-49**	66.5	33.5

Table 33. Distributions of Cases (n=21,895,936) and Deaths (n=382,009) by Age, Sex, Race, and Cross-Tabulated Age and Sex – United States as of 08 March 2021[21,a]

Event	Age Group	Age %	Sex	Sex %	Race[b]	Race %	Age Group	Age x Sex %	
								Males	Females
	50-64	14.5			**White**	63.1	**50-64**	65	35
	65-74	21.3			**M/O**	4.4	**65-74**	61.4	38.6
	75-84	27.7					**75-84**	55.8	44.2
	85+	32.1					**85+**	41.8	58.2

a. Percentage of missing demographic data varied by types of event and demographic.
b. Except for Hispanics/Latinos, all categories refer to non-Hispanics
Abbreviations: AI/AN=American Indian/Alaska Native, H/L=Hispanic/Latino, M/O=Multiple/Other, NH/PI=Native Hawaiian/Other Pacific Islander

In general, disease has been much less severe among ages 0-24 compared to ages ≥25 years, with 2.5% hospitalized, 0.8% admitted to an intensive care unit, and <0.1% dying among ages 0-24, versus 16.6% hospitalized, 8.6% intensive care, and 5% dying among ages ≥25 years.[22] Among hospitalized cases with COVID-19 in the US, approximately 90% are over 40 years old, and between 58% to 66% are at least 60 years old.[23] The majority (approximately 60%) of COVID-19 patients admitted to hospitals in the US have been male.[23,24,25,26,27]

African American COVID-19 patients have been reported to have an increased risk of hospitalization[24,28] and mortality,[29] compared to white patients in the United States. A CDC report examined demographic trends among US COVID-19 deaths from May to August of 2020.[30] During the observation period, the percentage of US COVID-19 deaths that were Hispanic increased from 16.3% in May to 26.4% in August, the only racial or ethnic group among whom the percentage of deaths increased during that time. In terms of setting, 64.3% of deaths occurred in inpatient hospitals and 21.5% in nursing homes or long-term care facilities.

As of 08 March 2021, the CDC estimated that the total number of *excess* deaths (as opposed to overall deaths in the preceding paragraph) across the US from 01 February 2020 to the present from all causes (COVID-19 and otherwise) ranged from 509,890-624,307.[31] A CDC report examining US excess deaths associated with race and age, restricted to the period 26 January 2020 to 03 October 2020, estimated that 66% of US excess deaths during that period were attributable to COVID-19.[32] By age, the largest increase in deaths compared to average expected deaths occurred among adults aged 25-44 (26.5% increase). By race, increases in deaths compared to expectation were largest among Hispanics (53.6% increase), Asian Americans (36.6% increase), African Americans (32.9% increase), and Native Americans and Native Alaskans (28.9% increase), all compared to an excess 11.9% deaths among non-Hispanic whites.

Risk Factors

While anyone can become infected with SARS-CoV-2, symptoms of COVID-19 disease can range from very mild (or no symptoms) to severe or fatal. A person's risk of initial infection

increases through spending time in close physical proximity to others, especially in indoor spaces with poor ventilation.[33] People living in long-term care facilities or high-density apartment homes, or working in occupations with close proximity to others (e.g. healthcare, transportation), have a higher risk of infection.[33,34,35] According to the CDC, people ages 18-29 have the highest risk of initial infection, while children age 4 and under have the lowest rate (Table 34).[36] Risk of infection is also higher among some ethnic minority groups.[37,38]

Table 34. Risk for COVID-19 Infection, Hospitalization, and Death by Age Group [36] and by Race/Ethnicity [37]

	Rate ratios		
Age Group (years)	**Cases**	**Hospitalization**	**Death**
0-4	<1	2	2
5-17 [a]	1	1	1
18-29	3	7	15
30-39	2	10	45
40-49	2	15	130
50-64	2	25	400
65-74	2	35	1100
75-84	2	55	2800
85+	2	80	7900
Race/Ethnicity			
Non-Hispanic White [b]	1	1	1
American Indian or Alaska Native, non-Hispanic	1.9	3.7	2.4
Asian, non-Hispanic	0.7	1.1	1.0
Black or African American, non-Hispanic	1.1	2.9	1.9
Hispanic or Latino	1.3	3.2	2.3

a. Rate ratios for each age group are relative to the 5—17-year age category.
b. Rate ratios for each race/ethnicity group are relative to the Non-Hispanic White category.

Risk for severe or fatal COVID-19 disease has been shown to increase with older age, male sex, or ethnic minority status.[36,37,38,39,40,41] Risks of hospitalization and death increase dramatically for every 10-year age group above age 17 (Table 34).[36,41] Table 34 also gives estimated rate ratios for COVID-19 hospitalization and death by race/ethnicity relative to white, non-Hispanic persons in the US. The highest risks of hospitalization and death were observed among American Indian or Alaska native persons (RR = 3.7 for hospitalization and 2.4 for death) and Hispanic or Latino persons (RR = 3.2 for hospitalization and 2.3 for death). These differences in risk among ethnic groups may be attributed to differences in underlying factors that are correlated with race/ethnicity including socioeconomic status, access to health care, and occupation-related virus exposure.[37]

Risk of severe or fatal COVID-19 disease is higher among persons who are current or former smokers, have lower socioeconomic status, have no or public insurance, or live in neighborhoods with higher rates of limited English proficiency.[38,40,41,42] The CDC has also recognized other socio-demographic groups who may need to take extra precautions against COVID-19 due to increased risk for severe illness: pregnant women; breastfeeding mothers; people with disabilities or developmental/behavioral disorders; people living in rural

communities, nursing homes, long-term care facilities, or prisons; people experiencing homelessness; and newly resettled refugee populations.[43]

Risk for severe or fatal COVID-19 disease also increases with the presence of chronic medical conditions, including obesity, respiratory diseases (e.g., COPD or asthma), cardiovascular disease, diabetes, cancer, liver disease, neurological diseases (e.g., stroke or dementia), chronic kidney disease, sickle cell disease, autoimmune conditions and immunosuppression, or higher scores on the WHO Clinical Progression Scale and Charlson Comorbidity Index.[38,39,40,41,42] Table 35 shows the estimated hazard ratios of COVID-19 mortality associated with these chronic conditions and socio-demographics from a cohort study of 17 million adults in England.[41]

Table 35. Hazard Ratios and 95% Confidence Intervals for COVID-19-related Death[41]

		COVID-19 death Hazard Ratio	
Characteristic	**Category**	**Adjusted for age and sex**	**Fully adjusted**
Age	18-39	0.05 (0.04-0.07)	0.06 (0.04-0.08)
	40-49	0.28 (0.23-0.33)	0.30 (0.25 - 0.36)
	50-59	1.00 (ref)	1.00 (ref)
	60-69	2.79 (2.52-3.10)	2.40 (2.16-2.66)
	70-79	8.62 (7.84-9.46)	6.07 (5.51-6.69)
	80+	38.29 (35.02-41.87)	20.60 (18.70-22.68)
Sex	Female	1.00 (ref)	1.00 (ref)
	Male	1.78 (1.71-1.85)	1.59 (1.53-1.65)
BMI (kg/m^2)	Not obese	1.00 (ref)	1.00 (ref)
	30-34.9 (obese class I)	1.23 (1.17–1.30)	1.05 (1.00–1.11)
	35-39.9 (obese class II)	1.81 (1.68–1.95)	1.40 (1.30–1.52)
	40+ (obese class III)	2.66 (2.39–2.95)	1.92 (1.72–2.13)
Smoking	Never	1.00 (ref)	1.00 (ref)
	Former	1.43 (1.37–1.49)	1.19 (1.14–1.24)
	Current	1.14 (1.05–1.23)	0.89 (0.82–0.97)
Ethnicity[a]	White	1.00 (ref)	1.00 (ref)
	Mixed	1.62 (1.26–2.08)	1.43 (1.11–1.84)
	South Asian	1.69 (1.54–1.84)	1.45 (1.32–1.58)
	Black	1.88 (1.65–2.14)	1.48 (1.29–1.69)
	Other	1.37 (1.13–1.65)	1.33 (1.10–1.61)
IMD quintile[e]	1 (least deprived)	1.00 (ref)	1.00 (ref)
	2	1.16 (1.08-1.23)	1.12 (1.05–1.19)
	3	1.31 (1.23–1.40)	1.22 (1.15–1.30)
	4	1.69 (1.59–1.79)	1.51 (1.42–1.61)
	5 (most deprived)	2.11 (1.98–2.25)	1.79 (1.68–1.91)
Blood pressure	Normal	1.00 (ref)	1.00 (ref)
	High BP or diagnosed hypertension	1.09 (1.05–1.14)	0.89 (0.85–0.93)
Respiratory disease excluding asthma		1.95 (1.86–2.04)	1.63 (1.55–1.71)
Asthma[b] (vs. none)	With no recent OCS use	1.13 (1.07–1.20)	0.99 (0.93–1.05)
	With recent OCS use	1.55 (1.39–1.73)	1.13 (1.01–1.26)

Table 35. Hazard Ratios and 95% Confidence Intervals for COVID-19-related Death[41]

		COVID-19 death Hazard Ratio	
Characteristic	**Category**	**Adjusted for age and sex**	**Fully adjusted**
Chronic heart disease		1.57 (1.51–1.64)	1.17 (1.12–1.22)
Diabetes[c] (vs. none)	With HbA1c < 58 mmol/mol	1.58 (1.51–1.66)	1.31 (1.24–1.37)
	With HbA1c ≥ 58 mmol/mol	2.61 (2.46–2.77)	1.95 (1.83–2.08)
	With no recent HbA1c measure	2.27 (2.06–2.50)	1.90 (1.72–2.09)
Cancer (non-hematological, vs. none)	Diagnosed <1 year ago	1.81 (1.58–2.07)	1.72 (1.50–1.96)
	Diagnosed 1-4.9 years ago	1.20 (1.10–1.32)	1.15 (1.05–1.27)
	Diagnosed ≥ 5 years ago	0.99 (0.93–1.06)	0.96 (0.91–1.03)
Hematological malignancy (vs. none)	Diagnosed <1 year ago	3.02 (2.24–4.08)	2.80 (2.08–3.78)
	Diagnosed 1-4.9 years ago	2.56 (2.14–3.06)	2.46 (2.06–2.95)
	Diagnosed ≥ 5 years ago	1.70 (1.46–1.98)	1.61 (1.39–1.87)
Reduced kidney function[d] (vs. none)	eGFR 30-60	1.56 (1.49–1.63)	1.33 (1.28–1.40)
	eGFR < 30	3.48 (3.23–3.75)	2.52 (2.33–2.72)
Liver disease		2.39 (2.06–2.77)	1.75 (1.51–2.03)
Stroke or dementia		2.57 (2.46–2.70)	2.16 (2.06–2.27)
Other neurological disease		3.08 (2.85–3.33)	2.58 (2.38–2.79)
Organ transplant		6.00 (4.73–7.61)	3.53 (2.77–4.49)
Asplenia		1.62 (1.19–2.21)	1.34 (0.98–1.83)
Rheumatoid arthritis, lupus, or psoriasis		1.30 (1.21–1.38)	1.19 (1.11–1.27)
Other immunosuppressive condition		2.75 (2.10–3.62)	2.21 (1.68–2.90)

a. Ethnicity hazard ratios were estimated from a model restricted to those with recorded ethnicity.
b. For OCS use, 'recent' refers to during the year before baseline.
c. Classification by HbA1c is based on measurements within 15 months of baseline.
d. eGFR is measured in ml min−1 per 1.73 m^2 and taken from the most recent serum creatinine measurement.
e. Index of Multiple Deprivation
Models were adjusted for age using a four-knot cubic spline for age, except for estimation of age-group hazard ratios. Ref, reference group; 95% CI, 95% confidence interval.

The main existing treatment options:

Through 28 February 2021, other COVID-19 vaccines were authorized and recommended for use in the United States including vaccines from Moderna (NCT04470427), and Johnson & Johnson/Janssen (NCT04505722). Others may subsequently be approved.

Natural history of the indicated condition in the untreated population, including mortality and morbidity:

Symptoms of COVID-19

The clinical manifestations of COVID-19 vary widely, from asymptomatic infection in 17-20%,[44,45] to critical illness and death. The most common symptoms of COVID-19 are fever, cough, and shortness of breath (Table 36).[46]

Table 36. Signs and symptoms among 291 pediatric (age <18 years) and 10,944 adult (age 18–64 years) patients[a] with laboratory confirmed COVID-19 — United States, 12 February– 2April 2020[46]

	No. (%) with sign/symptom	
Sign/Symptom	**Pediatric**	**Adult**
Fever, cough, or shortness of breath[b]	213 (73)	10,167 (93)
Fever[d]	163 (56)	7,794 (71)
Cough	158 (54)	8,775 (80)
Shortness of breath	39 (13)	4,674 (43)
Myalgia	66 (23)	6,713 (61)
Runny nose[c]	21 (7.2)	757 (6.9)
Sore throat	71 (24)	3,795 (35)
Headache	81 (28)	6,335 (58)
Nausea/Vomiting	31 (11)	1,746 (16)
Abdominal pain[d]	17 (5.8)	1,329 (12)
Diarrhea	37 (13)	3,353 (31)

a. Cases were included in the denominator if they had a known symptom status for fever, cough, shortness of breath, nausea/vomiting, and diarrhea. Total number of patients by age group: <18 years (N = 2,572), 18–64 years (N = 113,985).
b. Includes all cases with one or more of these symptoms.
c. Runny nose and abdominal pain were less frequently completed than other symptoms; therefore, percentages with these symptoms are likely underestimates.
d. Patients were included if they had information for either measured or subjective fever variables and were considered to have a fever if "yes" was indicated for either variable.

Progression and Timeline of Mild to Moderate Disease

Mild to moderate disease is defined as the absence of viral pneumonia and hypoxia. For those who develop symptoms, the incubation period is usually 4 to 5 days, with 97.5% experiencing symptoms within 11 days of exposure.[47,48] Those with mild COVID-19 recover at home with supportive care and guidance to self-isolate. Those with moderate disease are monitored at home and are sometimes recommended to be hospitalized if conditions worsen.[48] Data on rates of re-infection are limited but variants that are not neutralized by immune antisera, such as the recent South African variant, may lead to increased risk of re-infection in the future.[47]

Progression and Timeline of Severe Disease Requiring Hospitalization

Those with severe disease will require hospitalization to manage their illness. Based on data that have been systematically collected for the US by the CDC between 01 August 2020 and 02 March 2021, there were 1,814,606 new hospital admissions for patients with confirmed COVID-19 in the US.[49] For the week ending 28 February 2021, 10 patients per 100,000 population were hospitalized due to COVID-19 in 22 countries of the EU/EEA with available data.[50]

The most common symptoms in patients are fever (42-80%), shortness of breath (35-71%), fatigue (33-62%), cough (77-84%), chills (63%), myalgias (63%), headache (59%), and diarrhea (33%).[51,52,53,54] Approximately 17% to 40% of those hospitalized with COVID-19

experience severe symptoms necessitating intensive care.[23,28,51] More than 75% of patients hospitalized with COVID-19 require supplemental- oxygen.[55]

Studies early in the pandemic demonstrated that time from onset of illness to ARDS was 8-12 -days and time from onset of illness to ICU admission was 9.5–12 days.[47] In 17 countries of the EU/EEA with available data, 1.8 patients per 100,000 population were in the ICU due to COVID-19 for the week ending 28 February 2021.[50] A recent meta-analysis found that, of patients <19 years of age, 11% went to the ICU, non-invasive ventilation was administered among 12%, and 4% required mechanical ventilation.[45]

Mortality

As of 07 March 2021, there were 522,973 deaths reported in the US for all age groups among 28,771,749 cases (1.8% of cases).[49] As of 28 February 2021 there were 547,267 deaths reported for all age groups in the EU/EEA among 22,527,370 cases (2.4% of cases).[56] As of 7 March 2021, the UK has seen 124,736 deaths from COVID-19 in all age groups among 4,231,166 cases (2.9% of cases).[57] According to a recent meta-analysis of pediatric studies published through October 2020, the mortality for patients <19 years of age is 2%.[45]

Mortality data are also presented from Worldometer, an independent organization that publishes current, reliable COVID-19 statistics online.[17] The mortality of SARS-CoV-2 infection is defined as the cumulative number of deaths among detected cases.

As of 03 March 2021, the overall SARS-CoV-2 mortality for the EU + UK was 677,146 deaths, or 132 per 100,000 people. Reported mortality among EU countries and the UK ranged from 14 to 195 deaths per 100,000 (Table 32). Finland and Cyprus reported the lowest mortality; Czech Republic, Belgium and Slovenia reported the highest.[15]

In the US, as of 03 March 2021, the mortality was 531,652 deaths (160 per 100,000 people). Mortality in the US was similar to that of EU countries Hungary, Portugal, and Italy. [15]

Overall reported mortality among hospitalized COVID-19 patients varies from 12.8% to 26% in the EU and UK. [28,30,58,59] Mortality rates are declining over time, presumably due to an improved understanding of COVID-19 and its management.[58,60]

Complications of COVID-19 and Long-COVID

Complications of COVID-19 include impaired function of the heart, brain, lung, liver, kidney, and coagulation system.[23,25,54] Based on a meta-analysis of 42 studies, the risk of thromboembolism was 21% overall and 31% in the ICU, with the pooled odds of mortality being 74% higher among those who experienced thromboembolism compared to those who did not.[61]

COVID-19 symptoms can persist weeks or months beyond the acute infection.[62,63] The NICE guideline scope published on 30 October 2020 defined “Long COVID” signs and symptoms that continue or develop after acute COVID-19. It includes both ongoing symptomatic COVID-19 (from 4 to 12 weeks) and post-COVID-19 syndrome (12 weeks or more and for which signs and symptoms are not explained by an alternative diagnosis).[64]

A meta analysis of 31 studies among patients between 18 to 49 years of age found that COVID-19 symptoms were experienced for 14 days to 3 months post-infection, including persistent fatigue (39–73%), breathlessness (39–74%), decrease in quality of life (44–69%), impaired pulmonary function, abnormal CT findings including pulmonary fibrosis (39–83%), evidence of peri-/perimyo-/myocarditis (3–26%), changes in microstructural and functional brain integrity with persistent neurological symptoms (55%), increased incidence of psychiatric diagnoses (5.8% versus 2.5–3.4% in controls), and incomplete recovery of olfactory and gustatory dysfunction (33–36%).[65] Children who are infected with COVID-19 are at risk of subsequent multisystem inflammatory syndrome (MIS-C) and often develop a rash following resolution of COVID-19.[66,67,45]

Important co-morbidities:

Important comorbidities in hospitalized COVID-19 patients include hypertension, diabetes, obesity, cardiovascular disease, chronic pulmonary disease or asthma, chronic kidney disease, cancer, and chronic liver disease.[24,25,26,51,54] Prevalence of these conditions have been reported to be lower in mild cases and higher among fatal cases, as shown as shown for European countries in Table 37 below.

Table 37. Preconditions among COVID-19 Patients in EU/EEA and UK, by Severity of Disease. Case-based Data from TESSy Produced 04 March 2021

	EU/EEA, produced on 04 March 2021			
	Mild	**Hosp**	**Severe**	**Fatal**
Total N	1,155,969	214,784	35,468	67,011
Asplenia (%)	0	0	0	0
Asthma (%)	0.5	1.6	1.7	1.6
Cancer, malignancy (%)	2.1	7.2	9.7	9.3
Cardiac disorder, excluding hypertension (%)	6.2	18.4	20.7	24.7
Chronic lung disease, excluding asthma (%)	1.8	4.7	5.3	5.3
Current smoking (%)	0.9	0.3	0.4	0.1
Diabetes (%)	3.3	13.9	18.9	15.6
Haematological disorders (%)	0	0.3	0.1	0.2
HIV/other immune deficiency (%)	0.1	0.9	1	0.8
Hypertension (%)	0.7	3.9	4.4	6.3
Kidney-related condition, renal disease (%)	0.3	2.3	2.2	3.7
Liver-related condition, liver disease (%)	0.2	0.7	0.7	0.6
Neuromuscular disorder, chronic neurological (%)	0.6	2.4	1.6	4.2
Obesity (%)	0.2	0.2	0.4	0.2
Other endocrine disorder, excluding diabetes (%)	0.4	0.2	0.1	0.1
Rheumatic diseases including arthritis (%)	0	0	0	0
Tuberculosis (%)	0	0	0	0
None (%)	82.5	42.8	32.7	27.3

Abbreviation: Hosp = Hospitalized

Table 38 below summarizes comorbidities among US COVID-19 patients in a retrospective cohort study conducted among 629,953 individuals tested for COVID-19 in a large health system in the US Northwest between 01 March and 31 December 2020.[38] The most common comorbidities were similar in the full cohort and among those who tested positive: obesity, hypertension, diabetes, and asthma. Among those hospitalized for COVID-19, a large

number of comorbidities had elevated prevalence compared to the full cohort and those who tested positive: obesity, hypertension, diabetes, kidney disease, congestive heart failure, coronary artery disease, and chronic obstructive pulmonary disease.

Table 38. Comorbidities in individuals tested for COVID-19 in the Providence St. Joseph Health System – States of California, Oregon, and Washington, 01 March–31 December 2020[38]

Comorbidity	Tested (N= 629,953) %	Positive (N= 54,645) %	Hospitalized (N= 8,536) %
Hypertension	23.3	19.8	40.2
Diabetes	9.4	10.9	28.3
Weight			
Underweight	2.1	1.7	3.1
Normal	29.0	23.9	24.3
Overweight	31.7	32.6	30.3
Class 1 Obesity	19.8	22.3	21.2
Class 2 Obesity	9.6	11.1	10.9
Class 3 Obesity	7.7	8.6	10.3
Asthma	6.5	5.3	6.7
Chronic Obstructive Pulmonary Disease	4.0	2.6	8.3
Coronary Artery Disease	5.5	3.6	9.7
Myocardial Infarction	2.2	1.6	5.5
Congestive Heart Failure	5.3	3.9	13.2
Kidney Disease	5.6	5.3	17.2
Liver Disease	3.1	2.5	4.0
Cancer	6.1	3.0	6.3

2.1.2.f. Pharmacological Class Effects

There are 2 vaccines (including BNT162b2) with a mRNA platform authorized for emergency use in multiple US jurisdictions since 11 December 2020. Theoretical concerns in mRNA vaccines have included the risk of the presence of naked extracellular RNA in the body which may lead to edema or coagulation and concerns about aberrant immune responses to the RNA or lipid particles. The immunogenicity and efficacy data from study C4591001 are indicative of the vaccine delivery system's success in transfecting the RNA into the appropriate target cells to stimulate an immune response. The RNA itself cannot integrate into the DNA genome.[68,69] The probability of any sequences from the vaccine RNA being integrated into the human genome by a reverse transcription mediated mechanism is considered remote, no higher than the probability of host RNA sequences being re-inserted into the genome, especially given the small quantity of RNA in the vaccine, the barriers to transfected RNA reaching the nucleus, the non-replicating nature of the vaccine RNA, the limited stability of RNA in a cellular context, and the expected targeting of transfected cells for elimination by T cells elicited by the vaccine antigen expressed from the RNA.

3. PHARMACOVIGILANCE PLAN

3.1. Structure of the Pharmacovigilance Plan

3.1.1. Summary of Ongoing Safety Concerns

Table 39. Ongoing Safety Concerns

Important Identified Risks	Anaphylaxis
	Myocarditis and Pericarditis
Important Potential Risks	Vaccine-associated enhanced disease (VAED) including Vaccine-associated enhanced respiratory disease (VAERD)
Missing Information	Use in pregnancy and lactation
	Vaccine effectiveness
	Use in pediatric individuals <12 years of age

3.1.2. Routine Pharmacovigilance Practices

- Routine pharmacovigilance activities is a critical component of activities relating to the detection, assessment, understanding and prevention of risks. The objective of routine pharmacovigilance is to have processes in place to assure the ongoing and timely collection, processing, follow-up, and analysis of individual AE reports globally, following global safety Standard Operating Procedures and regulatory guidance.

- Pfizer, on behalf of the marketing authorization applicant (MAA), monitors the safety profile of its products, evaluates issues potentially impacting product benefit-risk profiles in a timely manner, and ensures that appropriate communication of relevant information is conveyed in a timely manner to regulatory authorities and other interested parties as appropriate and in accordance with international principles and prevailing regulations.

- Pfizer, on behalf of the MAA, conducts scientific data gathering activities for the detection and evaluation of AEs in order to ensure safety monitoring, which is commensurate with product characteristics.

- Signal detection activities include periodic literature review for the life cycle of the product. This includes reviewing the medical literature for individual case reports that should be entered into the safety database as well as periodic aggregate literature review for broader signal detection.

- Safety signal evaluation requires the collection, analysis and assessment of information to evaluate whether there is a potential causal association between an event and the administration of the product and includes subsequent qualitative or quantitative characterization of the relevant safety risk to determine appropriate pharmacovigilance and risk mitigation actions.

- Routine pharmacovigilance activities will include the use of DCAs. They are intended to facilitate the capture of clinical details about:
  - the nature and severity of COVID-19 illness in individuals who have received the COVID-19 vaccine and is anticipated to provide insight into potential cases of vaccine lack of effect or VAED.
  - potential anaphylactic reactions in individuals who have received the COVID-19 vaccine.
- A web-based AE reporting portal will be available for vaccine providers and recipients, to assist with anticipated high volume of reports (based on expected large target population). The portal will capture key adverse event data in the initial interaction and will provide automated intake into the Pfizer safety database via E2B for safety review.
- At the country level, the Drug Safety Unit performs routine pharmacovigilance activities including the collection of AEs from various sources and the reporting of AEs to the regulatory authority as per local regulatory guidelines.

3.1.3. Action Plan for Safety Issues

Action Plan for Important Identified Risks

Table 40. Action Plan for Important Identified Risk "Myocarditis and Pericarditis"

Actions proposed	• C4591009: A non-interventional post-approval safety study of the Pfizer--BioNTech COVID-19 mRNA vaccine in the United States. • C4591011: Active safety surveillance of the Pfizer-BioNTech COVID-19 vaccine in the US Department of Defense population following Emergency Use Authorization. • C4591012: Post-emergency use authorization active safety surveillance study among individuals in the Veteran's Affairs Health System receiving Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) vaccine.
Objective of proposed actions	• C4591009: To assess the occurrence of safety events of interest, including myocarditis and pericarditis, in the general US population, pregnant women, the immunocompromised and persons with a prior history of COVID-19 within selected data sources participating in the US Sentinel System. • C4591011: To assess whether individuals in the US DoD Military Health System (MHS) experience increased risk of safety events of interest, including myocarditis and pericarditis, following receipt of the Pfizer-BioNTech COVID-19 Vaccine. • C4591012: To assess whether individuals in the US Veteran's Affairs Health System experience increased risk of safety events of interest, including myocarditis and pericarditis, following receipt of the Pfizer-BioNTech COVID-19 Vaccine.
Rationale for proposed actions	• C4591009: Robust surveillance is needed to ensure comprehensive understanding of real-world safety of the Pfizer-BioNTech COVID-19 Vaccine in the general US population and in subcohorts of interest, including pregnant women, immunocompromised individuals and persons with a prior history of COVID-19 infection. • C4591011 and C4591012: Robust surveillance is needed to ensure comprehensive understanding of real-world safety. This surveillance strategy consists of complementary approaches to ensure timely signal identification and evaluation in populations who have received the Pfizer-BioNTech COVID-19 Vaccine under an Emergency Use Authorization (EUA).
Monitoring by the sponsor for safety issue and proposed actions	• C4591009: Post-approval observational studies using real-world data are needed to assess the association between Pfizer-BioNTech COVID-19 Vaccine and safety events of interest, among persons administered the vaccine in both the overall US population and in populations of interest (e.g., pregnant women, the immunocompromised and persons with a prior history of COVID-19 infection). This observational study will capture safety events (based on AESI) including myocarditis and pericarditis, in individuals of any age who received the Pfizer-BioNTech COVID-19 Vaccine since its availability under an EUA using electronic health records and claims data from data partners participating in the Sentinel System. This study, will capture hospitalizations, deaths and serious safety events of interest, including myocarditis and pericarditis, as well as selected pregnancy-related and birth outcomes. • C4591011 and C4591012: 1. The collection of safety data in vaccine recipients is critical to our understanding of the vaccine safety profile and to enable safety signal

Table 40. Action Plan for Important Identified Risk "Myocarditis and Pericarditis"

	detection and, if needed, further risk mitigation during the EUA. In addition to the collection and monitoring of AEs reported voluntarily by healthcare professionals providing the vaccine and by individuals receiving the vaccine, active surveillance studies of the Pfizer-BioNTech COVID-19 Vaccine under EUA are also planned. 2. Active surveillance of large numbers of individuals vaccinated with the Pfizer-BioNTech COVID-19 Vaccine is necessary to confirm the safety profile demonstrated in the clinical study in a broader population under real-world conditions. Pfizer-BioNTech is conducting active surveillance studies of individuals vaccinated with the Pfizer--BioNTech COVID-19 Vaccine under an EUA in populations prioritized in the early stages of the EUA, e.g., active military and elderly, as described in the study protocols C4591011 (study planned) and C4591012 (study ongoing) submitted to FDA on 29 January 2021. The study period is/will be approximately 30 months following availability of vaccine under EUA. The studies capture hospitalizations, deaths and serious safety events of interest, including myocarditis and pericarditis.
Milestones for evaluation and reporting	• C4591009: • Protocol submission: 31 August 2021 • Monitoring report submission: 31 October 2022 • Interim Analysis submission: 31 October 2023 • Final study report submission: 31 October 2025. • C4591011: • Interim study reports[a] will be submitted on the following dates based on data collected post-EUA in target populations: – 31 December 2021 – 30 June 2022 – 31 December 2022 • Final study reports submission: 31 December 2023. • C4591012 • Interim study reports will be submitted on the following dates based on data collected post-EUA in target populations: – 30 June 2021 – 31 December 2021 – 30 June 2022 – 31 December 2022 • Final study reports submission: 31 December 2023.

a. FDA was informed (Response to FDA 12 May 2021 - Information Request Regarding Active Surveillance Studies) that the first milestone (Interim Report submission due 30 June 2021) is delayed due to a change in study collaboration; therefore it has been removed from this table.

Table 41. Action Plan for Important Identified Risk "Anaphylaxis"

Actions proposed	• Communication of this important identified risk via label (Sections 4 - *Contraindications*, 5.1 - *Management of Acute Allergic Reactions,* Section 6 - *Adverse reactions* - and 6.2 - *Post Authorization Experience*). • C4591001: Phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals. • C4591009: A non-interventional post-approval safety study of the Pfizer--BioNTech COVID-19 mRNA vaccine in the United States. • C4591011: Active safety surveillance of the Pfizer-BioNTech COVID-19 vaccine in the US Department of Defense population following Emergency Use Authorization. • C4591012: Post-emergency use authorization active safety surveillance study among individuals in the Veteran's Affairs Health System receiving Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) vaccine.
Objective of proposed actions	• Labelling communicates the risk of anaphylaxis. • C4591001: To evaluate the safety, tolerability, immunogenicity, and efficacy of BNT162b2. Further, an unfavorable imbalance between the vaccine and control groups in the frequency of COVID-19 disease, in particular for severe COVID-19 disease, may indicate the occurrence of VAED/VAERD. Surveillance is planned for 2 years following Dose 2. • C4591009: To assess the occurrence of safety events of interest in the general US population, pregnant women, the immunocompromised and persons with a prior history of COVID-19 within selected data sources participating in the US Sentinel System. • C4591011: To assess whether individuals in the US DoD Military Health System (MHS) experience increased risk of safety events of interest, following receipt of the BNT162b2. • C4591012: To assess whether individuals in the US Veteran's Affairs Health System experience increased risk of safety events of interest, following receipt of the BNT162b2.
Rationale for proposed actions	• Labeling communicates to health care provider the risk of anaphylaxis. • C4591001: Long-term monitoring throughout the clinical study for up to 2 years to assess the risk for vaccine-associated enhanced disease. • C4591009: Robust surveillance is needed to ensure comprehensive understanding of real-world safety of the BNT162b2 in the general US population and in subcohorts of interest, including pregnant women, immunocompromised individuals and persons with a prior history of COVID-19 infection. • C4591011 and C4591012: Robust surveillance is needed to ensure comprehensive understanding of real-world safety. This surveillance strategy consists of complementary approaches to ensure timely signal identification and evaluation in populations expected to receive the BNT162b2 under an Emergency Use Authorization (EUA).
Monitoring by the sponsor for safety issue and proposed actions	• C4591001: Safety evaluations will include AESI, including anaphylaxis; these will be collected systemically and monitored throughout the Phase 3 study. • C4591009: Post-approval observational studies using real-world data are needed to assess the association between BNT162b2 and safety events of

Table 41. Action Plan for Important Identified Risk "Anaphylaxis"

	interest, among persons administered the vaccine in both the overall US population and in populations of interest (e.g., pregnant women, the immunocompromised and persons with a prior history of COVID-19 infection). This observational study will capture safety events (based on AESI) including anaphylaxis, in individuals of any age who received the BNT162b2 since its availability under an EUA using electronic health records and claims data from data partners participating in the Sentinel System. This study, will capture hospitalizations, deaths and serious safety events of interest, including anaphylaxis, as well as selected pregnancy-related and birth outcomes. • C4591011 and C4591012: 1. The collection of safety data in vaccine recipients is critical to our understanding of the vaccine safety profile and to enable safety signal detection and, if needed, further risk mitigation during the EUA. In addition to the collection and monitoring of AEs reported voluntarily by healthcare professionals providing the vaccine and by individuals receiving the vaccine, active surveillance studies of the BNT162b2 under EUA are also planned. 2. Active surveillance of large numbers of individuals vaccinated with the BNT162b2 is necessary to confirm the safety profile demonstrated in the clinical study in a broader population under real-world conditions. Pfizer-BioNTech plans to conduct active surveillance studies of individuals vaccinated with the BNT162b2 under an EUA in populations prioritized in the early stages of the EUA, e.g., active military and elderly, as described in the study protocols C4591011 and C4591012 submitted to FDA on 29 January 2021. The study period will be approximately 30 months following availability of vaccine under EUA. The studies will capture hospitalizations, deaths and serious safety events of interest, including anaphylaxis.
Milestones for evaluation and reporting	• C4591001 (ongoing Study): • CSR submission upon regulatory request: at any time • CSR submission 6 months post Dose 2: 31 May 2021 • Final CSR submission with supplemental follow-up: 31 August 2023. • C4591009: • Protocol submission: 31 August 2021 • Monitoring report submission: 31 October 2022 • Interim Analysis submission: 31 October 2023 • Final study report submission: 31 October 2025. • C4591011 ~~and C4591012:~~ • Interim study reports[a] will be submitted on the following dates based on data collected post-EUA in target populations: ~~30 June 2021~~ – 31 December 2021 – 30 June 2022 – 31 December 2022 • Final study reports submission: 31 December 2023. • C4591012

Table 41. Action Plan for Important Identified Risk "Anaphylaxis"

	• Interim study reports will be submitted on the following dates based on data collected post-EUA in target populations: – 30 June 2021 – 31 December 2021 – 30 June 2022 – 31 December 2022 • Final study reports submission: 31 December 2023.

a. FDA was informed (Response to FDA 12 May 2021 - Information Request Regarding Active Surveillance Studies) that the first milestone (Interim Report submission due 30 June 2021) is delayed due to a change in study collaboration;, therefore, it has been removed from in this table.

Action Plan for Important Potential Risks

Table 42. Action Plan for Important Potential Risk "Vaccine-associated enhanced disease (VAED) including Vaccine-associated enhanced respiratory disease (VAERD)"

Actions proposed	• C4591001: Phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals. • C4591008: HERO Together: A post-Emergency Use Authorization observational cohort study to evaluate the safety of the Pfizer-BioNTech COVID-19 Vaccine in US healthcare workers, their families, and their communities. • C4591009: A non-interventional post-approval safety study of the Pfizer--BioNTech COVID-19 mRNA vaccine in the United States. • C4591011: Active safety surveillance of the Pfizer--BioNTech COVID-19 vaccine in the US Department of Defense population following Emergency Use Authorization. • C4591012: Post-emergency use authorization active safety surveillance study among individuals in the Veteran's Affairs Health System receiving Pfizer--BioNTech Coronavirus Disease 2019 (COVID-19) vaccine.
Objective of proposed actions	• C4591001: to evaluate the safety, tolerability, immunogenicity, and efficacy of BNT162b2. An unfavorable imbalance between the vaccine and control groups in the frequency of COVID-19 disease, in particular for severe COVID-19 disease, may indicate the occurrence of VAED/VAERD. Surveillance is planned for 2 years following Dose 2. • C4591008, C4591009, C4591011, and C4591012: to characterize the real-world incidence of safety events of interest, including events indicative of severe or atypical COVID-19 disease, among individuals vaccinated with the BNT162b2 since EUA.
Rationale for proposed actions	• C4591001: Robust and long-term monitoring throughout the clinical study for up to 2 years to assess the risk for vaccine-associated enhanced disease. • C4591008, C4591009, C4591011 and C4591012: Robust surveillance is needed to ensure comprehensive understanding of real-world safety. This surveillance strategy consists of complementary approaches to ensure timely signal identification and evaluation in populations expected to receive the vaccine in the early stages of an EUA as well as with broader vaccination roll-out.

Table 42. Action Plan for Important Potential Risk "Vaccine-associated enhanced disease (VAED) including Vaccine-associated enhanced respiratory disease (VAERD)"

Monitoring by the sponsor for safety issue and proposed actions Monitoring by the sponsor for safety issue and proposed actions *(Cont'd)*	• C4591001: Protocol prespecified stopping and alert rules were set for detecting enhanced COVID-19. Participants in all stages of the study will be monitored for COVID-19 illness including severe COVID-19 from Visit 1 onward. Cases will undergo blinded review to identify whether any features of each case appear unusual, in particular greater severity. Indicators of severity may include accelerated deterioration, need for hospitalization, need for ventilation, or death. The Data Monitoring Committee, supported by an unblinded medical monitor, will look for adverse imbalances between vaccine and control groups in COVID-19 disease outcomes, in particular for cases of severe COVID-19, that may be a signal for vaccine-associated enhanced disease on an ongoing basis and at interim analyses. Stopping rules were set so that enrollment could be paused in the event of an adverse imbalance. Additional safety evaluations will include AESI that could represent symptoms of severe COVID-19 disease; these will be collected systemically and monitored throughout the Phase 3 study. • C4591008, C4591011, C4591012: The collection of safety data in vaccine recipients is critical to our understanding of the vaccine safety profile and to enable efficient safety signal detection and, if needed, further risk mitigation during the EUA. In addition to the collection and monitoring of AEs reported voluntarily by healthcare professionals providing the vaccine and by individuals receiving the vaccine, active surveillance studies of the BNT162b2 under EUA are also planned. Active surveillance of large numbers of individuals vaccinated with the BNT162b2 is necessary to confirm the safety profile demonstrated in the clinical study in a broader population under real-world conditions. Pfizer-BioNTech plans to conduct active surveillance studies of vaccinated individuals in populations prioritized in the early stages of the EUA, e.g., healthcare workers, active military, and elderly, as described in C4591008 protocol submitted to FDA on 28 January 2021; C4591011 protocol submitted to FDA on 29 January 2021 and C4591012 protocol submitted to FDA on 29 January 2021. The study period will be approximately 30 months following availability of vaccine under EUA. The studies will capture hospitalizations, deaths and serious safety events of interest, including severe COVID-19 (which, if associated with vaccination, may indicate VAED/VAERD). • C4591009: Surveillance of large numbers of individuals vaccinated with the BNT162b2 is necessary to confirm the safety profile demonstrated in the clinical study in a broader population under real-world conditions. This study is intended to capture a broader sample of vaccinated individuals of any age in the general US population using large scale data sources.
Milestones for evaluation and reporting	• C4591001 (ongoing Study): • CSR submission upon regulatory request: at any time • CSR submission 6 months post Dose 2: 31 May 2021 • Final CSR submission with supplemental follow-up: 31 August 2023. • Three observational post-authorization safety studies for EUA (C4591008, C4591011, and C4591012): • C4591008 and C4591012: Interim study reports will be submitted on the following dates based on data collected post-EUA in target populations: o 30 June 2021

Table 42. Action Plan for Important Potential Risk "Vaccine-associated enhanced disease (VAED) including Vaccine-associated enhanced respiratory disease (VAERD)"

	○ 31 December 2021 ○ 30 June 2022 ○ 31 December 2022 • Final study reports submission: 31 December 2023. • C4591011: Interim study reports[a] will be submitted on the following dates based on data collected post-EUA in target populations: ○ 31 December 2021 ○ 30 June 2022 ○ 31 December 2022 • Final study reports submission: 31 December 2023. • C4591009: • Protocol submission: 31 August 2021 • Monitoring report submission: 31 October 2022 • Interim Analysis submission: 31 October 2023 • Final study report submission: 31 October 2025.

a. FDA was informed (Response to FDA 12 May 2021 - Information Request Regarding Active Surveillance Studies) that the first milestone (Interim Report submission due 30 June 2021) is delayed due to a change in study collaboration:, therefore, it has been removed from in this table.

Action Plan for Missing Information

Table 43. Action Plan for Missing Information "Use in Pregnancy and Lactation"

Actions proposed	• C4591015: A phase 2/3, placebo-controlled, randomized, observer blind study to evaluate the safety, tolerability, and immunogenicity of a SARS-CoV-2 RNA vaccine candidate (BNT162b2) against COVID-19 in healthy pregnant women 18 years of age and older. • C4591009: A non-interventional post-approval safety study of the Pfizer--BioNTech COVID-19 mRNA vaccine in the United States. • C4591011: Active safety surveillance of the Pfizer-BioNTech COVID-19 Vaccine in the US Department of Defense population following Emergency Use Authorization. • C4591022: Pfizer-BioNTech COVID-19 Vaccine exposure during pregnancy: A non-interventional post-approval safety study of pregnancy and infant outcomes in the Organization of Teratology Information Specialists (OTIS)/MotherToBaby Pregnancy Registry.
Objective of proposed actions	• C4591015: To assess safety and immunogenicity of BNT162b2 in pregnant women. In addition, exploratory objectives include: To describe the immune response in infants born to breastfeeding maternal participants vaccinated with prophylactic BNT162b2 during pregnancy. To describe the safety of maternal immunization in infants born to breastfeeding maternal participants vaccinated with prophylactic BNT162b2 during pregnancy. • C4591009[a]: To assess whether pregnant women experience increased risk of safety events of interest following receipt of the BNT162b2.

Table 43. Action Plan for Missing Information "Use in Pregnancy and Lactation"

	• C4591011[a]: To assess whether sub-cohorts of interest, such as pregnant women, in the MHS experience increased risk of safety events of interest following receipt of the BNT162b2. • C4591022[a]: To assess whether pregnant women receiving BNT162b2 experience increased risk of pregnancy and infant safety outcomes, including major congenital malformations, spontaneous abortion, stillbirth, preterm delivery, small for gestational age, and small for age postnatal growth to one year of age.
Rationale for proposed actions	Acquisition of data in an unstudied population with potentially different safety considerations from the time vaccine is available.
Monitoring by the sponsor for safety issue and proposed actions	• C4591015: Monitoring via ongoing clinical study. • C4591009: The collection of safety data in vaccine recipients, including pregnant women, is critical to our understanding of the vaccine safety profile and to enable robust safety signal detection and evaluation and, if needed, further risk mitigation under BLA. • C4591011: 1. The collection of safety data in vaccine recipients is critical to our understanding of the vaccine safety profile and to enable efficient safety signal detection and, if needed, further risk mitigation. Active surveillance studies of the BNT162b2 under EUA are also planned. 2. Active surveillance of large numbers of individuals vaccinated with the BNT162b2 is necessary to confirm the safety profile demonstrated in the clinical study in a broader population under real-world conditions. Pfizer-BioNTech plans to conduct active surveillance studies of individuals vaccinated with the BNT162b2 under an EUA in populations prioritized in the early stages of the EUA, e.g., active military and their family members, as described in C4591011 (protocol submitted to FDA on 29 January 2021). The study period will be approximately 30 months following availability of vaccine under EUA. The study will capture hospitalizations, deaths and serious safety events of interest, including anaphylaxis. • C4591022: This study will monitor rates of pregnancy and infant outcomes in planned and unplanned pregnancies exposed to BNT162b2 using an established pregnancy registry. Women receiving BNT162b2 during pregnancy will be followed from exposure to one-year post-partum. Analyses will be conducted to evaluate if the pregnant women receiving the vaccine during pregnancy experience increased risk of pregnancy and infant outcomes compared with 1) pregnant women who are unvaccinated and 2) pregnant women who have received an influenza or tetanus, diphtheria, and acellular pertussis (Tdap) vaccine during pregnancy.
Milestones for evaluation and reporting	• C4591015: Primary endpoints completion: 30 April 2023. • C4591009: • Protocol submission: 31 August 2021 • Monitoring report submission: 31 October 2022 • Interim Analysis submission: 31 October 2023 • Final study report submission: 31 October 2025. • C4591011: • Interim study reports[b] will be submitted on the following dates based on data collected post-EUA in target populations:

Table 43. Action Plan for Missing Information "Use in Pregnancy and Lactation"

	~~○ 30 June 2021~~ ○ 31 December 2021 ○ 30 June 2022 ○ 31 December 2022 • Final study report submission: 31 December 2023. • C4591022: • Protocol submission: 01 July 2021 • Interim reports submission: ○ 31 January 2022 ○ 31 January 2023 ○ 31 January 2024 ○ 31 January 2025 • Final study report submission: 01 December 2025

a. Study assesses pregnancy only.
b. FDA was informed (Response to FDA 12 May 2021 - Information Request Regarding Active Surveillance Studies) that the first milestone (Interim Report submission due 30 June 2021) is delayed due to a change in study collaboration; therefore, it has been removed from in this table.

Table 44. Action Plan for Missing Information "Vaccine Effectiveness"

Action proposed	• C4591014: Pfizer-BioNTech COVID-19 BNT162b2 Vaccine Effectiveness Study - Kaiser Permanente Southern California. • WI235284: Determining RSV Burden and Outcomes in Pregnant Women and Older Adults Requiring Hospitalization. COVID-19 Amendment for COVID VE/ Sub-study 6. • WI255886: Avon Community Acquired Pneumonia Surveillance Study: A Pan-pandemic Acute Lower Respiratory Tract Disease Surveillance Study. • BNT162-01 cohort 13: Immunogenicity of Pfizer-BioNTech COVID-19 Vaccine in immunocompromised subjects, including assessment of antibody responses and cell-mediated responses.
Objective of proposed actions	• C4591014: To estimate the effectiveness of 2 doses of BNT162b2 against hospitalization and emergency department admission for acute respiratory illness due to SARS-CoV-2 infection. • WI235284: To estimate the effectiveness of 2 doses of BNT162b2 against hospitalization for acute respiratory illness due to SARS-CoV-2 infection. • WI255886: To estimate the effectiveness of 2 doses of BNT162b2 against hospitalization for acute respiratory illness due to SARS-CoV-2 infection. • BNT-162-01 cohort 13: To assess potentially protective immune responses in immunocompromised adults.
Rationale for proposed actions	• C4591014: To determine the effectiveness of BNT162b2 when administered outside of the clinical setting. • WI235284: To determine the effectiveness of BNT162b2 when administered outside of the clinical setting. • WI255886: To determine the effectiveness of BNT162b2 when administered outside of the clinical setting. • BNT-162-01 cohort 13: To determine whether the BNT162b2 has potential to protect immunocompromised adults.

Table 44. Action Plan for Missing Information "Vaccine Effectiveness"

Monitoring by the sponsor for safety issue and proposed actions	• C4591014: Use of primary and secondary data sources to monitor COVID-19 infection in vaccinated individuals. • WI235284: Use of primary and secondary data sources to monitor COVID-19 infection in vaccinated individuals. • WI255886: Use of primary and secondary data sources to monitor COVID-19 infection in vaccinated individuals. • BNT-162-01 cohort 13: Reactogenicity, AE and SAE assessment.
Milestones for evaluation and reporting	• C4591014: Final CSR submission: 30 June 2023. • WI235284: Final CSR submission: 30 June 2023. • WI255886: Final CSR submission: 30 June 2023. • BNT-162-01 cohort 13: First IA submission: 30 September 2021.

Table 45. Action Plan for Missing Information "Use in Paediatric Individuals <12 Years of Age"

Actions proposed	• C4591001 ≥12 to ≤15 years of age: Phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals[a]. Randomised placebo-controlled study in 2000 participants (1000 active recipients) of 2 doses of BNT162b2 at a 21-day interval. • C4591007 <12 years of age: Phase 1 open label dose-finding study to evaluate safety, tolerability, and immunogenicity and phase 2/3 placebo-controlled, observer- blinded safety, tolerability, and immunogenicity study of a SARS-CoV-2 RNA vaccine candidate against COVID-19 in healthy children <12 years of age. Phase 1: open-label dose finding portion up to 3 age groups (participants ≥5 to <12 years, ≥2 to <5 years, and ≥6 months to <2 years of age) with 16 participants per dose level. Dose finding is being initiated in this study in participants ≥5 to <12 years of age based on the acceptable blinded safety assessment of the 30-µg dose in 12- to 15-year-olds in the C4591001 study. The purpose of Phase 1 is to identify preferred dose level(s) of BNT162b2 from up to 3 different dose levels in each age group. Phase 2/3: Children ≥5 to <12 years of age are randomized 2:1 at selected dose level of BNT162b2 at a 21-day interval (2250 total subjects; 1500 active vaccine). Children 2 to < 5 years and 6 to 23 months of age randomized 2:1 placebo controlled at selected dose level of BNT162b2 at a 21-day interval (1125 total subjects per age group; 750 active vaccine per age group). • C4591009: A non-interventional post-approval safety study of the Pfizer-BioNTech COVID-19 mRNA vaccine in the United States.

Table 45. Action Plan for Missing Information "Use in Paediatric Individuals <12 Years of Age"

Objective of proposed actions	• C4591001 ≥12 to ≤15 years of age: Safety compared to placebo and immune-non-inferiority of neutralizing antibody immune response compared to subjects 16-25 years of age. • C4591007 <12 years of age: Dose selection. Safety compared to placebo and immune-non-inferiority by 3 age cohorts of neutralizing antibody immune response compared to subjects 16-25 years of age. Efficacy if sufficient cases accrue. • C4591009: To assess the occurrence of safety events of interest in a general US population (<12 and ≥12 to ≤15 years of age) within selected data sources participating in the Sentinel System.
Rationale for proposed actions	• C4591001 ≥12 to ≤15 years of age: Need to collect evidence of safety and effectiveness to support immunization in this age group. • C4591007 <12 years of age: Need to collect evidence of safety and effectiveness to support immunization in this age group. • C4591009: Long-term surveillance of large numbers of individuals (<12 and ≥12 to ≤15 years of age) vaccinated with the BNT162b2 is necessary to confirm the safety profile demonstrated in the clinical study in a broader population under real-world conditions.

Monitoring by the sponsor for safety issue and proposed actions	• C4591001 ≥12 to ≤15 years of age:
	  • Electronic diary for reactogenicity 7 days following each dose of vaccine.
	  • Adverse events for one month after second dose.
	  • Serious Adverse Events for 6 months after the second dose.
	  • Related SAEs and related deaths for 24 months after the second dose.
	  • Collection of COVID-19 and MIS-C cases up to 24 months after the second dose.
	• C4591007 <12 years of age:
	  • Electronic diary for reactogenicity 7 days following each dose of vaccine.
	  • Adverse events for one month after second dose.
	  • Serious Adverse Events for 6 months after the second dose.
	  • Related SAEs and related deaths for 24 months after the second dose.
	  • Collection of COVID-19 and MIS-C cases up to 24 months after the second dose.
	• C4591009: < 12 and ≥12 to ≤15 years of age
	  • Longitudinal medical care information on outpatient medication dispensing, vaccine administrations, and inpatient and outpatient diagnoses and procedures in addition to adjudication of select events via medical records.
	  • Incidence rates and comparative incidence rate ratios of safety events of interest (AESIs from FDA's BEST System[70] and CDC's Vaccine Safety Datalink[71] in addition to vaccine-associated enhanced respirator disease).
	  • Study period to start on date that BNT162b2 became available under EUA (December 11, 2020) and will end a minimum of 3 years after this date.
	  • Risk windows will be defined for safety events of interest that have a hypothesized increased risk during specific time periods following vaccination. For other safety events of interest, patients will be followed for a maximum of 1 year.

Table 45. Action Plan for Missing Information "Use in Paediatric Individuals <12 Years of Age"

Milestones for evaluation and reporting	• C4591001 ≥12 to ≤15 years of age:
	  • First report with up to 1-month post dose 2 (safety): 30 April 2021
	  • Further reports:
	  – 6-month post dose 2 (safety): 31 ~~July 2021~~October 2021[b]
	  – 24-month post dose 2 (safety): ~~31 January~~30 April 2023~~.~~[c].
	• C4591007 <12 years of age:
	  • First report with up to 1-month post dose 2 in ≥5 to <12 years of age (safety): 30 September 2021
	  • Further reports:
	  – 6-month post dose 2 (safety): 31 March 2022
	  – 24-month post dose 2 (safety): 30 September 2023.
	• C4591009:
	  • Protocol submission: 31 August 2021
	  • Monitoring report submission: 31 October 2022
	  • Interim Analysis submission: 31 October 2023
	  • Final study report submission: 31 October 2025.

a. Study originally included in the PVP to address the Missing Information "Use in pediatric individuals < 16 years of age".
b. Due date updated from 31 July 2021 because the last subject visit for this group will not be until September 2021.
c. Due updated from 31 January 2023 for the same reason above..

3.1.4. Summary of Actions to be Completed, Including Milestones

Table 46. Summary of Safety Concerns and Action Plans

Safety Concerns	Ongoing/Planned Action	Summary of Objectives	Milestones	Due dates
Myocarditis and Pericarditis	C4591009: A non-interventional post-approval safety study of the Pfizer-BioNTech COVID-19 mRNA vaccine in the United States. *Planned*	To assess the occurrence of safety events of interest, including myocarditis and pericarditis, in the general US population, pregnant women, the immunocompromised and persons with a prior history of COVID-19 within selected data sources participating in the US Sentinel System	• Protocol submission: • Monitoring report submission: • Interim analysis submission: • Final study report submission:	• 31 August 2021 • 31 October 2022 • 31 October 2023 • 31 October 2025
	C4591011: Active safety surveillance of the Pfizer-BioNTech COVID-19 Vaccine in the US Department of Defense population following Emergency Use Authorization *Planned*	To assess whether individuals in the US DoD Military Health System (MHS) experience increased risk of safety events of interest, including myocarditis and pericarditis, following receipt of the Pfizer-BioNTech COVID-19 Vaccine.	• Interim reports submission:[a] • Final study report submission:	• 31 December 2021 30 June 2022 31 December 2022 • 31 December 2023
	C4591012: Post-emergency use authorization active safety surveillance study among individuals in the Veteran's Affairs Health System receiving Pfizer-BioNTech COVID-19 Vaccine. *Ongoing*	To assess whether individuals in the US Veteran's Affairs Health System experience increased risk of safety events of interest, including myocarditis and pericarditis, following receipt of the Pfizer-BioNTech COVID-19 Vaccine	• Interim reports submission: • Final study report submission:	• 30 June 2021 31 December 2021 30 June 2022 31 December 2022 • 31 December 2023
Anaphylaxis	C4591001: Phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals.	To evaluate the safety, tolerability, immunogenicity, and efficacy of BNT162b2. An unfavorable imbalance between the vaccine and control groups in the frequency of COVID-19 disease, in particular for severe COVID-19 disease, may indicate the occurrence	• CSR submission upon regulatory request: • CSR submission 6-month post Dose 2: • Final CSR submission with supplemental follow-up:	• At any time • 31 May 2021 • 31 August 2023

Table 46. Summary of Safety Concerns and Action Plans

Safety Concerns	Ongoing/Planned Action	Summary of Objectives	Milestones	Due dates
	Ongoing	of VAED/VAERD. Surveillance is planned for 2 years following Dose 2.		
	C4591009: A non-interventional post-approval safety study of the Pfizer-BioNTech COVID-19 mRNA Vaccine in the United States. *Planned*	To assess the occurrence of safety events of interest in the general US population, pregnant women, the immunocompromised and persons with a prior history of COVID-19 within selected data sources participating in the US Sentinel System.	• Protocol submission: • Monitoring report submission: • Interim analysis submission: • Final study report submission:	• 31 August 2021 • 31 October 2022 • 31 October 2023 • 31 October 2025
	C4591011: Active safety surveillance of the Pfizer-BioNTech COVID-19 Vaccine in the US Department of Defense population following Emergency Use Authorization. *Planned*	To assess whether individuals in the US DoD Military Health System (MHS) experience increased risk of safety events of interest, following receipt of the BNT162b2.	• Interim reports submission~~:~~[a]: • Final study report submission:	• ~~30 June 2021~~ 31 December 2021 30 June 2022 31 December 2022 • 31 December 2023
Anaphylaxis *(Cont'd)*	C4591012: Post-emergency use authorization active safety surveillance study among individuals in the Veteran's Affairs Health System receiving Pfizer-BioNTech COVID-19 Vaccine. ~~*Planned*~~ Ongoing	To assess whether individuals in the US Veteran's Affairs Health System experience increased risk of safety events of interest, following receipt of the BNT162b2.	• Interim reports submission: • Final study report submission:	• 30 June 2021 31 December 2021 30 June 2022 31 December 2022 • 31 December 2023

Table 46. Summary of Safety Concerns and Action Plans

Safety Concerns	Ongoing/Planned Action	Summary of Objectives	Milestones	Due dates
Vaccine-associated enhanced disease (VAED) including vaccine-associated enhanced respiratory disease (VAERD)	C4591001: Phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals. *Ongoing*	To evaluate the safety, tolerability, immunogenicity, and efficacy of BNT162b2. An unfavorable imbalance between the vaccine and control groups in the frequency of COVID-19 disease, in particular for severe COVID-19 disease, may suggest the occurrence of VAED/VAERD. Surveillance is planned for 2 years following Dose 2	• CSR submission upon regulatory request: • CSR submission 6-month post Dose 2: • Final CSR submission with supplemental follow-up:	• Any time • 31 May 2021 • 31 August 2023
	C4591008~~/C4591011~~/C4591012: Post-authorization epidemiological safety studies using active and passive surveillance strategies for safety events, including severe or atypical COVID-19, among individuals receiving Pfizer-BioNTech COVID-19 Vaccine C4591008: *Ongoing* ~~*C4591011*~~/C4591012: ~~*Planned*~~*Ongoing*	To characterize the real-world incidence of safety events of interest, including events indicative of severe or atypical COVID-19 disease, among individuals vaccinated with the BNT162b2 since EUA	• Interim reports submission: • Final study report submission:	• 30 June 2021 31 December 2021 30 June 2022 31 December 2022 • 31 December 2023
	C4591011: Active safety surveillance of the Pfizer-BioNTech COVID-19 Vaccine in the US Department of Defense population following Emergency Use Authorization *Planned*	To characterize the real-world incidence of safety events of interest, including events indicative of severe or atypical COVID-19 disease, among individuals vaccinated with the BNT162b2 since EUA	• Interim reports submission[a] • Final study report submission	• 31 December 2021 30 June 2022 31 December 2022 • 31 December 2023
Vaccine-associated enhanced disease (VAED)	C4591009: A non-interventional post-approval safety study of the Pfizer-BioNTech COVID-19 mRNA Vaccine in the United States	To characterize the real-world incidence of safety events of interest, including events indicative of severe or atypical COVID-19 disease,	• Protocol submission: • Monitoring report submission:	• 31 August 2021 • 31 October 2022 • 31 October 2023

Table 46. Summary of Safety Concerns and Action Plans

Safety Concerns	Ongoing/Planned Action	Summary of Objectives	Milestones	Due dates
including vaccine-associated enhanced respiratory disease (VAERD) *(Cont'd)*	*Planned*	among individuals vaccinated with the BNT162b2	• Interim analysis submission: • Final study report submission:	• 31 October 2025
Use in pregnancy and lactation	C4591015: A phase 2/3, placebo-controlled, randomized, observer-blind study to evaluate the safety, tolerability, and immunogenicity of a SARS-CoV-2 RNA vaccine candidate (BNT162b2) against COVID-19 in healthy pregnant women 18 years of age and older. *Ongoing*	To assess safety and immunogenicity of BNT162b2 in pregnant women. Exploratory objectives include: To describe the immune response in infants born to breastfeeding maternal participants vaccinated with prophylactic BNT162b2 during pregnancy. To describe the safety of maternal immunization in infants born to breastfeeding maternal participants vaccinated with prophylactic BNT162b2 during pregnancy.	• Primary endpoints completion:	• 30 April 2023
Use in pregnancy and lactation *(Cont'd)*	C4591011: Active safety surveillance of the Pfizer-BioNTech COVID-19 Vaccine in the United States Department of Defense population following Emergency Use Authorization *Planned*	To assess whether sub-cohorts of interest, such as pregnant women, in the MHS experience increased risk of safety events of interest following receipt of the BNT162b2.	• Interim reports submission:[a] • Final study report submission:	• ~~30 June 2021~~31 December 2021 30 June 2022 31 December 2022 • 31 December 2023
	C4591009: A non-interventional post-approval safety study of the Pfizer-BioNTech COVID-19 mRNA Vaccine in the United States. *Planned*	To assess whether pregnant women, experience increased risk of safety events of interest following receipt of the BNT162b2.	• Protocol submission: • Monitoring report submission: • Interim analysis submission: • Final study report submission:	• 31 August 2021 • 31 October 2022 • 31 October 2023 • 31 October 2025

Table 46. Summary of Safety Concerns and Action Plans

Safety Concerns	Ongoing/Planned Action	Summary of Objectives	Milestones	Due dates
	C4591022: Pfizer-BioNTech COVID-19 Vaccine exposure during pregnancy: A non-interventional post-approval safety study of pregnancy and infant outcomes in the Organization of Teratology Information Specialists (OTIS)/MotherToBaby Pregnancy Registry	To assess whether pregnant women receiving BNT162b2 experience increased risk of pregnancy and infant safety outcomes, including major congenital malformations, spontaneous abortion, stillbirth, preterm delivery, small for gestational age, and small for age postnatal growth to one year of age.	• Protocol submission: • Interim reports submission: Final study report submission:	• 01 July 2021 • 31 January 2022 31 January 2023 31 January 2024 31 January 2025 01 December 2025
Vaccine effectiveness	C4591014: Pfizer-BioNTech COVID-19 BNT162b2 Vaccine Effectiveness Study - Kaiser Permanente Southern California. *Planned*	To estimate the effectiveness of 2 doses of BNT162b2 against hospitalization and emergency department admission for acute respiratory illness due to SARS-CoV-2 infection.	• Final CSR submission:	• 30 June 2023
Vaccine effectiveness *(Cont'd)*	WI235284: Determining RSV Burden and Outcomes in Pregnant Women and Older Adults Requiring Hospitalization. Amendment for COVID VE/ Sub-study 6. *Planned*	To estimate the effectiveness of 2 dosed of BNT162b2 against hospitalization for acute respiratory illness due to SARS-CoV-2 infection.	• Final CSR submission:	• 30 June 2023

Table 46. Summary of Safety Concerns and Action Plans

Safety Concerns	Ongoing/Planned Action	Summary of Objectives	Milestones	Due dates
	WI255886: Avon Community Acquired Pneumonia Surveillance Study: A Pan-pandemic Acute Lower Respiratory Tract Disease Surveillance. *Planned*	To estimate the effectiveness of 2 doses of BNT162b2 against hospitalization for acute respiratory illness due to SARS-CoV-2 infection.	• Final CSR submission:	• 30 June 2023
	BNT162-01 cohort 13: Immunogenicity of Pfizer-BioNTech COVID-19 Vaccine in immunocompromised subjects, including assessment of antibody responses and cell-mediated responses. *Ongoing*	To assess potentially protective immune responses in immunocompromised adults.	• First IA submission:	• 30 September 2021

Table 46. Summary of Safety Concerns and Action Plans

Safety Concerns	Ongoing/Planned Action	Summary of Objectives	Milestones	Due dates
Use in pediatric individuals <12 years of age	C4591001 ≥12 to ≤15 years of age: Phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals[b]. *Ongoing*	Safety compared to placebo and immune-non-inferiority of neutralizing antibody immune response compared to subjects 16-25 years of age.	• First report with up to 1-month post dose 2 (safety): • Report 6-month post dose 2 (safety): • Report 24-month post dose 2 (safety):	• 30 April 2021 • ~~31 July 2021~~ • ~~31 January 2023~~31 October 2021[c] • 30 April 2023[d]
	C4591007 <12 years of age: Phase 1 open label dose-finding study to evaluate safety, tolerability, and immunogenicity and phase 2/3 placebo-controlled, observer blinded safety, tolerability, and immunogenicity, study of a SARS-CoV-2 RNA vaccine candidate against COVID-19 in healthy children <12 years of age. *Ongoing (started in March)*	Dose selection. Safety compared to placebo and immune-non-inferiority by 3 age cohorts of neutralizing antibody immune response compared to subjects 16-25 years of age. Efficacy if sufficient cases accrue.	• First report with up to 1-month post dose 2 (safety) in ≥5 to <12 years of age: • Report 6-month post dose 2 (safety) in ≥5 to <12 years of age: • Report 24-month post dose 2 (safety) in ≥5 to <12 years of age:	• 30 September 2021 • 31 March 2022 • 30 September 2023
	C4591009: A non-interventional post-approval safety study of the Pfizer-BioNTech COVID-19 mRNA vaccine in the United States. *Planned*	To assess the occurrence of safety events of interest in a general US population (< 12 and ≥ 12 to ≤15 years of age) within selected data sources participating in the Sentinel System.	• Protocol submission: • Monitoring report submission: • Interim analysis submission: • Final study report submission:	• 31 August 2021 • 31 October 2022 • 31 October 2023 • 31 October 2025

a. FDA was informed (Response to FDA – 12 May 2021 – Information Request Regarding Active Surveillance Studies) that the first milestone (Interim Report submission due 30 June 2021) is delayed due to a change in study collaboration; therefore, it has been removed from this table.
b. Study originally included in the PVP to address the Missing Information "Use in pediatric individuals < 16 years of age.
c. Due date updated from 31 July 2021 because the last subject visit for this group will not be until September 2021.
d. Due updated from 31 January 2023 for the same reason above.

ANNEX

3.2. Pharmacovigilance Methods

- BNT162b2 Vaccine: BNT162b2 Data Capture Aids:
    - Pfizer-BioNTech COVID-19 Vaccine VAED Data Capture Aid.
    - Pfizer-BioNTech COVID-19 Vaccine Anaphylactic Reaction Data Capture Aid.

3.2.1. List of Studies Included in the Pharmacovigilance Plan

C4591001

C4591007

C4591008

C4591009

C4591011

C4591012

C4591014

C4591015

C4591022

BNT162-01 cohort 13

WI235284

WI255886

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BNT162b2 (COMIRNATY)

BLA STN 125742/0

Response to CBER Comment Regarding Analyses for Safety for the Two Age Groups

August 2021

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LIST OF TABLES

1. INTRODUCTION

Reference is made to BLA STN 125742/0 for COVID-19 mRNA Vaccine (COMIRNATY), for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals ≥16 years of age and to CBER's 29 July 2021 Information Request received via email from Laura Gottschalk, PhD, CBER, OVRR regarding safety for the following age groups: 1) 16 through 55 years, 2) 56 years and older.

CBER's request in ***bold italics*** is followed by Pfizer/BioNTech's response below.

2. REQUESTS

2.1. CBER Request

Our review of the information provided in your BLA STN 125742/0 for COMIRNATY (COVID-19 Vaccine, mRNA), for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older, is ongoing. We have the following request for additional information:

Please submit the analyses as presented in Table 7 (page 116) of the Summary of Clinical Safety for the following age groups: 1) 16 through 55 years, 2) 56 years and older.

Response

Table 7 in the Summary of Clinical Safety presents the incident rates of at least 1 adverse event from dose 1 to unblinding date in the Phase 2/3 Subjects ≥16 Years of Age (Safety Population). The corresponding analyses for the two requested age groups were presented in Tables 14.106 and 14.107 located in Module 5.3.5.1 C4591001 6-Month Update Interim CSR Section 14, which are also provided in this response (Table 1 and Table 2).

Table 1. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by Age Group – Phase 2/3 Subjects ≥16 Years of Age – Safety Population
Age Group: 16-55 Years

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=12995, TE[b]=49.7)			Placebo (N[a]=13026, TE[b]=49.1)		
Adverse Event	n[c]	IR (/100 PY)[d]	(95% CI[e])	n[c]	IR (/100 PY)[d]	(95% CI[e])
Any event	4396	88.4	(85.8, 91.0)	2136	43.5	(41.7, 45.4)
Related[f]	3484	70.0	(67.7, 72.4)	884	18.0	(16.8, 19.2)
Severe	193	3.9	(3.4, 4.5)	124	2.5	(2.1, 3.0)
Life-threatening	13	0.3	(0.1, 0.4)	20	0.4	(0.2, 0.6)
Any serious adverse event	103	2.1	(1.7, 2.5)	117	2.4	(2.0, 2.9)
Related[f]	3	0.1	(0.0, 0.2)	1	0.0	(0.0, 0.1)
Severe	56	1.1	(0.9, 1.5)	75	1.5	(1.2, 1.9)
Life-threatening	13	0.3	(0.1, 0.4)	20	0.4	(0.2, 0.6)
Any adverse event leading to withdrawal	22	0.4	(0.3, 0.7)	28	0.6	(0.4, 0.8)
Related[f]	9	0.2	(0.1, 0.3)	8	0.2	(0.1, 0.3)
Severe	5	0.1	(0.0, 0.2)	6	0.1	(0.0, 0.3)
Life-threatening	3	0.1	(0.0, 0.2)	5	0.1	(0.0, 0.2)
Death	3	0.1	(0.0, 0.2)	4	0.1	(0.0, 0.2)

a. N = number of subjects in the specified group.
b. TE = total exposure time in 100 person-years across all subjects in the specified group. Exposure time for a subject is the time from Dose 1 to the end of blinded follow-up. This value is the denominator for the incidence rate calculation.
c. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
d. Incidence rate (IR) is calculated as number of subjects reporting the event/total exposure time in 100 person-years (PY) across all subjects in the specified group.
e. 2-sided CI based on Poisson distribution.
f. Assessed by the investigator as related to investigational product.

Table 1. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by Age Group – Phase 2/3 Subjects ≥16 Years of Age – Safety Population
Age Group: 16-55 Years

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=12995, TE[b]=49.7)			Placebo (N[a]=13026, TE[b]=49.1)		
Adverse Event	n[c]	IR (/100 PY)[d]	(95% CI[e])	n[c]	IR (/100 PY)[d]	(95% CI[e])

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (02:10)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adae_s092_unb_age_p3_saf

Table 2. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by Age Group – Phase 2/3 Subjects ≥16 Years of Age – Safety Population
Age Group: >55 Years

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=8931, TE[b]=33.7)			Placebo (N[a]=8895, TE[b]=33.1)		
Adverse Event	n[c]	IR (/100 PY)[d]	(95% CI[e])	n[c]	IR (/100 PY)[d]	(95% CI[e])
Any event	2551	75.7	(72.8, 78.7)	1432	43.3	(41.1, 45.6)
Related[f]	1762	52.3	(49.9, 54.8)	429	13.0	(11.8, 14.3)
Severe	163	4.8	(4.1, 5.6)	132	4.0	(3.3, 4.7)
Life-threatening	35	1.0	(0.7, 1.4)	34	1.0	(0.7, 1.4)
Any serious adverse event	165	4.9	(4.2, 5.7)	151	4.6	(3.9, 5.4)
Related[f]	1	0.0	(0.0, 0.2)	0	0.0	(0.0, 0.1)
Severe	92	2.7	(2.2, 3.3)	81	2.4	(1.9, 3.0)

Table 2. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by Age Group – Phase 2/3 Subjects ≥16 Years of Age – Safety Population
Age Group: >55 Years

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=8931, TE[b]=33.7)			Placebo (N[a]=8895, TE[b]=33.1)		
Adverse Event	n[c]	IR (/100 PY)[d]	(95% CI[e])	n[c]	IR (/100 PY)[d]	(95% CI[e])
Life-threatening	35	1.0	(0.7, 1.4)	34	1.0	(0.7, 1.4)
Any adverse event leading to withdrawal	23	0.7	(0.4, 1.0)	23	0.7	(0.4, 1.0)
Related[f]	4	0.1	(0.0, 0.3)	4	0.1	(0.0, 0.3)
Severe	5	0.1	(0.0, 0.3)	6	0.2	(0.1, 0.4)
Life-threatening	12	0.4	(0.2, 0.6)	11	0.3	(0.2, 0.6)
Death	12	0.4	(0.2, 0.6)	10	0.3	(0.1, 0.6)

a. N = number of subjects in the specified group.
b. TE = total exposure time in 100 person-years across all subjects in the specified group. Exposure time for a subject is the time from Dose 1 to the end of blinded follow-up. This value is the denominator for the incidence rate calculation.
c. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
d. Incidence rate (IR) is calculated as number of subjects reporting the event/total exposure time in 100 person-years (PY) across all subjects in the specified group.
e. 2-sided CI based on Poisson distribution.
f. Assessed by the investigator as related to investigational product.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (02:10)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adae_s092_unb_age_p3_saf

3. REFERENCES

None

BNT162b2 (COMIRNATY)

BLA STN 125742/0

Response to CBER 22 July 2021 Information Request Regarding Clinical Shell Tables for Study C4591001

Follow-Up #2

August 2021

1. INTRODUCTION

Reference is made to BLA STN 125742/0 for COVID-19 mRNA Vaccine (COMIRNATY), for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals ≥16 years of age and to CBER's 22 July 2021 Information Request received via email from Laura Gottschalk, PhD, CBER, OVRR, regarding the request to provide additional sensitivity analysis in question 5b if it was not previously provided or conducted. This request was made initially on 22 July 2021 and Pfizer agreed to provide the results of the additional sensitivity analysis by 02 August 2021 in the 26 July 2021 responses submitted to CBER.

Reference is made to BLA STN 125742/0 for COVID-19 mRNA Vaccine (COMIRNATY), for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals ≥16 years of age and to CBER's 22 July 2022 Information Request received via email from Laura Gottshalk, PhD (CBER) regarding clinical shell tables for Study C4591001.

Further reference is made to the Response to CBER 22 July 2021 Information Request submitted to BLA 125742/0 on 26 July 2021 (Sequence Number 0018) and to the Response to CBER 22 July 2021 Information Request Follow-up #1 submitted to BLA 125549/0 on 28 July 2021 (Sequence Number 0020)

Please note the following:

- Responses to CBER 22 July 2021 Information Request Items 3, 4, 5, 7, 8 and 9 were submitted to BLA 125742/0 on 26 July 2021. **The present submission provides further follow-up to the information provided in this document for Item 5(b).**
- Response to CBER 22 July 2021 Information Request Items 1 and 2 were submitted to BLA 125742/0 on 28 July 2021.
- CBER 22 July 2021 Information Request Item 6 will be the subject of separate, future, follow-up Response.

CBER requests are provided below in ***bold italics*** with Sponsor responses in plain text.

2. REQUESTS

2.1. CBER Request 5

In the efficacy analyses, subjects at risk were determined (in part) by the "PDRMUPFL='N'" condition, which would exclude all subjects who had reported COVID symptoms but had missing or unknown PCR results at any time. It may be reasonable to exclude subjects who had reported COVID symptoms but had missing/unknown PCR results prior to 7 days after dose 2 for the efficacy analyses in subjects without evidence of infection, as this would define a more specific group of subjects without evidence of infection. However, based on your analyses, subjects who reported symptoms and had missing/unknown PCR results after 7 days post dose 2 were also excluded from the efficacy analyses, while these subjects were in fact at risk for the efficacy endpoint starting

from 7 days post dose 2. For example, Subject 10011087 was excluded since he/she reported symptoms on 01/09/2021 without any associated PCR result, which was ~144 days post dose 2.

a. Please explain why these subjects were not considered at risk for the respective efficacy endpoints, and comment on the impact of the exclusion on the VE results.

b. In Section 6.1.3.1.2 of the SAP, it is stated that "with MAR assumption, a missing efficacy endpoint (laboratory-confirmed COVID-19 results) may be imputed based on predicted probability using the fully conditional specification method." Please clarify whether this sensitivity analysis was conducted and the location of the sensitivity analyses if they were submitted. If not, please perform such a sensitivity analysis for subjects who reported COVID symptoms but had missing/unknown PCR results.

Sponsor Response

The response to Item 5(a) and an initial response to Item 5(b) was previously submitted to CBER on 26 July 2021 (Response to 22 July 2021 Information Request; Sequence Number 0018).

The additional sensitivity analysis to respond to Item 5(b) is provided in Table 1.

A total of 648 subjects (279 in BNT162b2 group and 369 in placebo group) in the evaluable population reported COVID-19 symptoms from 7 days post Dose 2 but had PCR results missing/unknown as of data cutoff 13 Mar 2021 (Table 2 of the Response to CBER 22 July 2021 Information Request Follow-up #1 submitted on 28 July 2021). Sensitivity analysis with missing data imputation described in the SAP, using the same methods as the original EUA database, was performed using the updated data.

It was expected that the missing data had minimal impact on the overall result. As shown in Table 1 below, average VE after imputation was over 70% even with up to 16-fold increase of positivity rate applied to the BNT162b2 group. With over 20-fold increase of positivity rate applied to the BNT162b2 group, median lower bound of the 95% CI for VE is still >60% and the percentage of times the posterior probability of VE >30% was greater than 98.6% is 100%.

Table 1. Table Sensitivity and Robustness Analysis of Missing Laboratory Results for Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

Assumed Missing Data Mechanism	Average Positive Rate (%) Across all Imputations (BNT162b2:Placebo)[a]	Infection Rates Based on Existing and Imputed Values (BNT162b2:Placebo)[b]	Median Posterior Probability of VE > 30%	Percentage of Posterior Probability of VE >30% greater than 98.6%	Median of Lower Limit of 95% CI for VE	Median VE (%)	Average VE (%)
MAR	4.0:28.5	4.21:45.31	100.00	100.00	88.56	90.78	90.76
MNAR1	10.1:28.5	5.01:45.31	100.00	100.00	86.55	88.97	88.98
MNAR2	23.3:28.5	6.76:45.31	100.00	100.00	82.30	85.12	85.14
MNAR3	45.3:28.5	9.69:45.31	100.00	100.00	75.36	78.79	78.69
MNAR4	69.1:28.5	12.85:45.31	100.00	100.00	67.71	71.78	71.75
MNAR5	85.9:28.5	15.08:45.31	100.00	100.00	62.36	66.81	66.85

Abbreviations: MAR = missing at random; MNAR = missing not at random; VE = vaccine efficacy.
Note: Each row of this table represents summary results from 500 imputations that were generated using SAS PROC MI Fully Conditional Specification (FCS) method. Each imputation filled in the missing laboratory results based on a logistic regression model at the subject level, under the assumed missing data mechanism.
a. Average positive rate for each vaccine group was calculated as the mean of positive rates across all imputations among subjects with missing data after each imputation. Under the MAR assumption, the imputation model assumes the probability of positive cases for each vaccine group to be the same as observed from subjects with no missing data in that group. Under each MNAR assumption, while keeping the imputation model for placebo group unchanged, an increase in the positive rate for the BTN162b2 group was assumed to reflect a potential conservative and unknowable MNAR scenario for efficacy results of the study.
b. Infection rate in each vaccine group was the number of cases divided by a total number of subjects in that vaccine group times 1000.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adc19ef Table Generation: 30JUL2021 (12:35)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA_RR/adc19ef_ve_7pd2_wo_sen1_eval_bla

3. REFERENCES

None

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ~~TRADENAME~~ COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older (1)

DOSAGE AND ADMINISTRATION

COMIRNATY is administered intramuscularly as a series of 2 doses (0 3 mL each) 3 weeks apart (2 3)

DOSAGE FORMS AND STRENGTHS

Suspension for injection After preparation, a single dose is 0 3 mL (3)

CONTRAINDICATIONS

Known history of a severe allergic reaction (e g , anaphylaxis) to any component of COMIRNATY (4)

WARNINGS AND PRECAUTIONS

- Postmarketing reports of adverse events suggest increased risks of myocarditis and pericarditis, particularly following the second dose (5 2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY Procedures should be in place to avoid injury from fainting (5 4)

ADVERSE REACTIONS

n clinical studies of participants 16 years of age and older, the most commonly reported adverse reactions (>10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, fever, and injection site swelling (6 1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed

Commented [A1]: Pfizer-BioNTech comment
The Sponsor has revised the placeholder "TRADENAME" to the FDA approved "COMIRNATY" tradename through the USPI. Only the first instance of this revision is shown in tracked mode.

Commented [A2]: FDA comment
Pfizer: we have inserted a place holder W/P for myocarditis/pericarditis based on the fact sheet language. We anticipate that this will be further revised.

Pfizer-BioNTech response
The Sponsor accepts the FDA proposed text and acknowledges the FDA comment.

Commented [A3]: FDA comment
Pfizer: Please provide percentages for each adverse reaction—i e., " were pain at the injection site (X%), fatigue (X%) broken out by age (16 through 55 yrs and 56 and older), "

Pfizer-BioNTech response
The Sponsor has not revised this text in the Highlights section as the requested information is not captured in the Full Prescribing Information (FPI). The FDA requested information is more appropriate for inclusion in the FPI vs the Highlights page. The Sponsor will review the Highlights page once the section 6 is further reviewed by FDA.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

2.1 Preparation for Administration

Prior to Dilution

- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2°C to 8°C (35°F to 46°F)] or at room temperature [up to 25°C (77°F)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of 0.9% Sodium Chloride Injection, USP (provided but shipped separately) to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use 0.9% Sodium Chloride Injection, USP as the diluent.
- After dilution, 1 vial contains 6 doses of 0.3 mL.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before use either by: o Allowing vial(s) to thaw in the refrigerator [2°C to 8°C (35°F to 46°F)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to ~~5 days (120 hours)~~1 month. o Allowing vial(s) to sit at room temperature [up to 25°C (77°F)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.

Commented [A4]: FDA comment
Pfizer: based on information in the BLA the saline diluent will be provided separately from the vials of vaccine. We have revised the text since the diluent is provided separately.

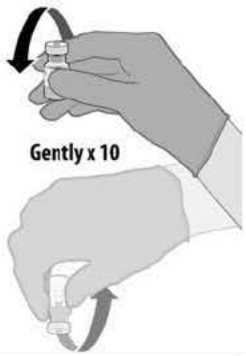
Pfizer-BioNTech response
The Sponsor is not in agreement to revise the text to specify only the provided sodium chloride can be used to dilute the vaccine. The Sponsor will be providing the sodium chloride separately but if an alternate brand of sodium chloride is used, there is no impact to product quality.

Pfizer-BioNTech proposed revision

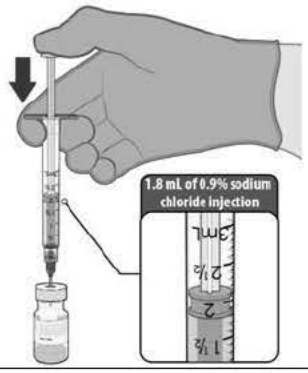
ONLY use ~~the provided~~ 0.9% Sodium Chloride Injection, USP as the diluent.

Commented [A5]: FDA comment
Pfizer: the storage time in the fact sheets is one month. Please explain why this is 5 days.

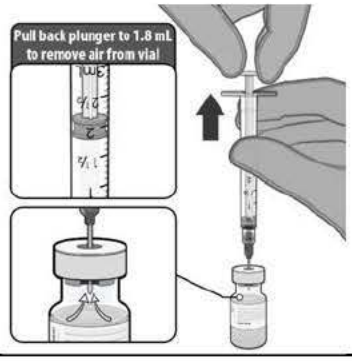
Pfizer-BioNTech response
The information has been revised to reflect "1 month" as aligned with the EUA Fact Sheet. The draft USPI was provided to FDA for review prior to the FDA approval of the revised 1-month storage time. The text has now been updated to reflect the "1 month" information.

<table>
<tr><td> 
</td><td>

Before dilution invert vaccine vial gently 10 times.
<u>Do not shake.</u>
Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain <u>white to off-white opaque amorphous particles</u>.
Do not use if liquid is discolored or if other particles are observed.

</td></tr>
<tr><td colspan="2">DILUTION</td></tr>
<tr><td> 
</td><td>

~~Obtain~~ Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent.
Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle).
Cleanse the vaccine vial stopper with a single-use antiseptic swab.
Add 1.8 mL of 0.9% Sodium Chloride Injection, USP into the vaccine vial.

</td></tr>
<tr><td> 
</td><td>

Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.

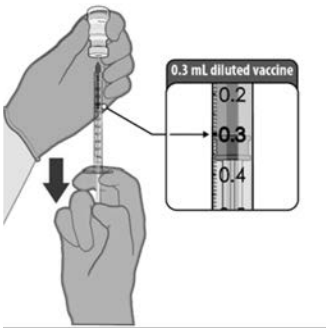
</td></tr>
</table>

Commented [A6]: Pfizer-BioNTech response
The Sponsor is not in agreement to revise the text to specify only the provided sodium chloride can be used to dilute the vaccine. The Sponsor will be providing the sodium chloride separately but if an alternate brand of sodium chloride is used, there is no impact to product quality.

Pfizer-BioNTech proposed revision

- ~~Obtain~~ Obtain ~~Use the provided~~ sterile 0 9% Sodium Chloride Injection, USP. Use only this as the diluent.

	• Gently invert the vial containing the COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Visually inspect each dose in the dosing syringe prior to administration. The vaccine will be an off-white suspension. During the visual inspection,

- verify the final dosing volume of 0.3 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

Administer COMIRNATY intramuscularly.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Reports of adverse events following use of COMIRNATY under EUA suggest increased risks of myocarditis and pericarditis, particularly following the second dose. Typically, onset of symptoms has been within a few days following receipt of COMIRNATY. Available data from short-term follow-up suggest that most individuals have had resolution of symptoms, but information is not yet available about potential long-term sequelae. The decision to administer COMIRNATY to an individual with a history of myocarditis or

Commented [A7]: FDA comment
Pfizer: We have inserted the text in the current fact sheet for vaccination providers as a placeholder but we expect that this will be further revised.

Text based on FS (changed "Pfizer-BioNTech COV D-19 Vaccine" to "TRADENAME"

Pfizer-BioNTech response
The Sponsor accepts the FDA proposed text and acknowledges the FDA comment.

pericarditis should take into account the individual's clinical circumstances. The CDC has published clinical considerations relevant to myocarditis and pericarditis associated with administration of COMIRNATY (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis html).

~~5.2 Concurrent Illness at Time of Vaccination~~

~~The administration of COMIRNATY should be postponed in individuals suffering from acute severe febrile illness.~~

5.3 Concurrent Illness at Time of Vaccination

The administration of COMIRNATY should be postponed in individuals suffering from acute severe febrile illness.

Commented [A8]: Pfizer-BioNTech comment
The Sponsor is not in agreement with the deletion of this information as this is important information for the healthcare provider.

5.~~3~~4 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.~~4~~5 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

~~5.4 Bleeding Precautions~~

~~Individuals receiving anticoagulant therapy or those with a bleeding disorder that would contraindicate intramuscular injection, should not be given the vaccine unless the potential benefit clearly outweighs the risk of administration.~~

5.6 Bleeding Precautions

Individuals receiving anticoagulant therapy or those with a bleeding disorder that would contraindicate intramuscular injection, should not be given the vaccine unless the potential benefit clearly outweighs the risk of administration.

Commented [A9]: Pfizer-BioNTech comment
The Sponsor is not in agreement with the deletion of this information as this is important information for the healthcare provider.

5.~~5~~7 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

~~In clinical studies with a data cut-off of March 13, 2021, adverse reactions in participants 16 years of age and older included pain at the injection site (84.3%), fatigue (64.7%), headache (57.1%), muscle pain (40.2%), chills (34.7%), joint pain (25.0%), fever (15.2%), injection site swelling (11.1%), injection site redness (9.9%), nausea (1.2%), malaise (0.6%), lymphadenopathy (0.4%), asthenia (0.3%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).~~

~~Severe allergic reactions, including anaphylaxis, have been reported following administration of COMIRNATY outside of clinical trials.~~

In clinical studies with a data cut-off of March 13, 2021, adverse reactions in participants 16 years of age and older included pain at the injection site (84.3%), fatigue (64.7%), headache (57.1%), muscle pain (40.2%),

chills (34.7%), joint pain (25.0%), fever (15.2%), injection site swelling (11.1%), injection site redness (9.9%), nausea (1.2%), malaise (0.6%), lymphadenopathy (0.4%), asthenia (0.3%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

Severe allergic reactions, including anaphylaxis, have been reported following administration of COMIRNATY outside of clinical trials.

Commented [A10]: Pfizer-BioNTech response
The Sponsor is not in agreement with the deletion of this information. The Sponsor proposes to retain this information as the deletion will have adverse reactions that are below the 10% threshold to be removed from the USPI.

Please refer to the Sponsor response in the Highlights page.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

Commented [A11]: FDA comment
Pfizer: We have included a couple of very high level comments in this section of the PI. Additional comments will be provided after review of this section.

Pfizer-BioNTech response
The Sponsor acknowledges the FDA's comment.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), ~~the~~ United States, Argentina, Brazil, ~~Europe,~~ Turkey, South Africa, and ~~South America~~Germany (Study- 2). Study BNT162-01 (Study 1) was a Phase 1/2, 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3, multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection (Phase 1) and efficacy (Phase 2/3) study that has enrolled approximately 46,000 participants, 12 years of age or older. Of these, approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) in Phase 2/3 are 16 years of age or older (including 378 and 376 participants~~adolescents~~ 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses.

Commented [A12]: FDA comment
Pfizer: Please revise text to clarify that Study 1 was conducted in Germany and that Study 2 was conducted in the United States, Argentina, Brazil, Turkey, South Africa, and Germany.

Pfizer-BioNTech response
The Sponsor accepts and has revised the text.

At the time of the analysis of Study 2 for the Emergency Use Authorization (EUA) with a data cut-off of November 14, 2020, there were 37,586 participants (18,801 COMIRNATY and 18,785 placebo) 16 years of age or older followed for a median of 2 months after the second dose of COMIRNATY. At the time of the analysis of Study 2 for the EUA with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

The safety evaluation in Study 2 is ongoing. The safety population includes participants enrolled by October 9, 2020, and includes safety data accrued through March 13, 2021. Participants 16 years and older in the reactogenicity subset are monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male and 49.1% were female, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants

16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 to 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	**Placebo Dose 1 N[a]=2908 n[b] (%)**	**COMIRNATY Dose 2 N[a]=2682 n[b] (%)**	**Placebo Dose 2 N[a]=2684 n[b] (%)**
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm

d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours

f Severity was not collected for use of antipyretic or pain medication

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination

No Grade 4 solicited local reactions were reported in participants 56 years of age and older

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, the information was included in the column header

b n = Number of participants with the specified reaction

c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm

d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header

b n = Number of participants with the specified reaction

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea

f Severity was not collected for use of antipyretic or pain medication

Table 5 and Table 6 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 16 years of age and older with confirmed stable HIV infection.

Table 5: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – HIV-Positive Participants 16 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Redness[c]				
Any (>2.0 cm)	2 (3.7)	3 (5.4)	4 (6.7)	1 (1.6)
Mild	2 (3.7)	1 (1.8)	3 (5.0)	1 (1.6)
Moderate	0	0	1 (1.7)	0
Severe	0	2 (3.6)	0	0
Swelling[c]				
Any (>2.0 cm)	3 (5.6)	1 (1.8)	5 (8.3)	0
Mild	2 (3.7)	0	2 (3.3)	0
Moderate	1 (1.9)	0	3 (5.0)	0
Severe	0	1 (1.8)	0	0

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Pain at the injection site[d]				
Any	34 (63.0)	9 (16.1)	32 (53.3)	5 (8.1)
Mild	26 (48.1)	8 (14.3)	22 (36.7)	5 (8.1)
Moderate	8 (14.8)	1 (1.8)	9 (15.0)	0
Severe	0	0	1 (1.7)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in HIV-positive participants 16 years of age and older
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention
a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, this information was included in the column header
b n = Number of participants with the specified reaction
c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm
d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 6: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – HIV-Positive Participants 16 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Fever				
≥38.0°C	1 (1.9)	4 (7.1)	9 (15.0)	5 (8.1)
≥38.0°C to 38.4°C	1 (1.9)	2 (3.6)	4 (6.7)	5 (8.1)
>38.4°C to 38.9°C	0	0	4 (6.7)	0
>38.9°C to 40.0°C	0	2 (3.6)	1 (1.7)	0
>40.0°C	0	0	0	0
Fatigue[c]				
Any	22 (40.7)	15 (26.8)	24 (40.0)	12 (19.4)
Mild	15 (27.8)	9 (16.1)	12 (20.0)	5 (8.1)
Moderate	7 (13.0)	5 (8.9)	9 (15.0)	7 (11.3)
Severe	0	1 (1.8)	3 (5.0)	0
Headache[c]				
Any	11 (20.4)	18 (32.1)	18 (30.0)	12 (19.4)
Mild	7 (13.0)	10 (17.9)	8 (13.3)	8 (12.9)
Moderate	4 (7.4)	7 (12.5)	8 (13.3)	4 (6.5)
Severe	0	1 (1.8)	2 (3.3)	0
Chills[c]				
Any	6 (11.1)	5 (8.9)	14 (23.3)	4 (6.5)
Mild	5 (9.3)	4 (7.1)	5 (8.3)	3 (4.8)
Moderate	1 (1.9)	1 (1.8)	8 (13.3)	1 (1.6)
Severe	0	0	1 (1.7)	0

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Vomiting[d]				
Any	1 (1.9)	3 (5.4)	2 (3.3)	2 (3.2)
Mild	1 (1.9)	1 (1.8)	1 (1.7)	1 (1.6)
Moderate	0	0	1 (1.7)	1 (1.6)
Severe	0	2 (3.6)	0	0
Diarrhea[e]				
Any	5 (9.3)	8 (14.3)	4 (6.7)	9 (14.5)
Mild	5 (9.3)	6 (10.7)	1 (1.7)	6 (9.7)
Moderate	0	1 (1.8)	2 (3.3)	3 (4.8)
Severe	0	1 (1.8)	1 (1.7)	0
New or worsened muscle pain[c]				
Any	9 (16.7)	10 (17.9)	10 (16.7)	5 (8.1)
Mild	7 (13.0)	7 (12.5)	5 (8.3)	1 (1.6)
Moderate	2 (3.7)	3 (5.4)	5 (8.3)	4 (6.5)
Severe	0	0	0	0
New or worsened joint pain[c]				
Any	5 (9.3)	7 (12.5)	10 (16.7)	5 (8.1)
Mild	5 (9.3)	4 (7.1)	4 (6.7)	1 (1.6)
Moderate	0	3 (5.4)	6 (10.0)	4 (6.5)
Severe	0	0	0	0
Use of antipyretic or pain medication[f]	7 (13.0)	8 (14.3)	16 (26.7)	7 (11.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

No Grade 4 solicited systemic reactions were reported in HIV-positive participants 16 years of age and older

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each event or use of antipyretic or pain medication was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours

f Severity was not collected for use of antipyretic or pain medication

Unsolicited Adverse Events

Upon issuance of the EUA for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began in a phased manner for participants in the study. Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 2.1 per 100 person-years among

COMIRNATY recipients and 2.4 per 100 person-years among placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported at an incidence rate of 4.9 per 100 person-years among COMIRNATY recipients and 4.6 per 100 person-years among placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 6.6 per 100 person-years among COMIRNATY recipients and 6.9 per 100 person-years among placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 88.4 per 100 person-years among participants who received COMIRNATY and 43.5 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include non-serious adverse events were reported at an incidence rate of 75.7 per 100 person-years among participants who received COMIRNATY and 43.3 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 95.8 per 100 person-years among participants who received COMIRNATY and 52.0 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

6.2 Post Marketing Experience

The following adverse reactions have been identified during post marketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
~~Gastrointestinal Disorders: diarrhea, vomiting~~
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A reproductive and developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions, twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a reproductive and developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

Commented [A13]: FDA comment
Pfizer- Please re-order list of systems alphabetically.

Pfizer-BioNTech response
The Sponsor accepts and has revised the list of systems alphabetically.

Commented [A14]: Pfizer-BioNTech comment
The Sponsor accepts the FDA proposed revisions with modifications. The Sponsor proposes to include the text "reproductive" in describing the study to be consistent with the text in the *Animal Data* section.

Pfizer-BioNTech proposed revision

A reproductive and developmental toxicity study [.]. These studies revealed no evidence of harm to the fetus due to the vaccine ~~(see *(see Animal Data below)*~~.

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Commented [A15]: Pfizer-BioNTech comment
The Sponsor accepts with FDA proposed text with a modification. The Sponsor proposes to use the term "individuals" for more precision.

Pfizer-BioNTech proposed revision
Safety and effectiveness of TRADENAME in ~~adolescents~~ individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative. The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In ~~studies~~ a developmental and reproductive toxicity study in rats with COMIRNATY, there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

14.1 Efficacy in Participants 16 Years of Age and Older

Study 2 is a multicenter, multinational, Phase 1/2/3, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or

Commented [A16]: Pfizer-BioNTech response
The Sponsor is not in agreement to revise the text to specify only the provided sodium chloride can be used to dilute the vaccine. The Sponsor will be providing the sodium chloride separately but if an alternate brand of sodium chloride is used, there is no impact to product quality.

Pfizer-BioNTech proposed revision

COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1 8 mL of ~~the provided~~ sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine.

Commented [A17]: FDA comment
Pfizer: this was revised to be consistent with the NP name

Pfizer-BioNTech response
The Sponsor accepts.

Commented [A18]: FDA comment
Pfizer: Subsection 8.1 refers to a single study. Please clarify if "studies" should be revised to "a study."

Pfizer-BioNTech response
The text has been revised to reflect the single developmental and reproductive toxicity study.

Commented [A19]: FDA comment
Pfizer: We have not reviewed this section. Comments will be provided after review.

Pfizer-BioNTech response
The Sponsor acknowledges the FDA comment.

hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In the Phase 2/3 portion of Study 2, based on data accrued through November 14, 2020, approximately 44,000 participants 12 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. The efficacy analyses included participants that received their second vaccination within 19 to 42 days after their first vaccination. The majority (93.1%) of vaccine recipients received the second dose 19 days to 23 days after Dose 1. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. Table 7 presents the specific demographic characteristics in the studied population.

Table 7: Demographics (Population For the Primary Efficacy Endpoint)[a]

	COMIRNATY (N=18,242) n (%)	**Placebo (N=18,379) n (%)**
Sex		
Male	9318 (51.1)	9225 (50.2)
Female	8924 (48.9)	9154 (49.8)
Age (years)		
Mean (SD)	50.6 (15.70)	50.4 (15.81)
Median	52.0	52.0
Min, max	(12, 89)	(12, 91)
Age group		
≥12 through 15 years	46 (0.3)	42 (0.2)
≥16 through 64 years	14,216 (77.9)	14,299 (77.8)
≥65 through 74 years	3176 (17.4)	3226 (17.6)
≥75 years	804 (4.4)	812 (4.4)
Race		
White	15,110 (82.8)	15,301 (83.3)
Black or African American	1617 (8.9)	1617 (8.8)
American Indian or Alaska Native	118 (0.6)	106 (0.6)
Asian	815 (4.5)	810 (4.4)
Native Hawaiian or other Pacific Islander	48 (0.3)	29 (0.2)
Other[b]	534 (2.9)	516 (2.8)
Ethnicity		
Hispanic or Latino	4886 (26.8)	4857 (26.4)
Not Hispanic or Latino	13,253 (72.7)	13,412 (73.0)
Not reported	103 (0.6)	110 (0.6)
Comorbidities[c]		
Yes	8432 (46.2)	8450 (46.0)
No	9810 (53.8)	9929 (54.0)

a All eligible randomized participants who receive all vaccination(s) as randomized within the predefined window, have no other important protocol deviations as determined by the clinician, and have no evidence of SARS-CoV-2 infection prior to 7 days after Dose 2

b Includes multiracial and not reported

c Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease:

- Chronic lung disease (e g , emphysema and chronic bronchitis, idiopathic pulmonary fibrosis, and cystic fibrosis) or moderate to severe asthma
- Significant cardiac disease (e g , heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and pulmonary hypertension)
- Obesity (body mass index ≥30 kg/m^2)
- Diabetes (Type 1, Type 2, or gestational)
- Liver disease
- Human Immunodeficiency Virus (HIV) infection (not included in the efficacy evaluation)

Efficacy Against COVID-19

The population in the primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 -through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

The vaccine efficacy information is presented in Table 8.

Table 8: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY Na=18,198 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=18,325 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CI)**
All participants[e]	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.3, 97.6)[f]
16 to 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)[g]
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)[g]
65 to 74 years	1 0.406 (3074)	14 0.406 (3095)	92.9 (53.1, 99.8)[g]
75 years and older	0 0.102 (774)	5 0.106 (785)	100.0 (-13.1, 100.0)[g]
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY Na=19,965 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=20,172 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CI)**
All participants[e]	9 2.332 (18,559)	169 2.345 (18,708)	94.6 (89.9, 97.3)[f]
16 to 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1	19	94.7

	0.530 (4044)	0.532 (4067)	(66.8, 99.9)[g]
65 to 74 years	1 0.424 (3239)	14 0.423 (3255)	92.9 (53.2, 99.8)[g]
75 years and older	0 0.106 (805)	5 0.109 (812)	100.0 (-12.1, 100.0)[g]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

a N = Number of participants in the specified group

b n1 = Number of participants meeting the endpoint definition

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

d n2 = Number of participants at risk for the endpoint

e No confirmed cases were identified in participants 12 to 15 years of age

f Two-sided credible interval for vaccine efficacy was calculated using a beta-binomial model with a beta (0 700102, 1) prior for θ=r(1-VE)/(1+r(1-VE)), where r is the ratio of surveillance time in the active vaccine group over that in the placebo group

g Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

Updated efficacy analyses were performed with additional confirmed COVID-19 cases accrued during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2 for participants in the efficacy population.

The updated vaccine efficacy information is presented in Table 9.

Table 9: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
16 through 64 years	70 4.859 (15,519)	710 4.654 (15,515)	90.6 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
65 through 74 years	6 0.994 (3350)	98 0.966 (3379)	94.1 (86.6, 97.9)
75 years and older	1 0.239 (842)	26 0.237 (847)	96.2 (76.9, 99.9)

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
16 through 64 years	74 5.073 (16,218)	727 4.879 (16,269)	90.2 (87.6, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)
65 through 74 years	6 1.021 (3450)	102 0.992 (3468)	94.3 (87.1, 98.0)
75 years and older	1 0.246 (865)	26 0.240 (858)	96.2 (77.2, 99.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

a N = Number of participants in the specified group

b n1 = Number of participants meeting the endpoint definition

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

d n2 = Number of participants at risk for the endpoint

e Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

f Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group (both without and with or without evidence of prior SARS-CoV-2 infection); 16 and 18 in the placebo group (without and with or without evidence of prior SARS-CoV-2 infection, respectively)

The updated subgroup analyses of vaccine efficacy by demographic characteristics are presented in Table 10 and Table 11.

Table 10: Vaccine Efficacy– First COVID-19 Occurrence From 7 Days After Dose 2 – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 by Demographic Characteristics – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	**COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)[e]**
Sex			
Male	42 3.246 (10,637)	399 3.047 (10,433)	90.1 (86.4, 93.0)
Female	35 3.001 (10,075)	451 2.956 (10,280)	92.4 (89.2, 94.7)
Ethnicity			

Subgroup	COMIRNATY Na=20,998 Cases n1b Surveillance Timec (n2d)	Placebo Na=21,096 Cases n1b Surveillance Timec (n2d)	Vaccine Efficacy % (95% CI)e
Hispanic or Latino	29 1.786 (5161)	241 1.711 (5120)	88.5 (83.0, 92.4)
Not Hispanic or Latino	47 4.429 (15,449)	609 4.259 (15,484)	92.6 (90.0, 94.6)
Race			
Black or African American	4 0.545 (1737)	48 0.527 (1737)	91.9 (78.0, 97.9)
White	67 5.208 (17,186)	747 5.026 (17,256)	91.3 (88.9, 93.4)
All others[f]	6 0.494 (1789)	55 0.451 (1720)	90.0 (76.9, 96.5)
Country			
Argentina	15 1.012 (2600)	108 0.986 (2586)	86.5 (76.7, 92.7)
Brazil	12 0.406 (1311)	80 0.374 (1293)	86.2 (74.5, 93.1)
Germany	0 0.047 (236)	1 0.048 (242)	100.0 (-3874.2, 100.0)
South Africa	0 0.080 (291)	9 0.074 (276)	100.0 (53.5, 100.0)
Turkey	0 0.027 (228)	5 0.025 (222)	100.0 (-0.1, 100.0)
United States	50 4.674 (16,046)	647 4.497 (16,094)	92.6 (90.1, 94.5)

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

a N = Number of participants in the specified group

b n1 = Number of participants meeting the endpoint definition

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

d n2 = Number of participants at risk for the endpoint

e Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

f All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories

Table 11: Vaccine Efficacy– First COVID-19 Occurrence From 7 Days After Dose 2 – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 by Demographic Characteristics – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Sex			
Male	44 3.376 (11,103)	411 3.181 (10,920)	89.9 (86.2, 92.8)
Female	37 3.133 (10,539)	462 3.093 (10,769)	92.1 (88.9, 94.5)
Ethnicity			
Hispanic or Latino	32 1.862 (5408)	245 1.794 (5391)	87.4 (81.8, 91.6)
Not Hispanic or Latino	48 4.615 (16,128)	628 4.445 (16,186)	92.6 (90.1, 94.6)
Race			
Black or African American	4 0.611 (1958)	49 0.601 (1985)	92.0 (78.1, 97.9)
White	69 5.379 (17,801)	768 5.191 (17,880)	91.3 (88.9, 93.3)
All others[f]	8 0.519 (1883)	56 0.481 (1824)	86.8 (72.1, 94.5)
Country			
Argentina	16 1.033 (2655)	110 1.017 (2670)	85.7 (75.7, 92.1)
Brazil	14 0.441 (1419)	82 0.408 (1401)	84.2 (71.9, 91.7)
Germany	0 0.047 (237)	1 0.048 (243)	100.0 (-3868.6, 100.0)
South Africa	0 0.099 (358)	10 0.096 (358)	100.0 (56.6, 100.0)
Turkey	0 0.029 (238)	6 0.026 (232)	100.0 (22.2, 100.0)
United States	51 4.861 (16,735)	664 4.678 (16,785)	92.6 (90.2, 94.6)

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

a N = Number of participants in the specified group

b n1 = Number of participants meeting the endpoint definition

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

d n2 = Number of participants at risk for the endpoint

e Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

f All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories

The updated subgroup analyses of vaccine efficacy by risk status in participants are presented in Table 12 and Table 13.

Table 12: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First COVID-19 occurrence from 7 days after Dose 2[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
At risk[g]			
Yes	35 2.797 (9167)	401 2.681 (9136)	91.6 (88.2, 94.3)
No	42 3.450 (11,545)	449 3.322 (11,577)	91.0 (87.6, 93.6)
Age group (years) and risk status			
16 through 64 and not at risk	41 2.776 (8887)	385 2.661 (8886)	89.8 (85.9, 92.8)
16 through 64 and at risk	29 2.083 (6632)	325 1.993 (6629)	91.5 (87.5, 94.4)
65 and older and not at risk	1 0.553 (1870)	53 0.546 (1922)	98.1 (89.2, 100.0)
65 and older and at risk	6 0.680 (2322)	71 0.656 (2304)	91.8 (81.4, 97.1)
Obese[h]			
Yes	27 2.103 (6796)	314 2.050 (6875)	91.6 (87.6, 94.6)
No	50 4.143 (13,911)	536 3.952 (13,833)	91.1 (88.1, 93.5)
Age group (years) and obesity status			
16 through 64 and not obese	46 3.178 (10,212)	444 3.028 (10,166)	90.1 (86.6, 92.9)
16 through 64 and obese	24 1.680 (5303)	266 1.624 (5344)	91.3 (86.7, 94.5)
65 and older and not obese	4 0.829 (2821)	79 0.793 (2800)	95.2 (87.1, 98.7)
65 and older and obese	3 0.404 (1370)	45 0.410 (1426)	93.2 (78.9, 98.7)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

a N = Number of participants in the specified group

b n1 = Number of participants meeting the endpoint definition

Subgroup	COMIRNATY Na=20,998 Cases n1b Surveillance Timec (n2d)	Placebo Na=21,096 Cases n1b Surveillance Timec (n2d)	Vaccine Efficacy % (95% CI)e

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

d n2 = Number of participants at risk for the endpoint

e Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time

f Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group

g At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age])

h Obese is defined as BMI ≥30 kg/m^2 For 12 through 15 years age group, obesity is defined as a BMI at or above the 95th percentile Refer to the CDC growth charts at https://www cdc gov/growthcharts/html_charts/bmiagerev htm

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY Na=22,166 Cases n1b Surveillance Timec (n2d)	Placebo Na=22,320 Cases n1b Surveillance Timec (n2d)	Vaccine Efficacy % (95% CI)e
First COVID-19 occurrence from 7 days after Dose 2f	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
At riskg			
Yes	36 2.925 (9601)	410 2.807 (9570)	91.6 (88.1, 94.2)
No	45 3.584 (12,041)	463 3.466 (12,119)	90.6 (87.2, 93.2)
Age group (years) and risk status			
16 through 64 and not at risk	44 2.887 (9254)	397 2.779 (9289)	89.3 (85.4, 92.4)
16 through 64 and at risk	30 2.186 (6964)	330 2.100 (6980)	91.3 (87.3, 94.2)
65 and older and not at risk	1 0.566 (1920)	55 0.559 (1966)	98.2 (89.6, 100.0)
65 and older and at risk	6 0.701 (2395)	73 0.672 (2360)	92.1 (82.0, 97.2)
Obeseh			
Yes	28 2.207 (7139)	319 2.158 (7235)	91.4 (87.4, 94.4)
No	53 4.301 (14,497)	554 4.114 (14,448)	90.8 (87.9, 93.2)
Age group (years) and obesity status			
16 through 64 and not obese	49 3.303 (10,629)	458 3.158 (10,614)	89.8 (86.2, 92.5)
16 through 64 and obese	25 1.768 (5584)	269 1.719 (5649)	91.0 (86.4, 94.3)

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
65 and older and not obese	4 0.850 (2899)	82 0.811 (2864)	95.3 (87.6, 98.8)
65 and older and obese	3 0.417 (1415)	46 0.420 (1462)	93.4 (79.5, 98.7)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

a N = number of participants in the specified group

b n1 = Number of participants meeting the endpoint definition

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

d n2 = Number of participants at risk for the endpoint

e Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time

f Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group

g At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age])

h Obese is defined as BMI ≥30 kg/m^2 For the 12 through 15 years of age group, obesity is defined as a BMI at or above the 95th percentile Refer to the CDC growth charts at https://www cdc gov/growthcharts/html_charts/bmiagerev htm

Efficacy Against Severe COVID-19

Updated efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 14) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 14: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants With or Without* Prior SARS-CoV-2 Infection Based on FDA† or Centers for Disease Control and Prevention (CDC)‡ Definition After Dose 1 or From 7 Days After Dose 2 in the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence Based on FDA Definition			
	COMIRNATY Cases n1[a] Surveillance Time (n2[b])	Placebo Cases n1[a] Surveillance Time (n2[b])	Vaccine Efficacy % (95% CI[c])
After Dose 1[d]	1 8.439[e] (22,505)	30 8.288[e] (22,435)	96.7 (80.3, 99.9)
7 days after Dose 2[f]	1 6.522[g] (21,649)	21 6.404[g] (21,730)	95.3 (70.9, 99.9)

Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time (n2[b])	**Placebo Cases n1[a] Surveillance Time (n2[b])**	**Vaccine Efficacy % (95% CI[c])**
After Dose 1[d]	1 8.427[e] (22,473)	45 8.269[e] (22,394)	97.8 (87.2, 99.9)
7 days after Dose 2[f]	0 6.514[g] (21,620)	32 6.391[g] (21,693)	100 (88.0, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

† Severe illness from COVID-19 as defined by FDA is confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death

a n1 = Number of participants meeting the endpoint definition

b n2 = Number of participants at risk for the endpoint

c Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

d Efficacy assessed based on the Dose 1 all available efficacy (modified intention-to-treat) population that included all randomized participants who received at least 1 dose of study intervention

e Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period

f Efficacy assessed based on the evaluable efficacy (7 Days) population that included all eligible randomized participants who receive all dose(s) of study intervention as randomized within the predefined window, have no other important protocol deviations as determined by the clinician

g Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. After dilution, 1 vial contains 6 doses of 0.3 mL.

Commented [A20]: FDA comment
Pfizer: Please include instructions on how to store the provided saline diluent.

Pfizer-BioNTech response
The Sponsor accepts and has included the storage information for the 0.9% Sodium Chloride Injection, USP diluent.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -80°C to -60°C (-112°F to -76°F) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -80°C to -60°C (-112°F to -76°F). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90°C to -60°C (-130°F to -76°F). Storage ~~within this temperature range~~of the vials between -96°C to -60°C (-141°F to -76°F) ~~-~~ is not considered an excursion from the recommended storage condition.

Commented [A21]: FDA comment
Pfizer: This is not consistent with the FS which states "Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition." Please revise if necessary.

Pfizer-BioNTech response
The information has been revised to align with the EUA Fact Sheet. The draft USPI was provided to FDA for review prior to the FDA approval of the revised statement. The text has now been updated.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -80°C to -60°C (-112°F to -76°F).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2°C to 8°C (35°F to 46°F)] for up to ~~5 days (120 hours)~~1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Commented [A22]: FDA comment
Pfizer: the storage time in the FS is "1 month". Please explain why this is 5 days.

Pfizer-BioNTech response
The information has been revised to reflect "1 month" to align with the EUA Fact Sheet. The draft USPI was provided to FDA for review prior to the FDA approval of the revised 1-month storage time. The information has now been updated to reflect the "1 month" information.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25°C (77°F)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours. ~~Any hours used for transport at 2°C to 8°C (35°F to 46°F) count against the 120-hour limit for storage at 2°C to 8°C (35°F to 46°F).~~

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers hhs.gov.

~~For general questions, visit the website or call the telephone number provided below.~~

~~Website~~	~~Telephone number~~
~~www.evdvaccine.com~~	~~1-877-829-2619 (1-877-VAX-CO19)~~

For general questions, visit the website or call the telephone number provided below.

Website	Telephone number
www.comirnatyhcp.com	1-877-829-2619 (1-877-VAX-CO19)

This product's labeling may have been updated. For the most recent prescribing information, please visit www.pfizer.com.

Commented [A23]: FDA comment
Pfizer: This statement is not in the FS. See comments above regarding whether storage of undiluted vials at 2-8C is for 5days or one month.

Pfizer-BioNTech response
The text has been revised to align with the EUA Fact Sheet. The draft USPI was provided to FDA for review prior to the FDA approval of the deleted text.

Commented [A24]: Pfizer-BioNTech comment
The Sponsor proposes to retain the inclusion of website, QR code and telephone contact information as it may provide helpful and current information for the healthcare provider. Updated QR codes and website have been proposed and may be further revised.

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LAB-1448-0.~~1~~2

US Govt. License No. x

~~CPT Code x~~CPT Code x

Commented [A25]: Pfizer-BioNTech comment
The Sponsor is not in agreement with the deletion of the placeholder information for the CPT Code.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

---------- INDICATIONS AND USAGE----------

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------

Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------

Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------

- Postmarketing reports of adverse events suggest increased risks of myocarditis and pericarditis, particularly following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------

In clinical studies of participants 16 years of age and older, the most commonly reported adverse reactions (>10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, fever, and injection site swelling. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

2.1 Preparation for Administration

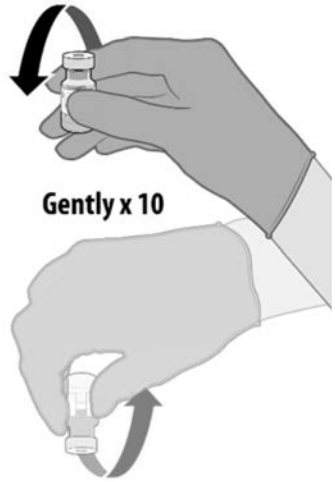
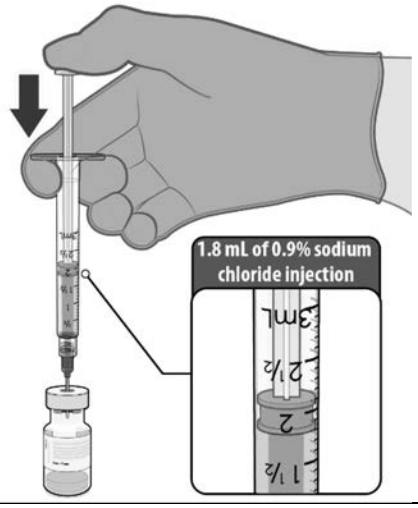
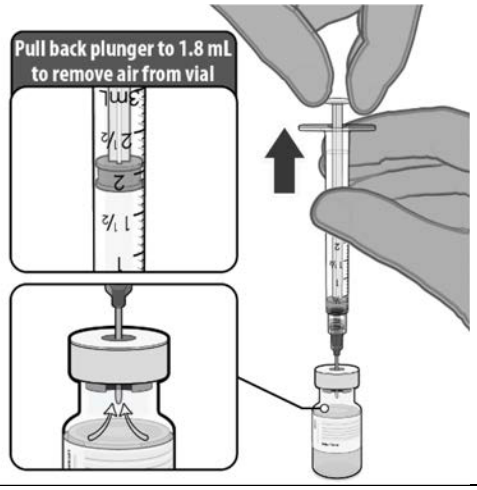
Prior to Dilution

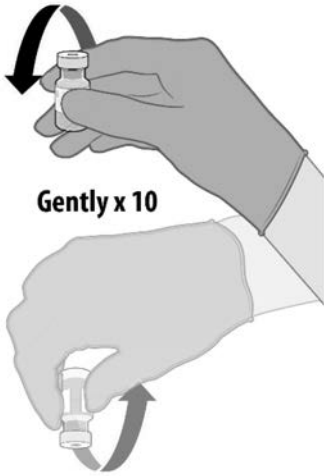
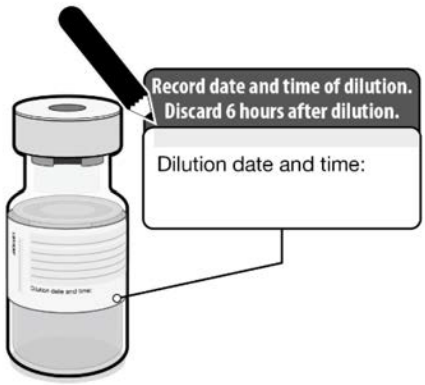
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

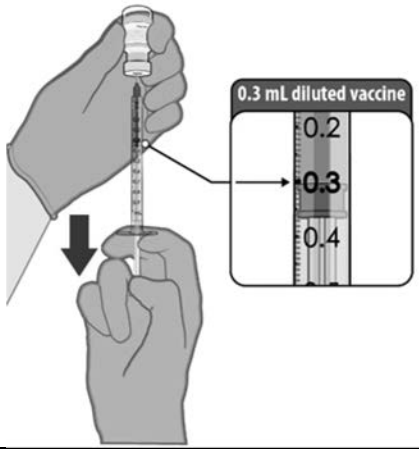
Dilution

- Dilute the vial contents using 1.8 mL of 0.9% Sodium Chloride Injection, USP (provided but shipped separately) to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use 0.9% Sodium Chloride Injection, USP as the diluent.
- After dilution, 1 vial contains 6 doses of 0.3 mL.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before use either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.

	• Before dilution invert vaccine vial gently 10 times. • Do not shake. • Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent. • Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Cleanse the vaccine vial stopper with a single-use antiseptic swab. • Add 1.8 mL of 0.9% Sodium Chloride Injection, USP into the vaccine vial.
	• Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.

	• Gently invert the vial containing the COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Visually inspect each dose in the dosing syringe prior to administration. The vaccine will be an off-white suspension. During the visual inspection,

- verify the final dosing volume of 0.3 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

Administer COMIRNATY intramuscularly.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Reports of adverse events following use of COMIRNATY under EUA suggest increased risks of myocarditis and pericarditis, particularly following the second dose. Typically, onset of symptoms has been within a few days following receipt of COMIRNATY. Available data from short-term follow-up suggest that most individuals have had resolution of symptoms, but information is not yet available about potential long-term sequelae. The decision to administer COMIRNATY to an individual with a history of myocarditis or

pericarditis should take into account the individual's clinical circumstances. The CDC has published clinical considerations relevant to myocarditis and pericarditis associated with administration of COMIRNATY (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Concurrent Illness at Time of Vaccination

The administration of COMIRNATY should be postponed in individuals suffering from acute severe febrile illness.

5.4 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.5 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.6 Bleeding Precautions

Individuals receiving anticoagulant therapy or those with a bleeding disorder that would contraindicate intramuscular injection, should not be given the vaccine unless the potential benefit clearly outweighs the risk of administration.

5.7 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies with a data cut-off of March 13, 2021, adverse reactions in participants 16 years of age and older included pain at the injection site (84.3%), fatigue (64.7%), headache (57.1%), muscle pain (40.2%), chills (34.7%), joint pain (25.0%), fever (15.2%), injection site swelling (11.1%), injection site redness (9.9%), nausea (1.2%), malaise (0.6%), lymphadenopathy (0.4%), asthenia (0.3%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

Severe allergic reactions, including anaphylaxis, have been reported following administration of COMIRNATY outside of clinical trials.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 1/2, 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001

(Study 2) is a Phase 1/2/3, multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection (Phase 1) and efficacy (Phase 2/3) study that has enrolled approximately 46,000 participants, 12 years of age or older. Of these, approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) in Phase 2/3 are 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses.

At the time of the analysis of Study 2 for the Emergency Use Authorization (EUA) with a data cut-off of November 14, 2020, there were 37,586 participants (18,801 COMIRNATY and 18,785 placebo) 16 years of age or older followed for a median of 2 months after the second dose of COMIRNATY. At the time of the analysis of Study 2 for the EUA with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

The safety evaluation in Study 2 is ongoing. The safety population includes participants enrolled by October 9, 2020, and includes safety data accrued through March 13, 2021. Participants 16 years and older in the reactogenicity subset are monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male and 49.1% were female, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 to 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.

f. Severity was not collected for use of antipyretic or pain medication.

Table 5 and Table 6 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 16 years of age and older with confirmed stable HIV infection.

Table 5: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – HIV-Positive Participants 16 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Redness[c]				
Any (>2.0 cm)	2 (3.7)	3 (5.4)	4 (6.7)	1 (1.6)
Mild	2 (3.7)	1 (1.8)	3 (5.0)	1 (1.6)
Moderate	0	0	1 (1.7)	0
Severe	0	2 (3.6)	0	0
Swelling[c]				
Any (>2.0 cm)	3 (5.6)	1 (1.8)	5 (8.3)	0
Mild	2 (3.7)	0	2 (3.3)	0
Moderate	1 (1.9)	0	3 (5.0)	0
Severe	0	1 (1.8)	0	0
Pain at the injection site[d]				
Any	34 (63.0)	9 (16.1)	32 (53.3)	5 (8.1)
Mild	26 (48.1)	8 (14.3)	22 (36.7)	5 (8.1)
Moderate	8 (14.8)	1 (1.8)	9 (15.0)	0
Severe	0	0	1 (1.7)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in HIV-positive participants 16 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 6: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – HIV-Positive Participants 16 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Fever				
≥38.0°C	1 (1.9)	4 (7.1)	9 (15.0)	5 (8.1)
≥38.0°C to 38.4°C	1 (1.9)	2 (3.6)	4 (6.7)	5 (8.1)
>38.4°C to 38.9°C	0	0	4 (6.7)	0
>38.9°C to 40.0°C	0	2 (3.6)	1 (1.7)	0
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Fatigue[c]				
Any	22 (40.7)	15 (26.8)	24 (40.0)	12 (19.4)
Mild	15 (27.8)	9 (16.1)	12 (20.0)	5 (8.1)
Moderate	7 (13.0)	5 (8.9)	9 (15.0)	7 (11.3)
Severe	0	1 (1.8)	3 (5.0)	0
Headache[c]				
Any	11 (20.4)	18 (32.1)	18 (30.0)	12 (19.4)
Mild	7 (13.0)	10 (17.9)	8 (13.3)	8 (12.9)
Moderate	4 (7.4)	7 (12.5)	8 (13.3)	4 (6.5)
Severe	0	1 (1.8)	2 (3.3)	0
Chills[c]				
Any	6 (11.1)	5 (8.9)	14 (23.3)	4 (6.5)
Mild	5 (9.3)	4 (7.1)	5 (8.3)	3 (4.8)
Moderate	1 (1.9)	1 (1.8)	8 (13.3)	1 (1.6)
Severe	0	0	1 (1.7)	0
Vomiting[d]				
Any	1 (1.9)	3 (5.4)	2 (3.3)	2 (3.2)
Mild	1 (1.9)	1 (1.8)	1 (1.7)	1 (1.6)
Moderate	0	0	1 (1.7)	1 (1.6)
Severe	0	2 (3.6)	0	0
Diarrhea[e]				
Any	5 (9.3)	8 (14.3)	4 (6.7)	9 (14.5)
Mild	5 (9.3)	6 (10.7)	1 (1.7)	6 (9.7)
Moderate	0	1 (1.8)	2 (3.3)	3 (4.8)
Severe	0	1 (1.8)	1 (1.7)	0
New or worsened muscle pain[c]				
Any	9 (16.7)	10 (17.9)	10 (16.7)	5 (8.1)
Mild	7 (13.0)	7 (12.5)	5 (8.3)	1 (1.6)
Moderate	2 (3.7)	3 (5.4)	5 (8.3)	4 (6.5)
Severe	0	0	0	0
New or worsened joint pain[c]				
Any	5 (9.3)	7 (12.5)	10 (16.7)	5 (8.1)
Mild	5 (9.3)	4 (7.1)	4 (6.7)	1 (1.6)
Moderate	0	3 (5.4)	6 (10.0)	4 (6.5)
Severe	0	0	0	0
Use of antipyretic or pain medication[f]	7 (13.0)	8 (14.3)	16 (26.7)	7 (11.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in HIV-positive participants 16 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each event or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.
f. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

Upon issuance of the EUA for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began in a phased manner for participants in the study. Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 2.1 per 100 person-years among COMIRNATY recipients and 2.4 per 100 person-years among placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported at an incidence rate of 4.9 per 100 person-years among COMIRNATY recipients and 4.6 per 100 person-years among placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 6.6 per 100 person-years among COMIRNATY recipients and 6.9 per 100 person-years among placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 88.4 per 100 person-years among participants who received COMIRNATY and 43.5 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include non-serious adverse events were reported at an incidence rate of 75.7 per 100 person-years among participants who received COMIRNATY and 43.3 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 95.8 per 100 person-years among participants who received

COMIRNATY and 52.0 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

6.2 Post Marketing Experience

The following adverse reactions have been identified during post marketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A reproductive and developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions, twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a reproductive and developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative. The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental and reproductive toxicity study in rats with COMIRNATY, there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

14.1 Efficacy in Participants 16 Years of Age and Older

Study 2 is a multicenter, multinational, Phase 1/2/3, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In the Phase 2/3 portion of Study 2, based on data accrued through November 14, 2020, approximately 44,000 participants 12 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. The efficacy analyses included participants that received their second vaccination within 19 to 42 days after their first vaccination. The majority (93.1%) of vaccine recipients received the second dose 19 days to 23 days after Dose 1. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. Table 7 presents the specific demographic characteristics in the studied population.

Table 7: Demographics (Population For the Primary Efficacy Endpoint)[a]

	COMIRNATY (N=18,242) n (%)	Placebo (N=18,379) n (%)
Sex		
Male	9318 (51.1)	9225 (50.2)
Female	8924 (48.9)	9154 (49.8)
Age (years)		
Mean (SD)	50.6 (15.70)	50.4 (15.81)
Median	52.0	52.0
Min, max	(12, 89)	(12, 91)
Age group		
≥12 through 15 years	46 (0.3)	42 (0.2)
≥16 through 64 years	14,216 (77.9)	14,299 (77.8)
≥65 through 74 years	3176 (17.4)	3226 (17.6)
≥75 years	804 (4.4)	812 (4.4)
Race		
White	15,110 (82.8)	15,301 (83.3)
Black or African American	1617 (8.9)	1617 (8.8)
American Indian or Alaska Native	118 (0.6)	106 (0.6)
Asian	815 (4.5)	810 (4.4)
Native Hawaiian or other Pacific Islander	48 (0.3)	29 (0.2)
Other[b]	534 (2.9)	516 (2.8)
Ethnicity		
Hispanic or Latino	4886 (26.8)	4857 (26.4)
Not Hispanic or Latino	13,253 (72.7)	13,412 (73.0)
Not reported	103 (0.6)	110 (0.6)
Comorbidities[c]		
Yes	8432 (46.2)	8450 (46.0)
No	9810 (53.8)	9929 (54.0)

a. All eligible randomized participants who receive all vaccination(s) as randomized within the predefined window, have no other important protocol deviations as determined by the clinician, and have no evidence of SARS-CoV-2 infection prior to 7 days after Dose 2.

b. Includes multiracial and not reported.

c. Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease:
- Chronic lung disease (e.g., emphysema and chronic bronchitis, idiopathic pulmonary fibrosis, and cystic fibrosis) or moderate to severe asthma
- Significant cardiac disease (e.g., heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and pulmonary hypertension)
- Obesity (body mass index ≥30 kg/m^2)
- Diabetes (Type 1, Type 2, or gestational)
- Liver disease
- Human Immunodeficiency Virus (HIV) infection (not included in the efficacy evaluation)

Efficacy Against COVID-19

The population in the primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

The vaccine efficacy information is presented in Table 8.

Table 8: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY Na=18,198 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=18,325 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CI)**
All participants[e]	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.3, 97.6)[f]
16 to 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)[g]
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)[g]
65 to 74 years	1 0.406 (3074)	14 0.406 (3095)	92.9 (53.1, 99.8)[g]
75 years and older	0 0.102 (774)	5 0.106 (785)	100.0 (-13.1, 100.0)[g]
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY Na=19,965 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=20,172 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CI)**
All participants[e]	9 2.332 (18,559)	169 2.345 (18,708)	94.6 (89.9, 97.3)[f]
16 to 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1 0.530 (4044)	19 0.532 (4067)	94.7 (66.8, 99.9)[g]
65 to 74 years	1 0.424 (3239)	14 0.423 (3255)	92.9 (53.2, 99.8)[g]
75 years and older	0 0.106 (805)	5 0.109 (812)	100.0 (-12.1, 100.0)[g]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. No confirmed cases were identified in participants 12 to 15 years of age.
f. Two-sided credible interval for vaccine efficacy was calculated using a beta-binomial model with a beta (0.700102, 1) prior for $\theta=r(1-VE)/(1+r(1-VE))$, where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.
g. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Updated efficacy analyses were performed with additional confirmed COVID-19 cases accrued during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2 for participants in the efficacy population.

The updated vaccine efficacy information is presented in Table 9.

Table 9: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
16 through 64 years	70 4.859 (15,519)	710 4.654 (15,515)	90.6 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
65 through 74 years	6 0.994 (3350)	98 0.966 (3379)	94.1 (86.6, 97.9)
75 years and older	1 0.239 (842)	26 0.237 (847)	96.2 (76.9, 99.9)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
16 through 64 years	74 5.073 (16,218)	727 4.879 (16,269)	90.2 (87.6, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)
65 through 74 years	6 1.021 (3450)	102 0.992 (3468)	94.3 (87.1, 98.0)
75 years and older	1 0.246 (865)	26 0.240 (858)	96.2 (77.2, 99.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group (both without and with or without evidence of prior SARS-CoV-2 infection); 16 and 18 in the placebo group (without and with or without evidence of prior SARS-CoV-2 infection, respectively).

The updated subgroup analyses of vaccine efficacy by demographic characteristics are presented in Table 10 and Table 11.

Table 10: Vaccine Efficacy– First COVID-19 Occurrence From 7 Days After Dose 2 – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 by Demographic Characteristics – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Sex			
Male	42 3.246 (10,637)	399 3.047 (10,433)	90.1 (86.4, 93.0)
Female	35 3.001 (10,075)	451 2.956 (10,280)	92.4 (89.2, 94.7)
Ethnicity			
Hispanic or Latino	29 1.786 (5161)	241 1.711 (5120)	88.5 (83.0, 92.4)
Not Hispanic or Latino	47 4.429 (15,449)	609 4.259 (15,484)	92.6 (90.0, 94.6)
Race			
Black or African American	4 0.545 (1737)	48 0.527 (1737)	91.9 (78.0, 97.9)
White	67 5.208 (17,186)	747 5.026 (17,256)	91.3 (88.9, 93.4)
All others[f]	6 0.494 (1789)	55 0.451 (1720)	90.0 (76.9, 96.5)

Subgroup	COMIRNATY Na=20,998 Cases n1b Surveillance Timec (n2d)	Placebo Na=21,096 Cases n1b Surveillance Timec (n2d)	Vaccine Efficacy % (95% CI)e
Country			
Argentina	15 1.012 (2600)	108 0.986 (2586)	86.5 (76.7, 92.7)
Brazil	12 0.406 (1311)	80 0.374 (1293)	86.2 (74.5, 93.1)
Germany	0 0.047 (236)	1 0.048 (242)	100.0 (-3874.2, 100.0)
South Africa	0 0.080 (291)	9 0.074 (276)	100.0 (53.5, 100.0)
Turkey	0 0.027 (228)	5 0.025 (222)	100.0 (-0.1, 100.0)
United States	50 4.674 (16,046)	647 4.497 (16,094)	92.6 (90.1, 94.5)

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).
Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group.

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
f. All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

Table 11: Vaccine Efficacy– First COVID-19 Occurrence From 7 Days After Dose 2 – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 by Demographic Characteristics – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY Na=22,166 Cases n1b Surveillance Timec (n2d)	Placebo Na=22,320 Cases n1b Surveillance Timec (n2d)	Vaccine Efficacy % (95% CI)e
Sex			
Male	44 3.376 (11,103)	411 3.181 (10,920)	89.9 (86.2, 92.8)
Female	37 3.133 (10,539)	462 3.093 (10,769)	92.1 (88.9, 94.5)

Subgroup	COMIRNATY Na=22,166 Cases n1b Surveillance Timec (n2d)	Placebo Na=22,320 Cases n1b Surveillance Timec (n2d)	Vaccine Efficacy % (95% CI)e
Ethnicity			
Hispanic or Latino	32 1.862 (5408)	245 1.794 (5391)	87.4 (81.8, 91.6)
Not Hispanic or Latino	48 4.615 (16,128)	628 4.445 (16,186)	92.6 (90.1, 94.6)
Race			
Black or African American	4 0.611 (1958)	49 0.601 (1985)	92.0 (78.1, 97.9)
White	69 5.379 (17,801)	768 5.191 (17,880)	91.3 (88.9, 93.3)
All others[f]	8 0.519 (1883)	56 0.481 (1824)	86.8 (72.1, 94.5)
Country			
Argentina	16 1.033 (2655)	110 1.017 (2670)	85.7 (75.7, 92.1)
Brazil	14 0.441 (1419)	82 0.408 (1401)	84.2 (71.9, 91.7)
Germany	0 0.047 (237)	1 0.048 (243)	100.0 (-3868.6, 100.0)
South Africa	0 0.099 (358)	10 0.096 (358)	100.0 (56.6, 100.0)
Turkey	0 0.029 (238)	6 0.026 (232)	100.0 (22.2, 100.0)
United States	51 4.861 (16,735)	664 4.678 (16,785)	92.6 (90.2, 94.6)

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group.

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
f. All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

The updated subgroup analyses of vaccine efficacy by risk status in participants are presented in Table 12 and Table 13.

Table 12: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY Na=20,998 Cases n1b Surveillance Timec (n2d)	Placebo Na=21,096 Cases n1b Surveillance Timec (n2d)	Vaccine Efficacy % (95% CI)e
First COVID-19 occurrence from 7 days after Dose 2f	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
At riskg			
Yes	35 2.797 (9167)	401 2.681 (9136)	91.6 (88.2, 94.3)
No	42 3.450 (11,545)	449 3.322 (11,577)	91.0 (87.6, 93.6)
Age group (years) and risk status			
16 through 64 and not at risk	41 2.776 (8887)	385 2.661 (8886)	89.8 (85.9, 92.8)
16 through 64 and at risk	29 2.083 (6632)	325 1.993 (6629)	91.5 (87.5, 94.4)
65 and older and not at risk	1 0.553 (1870)	53 0.546 (1922)	98.1 (89.2, 100.0)
65 and older and at risk	6 0.680 (2322)	71 0.656 (2304)	91.8 (81.4, 97.1)
Obeseh			
Yes	27 2.103 (6796)	314 2.050 (6875)	91.6 (87.6, 94.6)
No	50 4.143 (13,911)	536 3.952 (13,833)	91.1 (88.1, 93.5)
Age group (years) and obesity status			
16 through 64 and not obese	46 3.178 (10,212)	444 3.028 (10,166)	90.1 (86.6, 92.9)
16 through 64 and obese	24 1.680 (5303)	266 1.624 (5344)	91.3 (86.7, 94.5)
65 and older and not obese	4 0.829 (2821)	79 0.793 (2800)	95.2 (87.1, 98.7)
65 and older and obese	3 0.404 (1370)	45 0.410 (1426)	93.2 (78.9, 98.7)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group.

Subgroup	COMIRNATY Na=20,998 Cases n1b Surveillance Timec (n2d)	Placebo Na=21,096 Cases n1b Surveillance Timec (n2d)	Vaccine Efficacy % (95% CI)e

g. At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age]).
h. Obese is defined as BMI ≥30 kg/m^2. For 12 through 15 years age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY Na=22,166 Cases n1b Surveillance Timec (n2d)	Placebo Na=22,320 Cases n1b Surveillance Timec (n2d)	Vaccine Efficacy % (95% CI)e
First COVID-19 occurrence from 7 days after Dose 2f	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
At riskg			
Yes	36 2.925 (9601)	410 2.807 (9570)	91.6 (88.1, 94.2)
No	45 3.584 (12,041)	463 3.466 (12,119)	90.6 (87.2, 93.2)
Age group (years) and risk status			
16 through 64 and not at risk	44 2.887 (9254)	397 2.779 (9289)	89.3 (85.4, 92.4)
16 through 64 and at risk	30 2.186 (6964)	330 2.100 (6980)	91.3 (87.3, 94.2)
65 and older and not at risk	1 0.566 (1920)	55 0.559 (1966)	98.2 (89.6, 100.0)
65 and older and at risk	6 0.701 (2395)	73 0.672 (2360)	92.1 (82.0, 97.2)
Obeseh			
Yes	28 2.207 (7139)	319 2.158 (7235)	91.4 (87.4, 94.4)
No	53 4.301 (14,497)	554 4.114 (14,448)	90.8 (87.9, 93.2)
Age group (years) and obesity status			
16 through 64 and not obese	49 3.303 (10,629)	458 3.158 (10,614)	89.8 (86.2, 92.5)
16 through 64 and obese	25 1.768 (5584)	269 1.719 (5649)	91.0 (86.4, 94.3)
65 and older and not obese	4 0.850 (2899)	82 0.811 (2864)	95.3 (87.6, 98.8)
65 and older and obese	3 0.417 (1415)	46 0.420 (1462)	93.4 (79.5, 98.7)

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.
f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group.
g. At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age]).
h. Obese is defined as BMI ≥30 kg/m^2. For the 12 through 15 years of age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Efficacy Against Severe COVID-19

Updated efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 14) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 14: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants With or Without* Prior SARS-CoV-2 Infection Based on FDA† or Centers for Disease Control and Prevention (CDC)‡ Definition After Dose 1 or From 7 Days After Dose 2 in the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence Based on FDA Definition			
	COMIRNATY Cases n1[a] Surveillance Time (n2[b])	Placebo Cases n1[a] Surveillance Time (n2[b])	Vaccine Efficacy % (95% CI[c])
After Dose 1[d]	1 8.439[e] (22,505)	30 8.288[e] (22,435)	96.7 (80.3, 99.9)
7 days after Dose 2[f]	1 6.522[g] (21,649)	21 6.404[g] (21,730)	95.3 (70.9, 99.9)

Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time (n2[b])	**Placebo Cases n1[a] Surveillance Time (n2[b])**	**Vaccine Efficacy % (95% CI[c])**
After Dose 1[d]	1 8.427[e] (22,473)	45 8.269[e] (22,394)	97.8 (87.2, 99.9)
7 days after Dose 2[f]	0 6.514[g] (21,620)	32 6.391[g] (21,693)	100 (88.0, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 as defined by FDA is confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. n2 = Number of participants at risk for the endpoint.
c. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
d. Efficacy assessed based on the Dose 1 all available efficacy (modified intention-to-treat) population that included all randomized participants who received at least 1 dose of study intervention.
e. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.
f. Efficacy assessed based on the evaluable efficacy (7 Days) population that included all eligible randomized participants who receive all dose(s) of study intervention as randomized within the predefined window, have no other important protocol deviations as determined by the clinician.
g. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -80ºC to -60ºC (-112ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

For general questions, visit the website or call the telephone number provided below.

Website	Telephone number
www.comirnatyhcp.com	1-877-829-2619 (1-877-VAX-CO19)

This product's labeling may have been updated. For the most recent prescribing information, please visit www.pfizer.com.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.2

US Govt. License No. x

CPT Code x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing reports of adverse events suggest increased risks of myocarditis and pericarditis, particularly following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
In clinical studies of participants 16 years of age and older, the most commonly reported adverse reactions (>10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, fever, and injection site swelling. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

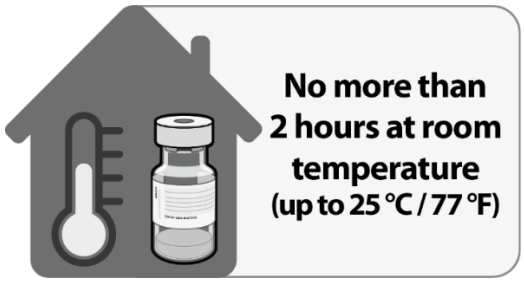
2.1 Preparation for Administration

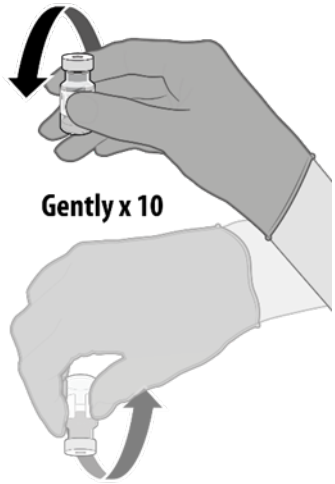
Prior to Dilution

- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

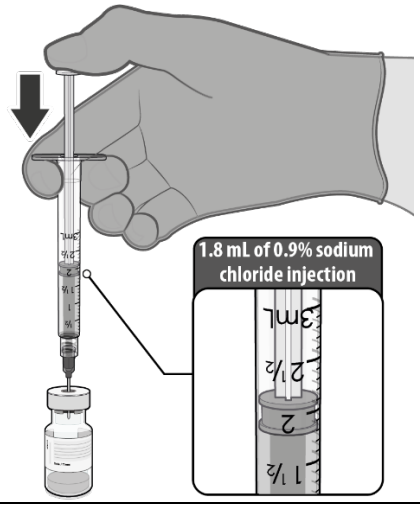
Dilution

- Dilute the vial contents using 1.8 mL of 0.9% Sodium Chloride Injection, USP (provided but shipped separately) to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use 0.9% Sodium Chloride Injection, USP as the diluent.
- After dilution, 1 vial contains 6 doses of 0.3 mL.
- Refer to dilution and dose preparation instructions in the panels below.

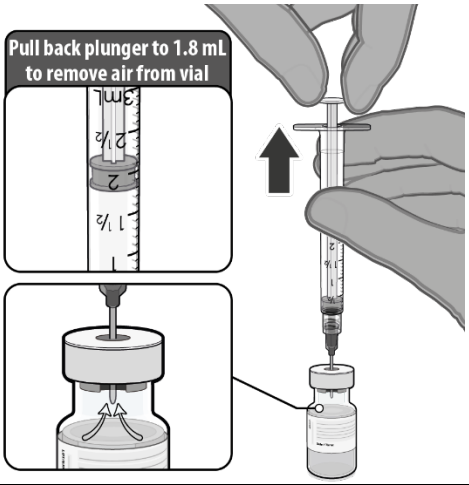
THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before use either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.

<table>
<tr><td> 
</td><td>

Before dilution invert vaccine vial gently 10 times.
Do not shake.
Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles.
Do not use if liquid is discolored or if other particles are observed.

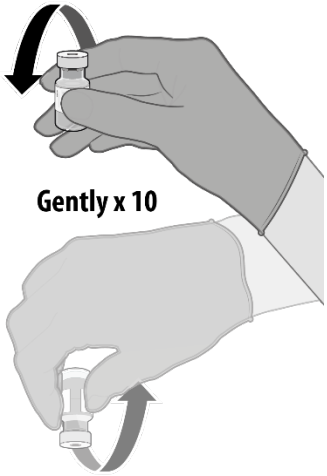
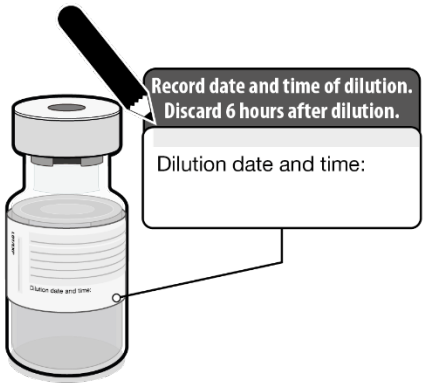
</td></tr>
<tr><td colspan="2">DILUTION</td></tr>
<tr><td> 
</td><td>

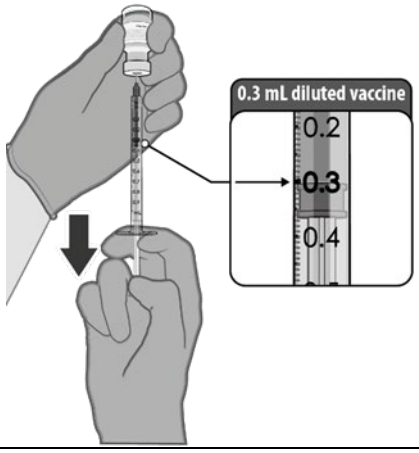
Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent.
Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle).
Cleanse the vaccine vial stopper with a single-use antiseptic swab.
Add 1.8 mL of 0.9% Sodium Chloride Injection, USP into the vaccine vial.

</td></tr>
<tr><td> 
</td><td>

Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.

</td></tr>
</table>

	• Gently invert the vial containing the COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Visually inspect each dose in the dosing syringe prior to administration. The vaccine will be an off-white suspension. During the visual inspection,

- verify the final dosing volume of 0.3 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

Administer COMIRNATY intramuscularly.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Reports of adverse events following use of COMIRNATY under EUA suggest increased risks of myocarditis and pericarditis, particularly following the second dose. Typically, onset of symptoms has been within a few days following receipt of COMIRNATY. Available data from short-term follow-up suggest that most individuals have had resolution of symptoms, but information is not yet available about potential long-term sequelae. The decision to administer COMIRNATY to an individual with a history of myocarditis or

pericarditis should take into account the individual's clinical circumstances. The CDC has published clinical considerations relevant to myocarditis and pericarditis associated with administration of COMIRNATY (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Concurrent Illness at Time of Vaccination

The administration of COMIRNATY should be postponed in individuals suffering from acute severe febrile illness.

5.4 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.5 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.6 Bleeding Precautions

Individuals receiving anticoagulant therapy or those with a bleeding disorder that would contraindicate intramuscular injection, should not be given the vaccine unless the potential benefit clearly outweighs the risk of administration.

5.7 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies with a data cut-off of March 13, 2021, adverse reactions in participants 16 years of age and older included pain at the injection site (84.3%), fatigue (64.7%), headache (57.1%), muscle pain (40.2%), chills (34.7%), joint pain (25.0%), fever (15.2%), injection site swelling (11.1%), injection site redness (9.9%), nausea (1.2%), malaise (0.6%), lymphadenopathy (0.4%), asthenia (0.3%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

Severe allergic reactions, including anaphylaxis, have been reported following administration of COMIRNATY outside of clinical trials.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 1/2, 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001

(Study 2) is a Phase 1/2/3, multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection (Phase 1) and efficacy (Phase 2/3) study that has enrolled approximately 46,000 participants, 12 years of age or older. Of these, approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) in Phase 2/3 are 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses.

At the time of the analysis of Study 2 for the Emergency Use Authorization (EUA) with a data cut-off of November 14, 2020, there were 37,586 participants (18,801 COMIRNATY and 18,785 placebo) 16 years of age or older followed for a median of 2 months after the second dose of COMIRNATY. At the time of the analysis of Study 2 for the EUA with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

The safety evaluation in Study 2 is ongoing. The safety population includes participants enrolled by October 9, 2020, and includes safety data accrued through March 13, 2021. Participants 16 years and older in the reactogenicity subset are monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male and 49.1% were female, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 to 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.

f. Severity was not collected for use of antipyretic or pain medication.

Table 5 and Table 6 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 16 years of age and older with confirmed stable HIV infection.

Table 5: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – HIV-Positive Participants 16 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Redness[c]				
Any (>2.0 cm)	2 (3.7)	3 (5.4)	4 (6.7)	1 (1.6)
Mild	2 (3.7)	1 (1.8)	3 (5.0)	1 (1.6)
Moderate	0	0	1 (1.7)	0
Severe	0	2 (3.6)	0	0
Swelling[c]				
Any (>2.0 cm)	3 (5.6)	1 (1.8)	5 (8.3)	0
Mild	2 (3.7)	0	2 (3.3)	0
Moderate	1 (1.9)	0	3 (5.0)	0
Severe	0	1 (1.8)	0	0
Pain at the injection site[d]				
Any	34 (63.0)	9 (16.1)	32 (53.3)	5 (8.1)
Mild	26 (48.1)	8 (14.3)	22 (36.7)	5 (8.1)
Moderate	8 (14.8)	1 (1.8)	9 (15.0)	0
Severe	0	0	1 (1.7)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in HIV-positive participants 16 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 6: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – HIV-Positive Participants 16 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Fever				
≥38.0°C	1 (1.9)	4 (7.1)	9 (15.0)	5 (8.1)
≥38.0°C to 38.4°C	1 (1.9)	2 (3.6)	4 (6.7)	5 (8.1)
>38.4°C to 38.9°C	0	0	4 (6.7)	0
>38.9°C to 40.0°C	0	2 (3.6)	1 (1.7)	0
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Fatigue[c]				
Any	22 (40.7)	15 (26.8)	24 (40.0)	12 (19.4)
Mild	15 (27.8)	9 (16.1)	12 (20.0)	5 (8.1)
Moderate	7 (13.0)	5 (8.9)	9 (15.0)	7 (11.3)
Severe	0	1 (1.8)	3 (5.0)	0
Headache[c]				
Any	11 (20.4)	18 (32.1)	18 (30.0)	12 (19.4)
Mild	7 (13.0)	10 (17.9)	8 (13.3)	8 (12.9)
Moderate	4 (7.4)	7 (12.5)	8 (13.3)	4 (6.5)
Severe	0	1 (1.8)	2 (3.3)	0
Chills[c]				
Any	6 (11.1)	5 (8.9)	14 (23.3)	4 (6.5)
Mild	5 (9.3)	4 (7.1)	5 (8.3)	3 (4.8)
Moderate	1 (1.9)	1 (1.8)	8 (13.3)	1 (1.6)
Severe	0	0	1 (1.7)	0
Vomiting[d]				
Any	1 (1.9)	3 (5.4)	2 (3.3)	2 (3.2)
Mild	1 (1.9)	1 (1.8)	1 (1.7)	1 (1.6)
Moderate	0	0	1 (1.7)	1 (1.6)
Severe	0	2 (3.6)	0	0
Diarrhea[e]				
Any	5 (9.3)	8 (14.3)	4 (6.7)	9 (14.5)
Mild	5 (9.3)	6 (10.7)	1 (1.7)	6 (9.7)
Moderate	0	1 (1.8)	2 (3.3)	3 (4.8)
Severe	0	1 (1.8)	1 (1.7)	0
New or worsened muscle pain[c]				
Any	9 (16.7)	10 (17.9)	10 (16.7)	5 (8.1)
Mild	7 (13.0)	7 (12.5)	5 (8.3)	1 (1.6)
Moderate	2 (3.7)	3 (5.4)	5 (8.3)	4 (6.5)
Severe	0	0	0	0
New or worsened joint pain[c]				
Any	5 (9.3)	7 (12.5)	10 (16.7)	5 (8.1)
Mild	5 (9.3)	4 (7.1)	4 (6.7)	1 (1.6)
Moderate	0	3 (5.4)	6 (10.0)	4 (6.5)
Severe	0	0	0	0
Use of antipyretic or pain medication[f]	7 (13.0)	8 (14.3)	16 (26.7)	7 (11.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in HIV-positive participants 16 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each event or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.
f. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

Upon issuance of the EUA for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began in a phased manner for participants in the study. Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 2.1 per 100 person-years among COMIRNATY recipients and 2.4 per 100 person-years among placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported at an incidence rate of 4.9 per 100 person-years among COMIRNATY recipients and 4.6 per 100 person-years among placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 6.6 per 100 person-years among COMIRNATY recipients and 6.9 per 100 person-years among placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 88.4 per 100 person-years among participants who received COMIRNATY and 43.5 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include non-serious adverse events were reported at an incidence rate of 75.7 per 100 person-years among participants who received COMIRNATY and 43.3 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 95.8 per 100 person-years among participants who received

COMIRNATY and 52.0 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

6.2 Post Marketing Experience

The following adverse reactions have been identified during post marketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A reproductive and developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions, twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a reproductive and developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative. The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental and reproductive toxicity study in rats with COMIRNATY, there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

14.1 Efficacy in Participants 16 Years of Age and Older

Study 2 is a multicenter, multinational, Phase 1/2/3, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In the Phase 2/3 portion of Study 2, based on data accrued through November 14, 2020, approximately 44,000 participants 12 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. The efficacy analyses included participants that received their second vaccination within 19 to 42 days after their first vaccination. The majority (93.1%) of vaccine recipients received the second dose 19 days to 23 days after Dose 1. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. Table 7 presents the specific demographic characteristics in the studied population.

Table 7: Demographics (Population For the Primary Efficacy Endpoint)[a]

	COMIRNATY (N=18,242) n (%)	Placebo (N=18,379) n (%)
Sex		
Male	9318 (51.1)	9225 (50.2)
Female	8924 (48.9)	9154 (49.8)
Age (years)		
Mean (SD)	50.6 (15.70)	50.4 (15.81)
Median	52.0	52.0
Min, max	(12, 89)	(12, 91)
Age group		
≥12 through 15 years	46 (0.3)	42 (0.2)
≥16 through 64 years	14,216 (77.9)	14,299 (77.8)
≥65 through 74 years	3176 (17.4)	3226 (17.6)
≥75 years	804 (4.4)	812 (4.4)
Race		
White	15,110 (82.8)	15,301 (83.3)
Black or African American	1617 (8.9)	1617 (8.8)
American Indian or Alaska Native	118 (0.6)	106 (0.6)
Asian	815 (4.5)	810 (4.4)
Native Hawaiian or other Pacific Islander	48 (0.3)	29 (0.2)
Other[b]	534 (2.9)	516 (2.8)
Ethnicity		
Hispanic or Latino	4886 (26.8)	4857 (26.4)
Not Hispanic or Latino	13,253 (72.7)	13,412 (73.0)
Not reported	103 (0.6)	110 (0.6)
Comorbidities[c]		
Yes	8432 (46.2)	8450 (46.0)
No	9810 (53.8)	9929 (54.0)

a. All eligible randomized participants who receive all vaccination(s) as randomized within the predefined window, have no other important protocol deviations as determined by the clinician, and have no evidence of SARS-CoV-2 infection prior to 7 days after Dose 2.

b. Includes multiracial and not reported.

c. Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease:
- Chronic lung disease (e.g., emphysema and chronic bronchitis, idiopathic pulmonary fibrosis, and cystic fibrosis) or moderate to severe asthma
- Significant cardiac disease (e.g., heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and pulmonary hypertension)
- Obesity (body mass index ≥30 kg/m^2)
- Diabetes (Type 1, Type 2, or gestational)
- Liver disease
- Human Immunodeficiency Virus (HIV) infection (not included in the efficacy evaluation)

Efficacy Against COVID-19

The population in the primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

The vaccine efficacy information is presented in Table 8.

Table 8: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=18,198 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.3, 97.6)[f]
16 to 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)[g]
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)[g]
65 to 74 years	1 0.406 (3074)	14 0.406 (3095)	92.9 (53.1, 99.8)[g]
75 years and older	0 0.102 (774)	5 0.106 (785)	100.0 (-13.1, 100.0)[g]
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=19,965 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,172 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	9 2.332 (18,559)	169 2.345 (18,708)	94.6 (89.9, 97.3)[f]
16 to 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1 0.530 (4044)	19 0.532 (4067)	94.7 (66.8, 99.9)[g]
65 to 74 years	1 0.424 (3239)	14 0.423 (3255)	92.9 (53.2, 99.8)[g]
75 years and older	0 0.106 (805)	5 0.109 (812)	100.0 (-12.1, 100.0)[g]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. No confirmed cases were identified in participants 12 to 15 years of age.
f. Two-sided credible interval for vaccine efficacy was calculated using a beta-binomial model with a beta (0.700102, 1) prior for θ=r(1-VE)/(1+r(1-VE)), where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.
g. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Updated efficacy analyses were performed with additional confirmed COVID-19 cases accrued during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2 for participants in the efficacy population.

The updated vaccine efficacy information is presented in Table 9.

Table 9: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
16 through 64 years	70 4.859 (15,519)	710 4.654 (15,515)	90.6 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
65 through 74 years	6 0.994 (3350)	98 0.966 (3379)	94.1 (86.6, 97.9)
75 years and older	1 0.239 (842)	26 0.237 (847)	96.2 (76.9, 99.9)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
16 through 64 years	74 5.073 (16,218)	727 4.879 (16,269)	90.2 (87.6, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)
65 through 74 years	6 1.021 (3450)	102 0.992 (3468)	94.3 (87.1, 98.0)
75 years and older	1 0.246 (865)	26 0.240 (858)	96.2 (77.2, 99.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group (both without and with or without evidence of prior SARS-CoV-2 infection); 16 and 18 in the placebo group (without and with or without evidence of prior SARS-CoV-2 infection, respectively).

The updated subgroup analyses of vaccine efficacy by demographic characteristics are presented in Table 10 and Table 11.

Table 10: Vaccine Efficacy– First COVID-19 Occurrence From 7 Days After Dose 2 – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 by Demographic Characteristics – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Sex			
Male	42 3.246 (10,637)	399 3.047 (10,433)	90.1 (86.4, 93.0)
Female	35 3.001 (10,075)	451 2.956 (10,280)	92.4 (89.2, 94.7)
Ethnicity			
Hispanic or Latino	29 1.786 (5161)	241 1.711 (5120)	88.5 (83.0, 92.4)
Not Hispanic or Latino	47 4.429 (15,449)	609 4.259 (15,484)	92.6 (90.0, 94.6)
Race			
Black or African American	4 0.545 (1737)	48 0.527 (1737)	91.9 (78.0, 97.9)
White	67 5.208 (17,186)	747 5.026 (17,256)	91.3 (88.9, 93.4)
All others[f]	6 0.494 (1789)	55 0.451 (1720)	90.0 (76.9, 96.5)

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Country			
Argentina	15 1.012 (2600)	108 0.986 (2586)	86.5 (76.7, 92.7)
Brazil	12 0.406 (1311)	80 0.374 (1293)	86.2 (74.5, 93.1)
Germany	0 0.047 (236)	1 0.048 (242)	100.0 (-3874.2, 100.0)
South Africa	0 0.080 (291)	9 0.074 (276)	100.0 (53.5, 100.0)
Turkey	0 0.027 (228)	5 0.025 (222)	100.0 (-0.1, 100.0)
United States	50 4.674 (16,046)	647 4.497 (16,094)	92.6 (90.1, 94.5)

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).
Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group.

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
f. All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

Table 11: Vaccine Efficacy– First COVID-19 Occurrence From 7 Days After Dose 2 – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 by Demographic Characteristics – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Sex			
Male	44 3.376 (11,103)	411 3.181 (10,920)	89.9 (86.2, 92.8)
Female	37 3.133 (10,539)	462 3.093 (10,769)	92.1 (88.9, 94.5)

Subgroup	COMIRNATY Na=22,166 Cases n1b Surveillance Timec (n2d)	Placebo Na=22,320 Cases n1b Surveillance Timec (n2d)	Vaccine Efficacy % (95% CI)e
Ethnicity			
Hispanic or Latino	32 1.862 (5408)	245 1.794 (5391)	87.4 (81.8, 91.6)
Not Hispanic or Latino	48 4.615 (16,128)	628 4.445 (16,186)	92.6 (90.1, 94.6)
Race			
Black or African American	4 0.611 (1958)	49 0.601 (1985)	92.0 (78.1, 97.9)
White	69 5.379 (17,801)	768 5.191 (17,880)	91.3 (88.9, 93.3)
All others[f]	8 0.519 (1883)	56 0.481 (1824)	86.8 (72.1, 94.5)
Country			
Argentina	16 1.033 (2655)	110 1.017 (2670)	85.7 (75.7, 92.1)
Brazil	14 0.441 (1419)	82 0.408 (1401)	84.2 (71.9, 91.7)
Germany	0 0.047 (237)	1 0.048 (243)	100.0 (-3868.6, 100.0)
South Africa	0 0.099 (358)	10 0.096 (358)	100.0 (56.6, 100.0)
Turkey	0 0.029 (238)	6 0.026 (232)	100.0 (22.2, 100.0)
United States	51 4.861 (16,735)	664 4.678 (16,785)	92.6 (90.2, 94.6)

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group.

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
f. All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

The updated subgroup analyses of vaccine efficacy by risk status in participants are presented in Table 12 and Table 13.

Table 12: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First COVID-19 occurrence from 7 days after Dose 2[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
At risk[g]			
Yes	35 2.797 (9167)	401 2.681 (9136)	91.6 (88.2, 94.3)
No	42 3.450 (11,545)	449 3.322 (11,577)	91.0 (87.6, 93.6)
Age group (years) and risk status			
16 through 64 and not at risk	41 2.776 (8887)	385 2.661 (8886)	89.8 (85.9, 92.8)
16 through 64 and at risk	29 2.083 (6632)	325 1.993 (6629)	91.5 (87.5, 94.4)
65 and older and not at risk	1 0.553 (1870)	53 0.546 (1922)	98.1 (89.2, 100.0)
65 and older and at risk	6 0.680 (2322)	71 0.656 (2304)	91.8 (81.4, 97.1)
Obese[h]			
Yes	27 2.103 (6796)	314 2.050 (6875)	91.6 (87.6, 94.6)
No	50 4.143 (13,911)	536 3.952 (13,833)	91.1 (88.1, 93.5)
Age group (years) and obesity status			
16 through 64 and not obese	46 3.178 (10,212)	444 3.028 (10,166)	90.1 (86.6, 92.9)
16 through 64 and obese	24 1.680 (5303)	266 1.624 (5344)	91.3 (86.7, 94.5)
65 and older and not obese	4 0.829 (2821)	79 0.793 (2800)	95.2 (87.1, 98.7)
65 and older and obese	3 0.404 (1370)	45 0.410 (1426)	93.2 (78.9, 98.7)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group.

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]

g. At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age]).
h. Obese is defined as BMI ≥30 kg/m^2. For 12 through 15 years age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First COVID-19 occurrence from 7 days after Dose 2[f]	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
At risk[g]			
Yes	36 2.925 (9601)	410 2.807 (9570)	91.6 (88.1, 94.2)
No	45 3.584 (12,041)	463 3.466 (12,119)	90.6 (87.2, 93.2)
Age group (years) and risk status			
16 through 64 and not at risk	44 2.887 (9254)	397 2.779 (9289)	89.3 (85.4, 92.4)
16 through 64 and at risk	30 2.186 (6964)	330 2.100 (6980)	91.3 (87.3, 94.2)
65 and older and not at risk	1 0.566 (1920)	55 0.559 (1966)	98.2 (89.6, 100.0)
65 and older and at risk	6 0.701 (2395)	73 0.672 (2360)	92.1 (82.0, 97.2)
Obese[h]			
Yes	28 2.207 (7139)	319 2.158 (7235)	91.4 (87.4, 94.4)
No	53 4.301 (14,497)	554 4.114 (14,448)	90.8 (87.9, 93.2)
Age group (years) and obesity status			
16 through 64 and not obese	49 3.303 (10,629)	458 3.158 (10,614)	89.8 (86.2, 92.5)
16 through 64 and obese	25 1.768 (5584)	269 1.719 (5649)	91.0 (86.4, 94.3)
65 and older and not obese	4 0.850 (2899)	82 0.811 (2864)	95.3 (87.6, 98.8)
65 and older and obese	3 0.417 (1415)	46 0.420 (1462)	93.4 (79.5, 98.7)

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.
f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group.
g. At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age]).
h. Obese is defined as BMI ≥30 kg/m^2. For the 12 through 15 years of age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Efficacy Against Severe COVID-19

Updated efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 14) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 14: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants With or Without* Prior SARS-CoV-2 Infection Based on FDA† or Centers for Disease Control and Prevention (CDC)‡ Definition After Dose 1 or From 7 Days After Dose 2 in the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence Based on FDA Definition			
	COMIRNATY Cases n1[a] Surveillance Time (n2[b])	Placebo Cases n1[a] Surveillance Time (n2[b])	Vaccine Efficacy % (95% CI[c])
After Dose 1[d]	1 8.439[e] (22,505)	30 8.288[e] (22,435)	96.7 (80.3, 99.9)
7 days after Dose 2[f]	1 6.522[g] (21,649)	21 6.404[g] (21,730)	95.3 (70.9, 99.9)

Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time (n2[b])	**Placebo Cases n1[a] Surveillance Time (n2[b])**	**Vaccine Efficacy % (95% CI[c])**
After Dose 1[d]	1 8.427[e] (22,473)	45 8.269[e] (22,394)	97.8 (87.2, 99.9)
7 days after Dose 2[f]	0 6.514[g] (21,620)	32 6.391[g] (21,693)	100 (88.0, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 as defined by FDA is confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. n2 = Number of participants at risk for the endpoint.
c. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
d. Efficacy assessed based on the Dose 1 all available efficacy (modified intention-to-treat) population that included all randomized participants who received at least 1 dose of study intervention.
e. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.
f. Efficacy assessed based on the evaluable efficacy (7 Days) population that included all eligible randomized participants who receive all dose(s) of study intervention as randomized within the predefined window, have no other important protocol deviations as determined by the clinician.
g. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -80ºC to -60ºC (-112ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

For general questions, visit the website or call the telephone number provided below.

Website	Telephone number
www.comirnatyhcp.com	1-877-829-2619 (1-877-VAX-CO19)

This product's labeling may have been updated. For the most recent prescribing information, please visit www.pfizer.com.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.2

US Govt. License No. x

CPT Code x

Table.A.1 Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Test Status – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population, Participants 16 Years of Age and Older (Data Cutoff March 13, 2021)

RT-PCR NP Swab Results and Serostatus at Different Time Points	BNT162b2 (N[a]=21047) Cases n1[b] Surveillance Time[c] (n2[d])	Placebo (N[a]=21210) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Pre-Dose 1 SARS-CoV-2 RT-PCR (NP swab)			
Positive	1 0.040 (127)	1 0.047 (154)	-17.9 (-9154.3, 98.5)
Negative	79 6.284 (20356)	853 6.048 (20395)	91.1 (88.8, 93.0)
Unknown	1 0.015 (50)	0 0.015 (46)	-∞ (NA, NA)
Pre-Dose 2 SARS-CoV-2 RT-PCR (NP swab)			
Positive	1 0.030 (101)	1 0.037 (130)	-24.7 (-9685.9, 98.4)
Negative	80 6.293 (20376)	849 6.061 (20423)	90.9 (88.6, 92.9)
Unknown	0 0.017 (56)	4 0.013 (42)	100.0 (-11.3, 100.0)

Table.A.1 Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Test Status – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population, Participants 16 Years of Age and Older (Data Cutoff March 13, 2021)

RT-PCR NP Swab Results and Serostatus at Different Time Points	BNT162b2 (N[a]=21047) Cases n1[b] Surveillance Time[c] (n2[d])	Placebo (N[a]=21210) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Subjects with negative PCR Pre-dose 1 and positive PCR Pre-dose 2			
Subjects with documented COVID-19 symptoms between Dose 1 and 2	0 0.000 (0)	0 0.001 (2)	
Subjects with no documented COVID-19 symptoms between Dose 1 and 2	0 0.016 (58)	1 0.019 (71)	
Pre-Dose 1 N-binding antibody			
Positive	3 0.169 (550)	5 0.181 (594)	36.0 (-228.7, 90.1)
Negative	78 6.147 (19896)	847 5.910 (19927)	91.1 (88.8, 93.1)
Unknown	0 0.023 (87)	2 0.019 (74)	100.0 (-348.8, 100.0)

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NA = Not applicable; NP = nasopharyngeal; RT-PCR = reverse transcription–polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

a. N = number of subjects in the specified group.

Table.A.1 Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Test Status – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population, Participants 16 Years of Age and Older (Data Cutoff March 13, 2021)

RT-PCR NP Swab Results and Serostatus at Different Time Points	BNT162b2 (N^a=21047) Cases n1[b] Surveillance Time[c] (n2[d])	Placebo (N^a=21210) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]

b. n1 = Number of subjects meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

Table.A.2 Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Test Status – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Dose 2 All-Available Efficacy Population, Participants 16 Years of Age and Older (Data Cutoff March 13, 2021)

RT-PCR NP Swab Results and Serostatus at Different Time Points	BNT162b2 (N[a]=21552) Cases n1[b] Surveillance Time[c] (n2[d])	Placebo (N[a]=21528) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Pre-Dose 1 SARS-CoV-2 RT-PCR (NP swab)			
Positive	1 0.041 (132)	1 0.048 (155)	-15.4 (-8959.5, 98.5)
Negative	80 6.422 (20836)	869 6.144 (20697)	91.2 (88.9, 93.1)
Unknown	1 0.016 (51)	0 0.016 (49)	-∞ (NA, NA)
Pre-Dose 2 SARS-CoV-2 RT-PCR (NP swab)			
Positive	1 0.031 (105)	1 0.038 (131)	-22.3 (-9503.8, 98.4)
Negative	81 6.431 (20857)	865 6.156 (20723)	91.0 (88.7, 93.0)
Unknown	0 0.017 (57)	4 0.013 (47)	100.0 (-16.4, 100.0)

Table.A.2 Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Test Status – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Dose 2 All-Available Efficacy Population, Participants 16 Years of Age and Older (Data Cutoff March 13, 2021)

RT-PCR NP Swab Results and Serostatus at Different Time Points	BNT162b2 (N[a]=21552) Cases n1[b] Surveillance Time[c] (n2[d])	Placebo (N[a]=21528) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Subjects with negative PCR Pre-dose 1 and positive PCR Pre-dose 2			
Subjects with documented COVID-19 symptoms between Dose 1 and 2	0 0.000 (0)	0 0.001 (2)	
Subjects with no documented COVID-19 symptoms between Dose 1 and 2	0 0.016 (61)	1 0.020 (72)	
Pre-Dose 1 N-binding antibody			
Positive	3 0.173 (563)	5 0.185 (608)	35.8 (-229.9, 90.0)
Negative	79 6.283 (20367)	863 6.002 (20218)	91.3 (89.0, 93.1)
Unknown	0 0.023 (89)	2 0.019 (75)	100.0 (-344.1, 100.0)

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NA = Not applicable; NP = nasopharyngeal; RT-PCR = reverse transcription–polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

a. N = number of subjects in the specified group.

Table.A.2 Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Test Status – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Dose 2 All-Available Efficacy Population, Participants 16 Years of Age and Older (Data Cutoff March 13, 2021)

RT-PCR NP Swab Results and Serostatus at Different Time Points	BNT162b2 (N^a=21552) Cases n1[b] Surveillance Time[c] (n2[d])	Placebo (N^a=21528) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]

b. n1 = Number of subjects meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

Table.D Disposition of Participants 16 Years of Age and Older, Phase 2/3 Subjects, Efficacy Population (Data Cutoff March 13, 2021)

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) n[a] (%)	**Placebo n[a] (%)**	**Total n[a] (%)**
Randomized[b]	22085 (100.0)	22080 (100.0)	44165 (100.0)
Dose 1 all-available efficacy population	22009 (99.7)	22008 (99.7)	44017 (99.7)
Subjects without evidence of infection before Dose 1	21172 (95.9)	21168 (95.9)	42340 (95.9)
Subjects excluded from Dose 1 all-available efficacy population	76 (0.3)	72 (0.3)	148 (0.3)
Reason for exclusion[c]			
Did not receive at least 1 vaccination	55 (0.2)	50 (0.2)	105 (0.2)
Data considered potentially unreliable due to lack of PI oversight identified as significant quality event	21 (0.1)	22 (0.1)	43 (0.1)
Dose 2 all-available efficacy population	21648 (98.0)	21624 (97.9)	43272 (98.0)
Subjects without evidence of infection prior to 7 days after Dose 2	20536 (93.0)	20487 (92.8)	41023 (92.9)
Subjects excluded from Dose 2 all-available efficacy population	437 (2.0)	456 (2.1)	893 (2.0)
Reason for exclusion[c]			
Did not receive 2 vaccinations	374 (1.7)	430 (1.9)	804 (1.8)
Data considered potentially unreliable due to lack of PI oversight identified as significant quality event	21 (0.1)	22 (0.1)	43 (0.1)
Unblinded prior to 7 days after Dose 2	44 (0.2)	11 (0.0)	55 (0.1)
Evaluable efficacy (7 days) population	21136 (95.7)	21300 (96.5)	42436 (96.1)
Subjects without evidence of infection prior to 7 days after Dose 2	20064 (90.8)	20197 (91.5)	40261 (91.2)
Subjects excluded from evaluable efficacy (7 days) population	949 (4.3)	780 (3.5)	1729 (3.9)
Reason for exclusion[c]			

Table.D Disposition of Participants 16 Years of Age and Older, Phase 2/3 Subjects, Efficacy Population (Data Cutoff March 13, 2021)

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) n[a] (%)	**Placebo n[a] (%)**	**Total n[a] (%)**
Randomized but did not meet all eligibility criteria	32 (0.1)	30 (0.1)	62 (0.1)
Data considered potentially unreliable due to lack of PI oversight identified as significant quality event	21 (0.1)	22 (0.1)	43 (0.1)
Did not receive all vaccinations as randomized or did not receive Dose 2 within the predefined window (19-42 days after Dose 1)	718 (3.3)	729 (3.3)	1447 (3.3)
Unblinded prior to 7 days after Dose 2	44 (0.2)	11 (0.0)	55 (0.1)
Had other important protocol deviations on or prior to 7 days after Dose 2	240 (1.1)	58 (0.3)	298 (0.7)

Note: HIV-positive subjects are included in this summary but not included in the analyses of the overall study objectives.
a. n = Number of subjects with the specified characteristic.
b. These values are the denominators for the percentage calculations.
c. Subjects may have been excluded for more than 1 reason.

Table.F Demographics and Other Baseline Characteristics, Participants 16 Years of Age and Older, With or Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy Population (Data Cutoff March 13, 2021)

	Vaccine Group (as Randomized)		
Characteristic	**BNT162b2 (30 µg) (N[a]=21136) n[b] (%)**	**Placebo (N[a]=21300) n[b] (%)**	**Total (N[a]=42436) n[b] (%)**
Sex: Female	10280 (48.6)	10579 (49.7)	20859 (49.2)
Sex: Male	10856 (51.4)	10721 (50.3)	21577 (50.8)
Age at Vaccination: Mean years (SD)	49.8 (15.99)	49.7 (16.03)	49.7 (16.01)
Age at Vaccination: Median (years)	51.0	51.0	51.0
Age at Vaccination: Min, max (years)	(16, 89)	(16, 91)	(16, 91)
Age Group: 16 to <18 years	370 (1.8)	362 (1.7)	732 (1.7)
Age Group: 18 to 55 years	12120 (57.3)	12252 (57.5)	24372 (57.4)
Age Group: >55 years	8646 (40.9)	8686 (40.8)	17332 (40.8)
Age Group: ≥65 years	4407 (20.9)	4429 (20.8)	8836 (20.8)
Race: American Indian or Alaska Native	204 (1.0)	190 (0.9)	394 (0.9)
Race: Asian	929 (4.4)	924 (4.3)	1853 (4.4)
Race: Black or African American	2009 (9.5)	2036 (9.6)	4045 (9.5)
Race: Native Hawaiian or Other Pacific Islander	56 (0.3)	32 (0.2)	88 (0.2)
Race: White	17304 (81.9)	17487 (82.1)	34791 (82.0)
Race: Multiracial	545 (2.6)	519 (2.4)	1064 (2.5)
Race: Not reported	89 (0.4)	112 (0.5)	201 (0.5)
Ethnicity: Hispanic or Latino	5403 (25.6)	5409 (25.4)	10812 (25.5)

Table.F Demographics and Other Baseline Characteristics, Participants 16 Years of Age and Older, With or Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy Population (Data Cutoff March 13, 2021)

Characteristic	Vaccine Group (as Randomized) BNT162b2 (30 µg) (N[a]=21136) n[b] (%)	Placebo (N[a]=21300) n[b] (%)	Total (N[a]=42436) n[b] (%)
Ethnicity: Not Hispanic or Latino	15628 (73.9)	15778 (74.1)	31406 (74.0)
Ethnicity: Not reported	105 (0.5)	113 (0.5)	218 (0.5)
Obesity: Yes[c]	7239 (34.2)	7386 (34.7)	14625 (34.5)
Obesity: No	13897 (65.8)	13914 (65.3)	27811 (65.5)
Comorbidities: Yes[d]	9712 (46.0)	9736 (45.7)	19448 (45.8)
Comorbidities: No	11424 (54.0)	11564 (54.3)	22988 (54.2)
Baseline evidence of prior SARS-CoV-2 infection: Negative[f]	20365 (96.4)	20511 (96.3)	40876 (96.3)
Baseline evidence of prior SARS-CoV-2 infection: Positive[e]	627 (3.0)	669 (3.1)	1296 (3.1)
Baseline evidence of prior SARS-CoV-2 infection: Missing	144 (0.7)	120 (0.6)	264 (0.6)
Country: Argentina	2686 (12.7)	2710 (12.7)	5396 (12.7)
Country: Brazil	1437 (6.8)	1432 (6.7)	2869 (6.8)
Country: Germany	240 (1.1)	243 (1.1)	483 (1.1)
Country: South Africa	391 (1.8)	392 (1.8)	783 (1.8)
Country: Turkey	241 (1.1)	238 (1.1)	479 (1.1)
Country: United States of America	16141 (76.4)	16285 (76.5)	32426 (76.4)

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: HIV-positive subjects are included in this summary but not included in the analyses of the overall study objectives.
a. N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.
b. n = Number of subjects with the specified characteristic.
c. Subjects who had BMI ≥30 kg/m^2.

Table.F Demographics and Other Baseline Characteristics, Participants 16 Years of Age and Older, With or Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy Population (Data Cutoff March 13, 2021)

	Vaccine Group (as Randomized)		
Characteristic	**BNT162b2 (30 µg) (N^a=21136) n^b (%)**	**Placebo (N^a=21300) n^b (%)**	**Total (N^a=42436) n^b (%)**

d. Number of subjects who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or BMI ≥30 kg/m^2.
e. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
f. Negative N-binding antibody result and negative NAAT result at Visit 1 and no medical history of COVID-19.

Table.G Final Analysis of Efficacy of BNT162b2 Against Confirmed COVID-19 From 7 Days After Dose 2 in Participants Without Evidence of Prior SARS-CoV-2 Infection – Evaluable Efficacy Population, 16 Years and Older (Data Cutoff November 2020)

Pre-specified Age Group	BNT162b2 (N^a=18152) Cases n1[b] Surveillance Time[c] (n2[d])	Placebo (N^a=18283) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]	Met Predefined Success Criterion
All participants	8 2.214 (17397)	162 2.222 (17498)	95.0 (90.0, 97.9)	NA
16 to 55 years	5 1.234 (9897)	114 1.239 (9955)	95.6 (89.4, 98.6)	NA
>55 years and older	3 0.980 (7500)	48 0.983 (7543)	93.7 (80.6, 98.8)	NA

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of subjects in the specified group.
b. n1 = Number of subjects meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

Table.H Updated Efficacy of BNT162b2 Against Confirmed COVID-19 From 7 Days After Dose 2 in Participants Without Evidence of Prior SARS-CoV-2 Infection – Evaluable Efficacy Population, 16 Years and Older (Data Cutoff March 13, 2021)

Pre-specified Age Group	BNT162b2 (N[a]=19993) Cases n1[b] Surveillance Time[c] (n2[d])	Placebo (N[a]=20118) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
All participants	77 6.092 (19711)	833 5.857 (19741)	91.1 (88.8, 93.1)
16 to 55 years	52 3.593 (11517)	568 3.439 (11533)	91.2 (88.3, 93.5)
>55 years and older	25 2.499 (8194)	265 2.417 (8208)	90.9 (86.2, 94.2)

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of subjects in the specified group.
b. n1 = Number of subjects meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

Table.I Updated Efficacy of BNT162b2 Against Confirmed COVID-19 From 7 Days After Dose 2 in Participants With or Without Evidence of Prior SARS-CoV-2 Infection – Evaluable Efficacy Population, 16 Years and Older (Data Cutoff March 13, 2021)

Pre-specified Age Group	BNT162b2 (N[a]=21047) Cases n1[b] Surveillance Time[c] (n2[d])	Placebo (N[a]=21210) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
All participants	81 6.340 (20533)	854 6.110 (20595)	90.9 (88.5, 92.8)
16 to 55 years	56 3.766 (12088)	584 3.619 (12142)	90.8 (87.9, 93.1)
>55 years and older	25 2.573 (8445)	270 2.492 (8453)	91.0 (86.5, 94.3)

Abbreviations: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

a. N = number of subjects in the specified group.

b. n1 = Number of subjects meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of subjects at risk for the endpoint.

e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

Table.J Subgroup Analyses of Updated Second Primary Endpoint: First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup, Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy Population, 16 Years and Older (Data Cutoff March 13, 2021)

	Vaccine Group (as Randomized)		
Efficacy Endpoint Subgroup	**BNT162b2 (30 µg) (N[a]=21047) Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo (N[a]=21210) Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy (%) (95% CI[e])**
First COVID-19 occurrence from 7 days after Dose 2			
Overall	81 6.340 (20533)	854 6.110 (20595)	90.9 (88.5, 92.8)
Age group: 16 to <18 years	0 0.065 (365)	11 0.061 (355)	100.0 (62.4, 100.0)
Age group: 18 to <65 years	74 5.008 (15853)	715 4.817 (15914)	90.0 (87.3, 92.3)
Age group: ≥65 years	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)
Age group: 65 to 74 years	6 1.021 (3450)	102 0.992 (3468)	94.3 (87.1, 98.0)
Age group: ≥75 years	1 0.246 (865)	26 0.240 (858)	96.2 (77.2, 99.9)

Table.J Subgroup Analyses of Updated Second Primary Endpoint: First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup, Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy Population, 16 Years and Older (Data Cutoff March 13, 2021)

Efficacy Endpoint Subgroup	Vaccine Group (as Randomized) BNT162b2 (30 µg) (N[a]=21047) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Group (as Randomized) Placebo (N[a]=21210) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy (%) (95% CI[e])
At risk: Yes[f]	36 2.887 (9359)	402 2.772 (9340)	91.4 (87.9, 94.1)
At risk: No	45 3.453 (11174)	452 3.338 (11255)	90.4 (86.9, 93.1)
Age group and Risk: 16-64 and not at risk	44 2.887 (9254)	397 2.779 (9289)	89.3 (85.4, 92.4)
Age group and Risk: 16-64 and at risk	30 2.186 (6964)	329 2.100 (6980)	91.2 (87.3, 94.2)
Age group and Risk: ≥65 and not at risk	1 0.566 (1920)	55 0.559 (1966)	98.2 (89.6, 100.0)
Age group and Risk: ≥65 and at risk	6 0.701 (2395)	73 0.672 (2360)	92.1 (82.0, 97.2)
Obese: Yes[g]	28 2.185 (6999)	314 2.139 (7111)	91.3 (87.1, 94.3)

Table.J Subgroup Analyses of Updated Second Primary Endpoint: First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup, Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy Population, 16 Years and Older (Data Cutoff March 13, 2021)

Efficacy Endpoint Subgroup	Vaccine Group (as Randomized) BNT162b2 (30 µg) (N[a]=21047) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Group (as Randomized) Placebo (N[a]=21210) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy (%) (95% CI[e])
Obese: No	53 4.153 (13528)	540 3.970 (13478)	90.6 (87.5, 93.1)
Age group and obese:16-64 and not obese	49 3.303 (10629)	458 3.158 (10614)	89.8 (86.2, 92.5)
Age group and obese:16-64 and obese	25 1.768 (5584)	268 1.719 (5649)	90.9 (86.3, 94.2)
Age group and obese: ≥65 and not obese	4 0.850 (2899)	82 0.811 (2864)	95.3 (87.6, 98.8)
Age group and obese: ≥65 and obese	3 0.417 (1415)	46 0.420 (1462)	93.4 (79.5, 98.7)
Sex: Female	37 3.051 (9985)	455 3.013 (10241)	92.0 (88.8, 94.4)
Sex: Male	44 3.289 (10548)	399 3.097 (10354)	89.6 (85.8, 92.6)

Table.J Subgroup Analyses of Updated Second Primary Endpoint: First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup, Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy Population, 16 Years and Older (Data Cutoff March 13, 2021)

Efficacy Endpoint Subgroup	Vaccine Group (as Randomized) BNT162b2 (30 µg) (N[a]=21047) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Group (as Randomized) Placebo (N[a]=21210) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy (%) (95% CI[e])
Ethnicity: Hispanic or Latino	32 1.841 (5280)	240 1.777 (5266)	87.1 (81.3, 91.4)
Ethnicity: Not Hispanic or Latino	48 4.466 (15149)	614 4.300 (15220)	92.5 (89.9, 94.5)
Ethnicity: Not reported	1 0.032 (104)	0 0.034 (109)	-∞ (NA, NA)
Race: American Indian or Alaska native	0 0.043 (196)	3 0.038 (180)	100.0 (-116.0, 100.0)
Race: Asian	3 0.258 (907)	24 0.247 (896)	88.0 (60.6, 97.7)
Race: Black or African American	4 0.602 (1909)	49 0.591 (1928)	92.0 (78.1, 97.9)
Race: Native Hawaiian or other Pacific Islander	0 0.016 (54)	1 0.008 (31)	100.0 (-1947.9, 100.0)

Table.J Subgroup Analyses of Updated Second Primary Endpoint: First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup, Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy Population, 16 Years and Older (Data Cutoff March 13, 2021)

Efficacy Endpoint Subgroup	Vaccine Group (as Randomized) BNT162b2 (30 µg) (N[a]=21047) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Group (as Randomized) Placebo (N[a]=21210) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy (%) (95% CI[e])
Race: White	69 5.234 (16846)	749 5.054 (16952)	91.1 (88.6, 93.2)
Race: Multiracial	5 0.160 (538)	22 0.140 (503)	80.1 (46.1, 94.1)
Race: Not reported	0 0.027 (83)	6 0.031 (105)	100.0 (1.4, 100.0)
Baseline SARS-CoV-2 Status:Positive[h]	3 0.183 (593)	6 0.195 (643)	46.7 (-149.5, 91.4)
Baseline SARS-CoV-2 Status:Negative[i]	77 6.119 (19805)	846 5.883 (19838)	91.2 (88.9, 93.2)
Baseline SARS-CoV-2 Status:Unknown	1 0.038 (135)	2 0.033 (114)	56.9 (-728.5, 99.3)
Country: Argentina	16 1.033 (2655)	110 1.017 (2670)	85.7 (75.7, 92.1)

Table.J Subgroup Analyses of Updated Second Primary Endpoint: First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup, Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy Population, 16 Years and Older (Data Cutoff March 13, 2021)

Efficacy Endpoint Subgroup	Vaccine Group (as Randomized) BNT162b2 (30 µg) (N[a]=21047) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Group (as Randomized) Placebo (N[a]=21210) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy (%) (95% CI[e])
Country: Brazil	14 0.441 (1419)	82 0.408 (1401)	84.2 (71.9, 91.7)
Country: Germany	0 0.047 (237)	1 0.048 (243)	100.0 (-3868.6, 100.0)
Country: South Africa	0 0.099 (358)	10 0.096 (358)	100.0 (56.6, 100.0)
Country: Turkey	0 0.029 (238)	6 0.026 (232)	100.0 (22.2, 100.0)
Country: United States	51 4.692 (15626)	645 4.515 (15691)	92.4 (89.9, 94.4)

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

a. N = number of subjects in the specified group.

b. n1 = Number of subjects meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of subjects at risk for the endpoint.

e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

Table.J Subgroup Analyses of Updated Second Primary Endpoint: First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup, Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy Population, 16 Years and Older (Data Cutoff March 13, 2021)

Efficacy Endpoint Subgroup	Vaccine Group (as Randomized) BNT162b2 (30 µg) (N[a]=21047) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Group (as Randomized) Placebo (N[a]=21210) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy (%) (95% CI[e])

f. Includes subjects who had at least one of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2).
g. Subjects (≥16 Years of age) who had BMI ≥30 kg/m^2.
h. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
i. Negative N-binding antibody result and negative NAAT result at Visit 1 and no medical history of COVID-19.

Table.K Demographic Characteristics, Participants 16 Years of Age and Older, With Protocol-Defined Case (Without Evidence of Infection Prior to 7 Days After Dose 2) (Data Cutoff March 13, 2021)

	Vaccine Group (as Randomized)		
Characteristic	**BNT162b2 (30 µg) (N[a]=77) n[b] (%)**	**Placebo (N[a]=833) n[b] (%)**	**Total (N[a]=910) n[b] (%)**
Age at Vaccination: Mean years (SD)	46.9 (14.79)	47.1 (15.58)	47.1 (15.51)
Age at Vaccination: Median (years)	50.0	47.0	48.0
Age at Vaccination: Min, max (years)	(19, 77)	(16, 88)	(16, 88)
Age Group: 16 to <18 years	0	10 (1.2)	10 (1.1)
Age Group: 18 to <65 years	70 (90.9)	699 (83.9)	769 (84.5)
Age Group: ≥65 years	7 (9.1)	124 (14.9)	131 (14.4)
Age Group: ≥65 to <75 years	6 (7.8)	98 (11.8)	104 (11.4)
Age Group: ≥75 years	1 (1.3)	26 (3.1)	27 (3.0)
Race: American Indian or Alaska Native	0	3 (0.4)	3 (0.3)
Race: Asian	3 (3.9)	23 (2.8)	26 (2.9)
Race: Black or African American	4 (5.2)	48 (5.8)	52 (5.7)
Race: Native Hawaiian or Other Pacific Islander	0	1 (0.1)	1 (0.1)
Race: White	67 (87.0)	730 (87.6)	797 (87.6)
Race: Multiracial	3 (3.9)	22 (2.6)	25 (2.7)
Race: Not reported	0	6 (0.7)	6 (0.7)
Sex: Female	35 (45.5)	444 (53.3)	479 (52.6)
Sex: Male	42 (54.5)	389 (46.7)	431 (47.4)
Ethnicity: Hispanic or Latino	29 (37.7)	236 (28.3)	265 (29.1)

Table.K Demographic Characteristics, Participants 16 Years of Age and Older, With Protocol-Defined Case (Without Evidence of Infection Prior to 7 Days After Dose 2) (Data Cutoff March 13, 2021)

Characteristic	Vaccine Group (as Randomized) BNT162b2 (30 µg) (N[a]=77) n[b] (%)	Placebo (N[a]=833) n[b] (%)	Total (N[a]=910) n[b] (%)
Ethnicity: Not Hispanic or Latino	47 (61.0)	597 (71.7)	644 (70.8)
Ethnicity: Not reported	1 (1.3)	0	1 (0.1)
Comorbidities: Yes[c]	35 (45.5)	395 (47.4)	430 (47.3)
Comorbidities: No	42 (54.5)	438 (52.6)	480 (52.7)
Obesity: Yes[d]	27 (35.1)	310 (37.2)	337 (37.0)
Obesity: No	50 (64.9)	523 (62.8)	573 (63.0)
Country: Argentina	15 (19.5)	108 (13.0)	123 (13.5)
Country: Brazil	12 (15.6)	80 (9.6)	92 (10.1)
Country: Germany	0	1 (0.1)	1 (0.1)
Country: South Africa	0	9 (1.1)	9 (1.0)
Country: Turkey	0	5 (0.6)	5 (0.5)
Country: United States	50 (64.9)	630 (75.6)	680 (74.7)

a. N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.
b. n = Number of subjects with the specified characteristic.
c. Number of subjects who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or BMI ≥30 kg/m^2.
d. Subjects who had BMI ≥30 kg/m^2.

Table.L Updated Vaccine Efficacy: First COVID-19 Occurrence From 7 Days After Dose 2, by Comorbidity Status, Among Participants Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy Population. Participants 16 Years of Age and Older (Data Cutoff March 13, 2021)

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=19993)	Placebo (N[a]=20118)	
Efficacy Endpoint Subgroup	**Cases n1[b] Surveillance Time[c] (n2[d])**	**Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy (%) (95% CI[e])**
First COVID-19 occurrence from 7 days after Dose 2			
Overall	77 6.092 (19711)	833 5.857 (19741)	91.1 (88.8, 93.1)
Comorbidity			
No comorbidity	42 3.329 (10757)	438 3.207 (10808)	90.8 (87.3, 93.4)
Any comorbidity[f]	35 2.763 (8954)	395 2.650 (8933)	91.5 (88.0, 94.2)
Any malignancy	3 0.228 (770)	27 0.213 (747)	89.6 (66.3, 98.0)
Cardiovascular	3 0.172 (584)	22 0.159 (555)	87.4 (58.1, 97.6)

Table.L Updated Vaccine Efficacy: First COVID-19 Occurrence From 7 Days After Dose 2, by Comorbidity Status, Among Participants Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy Population. Participants 16 Years of Age and Older (Data Cutoff March 13, 2021)

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=19993)	Placebo (N[a]=20118)	
Efficacy Endpoint Subgroup	Cases n1[b] Surveillance Time[c] (n2[d])	Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy (%) (95% CI[e])
Chronic pulmonary disease	8 0.474 (1582)	66 0.443 (1562)	88.7 (76.3, 95.3)
Diabetes	9 0.465 (1528)	60 0.444 (1513)	85.7 (70.9, 93.7)
Obese (≥30.0 kg/m^2)	27 2.083 (6673)	310 2.034 (6770)	91.5 (87.4, 94.5)
Hypertension	15 1.481 (4900)	190 1.427 (4895)	92.4 (87.1, 95.8)
Diabetes (including gestational diabetes)	9 0.468 (1537)	62 0.447 (1527)	86.1 (71.9, 93.9)

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of subjects in the specified group.

Table.L Updated Vaccine Efficacy: First COVID-19 Occurrence From 7 Days After Dose 2, by Comorbidity Status, Among Participants Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy Population. Participants 16 Years of Age and Older (Data Cutoff March 13, 2021)

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N^a=19993)	**Placebo (N^a=20118)**	
Efficacy Endpoint Subgroup	**Cases n1[b] Surveillance Time[c] (n2[d])**	**Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy (%) (95% CI[e])**

b. n1 = Number of subjects meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
f. Subject who had 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or BMI ≥30 kg/m^2.

Table.M First Severe COVID-19 Occurrence From 7 Days After Dose 2 – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Participants 16 Years of Age and Older – Evaluable Efficacy Population (Data Cutoff March 13, 2021)

Secondary Efficacy Endpoint	BNT162b2 (N[a]=19993) Cases n1[b] Surveillance Time[c] (n2[d])	Placebo (N[a]=20118) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First severe COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection	1 6.103 (19711)	21 5.971 (19741)	95.3 (71.0, 99.9)

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of subjects in the specified group.
b. n1 = Number of subjects meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

Table.N First Severe COVID-19 Occurrence After Dose 1 – Participants 16 Years of Age and Older – Dose 1 All-Available Efficacy Population (Data Cutoff March 13, 2021)

Secondary Efficacy Endpoint	BNT162b2 (N[a]=21909) Cases n1[b] Surveillance Time[c] (n2[d])	Placebo (N[a]=21908) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First severe case occurrence after Dose 1	1 8.181 (21385)	30 8.032 (21316)	96.7 (80.3, 99.9)
After Dose 1 to before Dose 2	0 1.285 (21385)	6 1.293 (21316)	100.0 (14.6, 100.0)
Dose 2 to 7 days after Dose 2	0 0.403 (21056)	1 0.402 (20962)	100.0 (-3783.8, 100.0)
≥7 Days after Dose 2	1 6.493 (21029)	23 6.337 (20940)	95.8 (73.9, 99.9)

Abbreviation: VE = vaccine efficacy.

a. N = number of subjects in the specified group.

b. n1 = Number of subjects meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.

d. n2 = Number of subjects at risk for the endpoint.

e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

Table.O Primary Efficacy Endpoint – Participants 16 Years of Age and Older – Dose 1 All-Available Efficacy Population (Data Cutoff March 13, 2021)

Efficacy Endpoint Subgroup	BNT162b2 (N[a]=21909) Cases n1[b] Surveillance Time[c] (n2[d])	Placebo (N[a]=21908) Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First COVID-19 occurrence after Dose 1	128 8.155 (21385)	998 7.874 (21315)	87.6 (85.1, 89.8)
After Dose 1 to before Dose 2	43 1.273 (21385)	98 1.266 (21315)	56.4 (37.0, 70.3)
Dose 2 to 7 days after Dose 2	3 0.403 (21049)	30 0.401 (20952)	90.0 (68.0, 98.1)
≥7 Days after Dose 2	82 6.479 (21019)	870 6.207 (20901)	91.0 (88.7, 92.9)

Abbreviation: VE = vaccine efficacy.

a. N = number of subjects in the specified group.

b. n1 = Number of subjects meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.

d. n2 = Number of subjects at risk for the endpoint.

e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

Table.B Study Disposition of Phase 2/3 Randomized Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N^a=22085) n^b (%)	**Placebo (N^a=22080) n^b (%)**	**Total (N^a=44165) n^b (%)**
Randomized	22085 (100.0)	22080 (100.0)	44165 (100.0)
Not vaccinated	55 (0.2)	50 (0.2)	105 (0.2)
Original blinded placebo-controlled follow-up period			
Vaccinated	22030 (99.8)	22030 (99.8)	44060 (99.8)
Dose 1	22030 (99.8)	22030 (99.8)	44060 (99.8)
Dose 2	21675 (98.1)	21650 (98.1)	43325 (98.1)
Discontinued from original blinded placebo-controlled vaccination period[c]	352 (1.6)	528 (2.4)	880 (2.0)
Reason for discontinuation			
Lost to follow-up	151 (0.7)	153 (0.7)	304 (0.7)
Withdrawal by subject	109 (0.5)	181 (0.8)	290 (0.7)
No longer meets eligibility criteria	26 (0.1)	120 (0.5)	146 (0.3)
Adverse event	27 (0.1)	26 (0.1)	53 (0.1)
Physician decision	5 (0.0)	8 (0.0)	13 (0.0)
Pregnancy	6 (0.0)	6 (0.0)	12 (0.0)
Protocol deviation	3 (0.0)	8 (0.0)	11 (0.0)
Death	3 (0.0)	4 (0.0)	7 (0.0)
Medication error without associated adverse event	3 (0.0)	2 (0.0)	5 (0.0)
Withdrawal by parent/guardian	1 (0.0)	0	1 (0.0)
Other	18 (0.1)	20 (0.1)	38 (0.1)
Unblinded before 1-month post–Dose 2 visit	253 (1.1)	240 (1.1)	493 (1.1)

Table.B Study Disposition of Phase 2/3 Randomized Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N^a=22085) n^b (%)	**Placebo (N^a=22080) n^b (%)**	**Total (N^a=44165) n^b (%)**
Completed 1-month post–Dose 2 visit	21382 (96.8)	21293 (96.4)	42675 (96.6)
Withdrawn from the study	343 (1.6)	484 (2.2)	827 (1.9)
Withdrawn after Dose 1 and before Dose 2	176 (0.8)	211 (1.0)	387 (0.9)
Withdrawn after Dose 2 and before 1-month post–Dose 2 visit	100 (0.5)	139 (0.6)	239 (0.5)
Withdrawn after 1-month post–Dose 2 visit	67 (0.3)	134 (0.6)	201 (0.5)
Reason for withdrawal from the study			
Lost to follow-up	174 (0.8)	191 (0.9)	365 (0.8)
Withdrawal by subject	122 (0.6)	226 (1.0)	348 (0.8)
Protocol deviation	11 (0.0)	24 (0.1)	35 (0.1)
Death	16 (0.1)	15 (0.1)	31 (0.1)
Adverse event	9 (0.0)	8 (0.0)	17 (0.0)
Physician decision	3 (0.0)	6 (0.0)	9 (0.0)
No longer meets eligibility criteria	1 (0.0)	4 (0.0)	5 (0.0)
Pregnancy	0	1 (0.0)	1 (0.0)
Medication error without associated adverse event	1 (0.0)	0	1 (0.0)
Withdrawal by parent/guardian	1 (0.0)	0	1 (0.0)
Other	5 (0.0)	9 (0.0)	14 (0.0)
Open-label follow-up period			
Originally randomized to BNT162b2	20404 (92.4)		
Received Dose 2/unplanned dose	87 (0.4)		
Completed 1-month post–Dose 2 visit	210 (1.0)		

Table.B Study Disposition of Phase 2/3 Randomized Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=22085) n[b] (%)	**Placebo (N[a]=22080) n[b] (%)**	**Total (N[a]=44165) n[b] (%)**
Completed 6-month post–Dose 2 visit	6414 (29.0)		
Withdrawn from the study	105 (0.5)		
Withdrawn before 6-month post–Dose 2 visit	103 (0.5)		
Withdrawn after 6-month post–Dose 2 visit	2 (0.0)		
Reason for withdrawal from the study			
Withdrawal by subject	56 (0.3)		
Protocol deviation	35 (0.2)		
Lost to follow-up	4 (0.0)		
Death	3 (0.0)		
Physician decision	2 (0.0)		
Adverse event	1 (0.0)		
No longer meets eligibility criteria	1 (0.0)		
Other	3 (0.0)		
Originally randomized to placebo		20948 (94.9)	
Completed 6-month post–Dose 2 visit		153 (0.7)	
Withdrawn from the study after unblinding and before Dose 3		497 (2.3)	
Received Dose 3 (first dose of BNT162b2 [30 µg])		19612 (88.8)	
Received Dose 4 (second dose of BNT162b2 [30 µg])		15986 (72.4)	
Discontinued from open-label vaccination period[d]		24 (0.1)	
Reason for discontinuation from open-label vaccination period			
Protocol deviation		6 (0.0)	

Table.B Study Disposition of Phase 2/3 Randomized Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=22085) n[b] (%)	Placebo (N[a]=22080) n[b] (%)	Total (N[a]=44165) n[b] (%)
Adverse event		5 (0.0)	
Withdrawal by subject		5 (0.0)	
Pregnancy		4 (0.0)	
Death		2 (0.0)	
Lost to follow-up		2 (0.0)	
Completed 1-month post–Dose 4 visit		7209 (32.6)	
Withdrawn from the study		14 (0.1)	
Withdrawn after Dose 3 and before Dose 4		11 (0.0)	
Withdrawn after Dose 4 and before 1-month post–Dose 4 visit		2 (0.0)	
Withdrawn after 1-month post–Dose 4 visit		1 (0.0)	
Reason for withdrawal from the study			
Withdrawal by subject		7 (0.0)	
Protocol deviation		3 (0.0)	
Death		2 (0.0)	
Adverse event		1 (0.0)	
Lost to follow-up		1 (0.0)	

Note: Human immunodeficiency virus (HIV)-positive subjects are included in this summary but analyzed and reported separately.
Note: Subjects randomized but did not sign informed consent or had a significant quality event due to lack of PI oversight are not included in any analysis population.
Note: Because of a dosing error, Subjects C4591001 1081 10811053, C4591001 1088 10881077, C4591001 1177 11771089 and C4591001 1231 12311057 received an additional dose of BNT162b2 (30 µg) at an unscheduled visit after receiving 1 dose of BNT162b2 (30 µg) and 1 dose of placebo.
a. N = number of randomized subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.

Table.B Study Disposition of Phase 2/3 Randomized Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N^a=22085) n^b (%)	**Placebo (N^a=22080) n^b (%)**	**Total (N^a=44165) n^b (%)**

b. n = Number of subjects with the specified characteristic.
c. Original blinded placebo-controlled vaccination period is defined as the time period from Dose 1 to 1 month post–Dose 2.
d. Open-label vaccination period is defined as the time period from Dose 3 (first dose of BNT162b2 [30 µg]) to 1 month post–Dose 4 (second dose of BNT162b2 [30 µg]).

Table.C Disposition of Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13 2021, Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N^a=22026) n^b (%)	**Placebo (N^a=22021) n^b (%)**	**Total (N^a=44050) n^b (%)**
Randomized			44165
Not vaccinated			105
Vaccinated	22026 (100.0)	22021 (100.0)	44050 (100.0)
Completed 1 dose	22026 (100.0)	22021 (100.0)	44050 (100.0)
Completed 2 doses	21674 (98.4)	21645 (98.3)	43319 (98.3)
Safety population	22026 (100.0)	22021 (100.0)	44050 (100.0)
Reactogenicity subset	5033 (22.9)	5032 (22.9)	10068 (22.9)
HIV-positive	100 (0.5)	100 (0.5)	200 (0.5)
Indeterminate vaccine			3 (0.0)
Participants excluded from safety population			115 (0.3)
Reason for exclusion			
Participant did not receive study vaccine			105 (0.2)
Unreliable data due to lack of PI oversight			10 (0.0)
Completed at least 6 months follow-up after Dose 2 in blinded placebo-controlled follow-up period	1778 (8.1)	1304 (5.9)	3082 (7.0)
Completed at least 6 months follow-up after Dose 2 in blinded and open-label follow-up period	12006 (54.5)		
Completed 1-month post–Dose 2 visit (vaccination period)	21378 (97.1)	21291 (96.7)	42669 (96.9)
Discontinued from vaccination period but continued in the study up to 1-month post–Dose 2 visit	350 (1.6)	520 (2.4)	873 (2.0)

Table.C Disposition of Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13 2021, Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N^a=22026) n^b (%)	**Placebo (N^a=22021) n^b (%)**	**Total (N^a=44050) n^b (%)**
Discontinued after Dose 1 and before Dose 2	233 (1.1)	359 (1.6)	595 (1.4)
Discontinued after Dose 2 and before 1-month post–Dose 2 visit	117 (0.5)	161 (0.7)	278 (0.6)
Reason for discontinuation from vaccination period			
Lost to follow-up	151 (0.7)	149 (0.7)	300 (0.7)
Withdrawal by subject	108 (0.5)	181 (0.8)	289 (0.7)
No longer meets eligibility criteria	25 (0.1)	120 (0.5)	145 (0.3)
Adverse event	27 (0.1)	26 (0.1)	53 (0.1)
Physician decision	5 (0.0)	7 (0.0)	12 (0.0)
Pregnancy	6 (0.0)	6 (0.0)	12 (0.0)
Protocol deviation	3 (0.0)	8 (0.0)	11 (0.0)
Death	3 (0.0)	4 (0.0)	7 (0.0)
Medication error without associated adverse event	2 (0.0)	0	5 (0.0)
Withdrawal by parent/guardian	1 (0.0)	0	1 (0.0)
Other	19 (0.1)	19 (0.1)	38 (0.1)
Withdrawn from study before 1-month post–Dose 2 visit	273 (1.2)	344 (1.6)	617 (1.4)
Withdrawn after Dose 1 and before Dose 2	173 (0.8)	205 (0.9)	378 (0.9)
Withdrawn after Dose 2 and before 1-month post–Dose 2 visit	100 (0.5)	139 (0.6)	239 (0.5)
Reason for withdrawal			
Lost to follow-up	151 (0.7)	153 (0.7)	304 (0.7)
Withdrawal by subject	101 (0.5)	168 (0.8)	269 (0.6)
Adverse event	9 (0.0)	7 (0.0)	16 (0.0)

Table.C Disposition of Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13 2021, Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=22026) n[b] (%)	**Placebo (N[a]=22021) n[b] (%)**	**Total (N[a]=44050) n[b] (%)**
Physician decision	3 (0.0)	5 (0.0)	8 (0.0)
Death	3 (0.0)	4 (0.0)	7 (0.0)
Protocol deviation	0	1 (0.0)	1 (0.0)
Medication error without associated adverse event	1 (0.0)	0	1 (0.0)
No longer meets eligibility criteria	0	1 (0.0)	1 (0.0)
Withdrawal by parent/guardian	1 (0.0)	0	1 (0.0)
Other	4 (0.0)	5 (0.0)	9 (0.0)

Note: Human immunodeficiency virus (HIV)-positive subjects are included in this summary but not included in the analyses of the overall study objectives.
Note: Subjects randomized but did not sign informed consent or had a significant quality event due to lack of PI oversight are not included in any analysis population.
Note: Because of a dosing error, Subjects C4591001 1081 10811053, C4591001 1088 10881077, C4591001 1177 11771089 and C4591001 1231 12311057 received an additional dose of BNT162b2 (30 µg) at an unscheduled visit after receiving 1 dose of BNT162b2 (30 µg) and 1 dose of placebo.
Note: "Indeterminate vaccine" refers to subjects whose vaccine group (as administered) could not be determined. These subjects were included in the number of subjects for "Total" column. These subjects were not included in the safety analysis but their safety data is listed separately.
a. N = number of randomized subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.
b. n = Number of subjects with the specified characteristic.

Table.E Demographics and Other Baseline Characteristics, Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021, Safety Population

Characteristic	Vaccine Group (as Administered) BNT162b2 (30 µg) (N[a]=22026) n[b] (%)	Placebo (N[a]=22021) n[b] (%)	Total (N[a]=44047) n[b] (%)
Sex: Female	10704 (48.6)	10923 (49.6)	21627 (49.1)
Sex: Male	11322 (51.4)	11098 (50.4)	22420 (50.9)
Age at Vaccination: Mean years (SD)	49.7 (15.99)	49.6 (16.05)	49.7 (16.02)
Age at Vaccination: Median (years)	51.0	51.0	51.0
Age at Vaccination: Min, max (years)	(16, 89)	(16, 91)	(16, 91)
Age Group: 16 to <18 years	378 (1.7)	376 (1.7)	754 (1.7)
Age Group: 18 to 55 years	12691 (57.6)	12719 (57.8)	25410 (57.7)
Age Group: >55 years	8957 (40.7)	8926 (40.5)	17883 (40.6)
Age Group: ≥65 years	4552 (20.7)	4545 (20.6)	9097 (20.7)
Race: American Indian or Alaska Native	221 (1.0)	217 (1.0)	438 (1.0)
Race: Asian	952 (4.3)	942 (4.3)	1894 (4.3)
Race: Black or African American	2098 (9.5)	2118 (9.6)	4216 (9.6)
Race: Native Hawaiian or Other Pacific Islander	58 (0.3)	32 (0.1)	90 (0.2)
Race: White	18056 (82.0)	18064 (82.0)	36120 (82.0)
Race: Multiracial	550 (2.5)	533 (2.4)	1083 (2.5)
Race: Not reported	91 (0.4)	115 (0.5)	206 (0.5)
Ethnicity: Hispanic or Latino	5704 (25.9)	5695 (25.9)	11399 (25.9)
Ethnicity: Not Hispanic or Latino	16211 (73.6)	16212 (73.6)	32423 (73.6)

Table.E Demographics and Other Baseline Characteristics, Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021, Safety Population

Characteristic	Vaccine Group (as Administered) BNT162b2 (30 µg) (N[a]=22026) n[b] (%)	Placebo (N[a]=22021) n[b] (%)	Total (N[a]=44047) n[b] (%)
Ethnicity: Not reported	111 (0.5)	114 (0.5)	225 (0.5)
Obesity: Yes[c]	7543 (34.2)	7629 (34.6)	15172 (34.4)
Obesity: No	14483 (65.8)	14392 (65.4)	28875 (65.6)
Comorbidities: Yes[d]	10119 (45.9)	10071 (45.7)	20190 (45.8)
Comorbidities: No	11907 (54.1)	11950 (54.3)	23857 (54.2)
Baseline evidence of prior SARS-CoV-2 infection: Negative[f]	21185 (96.2)	21180 (96.2)	42365 (96.2)
Baseline evidence of prior SARS-CoV-2 infection: Positive[e]	689 (3.1)	716 (3.3)	1405 (3.2)
Baseline evidence of prior SARS-CoV-2 infection: Missing	152 (0.7)	125 (0.6)	277 (0.6)
Country: Argentina	2883 (13.1)	2881 (13.1)	5764 (13.1)
Country: Brazil	1452 (6.6)	1448 (6.6)	2900 (6.6)
Country: Germany	249 (1.1)	250 (1.1)	499 (1.1)
Country: South Africa	401 (1.8)	399 (1.8)	800 (1.8)
Country: Turkey	249 (1.1)	249 (1.1)	498 (1.1)
Country: United States of America	16792 (76.2)	16794 (76.3)	33586 (76.3)

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: HIV-positive subjects are included in this summary but not included in the analyses of the overall study objectives.
a. N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.
b. n = Number of subjects with the specified characteristic.
c. Subjects who had BMI ≥30 kg/m^2.
d. Number of subjects who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or BMI ≥30 kg/m^2.
e. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.

Table.E Demographics and Other Baseline Characteristics, Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021, Safety Population

Characteristic	Vaccine Group (as Administered) BNT162b2 (30 µg) (N[a]=22026) n[b] (%)	Vaccine Group (as Administered) Placebo (N[a]=22021) n[b] (%)	Total (N[a]=44047) n[b] (%)

f. Negative N-binding antibody result and negative NAAT result at Visit 1 and no medical history of COVID-19.

Table.P Safety Overview, Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021, Safety Population

	BNT162b2 (30 µg) n/N (%)	Placebo n/N (%)
Immediate unsolicited AE within 30 minutes after vaccination		
Dose1	105/21926 (0.5)	81/21921 (0.4)
Dose2	71/21571 (0.3)	54/21549 (0.3)
Solicited injection site reaction within 7 days		
Dose1	3877/4907 (79.0)	639/4897 (13.0)
Dose2	3351/4542 (73.8)	483/4517 (10.7)
Solicited systemic AE within 7 days		
Dose1	2963/4907 (60.4)	2308/4897 (47.1)
Dose2	3237/4542 (71.3)	1542/4517 (34.1)
From Dose 1 through 1 month after Dose 2		
Unsolicited non-serious AE	6557/21926 (29.9)	2996/21921 (13.7)
SAE	127/21926 (0.6)	116/21921 (0.5)
Dose 1 to Data Cutoff March 13 2021 /Participant Unblinding (whichever is Earlier)		
SAE	268/21926 (1.2)	268/21921 (1.2)
Withdrawal due to AEs	45/21926 (0.2)	51/21921 (0.2)
Deaths	15/21926 (<0.1)	14/21921 (<0.1)

Note: MedDRA (v23.1) coding dictionary applied.
Note: Immediate AE refers to an AE reported in the 30-minute observation period after vaccination.

Table.Q Characteristics of Solicited Local and Systemic Adverse Reactions, Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021, Safety Population

	Vaccine Group (as Administered)			
Event	**BNT162b2 (30 µg)/Dose 1 n/N**	**BNT162b2 (30 µg)/Dose 2 n/N**	**Placebo/Dose 1 n/N**	**Placebo/Dose 2 n/N**
Redness				
Day of onset: Median (range)	2.0 (1, 7)	2.0 (1, 6)	1.0 (1, 5)	2.0 (1, 6)
Duration: Median (range)	2.0 (1, 20)	2.0 (1, 34)	1.0 (1, 10)	1.0 (1, 7)
Persisted beyond 7 days	8/4907	8/4542	1/4897	0
Swelling				
Day of onset: Median (range)	2.0 (1, 5)	2.0 (1, 5)	1.0 (1, 5)	1.0 (1, 5)
Duration: Median (range)	1.0 (1, 12)	2.0 (1, 34)	1.0 (1, 11)	1.5 (1, 5)
Persisted beyond 7 days	1/4907	6/4542	2/4897	0
Pain at injection site				
Day of onset: Median (range)	1.0 (1, 7)	1.0 (1, 7)	1.0 (1, 7)	1.0 (1, 7)
Duration: Median (range)	2.0 (1, 22)	2.0 (1, 70)	1.0 (1, 19)	1.0 (1, 35)
Persisted beyond 7 days	32/4907	35/4542	10/4897	4/4517
Any solicited local reaction				
Day of onset: Median (range)	2.0 (1, 7)	1.0 (1, 7)	1.0 (1, 7)	1.0 (1, 7)
Duration: Median (range)	2.0 (1, 22)	2.0 (1, 70)	1.0 (1, 19)	1.0 (1, 35)
Persisted beyond 7 days	41/4907	40/4542	11/4897	4/4517
Chills				
Day of onset: Median (range)	2.0 (1, 7)	2.0 (1, 7)	2.0 (1, 7)	2.0 (1, 7)
Duration: Median (range)	1.0 (1, 11)	1.0 (1, 11)	1.0 (1, 31)	1.0 (1, 16)
Persisted beyond 7 days	7/4907	2/4542	6/4897	6/4517

Table.Q Characteristics of Solicited Local and Systemic Adverse Reactions, Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021, Safety Population

	Vaccine Group (as Administered)			
Event	**BNT162b2 (30 µg)/Dose 1 n/N**	**BNT162b2 (30 µg)/Dose 2 n/N**	**Placebo/Dose 1 n/N**	**Placebo/Dose 2 n/N**
Diarrhea				
Day of onset: Median (range)	3.0 (1, 7)	3.0 (1, 7)	3.0 (1, 7)	3.0 (1, 7)
Duration: Median (range)	1.0 (1, 39)	1.0 (1, 31)	1.0 (1, 23)	1.0 (1, 33)
Persisted beyond 7 days	7/4907	6/4542	12/4897	5/4517
Fatigue				
Day of onset: Median (range)	2.0 (1, 7)	2.0 (1, 7)	2.0 (1, 7)	2.0 (1, 7)
Duration: Median (range)	1.0 (1, 34)	1.0 (1, 35)	1.0 (1, 23)	1.0 (1, 69)
Persisted beyond 7 days	84/4907	61/4542	93/4897	45/4517
Fever				
Day of onset: Median (range)	2.0 (1, 7)	2.0 (1, 7)	4.0 (1, 7)	4.0 (1, 7)
Duration: Median (range)	1.0 (1, 7)	1.0 (1, 8)	1.0 (1, 8)	1.0 (1, 6)
Persisted beyond 7 days	0	1/4542	1/4897	0
Joint pain				
Day of onset: Median (range)	2.0 (1, 7)	2.0 (1, 7)	3.0 (1, 7)	3.0 (1, 7)
Duration: Median (range)	1.0 (1, 36)	1.0 (1, 32)	1.0 (1, 17)	1.0 (1, 16)
Persisted beyond 7 days	7/4907	13/4542	8/4897	9/4517
Muscle pain				
Day of onset: Median (range)	2.0 (1, 7)	2.0 (1, 7)	3.0 (1, 7)	2.0 (1, 7)
Duration: Median (range)	1.0 (1, 17)	1.0 (1, 23)	1.0 (1, 31)	1.0 (1, 27)
Persisted beyond 7 days	11/4907	7/4542	15/4897	12/4517
Vomiting				

Table.Q Characteristics of Solicited Local and Systemic Adverse Reactions, Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021, Safety Population

	Vaccine Group (as Administered)			
Event	**BNT162b2 (30 µg)/Dose 1 n/N**	**BNT162b2 (30 µg)/Dose 2 n/N**	**Placebo/Dose 1 n/N**	**Placebo/Dose 2 n/N**
Day of onset: Median (range)	3.0 (1, 7)	2.0 (1, 7)	4.0 (1, 7)	4.0 (1, 7)
Duration: Median (range)	1.0 (1, 6)	1.0 (1, 37)	1.0 (1, 4)	1.0 (1, 6)
Persisted beyond 7 days	0	3/4542	0	0
Headache				
Day of onset: Median (range)	2.0 (1, 7)	2.0 (1, 7)	2.0 (1, 7)	2.0 (1, 7)
Duration: Median (range)	1.0 (1, 25)	1.0 (1, 25)	1.0 (1, 22)	1.0 (1, 35)
Persisted beyond 7 days	50/4907	30/4542	61/4897	32/4517
Any solicited systemic reaction				
Day of onset: Median (range)	2.0 (1, 7)	2.0 (1, 7)	2.0 (1, 7)	2.0 (1, 7)
Duration: Median (range)	1.0 (1, 39)	1.0 (1, 37)	1.0 (1, 31)	1.0 (1, 69)
Persisted beyond 7 days	138/4907	94/4542	139/4897	74/4517

Table.R Frequency of Unsolicited AEs with Occurrence in ≥1% of Phase 2/3 Participants in Any Treatment Group From Dose 1 to 1 Month After Dose 2, 16 Years of Age and Older, Safety Population

	BNT162b2 (30 µg) (N=21926)		Placebo (N=21921)	
SYSTEM ORGAN CLASS and Preferred Term	**Any n (%)**	**Severe n (%)**	**Any n (%)**	**Severe n (%)**
GASTROINTESTINAL DISORDERS				
Diarrhoea	248(1.1)	4 (0.0)	188(0.9)	5 (0.0)
Nausea	274(1.2)	1 (0.0)	87(0.4)	2 (0.0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
Chills	1365(6.2)	18 (0.1)	120(0.5)	0 (0.0)
Fatigue	1463(6.7)	24 (0.1)	379(1.7)	2 (0.0)
Injection site pain	2915(13.3)	19 (0.1)	397(1.8)	0 (0.0)
Pain	628(2.9)	9 (0.0)	61(0.3)	0 (0.0)
Pyrexia	1517(6.9)	38 (0.2)	77(0.4)	1 (0.0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS				
Arthralgia	268(1.2)	4 (0.0)	102(0.5)	6 (0.0)
Myalgia	1239(5.7)	21 (0.1)	168(0.8)	3 (0.0)
NERVOUS SYSTEM DISORDERS				
Headache	1339(6.1)	25 (0.1)	424(1.9)	10 (0.0)

MedDRA v23.1 coding dictionary applied.

Table.R.1 Frequency of Unsolicited AEs with Occurrence in ≥1% of Phase 2/3 Participants in Any Treatment Group From Dose 1 to Data Cutoff March 13 2021 /Unblinding (whichever is Earlier), 16 Years of Age and Older, Safety Population

	BNT162b2 (30 µg) (N=21926)		Placebo (N=21921)	
SYSTEM ORGAN CLASS and Preferred Term	**Any n (%)**	**Severe n (%)**	**Any n (%)**	**Severe n (%)**
	n (%)		**n (%)**	
GASTROINTESTINAL DISORDERS				
Diarrhoea	255(1.2)	4 (0.0)	189(0.9)	5 (0.0)
Nausea	277(1.3)	1 (0.0)	88(0.4)	2 (0.0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
Chills	1368(6.2)	18 (0.1)	121(0.6)	0 (0.0)
Fatigue	1466(6.7)	24 (0.1)	379(1.7)	2 (0.0)
Injection site pain	2917(13.3)	19 (0.1)	399(1.8)	0 (0.0)
Pain	628(2.9)	9 (0.0)	62(0.3)	0 (0.0)
Pyrexia	1520(6.9)	38 (0.2)	78(0.4)	1 (0.0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS				
Arthralgia	281(1.3)	5 (0.0)	122(0.6)	7 (0.0)
Myalgia	1245(5.7)	21 (0.1)	170(0.8)	3 (0.0)
NERVOUS SYSTEM DISORDERS				
Headache	1348(6.1)	25 (0.1)	429(2.0)	12 (0.1)

MedDRA v23.1 coding dictionary applied.

Table.R.2 Frequency of Unsolicited AEs with Occurrence in ≥1% of Phase 2/3 Participants From Unblinding Date to Cutoff Date (13MAR2021)
– Open-Label Follow-up Period– Participants Who Originally Received BNT162b2 – 16 Years of Age and Older, Safety Population

Table not created

No subject meets the reporting criteria

MedDRA v23.1 coding dictionary applied.

Table.R.3 Frequency of Unsolicited AEs with Occurrence in ≥1% of Phase 2/3 Participants From Dose 3 to Cutoff Date (13MAR2021) – Open-Label Follow-up Period – Participants Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – 16 Years of Age and Older, Safety Population

	BNT162b2 (30 µg) (N=19525)	
SYSTEM ORGAN CLASS and Preferred Term	**Any n (%)**	**Severe n (%)**
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS		
Chills	994(5.1)	15 (0.1)
Fatigue	1379(7.1)	23 (0.1)
Injection site pain	2944(15.1)	19 (0.1)
Pain	394(2.0)	5 (0.0)
Pyrexia	906(4.6)	18 (0.1)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS		
Myalgia	925(4.7)	15 (0.1)
NERVOUS SYSTEM DISORDERS		
Headache	1108(5.7)	18 (0.1)

Note: Dose 3 = First dose of BNT162b2 (30 µg).
MedDRA v23.1 coding dictionary applied.

Table.S Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Participants ≥16 Years of Age – Safety Population (Data Cutoff March 13, 2021)

		Vaccine Group (as Administered)	
		BNT162b2 (30 µg) (N[a]=21926)	Placebo (N[a]=21921)
SMQ	Overall SMQ System Organ Class Preferred Term	n[b] (%)	n[b] (%)
	Subjects with any unsolicited adverse events within SMQ	224 (1.02)	217 (0.99)
Angioedema (SMQ)	Any unsolicited adverse events within Angioedema (SMQ)	30 (0.14)	29 (0.13)
	Eye disorders	2 (0.01)	2 (0.01)
	Conjunctival oedema	0	1 (0.00)
	Eye swelling	0	1 (0.00)
	Eyelid oedema	1 (0.00)	0
	Swelling of eyelid	1 (0.00)	0
	Gastrointestinal disorders	6 (0.03)	3 (0.01)
	Gingival swelling	0	1 (0.00)
	Lip oedema	1 (0.00)	0
	Lip swelling	2 (0.01)	1 (0.00)
	Swollen tongue	2 (0.01)	1 (0.00)
	Tongue oedema	1 (0.00)	0
	General disorders and administration site conditions	4 (0.02)	7 (0.03)
	Face oedema	2 (0.01)	0
	Swelling face	2 (0.01)	7 (0.03)
	Respiratory, thoracic and mediastinal disorders	1 (0.00)	3 (0.01)

Table.S Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Participants ≥16 Years of Age – Safety Population (Data Cutoff March 13, 2021)

		Vaccine Group (as Administered)	
		BNT162b2 (30 µg) (N[a]=21926)	Placebo (N[a]=21921)
SMQ	Overall SMQ System Organ Class Preferred Term	n[b] (%)	n[b] (%)
	Pharyngeal swelling	1 (0.00)	3 (0.01)
	Skin and subcutaneous tissue disorders	21 (0.10)	18 (0.08)
	Angioedema	3 (0.01)	2 (0.01)
	Urticaria	18 (0.08)	15 (0.07)
	Urticaria papular	0	1 (0.00)
Arthritis (SMQ)	Any unsolicited adverse events within Arthritis (SMQ)	35 (0.16)	48 (0.22)
	Infections and infestations	1 (0.00)	0
	Arthritis bacterial	1 (0.00)	0
	Metabolism and nutrition disorders	5 (0.02)	3 (0.01)
	Gout	5 (0.02)	3 (0.01)
	Musculoskeletal and connective tissue disorders	29 (0.13)	45 (0.21)
	Arthritis	6 (0.03)	6 (0.03)
	Arthritis reactive	1 (0.00)	0
	Osteoarthritis	15 (0.07)	23 (0.10)
	Patellofemoral pain syndrome	0	1 (0.00)
	Periarthritis	4 (0.02)	1 (0.00)
	Polyarthritis	0	1 (0.00)
	Rheumatoid arthritis	0	2 (0.01)

Table.S Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Participants ≥16 Years of Age – Safety Population (Data Cutoff March 13, 2021)

		Vaccine Group (as Administered)	
		BNT162b2 (30 µg) (N[a]=21926)	Placebo (N[a]=21921)
SMQ	Overall SMQ System Organ Class Preferred Term	n[b] (%)	n[b] (%)
	Spinal osteoarthritis	2 (0.01)	4 (0.02)
	Spondylitis	1 (0.00)	1 (0.00)
	Synovitis	0	2 (0.01)
	Temporomandibular joint syndrome	1 (0.00)	4 (0.02)
Convulsions (SMQ)	Any unsolicited adverse events within Convulsions (SMQ)	2 (0.01)	2 (0.01)
	Nervous system disorders	2 (0.01)	2 (0.01)
	Generalised tonic-clonic seizure	0	1 (0.00)
	Seizure	2 (0.01)	1 (0.00)
Demyelination (SMQ)	Any unsolicited adverse events within Demyelination (SMQ)	2 (0.01)	1 (0.00)
	Nervous system disorders	2 (0.01)	1 (0.00)
	Guillain-Barre syndrome	0	1 (0.00)
	Optic neuritis	2 (0.01)	0
Hypersensitivity (SMQ)	Any unsolicited adverse events within Hypersensitivity (SMQ)	182 (0.83)	161 (0.73)
	Ear and labyrinth disorders	0	1 (0.00)
	Allergic otitis media	0	1 (0.00)
	Eye disorders	5 (0.02)	5 (0.02)
	Conjunctival oedema	0	1 (0.00)
	Conjunctivitis allergic	3 (0.01)	2 (0.01)

Table.S Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Participants ≥16 Years of Age – Safety Population (Data Cutoff March 13, 2021)

SMQ	Overall SMQ System Organ Class Preferred Term	Vaccine Group (as Administered) BNT162b2 (30 µg) (N[a]=21926) n[b] (%)	Vaccine Group (as Administered) Placebo (N[a]=21921) n[b] (%)
	Eye allergy	0	1 (0.00)
	Eye swelling	0	1 (0.00)
	Eyelid oedema	1 (0.00)	0
	Swelling of eyelid	1 (0.00)	0
	Gastrointestinal disorders	6 (0.03)	3 (0.01)
	Gingival swelling	0	1 (0.00)
	Lip oedema	1 (0.00)	0
	Lip swelling	2 (0.01)	1 (0.00)
	Swollen tongue	2 (0.01)	1 (0.00)
	Tongue oedema	1 (0.00)	0
	General disorders and administration site conditions	8 (0.04)	9 (0.04)
	Application site rash	0	1 (0.00)
	Face oedema	2 (0.01)	0
	Injection site dermatitis	1 (0.00)	0
	Injection site rash	2 (0.01)	1 (0.00)
	Injection site urticaria	1 (0.00)	0
	Swelling face	2 (0.01)	7 (0.03)
	Immune system disorders	10 (0.05)	13 (0.06)

Table.S Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Participants ≥16 Years of Age – Safety Population (Data Cutoff March 13, 2021)

		Vaccine Group (as Administered)	
		BNT162b2 (30 µg) (N[a]=21926)	Placebo (N[a]=21921)
SMQ	Overall SMQ System Organ Class Preferred Term	n[b] (%)	n[b] (%)
	Anaphylactic reaction	1 (0.00)	0
	Anaphylactic shock	0	1 (0.00)
	Drug hypersensitivity	7 (0.03)	7 (0.03)
	Hypersensitivity	2 (0.01)	5 (0.02)
	Infections and infestations	5 (0.02)	1 (0.00)
	Dermatitis infected	0	1 (0.00)
	Pustule	3 (0.01)	0
	Rash pustular	2 (0.01)	0
	Injury, poisoning and procedural complications	3 (0.01)	0
	Administration related reaction	2 (0.01)	0
	Stoma site rash	1 (0.00)	0
	Investigations	1 (0.00)	0
	Blood immunoglobulin E increased	1 (0.00)	0
	Respiratory, thoracic and mediastinal disorders	19 (0.09)	21 (0.10)
	Allergic respiratory disease	0	1 (0.00)
	Allergic sinusitis	2 (0.01)	0
	Bronchospasm	3 (0.01)	3 (0.01)
	Pharyngeal swelling	1 (0.00)	3 (0.01)

Table.S Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Participants ≥16 Years of Age – Safety Population (Data Cutoff March 13, 2021)

		Vaccine Group (as Administered)	
		BNT162b2 (30 µg) (N[a]=21926)	Placebo (N[a]=21921)
SMQ	Overall SMQ System Organ Class Preferred Term	n[b] (%)	n[b] (%)
	Rhinitis allergic	13 (0.06)	14 (0.06)
	Skin and subcutaneous tissue disorders	134 (0.61)	119 (0.54)
	Angioedema	3 (0.01)	2 (0.01)
	Dermatitis	5 (0.02)	4 (0.02)
	Dermatitis acneiform	1 (0.00)	0
	Dermatitis allergic	3 (0.01)	5 (0.02)
	Dermatitis atopic	0	1 (0.00)
	Dermatitis bullous	0	1 (0.00)
	Dermatitis contact	14 (0.06)	21 (0.10)
	Dermatitis exfoliative	1 (0.00)	0
	Drug eruption	0	2 (0.01)
	Eczema	7 (0.03)	3 (0.01)
	Erythema nodosum	1 (0.00)	0
	Fixed eruption	1 (0.00)	0
	Hand dermatitis	2 (0.01)	2 (0.01)
	Perioral dermatitis	0	1 (0.00)
	Pruritus allergic	0	2 (0.01)
	Rash	62 (0.28)	52 (0.24)

Table.S Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Participants ≥16 Years of Age – Safety Population (Data Cutoff March 13, 2021)

		Vaccine Group (as Administered)	
		BNT162b2 (30 µg) (N[a]=21926)	Placebo (N[a]=21921)
SMQ	Overall SMQ System Organ Class Preferred Term	n[b] (%)	n[b] (%)
	Rash erythematous	2 (0.01)	3 (0.01)
	Rash maculo-papular	7 (0.03)	4 (0.02)
	Rash papular	1 (0.00)	0
	Rash pruritic	8 (0.04)	6 (0.03)
	Urticaria	18 (0.08)	15 (0.07)
	Urticaria contact	0	1 (0.00)
	Urticaria papular	0	1 (0.00)
Peripheral neuropathy (SMQ)	Any unsolicited adverse events within Peripheral neuropathy (SMQ)	3 (0.01)	6 (0.03)
	Nervous system disorders	3 (0.01)	6 (0.03)
	Guillain-Barre syndrome	0	1 (0.00)
	Neuralgia	1 (0.00)	1 (0.00)
	Neuritis	0	1 (0.00)
	Neuropathy peripheral	1 (0.00)	3 (0.01)
	Peripheral sensory neuropathy	1 (0.00)	0

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event," n = the number of subjects reporting at least 1 occurrence of any event.

Table.T SAEs considered related by Investigator – Phase 2/3 Participants 16 Years of Age and Older, Safety Population (Data Cutoff March 13, 2021)

Product (Vaccine or Placebo)	SAE	Dose/Rel Day[a]	Demographics: Age/Sex/Risk Factors from Charlson Index	Resolution	Related per Investigator
BNT162b2	Shoulder injury related to vaccine administration	2/1	30 F; no relevant medical history	Resolved	Yes
BNT162b2	Paraesthesia	2/47	53 F; no relevant medical history	Resolving	Yes
BNT162b2	Ventricular arrhythmia	2/1	71 F; Any malignancy	Resolved	Yes
BNT162b2	Lymphadenopathy	1/13	48 F; no relevant medical history	Resolved	Yes
BNT162b2	Myocardial infarction	2/71#	41 M; no relevant medical history	Resolved	Yes
Placebo	Psoriatic arthropathy	2/38	25 M; no relevant medical history	Not Resolved	Yes
Placebo crossover to BNT162b2	Anaphylactoid reaction	3/3#	17 F; Chronic pulmonary disease	Resolved	Yes

Note: MedDRA (v23.1) coding dictionary applied.
Note: # = SAE occurring on or after unblinding.
a. Relative day (Rel Day) = date of SAE - date of last vaccination + 1.

Table.U Deaths, Phase 2/3 Participants 16 Years of Age and Older, Safety Population, (Data Cutoff March 13, 2021)

Product - Number of doses received	Subject Number	Dose/Rel Day[a]	Primary Cause of Death	Positive COVID-19 test (Y/N)	Age/Sex/ Race/Ethnicity	Demographics: Risk Factors from Charlson Index
BNT162b2 - 2	C4591001 1007 10071101∞	2/63	Cardiac arrest	N	56/F/White/Not Hispanic or Latino	Chronic pulmonary disease
BNT162b2 - 2	C4591001 1021 10211127∞	2/88	Cardiac failure congestive	Y	54/M/Black or African American/Not Hispanic or Latino	Chronic pulmonary disease, Congestive heart failure
BNT162b2 - 2	C4591001 1036 10361140∞#	2/91	Road traffic accident	N	64/M/White/Not Hispanic or Latino	
BNT162b2 - 2	C4591001 1039 10391010∞	2/71	Arteriosclerosis	N	84/M/White/Not Hispanic or Latino	Cerebrovascular disease
BNT162b2 - 2	C4591001 1084 10841266∞	2/121	Sepsis	N	77/M/White/Hispanic or Latino	Congestive heart failure, Diabetes without chronic complication, Peripheral vascular disease
BNT162b2 - 2	C4591001 1088 10881139∞#	2/143	Metastases to lung	N	82/M/White/Not Hispanic or Latino	Chronic pulmonary disease
BNT162b2 - 2	C4591001 1089 10891073∞	2/70	Chronic obstructive pulmonary disease	N	63/F/White/Not Hispanic or Latino	Any malignancy, Chronic pulmonary disease, Diabetes with chronic complication, Diabetes without chronic complication, Myocardial infarction
BNT162b2 - 2	C4591001 1097 10971023∞	2/98	Septic shock	N	86/F/White/Not Hispanic or Latino	
BNT162b2 - 2	C4591001 1114 11141050∞	2/42	Unevaluable event	N	63/F/White/Not Hispanic or Latino	Rheumatic disease
BNT162b2	C4591001 1120	2/73	Cardiac arrest	N	58/F/White/Not Hispanic or	Diabetes without chronic complication

Table.U Deaths, Phase 2/3 Participants 16 Years of Age and Older, Safety Population, (Data Cutoff March 13, 2021)

Product - Number of doses received	Subject Number	Dose/Rel Day[a]	Primary Cause of Death	Positive COVID-19 test (Y/N)	Age/Sex/ Race/Ethnicity	Demographics: Risk Factors from Charlson Index
- 2	11201050∞				Latino	
BNT162b2 - 2	C4591001 1120 11201266∞	2/113	Lung cancer metastatic	N	51/M/White/Not Hispanic or Latino	
BNT162b2 - 2	C4591001 1127 11271112∞	2/86	Cardio-respiratory arrest	N	53/M/Multiple/Not Hispanic or Latino	Chronic pulmonary disease, Myocardial infarction
BNT162b2 - 2	C4591001 1129 11291166∞#	2/129	Myocardial infarction	N	78/F/White/Not Hispanic or Latino	
BNT162b2 - 2	C4591001 1136 11361102∞	2/31	Cardiac arrest	N	76/M/White/Not Hispanic or Latino	
BNT162b2 - 2	C4591001 1140 11401117∞	2/117	Cardiac arrest	N	58/M/White/Not Hispanic or Latino	
BNT162b2 - 1	C4591001 1152 11521497∞	1/36	Shigella sepsis	N	72/M/White/Hispanic or Latino	Diabetes without chronic complication
BNT162b2 - 2	C4591001 1156 11561160∞†	2/74	Road traffic accident	N	62/F/Black or African American/Not Hispanic or Latino	AIDS/HIV, Chronic pulmonary disease
BNT162b2 - 1	C4591001 1162 11621327∞	1/4	Arteriosclerosis	Y	60/M/White/Not Hispanic or Latino	
BNT162b2 - 2	C4591001 1252 12521010∞	2/110	COVID-19 pneumonia	N	80/M/White/Not Hispanic or Latino	
Placebo - 2	C4591001 1019 10191146	2/87	Metastases to liver	N	67/M/White/Not Hispanic or Latino	Chronic pulmonary disease
Placebo - 2	C4591001 1027 10271191#	2/135	Respiratory failure	Y	68/F/Black or African American/Not Hispanic or	Any malignancy, Chronic pulmonary disease

Table.U Deaths, Phase 2/3 Participants 16 Years of Age and Older, Safety Population, (Data Cutoff March 13, 2021)

Product - Number of doses received	Subject Number	Dose/Rel Day[a]	Primary Cause of Death	Positive COVID-19 test (Y/N)	Age/Sex/ Race/Ethnicity	Demographics: Risk Factors from Charlson Index
					Latino	
Placebo - 1	C4591001 1066 10661350	1/16	Myocardial infarction	N	58/M/White/Not Hispanic or Latino	Congestive heart failure, Myocardial infarction
Placebo - 2	C4591001 1081 10811194	2/37	Myocardial infarction	N	51/F/White/Not Hispanic or Latino	Chronic pulmonary disease
Placebo - 2	C4591001 1084 10841470	2/83	Multiple organ dysfunction syndrome	N	65/M/White/Hispanic or Latino	Chronic pulmonary disease
Placebo - 2	C4591001 1088 10881126	2/70	Cardiac arrest	Y	65/M/White/Not Hispanic or Latino	
Placebo - 2	C4591001 1089 10891088	2/125	Dementia	N	82/F/White/Not Hispanic or Latino	Dementia
Placebo - 2	C4591001 1094 10941112	2/81	Acute respiratory failure	N	57/F/White/Hispanic or Latino	Chronic pulmonary disease, Diabetes without chronic complication
Placebo - 2	C4591001 1128 11281009	2/102	Pneumonia	N	66/M/White/Not Hispanic or Latino	Diabetes without chronic complication, Myocardial infarction
Placebo - 2	C4591001 1131 11311204*#	3/26	Cardio-respiratory arrest	N	84/M/White/Not Hispanic or Latino	Cerebrovascular disease, Peripheral vascular disease
Placebo - 2	C4591001 1135 11351033*#	3/5		N	67/M/White/Not Hispanic or Latino	
Placebo - 1	C4591001 1152 11521085	1/8	Death	N	42/F/White/Not Hispanic or Latino	Any malignancy
Placebo - 2	C4591001 1156 11561124	2/32	Overdose	N	53/M/White/Not Hispanic or Latino	

Table.U Deaths, Phase 2/3 Participants 16 Years of Age and Older, Safety Population, (Data Cutoff March 13, 2021)

Product - Number of doses received	Subject Number	Dose/Rel Day[a]	Primary Cause of Death	Positive COVID-19 test (Y/N)	Age/Sex/ Race/Ethnicity	Demographics: Risk Factors from Charlson Index
Placebo - 2	C4591001 1168 11681083	2/65	Aortic rupture	N	64/M/White/Not Hispanic or Latino	
Placebo - 2	C4591001 1207 12071055#	2/76	Pneumonia bacterial	N	65/M/White/Not Hispanic or Latino	Diabetes without chronic complication, Mild liver disease
Placebo - 2	C4591001 1229 12291083†	2/76	COVID-19 pneumonia	N	55/F/Black or African American/Not Hispanic or Latino	AIDS/HIV, Chronic pulmonary disease
Placebo - 2	C4591001 1231 12313972	2/16	Haemorrhagic stroke	N	61/F/White/Hispanic or Latino	
Placebo - 2	C4591001 1231 12314987	2/82	Cardio-respiratory arrest	N	47/M/White/Hispanic or Latino	
Placebo - 2	C4591001 1231 12315324	2/136	Multiple organ dysfunction syndrome	Y	58/F/White/Hispanic or Latino	

Note: MedDRA (v23.1) coding dictionary applied.
Note: † = Human immunodeficiency virus (HIV)-positive subject, # = death occurring on or after unblinding, * = subjects who originally received placebo and then received BNT162b2 after unblinding, ∞ = subjects who originally received BNT162b2.
a. Relative day (Rel Day)= date of death - date of last vaccination + 1.

Table V. Clinical Trials Submitted in Support of Safety and Effectiveness of the Pfizer-BioNTech COVID-19 Vaccine

Study Number/ Country	Study Description	Number of BNT162b2 (30 µg) subjects (N)	Number of placebo subjects (N)	Study Status
C4591001 Phase 1	A Phase 1/2/3 Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Individuals	24	6	Ongoing
C4591001 Phase 2/3		22085	22080	Ongoing
Argentina		2887	2889	
Brazil		1452	1448	
Germany		250	250	
South Africa		401	399	
Turkey		251	249	
USA		16844	16845	
BNT162-01 Phase 1/2 Germany (BNT162b2 30 µg)	A multi-site, Phase I/II, 2-part, dose escalation trial investigating the safety and immunogenicity of four prophylactic SARS-CoV-2 RNA vaccines against COVID-19 using different dosing regimens in healthy adults	24	0	Ongoing

N= total number of randomized participants 16 years of age and older, as of March 13, 2021.

Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup
– Blinded Placebo-Controlled Follow-up Period
– Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2
– Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=21047)		Placebo (N[a]=21210)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
First COVID-19 occurrence from 7 days after Dose 2						
Overall	81	6.340 (20533)	854	6.110 (20595)	90.9	(88.5, 92.8)
Age group (years)						
16 to 55	56	3.766 (12088)	584	3.619 (12142)	90.8	(87.9, 93.1)
>55	25	2.573 (8445)	270	2.492 (8453)	91.0	(86.5, 94.3)
≥65	7	1.267 (4315)	128	1.232 (4326)	94.7	(88.7, 97.9)
16 to 17	0	0.065 (365)	11	0.061 (355)	100.0	(62.4, 100.0)
16 to 25	10	0.511 (1734)	84	0.498 (1740)	88.4	(77.6, 94.6)
16 to 64	74	5.073 (16218)	726	4.879 (16269)	90.2	(87.5, 92.4)
18 to 64	74	5.008 (15853)	715	4.817 (15914)	90.0	(87.3, 92.3)
55 to 64	21	1.442 (4563)	158	1.386 (4559)	87.2	(79.8, 92.3)
65 to 74	6	1.021 (3450)	102	0.992 (3468)	94.3	(87.1, 98.0)
≥75	1	0.246 (865)	26	0.240 (858)	96.2	(77.2, 99.9)
75 to 85	1	0.244 (860)	25	0.238 (852)	96.1	(76.2, 99.9)
>85	0	0.001 (5)	1	0.001 (6)	100.0	(-4055.9, 100.0)
Sex						
Male	44	3.289 (10548)	399	3.097 (10354)	89.6	(85.8, 92.6)

Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup
– Blinded Placebo-Controlled Follow-up Period
– Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2
– Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=21047)		Placebo (N[a]=21210)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
Female	37	3.051 (9985)	455	3.013 (10241)	92.0	(88.8, 94.4)
Race						
White	69	5.234 (16846)	749	5.054 (16952)	91.1	(88.6, 93.2)
Black or African American	4	0.602 (1909)	49	0.591 (1928)	92.0	(78.1, 97.9)
American Indian or Alaska Native	0	0.043 (196)	3	0.038 (180)	100.0	(-116.0, 100.0)
Asian	3	0.258 (907)	24	0.247 (896)	88.0	(60.6, 97.7)
Native Hawaiian or other Pacific Islander	0	0.016 (54)	1	0.008 (31)	100.0	(-1947.9, 100.0)
Multiracial	5	0.160 (538)	22	0.140 (503)	80.1	(46.1, 94.1)
Not reported	0	0.027 (83)	6	0.031 (105)	100.0	(1.4, 100.0)
All others[f]	8	0.504 (1778)	56	0.465 (1715)	86.8	(72.2, 94.6)
Ethnicity						
Hispanic/Latino	32	1.841 (5280)	240	1.777 (5266)	87.1	(81.3, 91.4)
Non-Hispanic/non-Latino	48	4.466 (15149)	614	4.300 (15220)	92.5	(89.9, 94.5)
Not reported	1	0.032 (104)	0	0.034 (109)	-∞	(NA, NA)
Country						
Argentina	16	1.033 (2655)	110	1.017 (2670)	85.7	(75.7, 92.1)
Brazil	14	0.441 (1419)	82	0.408 (1401)	84.2	(71.9, 91.7)

Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup
– Blinded Placebo-Controlled Follow-up Period
– Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2
– Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=21047)		Placebo (N[a]=21210)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
Germany	0	0.047 (237)	1	0.048 (243)	100.0	(-3868.6, 100.0)
South Africa	0	0.099 (358)	10	0.096 (358)	100.0	(56.6, 100.0)
Turkey	0	0.029 (238)	6	0.026 (232)	100.0	(22.2, 100.0)
USA	51	4.692 (15626)	645	4.515 (15691)	92.4	(89.9, 94.4)
Prior SARS-CoV-2 Status						
Positive at baseline[g]	3	0.183 (593)	6	0.195 (643)	46.7	(-149.5, 91.4)
Positive N-binding only	2	0.143 (466)	5	0.147 (488)	58.8	(-151.9, 96.1)
Positive NAAT only	0	0.013 (43)	1	0.014 (48)	100.0	(-3922.5, 100.0)
Positive NAAT and N-binding	1	0.027 (84)	0	0.034 (106)	-∞	(NA, NA)
Negative at baseline but positive prior to 7 days after Dose 2[h]	0	0.011 (40)	1	0.013 (50)	100.0	(-4759.2, 100.0)
Negative prior to 7 days after Dose 2[i]	77	6.092 (19711)	833	5.856 (19740)	91.1	(88.8, 93.1)
Unknown	1	0.054 (189)	14	0.046 (162)	93.9	(59.9, 99.9)

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

a. N = number of subjects in the specified group.
b. n1 = Number of subjects meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup
– Blinded Placebo-Controlled Follow-up Period
– Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2
– Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=21047)		Placebo (N[a]=21210)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])

f. All others = American Indian or Alaska native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.
g. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
h. Negative N-binding antibody result and negative NAAT result at Visit 1, positive NAAT result at Visit 2 or at unscheduled visit, if any, prior to 7 days after Dose 2.
i. Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1 and Visit 2, and negative NAAT result at unscheduled visit, if any, prior to 7 days after Dose 2.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adc19ef Table Generation: 06AUG2021 (08:53)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA_Efficacy_v2/adc19ef_ve_cov_7pd2_sg_eval

Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup
– Blinded Placebo-Controlled Follow-up Period
– Subjects ≥16 Years of Age and Without Evidence of Infection Prior to 7 Days After Dose 2
– Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=19993)		Placebo (N[a]=20118)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
First COVID-19 occurrence from 7 days after Dose 2						
Overall	77	6.092 (19711)	833	5.857 (19741)	91.1	(88.8, 93.1)
Age group (years)						
16 to 55	52	3.593 (11517)	568	3.439 (11533)	91.2	(88.3, 93.5)
>55	25	2.499 (8194)	265	2.417 (8208)	90.9	(86.2, 94.2)
≥65	7	1.233 (4192)	124	1.202 (4226)	94.5	(88.3, 97.8)
16 to 17	0	0.061 (342)	10	0.057 (331)	100.0	(58.2, 100.0)
16 to 25	8	0.482 (1629)	80	0.466 (1622)	90.3	(80.0, 96.0)
16 to 64	70	4.859 (15519)	709	4.654 (15515)	90.5	(87.9, 92.7)
18 to 64	70	4.798 (15177)	699	4.597 (15184)	90.4	(87.7, 92.6)
55 to 64	21	1.399 (4426)	156	1.334 (4388)	87.2	(79.7, 92.3)
65 to 74	6	0.994 (3350)	98	0.966 (3379)	94.1	(86.6, 97.9)
≥75	1	0.239 (842)	26	0.237 (847)	96.2	(76.9, 99.9)
75 to 85	1	0.238 (837)	25	0.235 (841)	96.0	(75.9, 99.9)
>85	0	0.001 (5)	1	0.001 (6)	100.0	(-4055.9, 100.0)
Sex						
Male	42	3.167 (10138)	389	2.972 (9934)	89.9	(86.0, 92.8)

Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup
– Blinded Placebo-Controlled Follow-up Period
– Subjects ≥16 Years of Age and Without Evidence of Infection Prior to 7 Days After Dose 2
– Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=19993)		Placebo (N[a]=20118)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
Female	35	2.926 (9573)	444	2.885 (9807)	92.2	(89.0, 94.7)
Race						
White	67	5.076 (16321)	730	4.902 (16432)	91.1	(88.6, 93.2)
Black or African American	4	0.537 (1697)	48	0.519 (1690)	92.0	(78.0, 97.9)
American Indian or Alaska Native	0	0.040 (183)	3	0.037 (175)	100.0	(-120.7, 100.0)
Asian	3	0.251 (883)	23	0.239 (869)	87.6	(58.9, 97.6)
Native Hawaiian or other Pacific Islander	0	0.015 (51)	1	0.008 (30)	100.0	(-2017.6, 100.0)
Multiracial	3	0.148 (497)	22	0.124 (447)	88.6	(62.1, 97.8)
Not reported	0	0.025 (79)	6	0.029 (98)	100.0	(3.8, 100.0)
All others[f]	6	0.480 (1693)	55	0.436 (1619)	90.1	(77.0, 96.5)
Ethnicity						
Hispanic/Latino	29	1.768 (5052)	236	1.696 (5015)	88.2	(82.6, 92.3)
Non-Hispanic/non-Latino	47	4.293 (14559)	597	4.128 (14620)	92.4	(89.8, 94.5)
Not reported	1	0.031 (100)	0	0.033 (106)	-∞	(NA, NA)
Country						
Argentina	15	1.012 (2600)	108	0.986 (2586)	86.5	(76.7, 92.7)
Brazil	12	0.406 (1311)	80	0.374 (1293)	86.2	(74.5, 93.1)

Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup
– Blinded Placebo-Controlled Follow-up Period
– Subjects ≥16 Years of Age and Without Evidence of Infection Prior to 7 Days After Dose 2
– Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=19993)		Placebo (N[a]=20118)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
Germany	0	0.047 (236)	1	0.048 (242)	100.0	(-3874.2, 100.0)
South Africa	0	0.080 (291)	9	0.074 (276)	100.0	(53.5, 100.0)
Turkey	0	0.027 (228)	5	0.025 (222)	100.0	(-0.1, 100.0)
USA	50	4.519 (15045)	630	4.350 (15122)	92.4	(89.8, 94.4)

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test;
SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.
Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.
a. N = number of subjects in the specified group.
b. n1 = Number of subjects meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
f. All others = American Indian or Alaska native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adc19ef Table Generation: 06AUG2021 (08:52)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA_Efficacy_v2/adc19ef_ve_cov_7pd2_wo_sg_eval

Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC-Definition From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=21047)		Placebo (N[a]=21210)			
Efficacy Endpoint	**n1[b]**	**Surveillance Time[c] (n2[d])**	**n1[b]**	**Surveillance Time[c] (n2[d])**	**VE (%)**	**(95% CI[e])**
First severe COVID-19 occurrence based on CDC-definition from 7 days after Dose 2	0	6.345 (20513)	31	6.225 (20593)	100.0	(87.6, 100.0)

Abbreviation: VE = vaccine efficacy.

a. N = number of subjects in the specified group.

b. n1 = Number of subjects meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of subjects at risk for the endpoint.

e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:19) Source Data: adc19ef Table Generation: 06AUG2021 (09:21)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA_Efficacy_v2/adc19ef_ve_sev_7pd2_cdc_eval

Vaccine Efficacy – First Severe COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) (N[a]=21047)		Placebo (N[a]=21210)				
Efficacy Endpoint	**n1[b]**	**Surveillance Time[c] (n2[d])**	**n1[b]**	**Surveillance Time[c] (n2[d])**	**VE (%)**	**(95% CI[e])**	**Pr (VE >30% | data)[f]**
First severe COVID-19 occurrence from 7 days after Dose 2	1	6.353 (20540)	21	6.237 (20629)	95.3	(70.9, 99.9)	>0.9999

Abbreviation: VE = vaccine efficacy.

a. N = number of subjects in the specified group.

b. n1 = Number of subjects meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of subjects at risk for the endpoint.

e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:19) Source Data: adc19ef Table Generation: 06AUG2021 (09:07)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA_Efficacy_v2/adc19ef_ve_sev_cov_7pd2_eval

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older (1)

DOSAGE AND ADMINISTRATION

- For intramuscular injection ~~administration~~ only (2 [2])
- COMIRNATY is administered intramuscularly as a series of 2 doses (0 3 mL each) 3 weeks apart (2 3)

DOSAGE FORMS AND STRENGTHS

Suspension for injection After preparation, a single dose is 0 3 mL (3)

CONTRAINDICATIONS

Known history of a severe allergic reaction (e g , anaphylaxis) to any component of COMIRNATY (4)

WARNINGS AND PRECAUTIONS

- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose (5 2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY Procedures should be in place to avoid injury from fainting (5 4)

ADVERSE REACTIONS

- In clinical studies of participants 16 through 55 years of age ~~and older~~, the most commonly reported adverse reactions (~~≥~~>10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, fever, and injection site swelling (6 1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (>10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, injection site swelling, fever, and injection site redness (6 1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed

Commented [A2]: Pfizer-BioNTech accepts FDA revision.

Commented [A3]: FDA comment
Pfizer,
Please see section 6 for a statement to include in highlights.

Pfizer-BioNTech response
The Sponsor accepts and has included the listing of adverse reactions occurring at >10% in participants 16-55 years of age and 56 years of age and older.

Commented [A1]: Pfizer-BioNTech proposes to revise for consistency with FPI.

Commented [A4]: FDA comment
Pfizer,
Please make table of contents consistent with Full PI.

Pfizer-BioNTech response
The Sponsor accepts and has revised the table of contents consistent with the Full Prescribing Information.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

Commented [A5]: Pfizer-BioNTech accepts FDA revisions to this section.

2.1 Preparation for Administration

Prior to Dilution

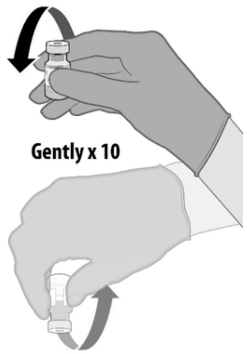
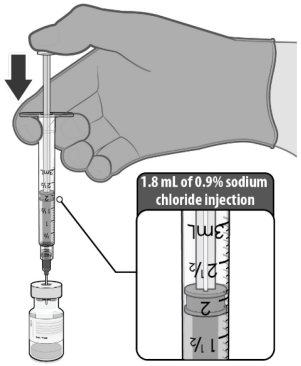
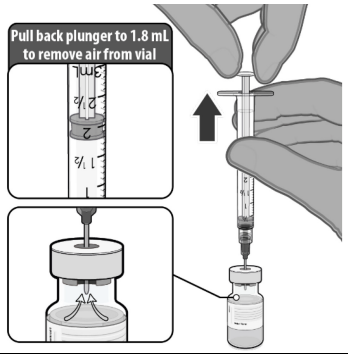
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2°C to 8°C (35°F to 46°F)] or at room temperature [up to 25°C (77°F)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

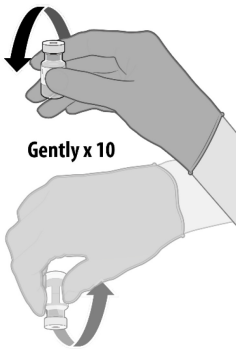
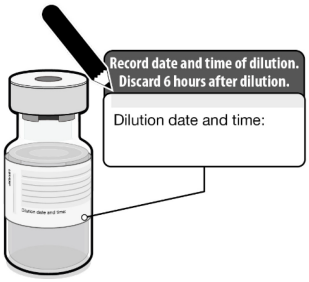
Dilution

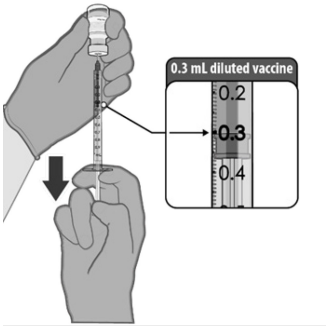
- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or an alternate brand of sterile 0.9% Sodium Chloride Injection, USP as the diluent.
- Provided diluent vials are single-use only and should be discarded after 1.8 mL is withdrawn. Do not use provided diluent vials to dilute multiple vials of COMIRNATY.
- After dilution, 1 vial contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

Commented [A6]: Pfizer BioNTech proposes to add this information to address the query received separately from CBER related to the number of uses of provided diluent vials.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2°C to 8°C (35°F to 46°F)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25°C (77°F)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.

	• Before dilution invert vaccine vial gently 10 times. • Do not shake. • Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Cleanse the vaccine vial stopper with a single-use antiseptic swab. • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.
	• Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.

	• Gently invert the vial containing the COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

2.2 Administration Information

For intramuscular injection only.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Visually inspect each dose in the dosing syringe prior to administration. The vaccine will be an off-white suspension. During the visual inspection,

- verify the final dosing volume of 0.3 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Commented [A7]: Pfizer-BioNTech accepts FDA revisions to this subsection.

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk has been highest in adolescent and young adult males under 40 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of symptoms. Information is not yet available about potential long-term sequelae. The CDC has published

considerations for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies with a data cut-off of March 13, 2021, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies with a data cut-off of March 13, 2021, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

In clinical studies with a data cut-off of March 13, 2021, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies with a data cut-off of March 13, 2021, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine

Commented [A8]: Pfizer-BioNTech accepts FDA deletion of this information "In clinical studies with a data cut-off of March 13, 2021, adverse reactions in participants 16 years of age and older included pain at the injection site (84.3%), fatigue (64.7%), headache (57.1%), muscle pain (40.2%), chills (34.7%), joint pain (25.0%), fever (15.2%), injection site swelling (11.1%), injection site redness (9.9%), nausea (1.2%), malaise (0.6%), lymphadenopathy (0.4%), asthenia (0.3%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%)
Severe allergic reactions, including anaphylaxis, have been reported following administration of COMIRNATY outside of clinical trials " and has provided updated proposal below

Commented [A9]: FDA comment
Pfizer,
Please complete the sentences and include in the Highlights.

Pfizer-BioNTech response
The Sponsor accepts and has updated the text as requested in section 6 of the Full Prescribing Information and in the Highlights page. The Sponsor has revised the FDA proposed text to list the adverse reactions by "≥" 10%. The Sponsor has also included the adverse reactions reported <10% by participants 16 to 55 years of age and 56 years of age and older.

candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 ~~TRADENAME~~COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection~~disease~~ was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were ≥65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 ~~to~~ through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Commented [A10]: **Pfizer BioNTech** agrees with the minor FDA revisions to this section with one modification to update TRADENAME to Comirnaty.

Commented [A11]: **Pfizer BioNTech** proposes to modify for consistency throughout the label.

Commented [A12]: **Pfizer BioNTech** accepts FDA addition of this statement.

Commented [A13]: **Pfizer BioNTech** agrees with FDA deletion of the following statement "At the time of the analysis of Study 2 for the Emergency Use Authorization (EUA) with a data cut-off of November 14, 2020, there were 37,586 participants (18,801 COMIRNATY and 18,785 placebo) 16 years of age or older followed for a median of 2 months after the second dose of COMIRNATY." as well as the minor modifications to this paragraph.

Commented [A14]: **Pfizer BioNTech** agrees with FDA deletion of the following statement "The safety evaluation in Study 2 is ongoing The safety population includes participants enrolled by October 9, 2020, and includes safety data accrued through March 13, 2021 "

Commented [A15]: **FDA comment**
Pfizer: Please also include the age demographics for percentages of participants who are 16 through 64 years and ≥65 years of age.

Pfizer-BioNTech response
Pfizer has updated the label as per FDA request.
Source: Table E Demographics and Other Baseline Characteristics, Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021, Safety Population in label bundle, age group >=65 years row.

Commented [A16]: **Pfizer BioNTech** proposes to modify for consistency throughout the label.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm

d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

Commented [A17]: Pfizer: Please add footnotes to Tables 1-4, that participants with chronic, stable HIV disease were excluded.

Pfizer-BioNTech response
The Sponsor accepts and has added the footnote to Tables 1-4.

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours

f Severity was not collected for use of antipyretic or pain medication

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in participants 56 years of age and older

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, the information was included in the column header

b n = Number of participants with the specified reaction

c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm

d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[c]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header

b n = Number of participants with the specified reaction

	COMIRNATY Dose 1 N^a=2008 n^b (%)	Placebo Dose 1 N^a=1989 n^b (%)	COMIRNATY Dose 2 N^a=1860 n^b (%)	Placebo Dose 2 N^a=1833 n^b (%)

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea

f Severity was not collected for use of antipyretic or pain medication

~~Table 5 and Table 6 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 16 years of age and older with confirmed stable HIV infection.~~

In participants with chronic, stable HIV infection after receiving Dose 2, local reactions and systemic events were similar to those observed for all participants 16 years of age and older by severity, onset day, and median duration. The frequency of pain at the injection site was similar after Dose 1 compared with Dose 2 of COMIRNATY (63.0% versus 53.3%). The frequency of redness and swelling was similar after Dose 1 compared with Dose 2 of COMIRNATY (redness: 3.7% versus 6.7%; swelling: 5.6% versus 8.3%, respectively). There was 1 (1.7%) severe reaction (pain at the injection site) reported after Dose 2 of COMIRNATY and no Grade 4 local reactions were reported. Fever, headache, chills, and joint pain increased in frequency from Dose 1 to Dose 2 while fatigue, vomiting, diarrhea, and muscle pain were similar after each dose of COMIRNATY. There were no severe systemic events after Dose 1 of COMIRNATY but after Dose 2, there was 1 (1.7%) severe fever (>38.9°C to 40.0°C), 3 (5.0%) participants with severe fatigue, 2 (3.3%) participants with severe headache, 1 (1.7%) participant with severe chills, and 1 (1.7%) participant with severe diarrhea. There were no Grade 4 systemic events reported after either dose.

Commented [A18]: Pfizer: Please describe local and systemic reactogenicity for the stable, chronic HIV+ participants in text to indicate that the frequencies of local and solicited reactions were generally the same or less frequent as compared to the overall safety population described in Tables 1-4.

Pfizer-BioNTech response
The Sponsor accepts deletion of the 2 HIV tables and has proposed summary text.

~~**Table 5: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – HIV-Positive Participants 16 Years of Age and Older – Reactogenicity Subset of the Safety Population[a]**~~

	COMIRNATY Dose 1 N^a=54 n^b (%)	Placebo Dose 1 N^a=56 n^b (%)	COMIRNATY Dose 2 N^a=60 n^b (%)	Placebo Dose 2 N^a=62 n^b (%)
Redness[c]				
Any (>2.0 cm)	2 (3.7)	3 (5.4)	4 (6.7)	1 (1.6)
Mild	2 (3.7)	1 (1.8)	3 (5.0)	1 (1.6)
Moderate	0	0	1 (1.7)	0
Severe	0	2 (3.6)	0	0
Swelling[c]				
Any (>2.0 cm)	3 (5.6)	1 (1.8)	5 (8.3)	0
Mild	2 (3.7)	0	2 (3.3)	0
Moderate	1 (1.9)	0	3 (5.0)	0
Severe	0	1 (1.8)	0	0

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Pain at the injection site[d]				
Any	34 (63.0)	9 (16.1)	32 (53.3)	5 (8.1)
Mild	26 (48.1)	8 (14.3)	22 (36.7)	5 (8.1)
Moderate	8 (14.8)	1 (1.8)	9 (15.0)	0
Severe	0	0	1 (1.7)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in HIV-positive participants 16 years of age and older
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention
a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header
b n = Number of participants with the specified reaction
c Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm
d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 6: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – HIV-Positive Participants 16 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Fever				
≥38.0°C	1 (1.9)	4 (7.1)	9 (15.0)	5 (8.1)
≥38.0°C to 38.4°C	1 (1.9)	2 (3.6)	4 (6.7)	5 (8.1)
>38.4°C to 38.9°C	0	0	4 (6.7)	0
>38.9°C to 40.0°C	0	2 (3.6)	1 (1.7)	0
>40.0°C	0	0	0	0
Fatigue[e]				
Any	22 (40.7)	15 (26.8)	24 (40.0)	12 (19.4)
Mild	15 (27.8)	9 (16.1)	12 (20.0)	5 (8.1)
Moderate	7 (13.0)	5 (8.9)	9 (15.0)	7 (11.3)
Severe	0	1 (1.8)	3 (5.0)	0
Headache[e]				
Any	11 (20.4)	18 (32.1)	18 (30.0)	12 (19.4)
Mild	7 (13.0)	10 (17.9)	8 (13.3)	8 (12.9)
Moderate	4 (7.4)	7 (12.5)	8 (13.3)	4 (6.5)
Severe	0	1 (1.8)	2 (3.3)	0
Chills[e]				
Any	6 (11.1)	5 (8.9)	14 (23.3)	4 (6.5)
Mild	5 (9.3)	4 (7.1)	5 (8.3)	3 (4.8)
Moderate	1 (1.9)	1 (1.8)	8 (13.3)	1 (1.6)
Severe	0	0	1 (1.7)	0

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Vomiting[d]				
Any	1 (1.9)	3 (5.4)	2 (3.3)	2 (3.2)
Mild	1 (1.9)	1 (1.8)	1 (1.7)	1 (1.6)
Moderate	0	0	1 (1.7)	1 (1.6)
Severe	0	2 (3.6)	0	0
Diarrhea[e]				
Any	5 (9.3)	8 (14.3)	4 (6.7)	9 (14.5)
Mild	5 (9.3)	6 (10.7)	1 (1.7)	6 (9.7)
Moderate	0	1 (1.8)	2 (3.3)	3 (4.8)
Severe	0	1 (1.8)	1 (1.7)	0
New or worsened muscle pain[c]				
Any	9 (16.7)	10 (17.9)	10 (16.7)	5 (8.1)
Mild	7 (13.0)	7 (12.5)	5 (8.3)	1 (1.6)
Moderate	2 (3.7)	3 (5.4)	5 (8.3)	4 (6.5)
Severe	0	0	0	0
New or worsened joint pain[c]				
Any	5 (9.3)	7 (12.5)	10 (16.7)	5 (8.1)
Mild	5 (9.3)	4 (7.1)	4 (6.7)	1 (1.6)
Moderate	0	3 (5.4)	6 (10.0)	4 (6.5)
Severe	0	0	0	0
Use of antipyretic or pain medication[f]	7 (13.0)	8 (14.3)	16 (26.7)	7 (11.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in HIV-positive participants 16 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each event or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b n = Number of participants with the specified reaction.

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

Upon issuance of the EUA for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Unblinded participants originally randomized to COMIRNATY and placebo recipients administered COMIRNATY continued to be followed for unsolicited adverse events including serious adverse events, throughout the study [from Dose 1 of COMIRNATY through 1 month (all unsolicited adverse events) and 6 months (serious adverse events) after the last vaccination]. Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began in a phased manner for

Commented [A19]: FDA comment
Pfizer: Please add a subsection to provide a description of the safety evaluation for the original BNT162b2 recipients who have at least 6 months of follow up post dose 2, through blinded and unblinded time periods.

Pfizer-BioNTech response
The Sponsor accepts and has provided the requested text.

participants in the study. Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 2.1 per 100 person-years among COMIRNATY recipients and 2.4 per 100 person-years among placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported at an incidence rate of 4.9 per 100 person-years among COMIRNATY recipients and 4.6 per 100 person-years among placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 6.6 per 100 person-years among COMIRNATY recipients and 6.9 per 100 person-years among placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 88.4 per 100 person-years among participants who received COMIRNATY and 43.5 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include non-serious adverse events were reported at an incidence rate of 75.7 per 100 person-years among participants who received COMIRNATY and 43.3 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 95.8 per 100 person-years among participants who received COMIRNATY and 52.0 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to

Commented [A20]: FDA comment
Pfizer: Please delete this sentence and revise this introduction to describe the variable exposure caused by the unblinding that occurred in a phased manner, to include the actual difference in duration of follow up between groups. We will then report the following events as frequencies n/N (%) rather than incidence rates, as revised below.

Pfizer-BioNTech response
The Sponsor is not in agreement with FDA request and the FDA proposed revisions to the SAE and AE paragraphs. Proportion is more appropriate to summarize adverse events over a specified period of time for all participants. In this study however, participants had differential follow-up time due to the phased manner for unblinding, with approximately 42% of subjects with <4 months of follow up and approximately 58% with >+4 months follow-up. Pfizer therefore proposes to report incidence rates for safety events accounting for the differential follow-up time as a more accurate statistical summary of the safety results.

Commented [A21]: Pfizer BioNTech accepts FDA addition of the statement "From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8) "

determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-marketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions, twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any

Commented [A22]: FDA comment
Pfizer,
This subsection should focus on adverse reactions not observed in clinical trials. Please provide a rationale for inclusion of diarrhea, vomiting and pain in extremity (arm).

Pfizer-BioNTech response
The Sponsor identified Diarrhea, Vomiting and Pain in extremity (arm) as adverse reactions caused by the vaccine in the post-authorization setting, not the clinical study setting. In the clinical study, there was not differentiation in the frequency of these events between the placebo vs vaccine groups. Please refer to the Clinical Overview submitted with this response for a complete justification of these terms.

Commented [A23]: FDA comment
Pfizer,
Please add the PTs for "Dizziness" and "Dyspnea" and their corresponding SOCs to section 6.2

Pfizer-BioNTech response
The Sponsor is not in agreement with the FDA request. The Sponsor does not consider Dizziness and Dyspnea as adverse reactions independent of potential symptoms of a Vaccination stress-related response due to the vaccination process.

Commented [A24]: FDA comment
Pfizer,
Please include information regarding Pregnancy Exposure Registry for COM RNATY to monitor pregnancy outcomes in women exposed to COM RNATY during pregnancy. Please list the telephone number for the health care providers to call and register women who receive COM RNATY during pregnancy.

Pfizer-BioNTech response
The Sponsor is not in agreement with the inclusion of the Pregnancy Exposure Registry. The study registry is performed by the University of California San Diego (UCSD) with a limited enrollment of vaccinated pregnant women with COMIRNATY. The recruitment is handled by UCSD using their established registry procedures.

Commented [A25]: Pfizer-BioNTech accepts deletion of "reproductive and" from this sentence.

Commented [A26]: Pfizer-BioNTech accepts deletion of "reproductive and" from this sentence.

potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

Commented [A27]: Pfizer-BioNTech accepts FDA editorial revisions to this section.

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY~~,~~ ~~t~~There were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

Commented [A28]: Pfizer-BioNTech accepts deletion of "and reproductive" from this sentence.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is a multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Commented [A29]: Pfizer BioNTech agrees with FDA deletion of the following statement "The efficacy analyses included participants that received their second vaccination within 19 to 42 days after their first vaccination. The majority (93.1%) of vaccine recipients received the second dose 19 days to 23 days after Dose 1." as well as the other edits within this paragraph.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. ~~Table 7 presents the specific demographic characteristics in the studied population.~~ Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.5% were male and 48.6% or 49.5% were female, 4.8% or 4.6% were 12 through 15 years of age, 75.1% or 75.1% were 16 through 64 years of age, 20.1% or 20.3% were 65 years of age and older, 16.1% or 16.3% were 65 through 74 years of age, 4.0% or 4.0% ≥75 years of age and older, 82.9% or 83.1% were White, 8.5% or 8.6% were Black or African American, 0.9% or 0.9% were American Indian or Alaska Native, 4.6% or 4.5% were Asian, 0.3% or 0.1% Native Hawaiian or other Pacific Islander, 24.9% or 24.6% were Hispanic/Latino, 74.6% or 74.8% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 44.6% or 44.4% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2 (16 years of age and older) or BMI ≥95th percentile (12 through 15 years of age)], respectively. The mean age at vaccination was 48.3 or 48.2 years and median age was 50.0 or 50.0 in participants who received COMIRNATY or placebo, respectively.

Table 7: Demographics (Population For the Primary Efficacy Endpoint)[a]

	COMIRNATY (N=18,242) n (%)	Placebo (N=18,379) n (%)
Sex		
Male	9318 (51.1)	9225 (50.2)
Female	8924 (48.9)	9154 (49.8)
Age (years)		
Mean (SD)	50.6 (15.70)	50.4 (15.81)
Median	52.0	52.0
Min, max	(12, 89)	(12, 91)
Age group		
≥12 through 15 years	46 (0.3)	42 (0.2)
≥16 through 64 years	14,216 (77.9)	14,299 (77.8)
≥65 through 74 years	3176 (17.4)	3226 (17.6)
≥75 years	804 (4.4)	812 (4.4)
Race		
White	15,110 (82.8)	15,301 (83.3)
Black or African American	1617 (8.9)	1617 (8.8)
American Indian or Alaska Native	118 (0.6)	106 (0.6)
Asian	815 (4.5)	810 (4.4)
Native Hawaiian or other Pacific Islander	48 (0.3)	29 (0.2)
Other[b]	534 (2.9)	516 (2.8)
Ethnicity		
Hispanic or Latino	4886 (26.8)	4857 (26.4)
Not Hispanic or Latino	13,253 (72.7)	13,412 (73.0)
Not reported	103 (0.6)	110 (0.6)
Comorbidities[c]		
Yes	8432 (46.2)	8450 (46.0)
No	9810 (53.8)	9929 (54.0)

a All eligible randomized participants who receive all vaccination(s) as randomized within the predefined window, have no other important protocol deviations as determined by the clinician, and have no evidence of SARS-CoV-2 infection prior to 7 days after Dose 2.

b Includes multiracial and not reported.

c Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease:

- Chronic lung disease (e.g., emphysema and chronic bronchitis, idiopathic pulmonary fibrosis, and cystic fibrosis) or moderate to severe asthma
- Significant cardiac disease (e.g., heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and pulmonary hypertension)
- Obesity (body mass index: ≥30 kg/m^2)
- Diabetes (Type 1, Type 2, or gestational)
- Liver disease
- Human Immunodeficiency Virus (HIV) infection (not included in the efficacy evaluation)

Commented [A30]: FDA Comment
Pfizer: Please delete this table and describe demographics of the efficacy population using the March 2021 data cutoff, to also include percentages of the participants in the age group ≥65 years, and those with comorbidities (with a definition).

Pfizer-BioNTech response
Pfizer-BioNTech has updated the label as per FDA request.

Efficacy Against COVID-19

The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

Commented [A31]: Pfizer BioNTech agrees with FDA addition of this information.

The vaccine efficacy information is presented in Table ~~8~~5.

Table ~~5~~8: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

Subgroup	COMIRNATY N[a]=18,198 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)
First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
All participants[e]	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.3, 97.6)[f]
16 to 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)[g]
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)[g]
65 to 74 years	1 0.406 (3074)	14 0.406 (3095)	92.9 (53.1, 99.8)[g]
75 years and older	0 0.102 (774)	5 0.106 (785)	100.0 (-13.1, 100.0)[g]
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=19,965 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,172 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	9 2.332 (18,559)	169 2.345 (18,708)	94.6 (89.9, 97.3)[f]
16 to 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1 0.530 (4044)	19 0.532 (4067)	94.7 (66.8, 99.9)[g]
65 to 74 years	1 0.424 (3239)	14 0.423 (3255)	92.9 (53.2, 99.8)[g]
75 years and older	0 0.106 (805)	5 0.109 (812)	100.0 (-12.1, 100.0)[g]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

a N = Number of participants in the specified group

b n1 = Number of participants meeting the endpoint definition

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

d n2 = Number of participants at risk for the endpoint

Commented [A32]: FDA comment
Pfizer: Please describe the primary efficacy analysis in text as outlined below and remove Table 8.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, VE against confirmed COV D-19 occurring at least 7 days after Dose 2 was 95.0%. The case split was 8 COVID-19 cases in the BNT162b2 group compared to 162 COV D-19 cases in the placebo group. The 95% credible interval for the vaccine efficacy was 90 3% to 97.6%, indicating that the true VE is at least 90.3% with a 97.5% probability, which met the pre-specified success criterion.

Pfizer-BioNTech response
The Sponsor proposes to retain the information as presented in the table as it is more informative and clearer for the healthcare provider.

e No confirmed cases were identified in participants 12 to 15 years of age
f Two-sided credible interval for vaccine efficacy was calculated using a beta-binomial model with a beta (0 700102, 1) prior for θ=r(1-VE)/(1+r(1-VE)), where r is the ratio of surveillance time in the active vaccine group over that in the placebo group
g Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021~~0~~, representing up to 6 months of follow-up after Dose 2. Overall, 59.2% of participants in the COMIRNATY group and 57.3% of participants in the placebo group had ≥4 months of follow-up time after Dose 2 in the blinded placebo-controlled follow-up period.
~~Updated efficacy analyses were performed with additional confirmed COVID-19 cases accrued during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2 for participants in the efficacy population.~~

The updated vaccine efficacy information is presented in Table ~~9~~6.

Table ~~9~~6: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	COMIRNATY N[a]=~~20,998~~19,993 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=~~21,096~~20,118 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI[e])
All participants[f]	77 ~~6.247 (20,712)~~6.092 (19,711)	~~850~~833 ~~6.003 (20,713)~~5.857 (19,741)	~~91.3~~91.1 ~~(89.0, 93.2)~~(88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	~~710~~709 ~~4.654 (15,515)~~4.654 (15,515)	~~90.6~~90.5 ~~(87.9, 92.7)~~(87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
~~65 through 74 years~~	~~6~~ ~~0.994 (3350)~~	~~98~~ ~~0.966 (3379)~~	~~94.1~~ ~~(86.6, 97.9)~~
~~75 years and older~~	~~1~~ ~~0.239 (842)~~	~~26~~ ~~0.237 (847)~~	~~96.2~~ ~~(76.9, 99.9)~~

Commented [A33]: FDA comment
Pfizer: Please insert a sentence describing the percentage of participants with blinded placebo-controlled follow up ≥4months, to mirror the description of the Safety population.

Pfizer-BioNTech response
Pfizer-BioNTech has updated the label as per FDA request.

Commented [A34]: FDA comment
Pfizer: Please revise Updated VE tables to display VE for participants 16 years of age and older (exclude participants 12-15 years of age) for only confirmed cases that we agree upon (exclude participant 10031167 from all analyses, as previously communicated).

Please also delete the last 2 rows of each portion of the table: 65 through 74 years and 75 years and older.

Pfizer-BioNTech response
Pfizer has updated the table as per FDA request.
Source: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup– Blinded Placebo-Controlled Follow-up Period– Subjects ≥16 Years of Age and Without Evidence of Infection Prior to 7 Days After Dose 2– Evaluable Efficacy (7 Days) Population

Commented [A35]: Pfizer BioNTech accepts deletion of the 65 through 74 years and 75 years and older rows.

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	COMIRNATY N[a]=~~22,166~~21,047 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=~~22,320~~21,210 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI[e])
All participants[f]	81 ~~6.509 (21,642)~~6.340 (20.533)	~~873~~854 ~~6.274 (21,689)~~6.110 (20.595)	~~91.1~~90.9 ~~(88.8, 93.0)~~(88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	~~727~~726 ~~4.879 (16,269)~~4.879 (16.269)	90.2 ~~(87.6, 92.4)~~(87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)
~~65 through 74 years~~	~~6~~ ~~1.021 (3450)~~	~~102~~ ~~0.992 (3468)~~	~~94.3~~ ~~(87.1, 98.0)~~
~~75 years and older~~	~~1~~ ~~0.246 (865)~~	~~26~~ ~~0.240 (858)~~	~~96.3~~ ~~(77.2, 99.9)~~

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

a N = Number of participants in the specified group

b n1 = Number of participants meeting the endpoint definition

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

d n2 = Number of participants at risk for the endpoint

e Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

~~f Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group (both without and with or without evidence of prior SARS-CoV-2 infection); 16 and 18 in the placebo group (without and with or without evidence of prior SARS-CoV-2 infection, respectively).~~

Subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, geographies, and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

~~The updated subgroup analyses of vaccine efficacy by demographic characteristics are presented in Table 10 and Table 11.~~

~~**Table 10: Vaccine Efficacy - First COVID-19 Occurrence From 7 Days After Dose 2 - Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 by Demographic Characteristics - Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period**~~

Commented [A36]: Pfizer BioNTech accepts deletion of the 65 through 74 years and 75 years and older rows.

Commented [A37]: FDA comment
Pfizer: This footnote should be removed based on our comment above to exclude all participants 12-15 years of age from this analysis.

Pfizer-BioNTech
The Sponsor accepts and has deleted the footnote.

Commented [A38]: FDA comment
Pfizer: Please delete Table 10-13.

Pfizer-BioNTech
The Sponsor accepts and has deleted Tables 10-13 and proposes a summary statement of the vaccine efficacy.

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Sex			
Male	42 3.246 (10,637)	399 3.047 (10,433)	90.1 (86.4, 93.0)
Female	35 3.001 (10,075)	451 2.956 (10,280)	92.4 (89.2, 94.7)
Ethnicity			
Hispanic or Latino	29 1.786 (5161)	241 1.711 (5120)	88.5 (83.0, 92.4)
Not Hispanic or Latino	47 4.429 (15,449)	609 4.259 (15,484)	92.6 (90.0, 94.6)
Race			
Black or African American	4 0.545 (1737)	48 0.527 (1737)	91.9 (78.0, 97.9)
White	67 5.208 (17,186)	747 5.026 (17,256)	91.3 (88.9, 93.4)
All others[f]	6 0.494 (1789)	55 0.451 (1720)	90.0 (76.9, 96.5)
Country			
Argentina	15 1.012 (2600)	108 0.986 (2586)	86.5 (76.7, 92.7)
Brazil	12 0.406 (1311)	80 0.374 (1293)	86.2 (74.5, 93.1)
Germany	0 0.047 (236)	1 0.048 (242)	100.0 (-3874.2, 100.0)
South Africa	0 0.080 (291)	9 0.074 (276)	100.0 (53.5, 100.0)
Turkey	0 0.027 (228)	5 0.025 (222)	100.0 (-0.1, 100.0)
United States	50 4.674 (16,046)	647 4.497 (16,094)	92.6 (90.1, 94.5)

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

a N = Number of participants in the specified group

b n1 = Number of participants meeting the endpoint definition

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

d n2 = Number of participants at risk for the endpoint

e Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

f All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories

Table 11: Vaccine Efficacy - First COVID-19 Occurrence From 7 Days After Dose 2 - Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 by Demographic Characteristics - Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Sex			
Male	44 3.376 (11,103)	411 3.181 (10,920)	89.9 (86.2, 92.8)
Female	37 3.133 (10,539)	462 3.093 (10,769)	92.1 (88.9, 94.5)
Ethnicity			
Hispanic or Latino	32 1.862 (5408)	245 1.794 (5391)	87.4 (81.8, 91.6)
Not Hispanic or Latino	48 4.615 (16,128)	628 4.445 (16,186)	92.6 (90.1, 94.6)
Race			
Black or African American	4 0.611 (1958)	49 0.601 (1985)	92.0 (78.1, 97.9)
White	69 5.379 (17,801)	768 5.191 (17,880)	91.3 (88.9, 93.3)
All others[f]	8 0.519 (1883)	56 0.481 (1824)	86.8 (72.1, 94.5)
Country			
Argentina	16 1.033 (2655)	110 1.017 (2670)	85.7 (75.7, 92.1)
Brazil	14 0.441 (1419)	82 0.408 (1401)	84.2 (71.9, 91.7)
Germany	0 0.047 (237)	1 0.048 (243)	100.0 (-3868.6, 100.0)
South Africa	0 0.099 (358)	10 0.096 (358)	100.0 (56.6, 100.0)
Turkey	0 0.029 (238)	6 0.026 (232)	100.0 (22.2, 100.0)
United States	51 4.861 (16,735)	664 4.678 (16,785)	92.6 (90.2, 94.6)

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]

Notes: Confirmed cases were determined by Reverse Transcription Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

a N = Number of participants in the specified group

b n1 = Number of participants meeting the endpoint definition

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

d n2 = Number of participants at risk for the endpoint

e Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

f All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories

The updated subgroup analyses of vaccine efficacy by risk status in participants are presented in Table 12 and Table 13.

Table 12: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First COVID-19 occurrence from 7 days after Dose 2[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
At risk[g]			
Yes	35 2.797 (9167)	401 2.681 (9136)	91.6 (88.2, 94.3)
No	42 3.450 (11,545)	449 3.322 (11,577)	91.0 (87.6, 93.6)
Age group (years) and risk status			
16 through 64 and not at risk	41 2.776 (8887)	385 2.661 (8886)	89.8 (85.9, 92.8)
16 through 64 and at risk	29 2.083 (6632)	325 1.993 (6629)	91.5 (87.5, 94.4)
65 and older and not at risk	1 0.553 (1870)	53 0.546 (1922)	98.1 (89.2, 100.0)
65 and older and at risk	6 0.680 (2322)	71 0.656 (2304)	91.8 (81.4, 97.1)
Obese[h]			

Subgroup	COMIRNATY Na=20,998 Cases n1b Surveillance Timec (n2d)	Placebo Na=21,096 Cases n1b Surveillance Timec (n2d)	Vaccine Efficacy % (95% CI)e
Yes	27 2.103 (6796)	314 2.050 (6875)	91.6 (87.6, 94.6)
No	50 4.143 (13,911)	536 3.952 (13,833)	91.1 (88.1, 93.5)
Age group (years) and obesity status			
16 through 64 and not obese	46 3.178 (10,212)	444 3.028 (10,166)	90.1 (86.6, 92.9)
16 through 64 and obese	24 1.680 (5303)	266 1.624 (5344)	91.3 (86.7, 94.5)
65 and older and not obese	4 0.829 (2821)	79 0.793 (2800)	95.2 (87.1, 98.7)
65 and older and obese	3 0.404 (1370)	45 0.410 (1426)	93.2 (78.9, 98.7)

Note: Confirmed cases were determined by Reverse Transcription Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a N = Number of participants in the specified group.

b n1 = Number of participants meeting the endpoint definition.

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d n2 = Number of participants at risk for the endpoint.

e Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

f Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group.

g At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age]).

h Obese is defined as BMI ≥30 kg/m^2. For 12 through 15 years age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY Na=22,166 Cases n1b Surveillance Timec (n2d)	Placebo Na=22,320 Cases n1b Surveillance Timec (n2d)	Vaccine Efficacy % (95% CI)e
First COVID-19 occurrence from 7 days after Dose 2f	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
At riskg:			
Yes	36 2.925 (9601)	410 2.807 (9570)	91.6 (88.1, 94.2)
No	45 3.584 (12,041)	463 3.466 (12,119)	90.6 (87.2, 93.2)

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Age group (years) and risk status			
16 through 64 and not at risk	44 2.887 (9254)	397 2.779 (9289)	89.3 (85.4, 92.4)
16 through 64 and at risk	30 2.186 (6964)	330 2.100 (6980)	91.3 (87.3, 94.2)
65 and older and not at risk	1 0.566 (1920)	55 0.559 (1966)	98.2 (89.6, 100.0)
65 and older and at risk	6 0.701 (2395)	73 0.672 (2360)	92.1 (82.0, 97.2)
Obese[h]			
Yes	28 2.207 (7139)	319 2.158 (7235)	91.4 (87.4, 94.4)
No	53 4.301 (14,497)	554 4.114 (14,448)	90.8 (87.9, 93.2)
Age group (years) and obesity status			
16 through 64 and not obese	49 3.303 (10,629)	458 3.158 (10,614)	89.8 (86.2, 92.5)
16 through 64 and obese	25 1.768 (5584)	269 1.719 (5649)	91.0 (86.4, 94.3)
65 and older and not obese	4 0.850 (2899)	82 0.811 (2864)	95.3 (87.6, 98.8)
65 and older and obese	3 0.417 (1415)	46 0.420 (1462)	93.4 (79.5, 98.7)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a N = number of participants in the specified group.

b n1 = Number of participants meeting the endpoint definition.

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d n2 = Number of participants at risk for the endpoint.

e Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

f Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group.

g At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m² or BMI ≥95th percentile [12 through 15 years of age]).

h Obese is defined as BMI ≥30 kg/m². For the 12 through 15 years of age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Efficacy Against Severe COVID-19

Updated efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table ~~14~~7) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table ~~14~~7: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older ~~and~~ With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition ~~After Dose 1 or~~ From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population ~~in~~ During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[cb])	Placebo Cases n1[a] Surveillance Time[b] (n2[cb])	Vaccine Efficacy % (95% CI[de])
~~After Dose 1[d]~~	~~1~~ ~~8,439[e] (22,505)~~	~~30~~ ~~8,288[e] (22,435)~~	~~96.7~~ ~~(80.3, 99.9)~~
7 days after Dose 2[fd]	1 ~~6,522[ge] (21,649)~~6,353 (20,540)	21 ~~6,404[ge] (21,730)~~6,237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[cb])	Placebo Cases n1[a] Surveillance Time[b] (n2[cb])	Vaccine Efficacy % (95% CI[de])
~~After Dose 1[d]~~	~~1~~ ~~8,427[e] (22,473)~~	~~45~~ ~~8,269[e] (22,394)~~	~~97.8~~ ~~(87.2, 99.9)~~
7 days after Dose 2[fd]	0 ~~6,514[ge] (21,620)~~6,345 (20,513)	~~32~~31 ~~6,391[ge] (21,693)~~6,225 (20,593)	100 ~~(88.0, 100.0)~~(87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death

Commented [A39]: FDA comment
Pfizer: Please revise this table as follows:
1.Remove the rows for severe cases after Dose 1
2.Remove the specification of the FDA Definition of Severe Disease, as revised.

Pfizer-BioNTech response
The Sponsor accepts the FDA requests. The original table presented results for all participants 12 years of age or older. To be consistent with other updated VE analyses in the label, e.g. Table 6, 7 days after Dose 2 results were updated for participants 16 years of age or older. Pfizer BioNTech also proposes to add population to table title and rearranged footnote to be consistent with Table 6.

Commented [A40]: Pfizer BioNTech accepts the replacement of "FDA" with "Protocol" in the table title and footnotes.

Commented [A41]: Source: Vaccine Efficacy – First Severe COVID-19 Occurrence From 7 Days After Dose 2– Blinded Placebo-Controlled Follow-up Period– Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2– Evaluable Efficacy (7 Days) Population

Commented [A42]: Source: Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC-Definition From 7 Days After Dose 2– Blinded Placebo-Controlled Follow-up Period – Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2– Evaluable Efficacy (7 Days) Population

[I] Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death

a n1 = Number of participants meeting the endpoint definition

b Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

c n2 = Number of participants at risk for the endpoint

de Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

~~d Efficacy assessed based on the Dose 1 all available efficacy (modified intention-to-treat) population that included all randomized participants who received at least 1 dose of study intervention.~~

~~e Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.~~

fd ~~Efficacy assessed based on the evaluable efficacy (7 Days) population that included all eligible randomized participants who receive all dose(s) of study intervention as randomized within the predefined window, have no other important protocol deviations as determined by the clinician.~~

ge ~~Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.~~

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as a 10 mL single-use vial manufactured by Hospira, Inc (NDC 0409-4888-10), or a 2 mL single-use vial manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

Commented [A43]: FDA comment
Pfizer,
Please include a description of the vials from each of the two suppliers and include NDC numbers for cartons and containers of diluent from each of the manufacturers.

Pfizer-BioNTech response
Pfizer-BioNTech has updated the label as per FDA request.

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -80ºC to -60ºC (-112ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -80°C to -60°C (-112°F to -76°F).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2°C to 8°C (35°F to 46°F)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25°C (77°F)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

~~There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by calling ……~~

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

Commented [A44]: Pfizer-BioNTech comment
The Sponsor is not in agreement with the inclusion of the Pregnancy Exposure Registry. The study registry is performed by the USD with a limited enrollment of vaccinated pregnant women with COM RNATY. The recruitment will be handled by the UCSD procedures.

Commented [A45]: FDA comment
Pfizer,
We do not concur; please delete.

Pfizer-BioNTech response
The Sponsor accepts deletion of the website and telephone number for general questions.

This product's labeling may have been updated. For the most recent prescribing information, please visit ~~www.pfizer.com~~www.comirnatyglobal.com.

Commented [A46]: Pfizer BioNTech proposes to update the website link.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.~~2~~3

US Govt. License No. x

CPT Code x

Commented [A47]: FDA comment
Pfizer,
CPT codes are not typically included in labeling. Please provide a rationale for inclusion.

Pfizer-BioNTech response
The Sponsor proposes to retain the CPT code in the label for consistency with other Pfizer Vaccine label such as Trumenba and Prevnar 13.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, fever, and injection site swelling. (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, injection site swelling, fever, and injection site redness. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

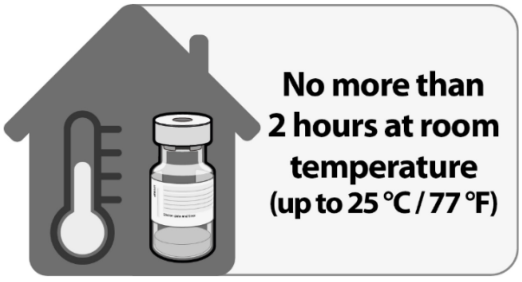
2.1 Preparation for Administration

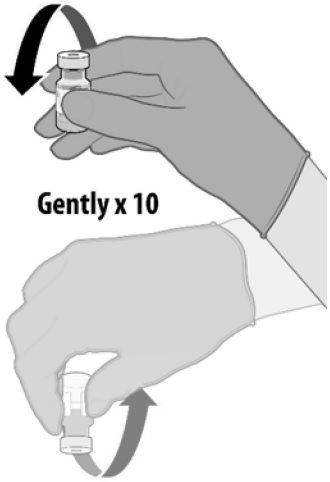
Prior to Dilution

- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

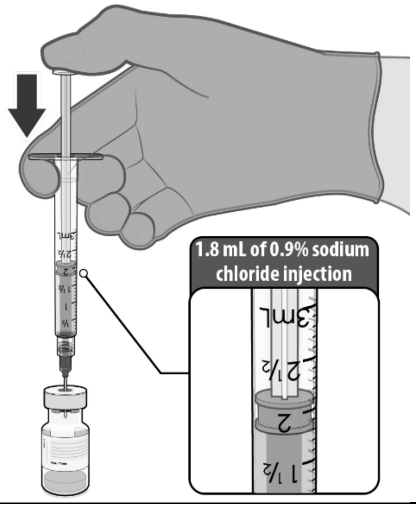
Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or an alternate brand of sterile 0.9% Sodium Chloride Injection, USP as the diluent.
- Provided diluent vials are single-use only and should be discarded after 1.8 mL is withdrawn. Do not use provided diluent vials to dilute multiple vials of COMIRNATY.
- After dilution, 1 vial contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

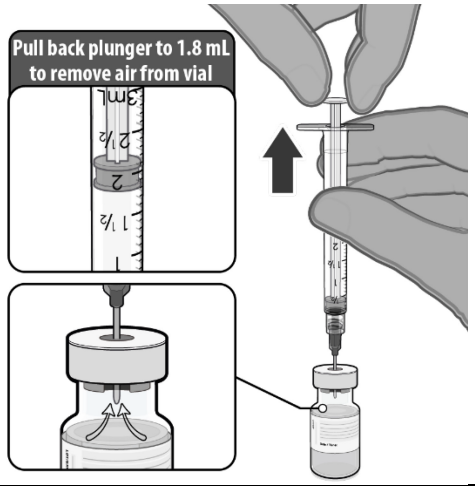
THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.

<table>
<tr><td> 
</td><td>

- Before dilution invert vaccine vial gently 10 times.
- Do not shake.
- Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles.
- Do not use if liquid is discolored or if other particles are observed.

</td></tr>
<tr><td colspan="2">DILUTION</td></tr>
<tr><td> 
</td><td>

- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent.
- Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle).
- Cleanse the vaccine vial stopper with a single-use antiseptic swab.
- Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

</td></tr>
<tr><td> 
</td><td>

- Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.

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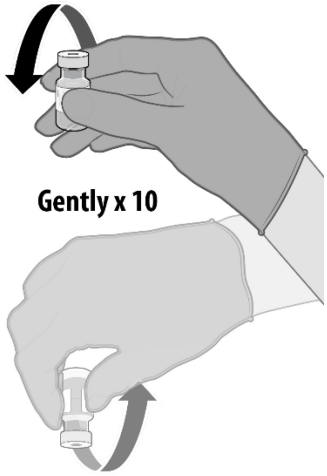
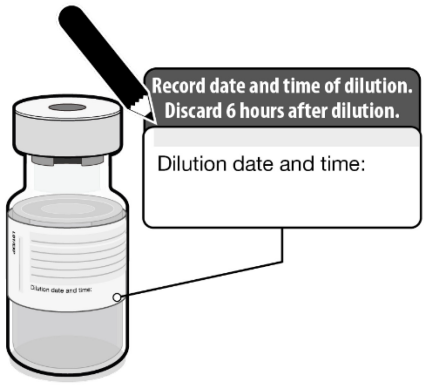
</table>

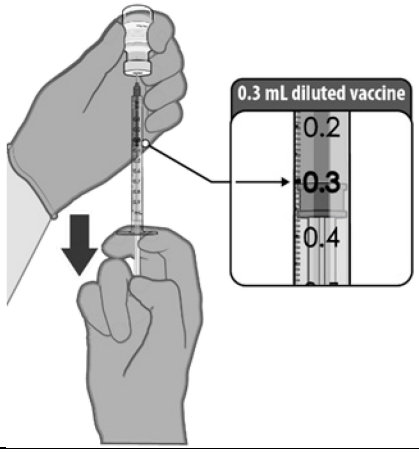


- Gently invert the vial containing the COMIRNATY 10 times to mix.
- Do not shake.
- Inspect the vaccine in the vial.
- The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.



- Record the date and time of dilution on the COMIRNATY vial label.
- Store between 2°C to 25°C (35°F to 77°F).
- Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY



- Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles.
- Each dose must contain 0.3 mL of vaccine.
- If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- Administer immediately.

2.2 Administration Information

For intramuscular injection only.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Visually inspect each dose in the dosing syringe prior to administration. The vaccine will be an off-white suspension. During the visual inspection,

- verify the final dosing volume of 0.3 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk has been highest in adolescent and young adult males under 40 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of symptoms. Information is not yet available about potential long-term sequelae. The CDC has published

considerations for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies with a data cut-off of March 13, 2021, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies with a data cut-off of March 13, 2021, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

In clinical studies with a data cut-off of March 13, 2021, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies with a data cut-off of March 13, 2021, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine

candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection after receiving Dose 2, local reactions and systemic events were similar to those observed for all participants 16 years of age and older by severity, onset day, and median duration. The frequency of pain at the injection site was similar after Dose 1 compared with Dose 2 of COMIRNATY (63.0% versus 53.3%). The frequency of redness and swelling was similar after Dose 1 compared with Dose 2 of COMIRNATY (redness: 3.7% versus 6.7%; swelling: 5.6% versus 8.3%, respectively). There was 1 (1.7%) severe reaction (pain at the injection site) reported after Dose 2 of COMIRNATY and no Grade 4 local reactions were reported. Fever, headache, chills, and joint pain increased in frequency from Dose 1 to Dose 2 while fatigue, vomiting, diarrhea, and muscle pain were similar after each dose of COMIRNATY. There were no severe systemic events after Dose 1 of COMIRNATY but after Dose 2, there was 1 (1.7%) severe fever (>38.9°C to 40.0°C), 3 (5.0%) participants with severe fatigue, 2 (3.3%) participants with severe headache, 1 (1.7%) participant with severe chills, and 1 (1.7%) participant with severe diarrhea. There were no Grade 4 systemic events reported after either dose.

Unsolicited Adverse Events

Upon issuance of the EUA for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Unblinded participants originally randomized to COMIRNATY and placebo recipients administered COMIRNATY continued to be followed for unsolicited adverse events including serious adverse events, throughout the study [from Dose 1 of COMIRNATY through 1 month (all unsolicited adverse events) and 6 months (serious adverse events) after the last vaccination]. Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began in a phased manner for participants in the study. Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 2.1 per 100 person-years among COMIRNATY recipients and 2.4 per 100 person-years among placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported at an incidence rate of 4.9 per 100 person-years among COMIRNATY recipients and 4.6 per 100 person-years among placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the

participant unblinding date in ongoing follow-up were reported at an incidence rate of 6.6 per 100 person-years among COMIRNATY recipients and 6.9 per 100 person-years among placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 88.4 per 100 person-years among participants who received COMIRNATY and 43.5 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include non-serious adverse events were reported at an incidence rate of 75.7 per 100 person-years among participants who received COMIRNATY and 43.3 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 95.8 per 100 person-years among participants who received COMIRNATY and 52.0 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions, twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY. There were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is a multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised

and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.5% were male and 48.6% or 49.5% were female, 4.8% or 4.6% were 12 through 15 years of age, 75.1% or 75.1% were 16 through 64 years of age, 20.1% or 20.3% were 65 years of age and older, 16.1% or 16.3% were 65 through 74 years of age, 4.0% or 4.0% 75 years of age and older, 82.9% or 83.1% were White, 8.5% or 8.6% were Black or African American, 0.9% or 0.9% were American Indian or Alaska Native, 4.6% or 4.5% were Asian, 0.3% or 0.1% Native Hawaiian or other Pacific Islander, 24.9% or 24.6% were Hispanic/Latino, 74.6% or 74.8% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 44.6% or 44.4% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) $\geq$30 kg/m^2 (16 years of age and older) or BMI $\geq$95th percentile (12 through 15 years of age)], respectively. The mean age at vaccination was 48.3 or 48.2 years and median age was 50.0 or 50.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

The vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=18,198 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.3, 97.6)[f]
16 to 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)[g]
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)[g]
65 to 74 years	1 0.406 (3074)	14 0.406 (3095)	92.9 (53.1, 99.8)[g]
75 years and older	0 0.102 (774)	5 0.106 (785)	100.0 (-13.1, 100.0)[g]
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=19,965 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,172 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	9 2.332 (18,559)	169 2.345 (18,708)	94.6 (89.9, 97.3)[f]
16 to 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1 0.530 (4044)	19 0.532 (4067)	94.7 (66.8, 99.9)[g]
65 to 74 years	1 0.424 (3239)	14 0.423 (3255)	92.9 (53.2, 99.8)[g]
75 years and older	0 0.106 (805)	5 0.109 (812)	100.0 (-12.1, 100.0)[g]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. No confirmed cases were identified in participants 12 to 15 years of age.

f. Two-sided credible interval for vaccine efficacy was calculated using a beta-binomial model with a beta (0.700102, 1) prior for θ=r(1-VE)/(1+r(1-VE)), where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.
g. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. Overall, 59.2% of participants in the COMIRNATY group and 57.3% of participants in the placebo group had ≥4 months of follow-up time after Dose 2 in the blinded placebo-controlled follow-up period.

The updated vaccine efficacy information is presented in Table 6.

Table 6: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY Na=19,993 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=20,118 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY Na=21,047 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=21,210 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, geographies, and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Updated efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 7) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 7: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as a 10 mL single-use vial manufactured by Hospira, Inc (NDC 0409-4888-10), or a 2 mL single-use vial manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -80ºC to -60ºC (-112ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F).

Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit www.comirnatyglobal.com.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.3

US Govt. License No. x

CPT Code x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection ~~administration~~ only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age ~~and older~~, the most commonly reported adverse reactions (~~>~~≥10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, fever, and injection site swelling. (6 1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, injection site swelling, fever, and injection site redness. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

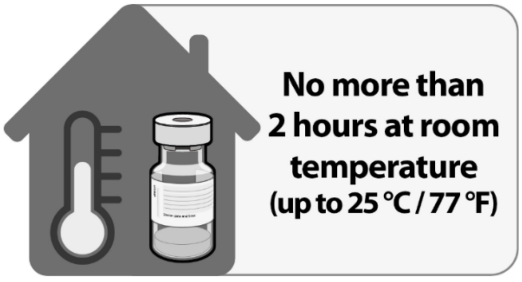
2.1 Preparation for Administration

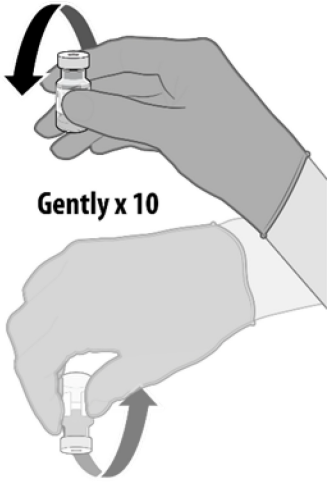
Prior to Dilution

- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or an alternate brand of sterile 0.9% Sodium Chloride Injection, USP as the diluent.
- Provided diluent vials are single-use only and should be discarded after 1.8 mL is withdrawn. Do not use provided diluent vials to dilute multiple vials of COMIRNATY.
- After dilution, 1 vial contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.

<table>
<tr><td> 
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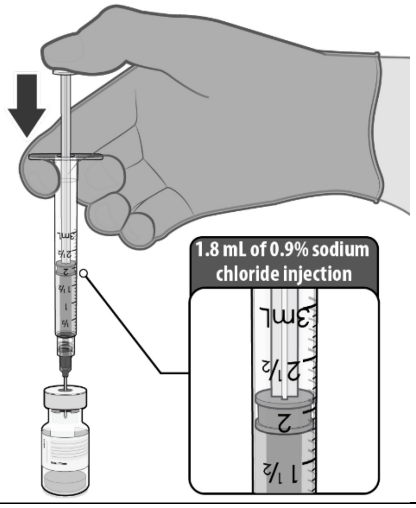
- Before dilution invert vaccine vial gently 10 times.
- Do not shake.
- Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles.
- Do not use if liquid is discolored or if other particles are observed.

</td></tr>
<tr><td colspan="2">DILUTION</td></tr>
<tr><td> 
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- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent.
- Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle).
- Cleanse the vaccine vial stopper with a single-use antiseptic swab.
- Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

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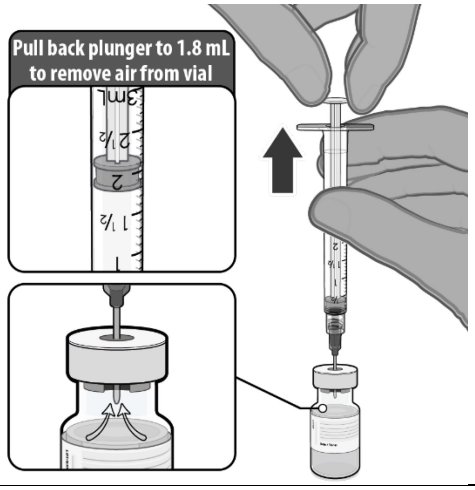
<tr><td> 
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- Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.

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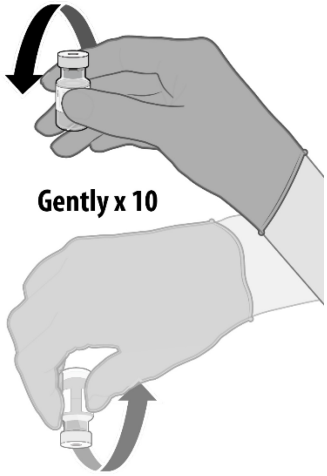
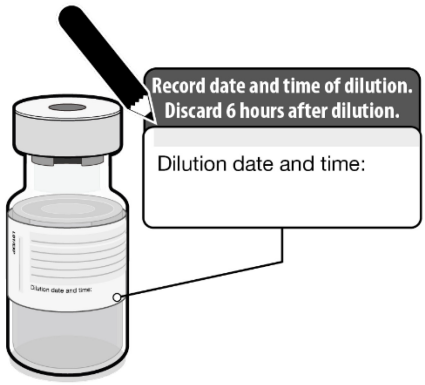
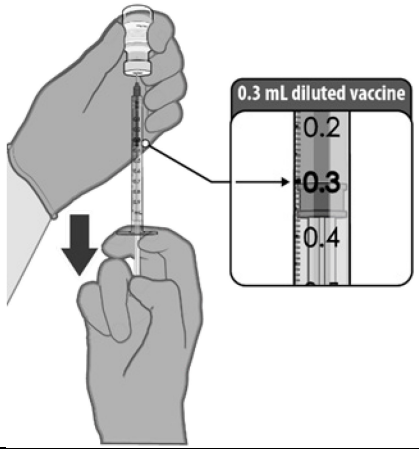


- Gently invert the vial containing the COMIRNATY 10 times to mix.
- Do not shake.
- Inspect the vaccine in the vial.
- The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.



- Record the date and time of dilution on the COMIRNATY vial label.
- Store between 2°C to 25°C (35°F to 77°F).
- Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY



- Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles.
- Each dose must contain 0.3 mL of vaccine.
- If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- Administer immediately.

2.2 Administration Information

For intramuscular injection only.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Visually inspect each dose in the dosing syringe prior to administration. The vaccine will be an off-white suspension. During the visual inspection,

- verify the final dosing volume of 0.3 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk has been highest in adolescent and young adult males under 40 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of symptoms. Information is not yet available about potential long-term sequelae. The CDC has published

considerations for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies with a data cut-off of March 13, 2021, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies with a data cut-off of March 13, 2021, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

In clinical studies with a data cut-off of March 13, 2021, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise- (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies with a data cut-off of March 13, 2021, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine

candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 ~~TRADENAME~~COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection~~disease~~ was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were ≥65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 ~~to~~ through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

~~Table 5 and Table 6 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 16 years of age and older with confirmed stable HIV infection.~~

In participants with chronic, stable HIV infection after receiving Dose 2, local reactions and systemic events were similar to those observed for all participants 16 years of age and older by severity, onset day, and median duration. The frequency of pain at the injection site was similar after Dose 1 compared with Dose 2 of COMIRNATY (63.0% versus 53.3%). The frequency of redness and swelling was similar after Dose 1 compared with Dose 2 of COMIRNATY (redness: 3.7% versus 6.7%; swelling: 5.6% versus 8.3%, respectively). There was 1 (1.7%) severe reaction (pain at the injection site) reported after Dose 2 of COMIRNATY and no Grade 4 local reactions were reported. Fever, headache, chills, and joint pain increased in frequency from Dose 1 to Dose 2 while fatigue, vomiting, diarrhea, and muscle pain were similar after each dose of COMIRNATY. There were no severe systemic events after Dose 1 of COMIRNATY but after Dose 2, there was 1 (1.7%) severe fever (>38.9°C to 40.0°C), 3 (5.0%) participants with severe fatigue, 2 (3.3%) participants with severe headache, 1 (1.7%) participant with severe chills, and 1 (1.7%) participant with severe diarrhea. There were no Grade 4 systemic events reported after either dose.

~~**Table 5: Study 2 Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose HIV-Positive Participants 16 Years of Age and Older Reactogenicity Subset of the Safety Population***~~

	~~COMIRNATY Dose 1 N[a]=54 n[b] (%)~~	~~Placebo Dose 1 N[a]=56 n[b] (%)~~	~~COMIRNATY Dose 2 N[a]=60 n[b] (%)~~	~~Placebo Dose 2 N[a]=62 n[b] (%)~~
~~Redness[e]~~				
~~Any (>2.0 cm)~~	~~2 (3.7)~~	~~3 (5.4)~~	~~4 (6.7)~~	~~1 (1.6)~~
~~Mild~~	~~2 (3.7)~~	~~1 (1.8)~~	~~3 (5.0)~~	~~1 (1.6)~~
~~Moderate~~	~~0~~	~~0~~	~~1 (1.7)~~	~~0~~
~~Severe~~	~~0~~	~~2 (3.6)~~	~~0~~	~~0~~
~~Swelling[e]~~				
~~Any (>2.0 cm)~~	~~3 (5.6)~~	~~1 (1.8)~~	~~5 (8.3)~~	~~0~~
~~Mild~~	~~2 (3.7)~~	~~0~~	~~2 (3.3)~~	~~0~~
~~Moderate~~	~~1 (1.9)~~	~~0~~	~~3 (5.0)~~	~~0~~
~~Severe~~	~~0~~	~~1 (1.8)~~	~~0~~	~~0~~

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Pain at the injection site[d]				
Any	34 (63.0)	9 (16.1)	32 (53.3)	5 (8.1)
Mild	26 (48.1)	8 (14.3)	22 (36.7)	5 (8.1)
Moderate	8 (14.8)	1 (1.8)	9 (15.0)	0
Severe	0	0	1 (1.7)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in HIV-positive participants 16 years of age and older.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 6: Study 2 Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose HIV-Positive Participants 16 Years of Age and Older Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Fever				
≥38.0°C	1 (1.9)	4 (7.1)	9 (15.0)	5 (8.1)
≥38.0°C to 38.4°C	1 (1.9)	2 (3.6)	4 (6.7)	5 (8.1)
>38.4°C to 38.9°C	0	0	4 (6.7)	0
>38.9°C to 40.0°C	0	2 (3.6)	1 (1.7)	0
>40.0°C	0	0	0	0
Fatigue[e]				
Any	22 (40.7)	15 (26.8)	24 (40.0)	12 (19.4)
Mild	15 (27.8)	9 (16.1)	12 (20.0)	5 (8.1)
Moderate	7 (13.0)	5 (8.9)	9 (15.0)	7 (11.3)
Severe	0	1 (1.8)	3 (5.0)	0
Headache[e]				
Any	11 (20.4)	18 (32.1)	18 (30.0)	12 (19.4)
Mild	7 (13.0)	10 (17.9)	8 (13.3)	8 (12.9)
Moderate	4 (7.4)	7 (12.5)	8 (13.3)	4 (6.5)
Severe	0	1 (1.8)	2 (3.3)	0
Chills[e]				
Any	6 (11.1)	5 (8.9)	14 (23.3)	4 (6.5)
Mild	5 (9.3)	4 (7.1)	5 (8.3)	3 (4.8)
Moderate	1 (1.9)	1 (1.8)	8 (13.3)	1 (1.6)
Severe	0	0	1 (1.7)	0

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Vomiting[d]				
Any	1 (1.9)	3 (5.4)	2 (3.3)	2 (3.2)
Mild	1 (1.9)	1 (1.8)	1 (1.7)	1 (1.6)
Moderate	0	0	1 (1.7)	1 (1.6)
Severe	0	2 (3.6)	0	0
Diarrhea[e]				
Any	5 (9.3)	8 (14.3)	4 (6.7)	9 (14.5)
Mild	5 (9.3)	6 (10.7)	1 (1.7)	6 (9.7)
Moderate	0	1 (1.8)	2 (3.3)	3 (4.8)
Severe	0	1 (1.8)	1 (1.7)	0
New or worsened muscle pain[e]				
Any	9 (16.7)	10 (17.9)	10 (16.7)	5 (8.1)
Mild	7 (13.0)	7 (12.5)	5 (8.3)	1 (1.6)
Moderate	2 (3.7)	3 (5.4)	5 (8.3)	4 (6.5)
Severe	0	0	0	0
New or worsened joint pain[e]				
Any	5 (9.3)	7 (12.5)	10 (16.7)	5 (8.1)
Mild	5 (9.3)	4 (7.1)	4 (6.7)	1 (1.6)
Moderate	0	3 (5.4)	6 (10.0)	4 (6.5)
Severe	0	0	0	0
Use of antipyretic or pain medication[f]	7 (13.0)	8 (14.3)	16 (26.7)	7 (11.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.
No Grade 4 solicited systemic reactions were reported in HIV-positive participants 16 years of age and older.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each event or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.
f. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

Upon issuance of the EUA for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Unblinded participants originally randomized to COMIRNATY and placebo recipients administered COMIRNATY continued to be followed for unsolicited adverse events including serious adverse events, throughout the study [from Dose 1 of COMIRNATY through 1 month (all unsolicited adverse events) and 6 months (serious adverse events) after the last vaccination]. Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began in a phased manner for

participants in the study. Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 2.1 per 100 person-years among COMIRNATY recipients and 2.4 per 100 person-years among placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported at an incidence rate of 4.9 per 100 person-years among COMIRNATY recipients and 4.6 per 100 person-years among placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 6.6 per 100 person-years among COMIRNATY recipients and 6.9 per 100 person-years among placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 88.4 per 100 person-years among participants who received COMIRNATY and 43.5 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include non-serious adverse events were reported at an incidence rate of 75.7 per 100 person-years among participants who received COMIRNATY and 43.3 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 95.8 per 100 person-years among participants who received COMIRNATY and 52.0 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to

determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-marketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions, twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any

potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY~~,~~. ~~t~~There were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is a multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. ~~Table 7 presents the specific demographic characteristics in the studied population.~~ Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.5% were male and 48.6% or 49.5% were female, 4.8% or 4.6% were 12 through 15 years of age, 75.1% or 75.1% were 16 through 64 years of age, 20.1% or 20.3% were 65 years of age and older, 16.1% or 16.3% were 65 through 74 years of age, 4.0% or 4.0% ≥75 years of age and older, 82.9% or 83.1% were White, 8.5% or 8.6% were Black or African American, 0.9% or 0.9% were American Indian or Alaska Native, 4.6% or 4.5% were Asian, 0.3% or 0.1% Native Hawaiian or other Pacific Islander, 24.9% or 24.6% were Hispanic/Latino, 74.6% or 74.8% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 44.6% or 44.4% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2 (16 years of age and older) or BMI ≥95^{th} percentile (12 through 15 years of age)], respectively. The mean age at vaccination was 48.3 or 48.2 years and median age was 50.0 or 50.0 in participants who received COMIRNATY or placebo, respectively.

Table 7: Demographics (Population For the Primary Efficacy Endpoint)[a]

	COMIRNATY (N=18,242) n (%)	Placebo (N=18,379) n (%)
Sex		
Male	9318 (51.1)	9225 (50.2)
Female	8924 (48.9)	9154 (49.8)
Age (years)		
Mean (SD)	50.6 (15.70)	50.4 (15.81)
Median	52.0	52.0
Min, max	(12, 89)	(12, 91)
Age group		
≥12 through 15 years	46 (0.3)	42 (0.2)
≥16 through 64 years	14,216 (77.9)	14,299 (77.8)
≥65 through 74 years	3176 (17.4)	3226 (17.6)
≥75 years	804 (4.4)	812 (4.4)
Race		
White	15,110 (82.8)	15,301 (83.3)
Black or African American	1617 (8.9)	1617 (8.8)
American Indian or Alaska Native	118 (0.6)	106 (0.6)
Asian	815 (4.5)	810 (4.4)
Native Hawaiian or other Pacific Islander	48 (0.3)	29 (0.2)
Other[b]	534 (2.9)	516 (2.8)
Ethnicity		
Hispanic or Latino	4886 (26.8)	4857 (26.4)
Not Hispanic or Latino	13,253 (72.7)	13,412 (73.0)
Not reported	103 (0.6)	110 (0.6)
Comorbidities[c]		
Yes	8432 (46.2)	8450 (46.0)
No	9810 (53.8)	9929 (54.0)

a. All eligible randomized participants who receive all vaccination(s) as randomized within the predefined window, have no other important protocol deviations as determined by the clinician, and have no evidence of SARS-CoV-2 infection prior to 7 days after Dose 2.

b. Includes multiracial and not reported.

c. Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease:

- Chronic lung disease (e.g., emphysema and chronic bronchitis, idiopathic pulmonary fibrosis, and cystic fibrosis) or moderate to severe asthma
- Significant cardiac disease (e.g., heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and pulmonary hypertension)
- Obesity (body mass index ≥30 kg/m^2)
- Diabetes (Type 1, Type 2, or gestational)
- Liver disease
- Human Immunodeficiency Virus (HIV) infection (not included in the efficacy evaluation)

Efficacy Against COVID-19

The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

The vaccine efficacy information is presented in Table 85.

Table 58: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=18,198 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.3, 97.6)[f]
16 to 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)[g]
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)[g]
65 to 74 years	1 0.406 (3074)	14 0.406 (3095)	92.9 (53.1, 99.8)[g]
75 years and older	0 0.102 (774)	5 0.106 (785)	100.0 (-13.1, 100.0)[g]
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=19,965 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,172 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	9 2.332 (18,559)	169 2.345 (18,708)	94.6 (89.9, 97.3)[f]
16 to 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1 0.530 (4044)	19 0.532 (4067)	94.7 (66.8, 99.9)[g]
65 to 74 years	1 0.424 (3239)	14 0.423 (3255)	92.9 (53.2, 99.8)[g]
75 years and older	0 0.106 (805)	5 0.109 (812)	100.0 (-12.1, 100.0)[g]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. No confirmed cases were identified in participants 12 to 15 years of age.
f. Two-sided credible interval for vaccine efficacy was calculated using a beta-binomial model with a beta (0.700102, 1) prior for θ=r(1-VE)/(1+r(1-VE)), where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.
g. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021~~0~~, representing up to 6 months of follow-up after Dose 2. Overall, 59.2% of participants in the COMIRNATY group and 57.3% of participants in the placebo group had ≥4 months of follow-up time after Dose 2 in the blinded placebo-controlled follow-up period.
~~Updated efficacy analyses were performed with additional confirmed COVID-19 cases accrued during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2 for participants in the efficacy population.~~

The updated vaccine efficacy information is presented in Table ~~9~~6.

Table ~~9~~6: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY** **N[a]=~~20,998~~19,993** **Cases** **n1[b]** **Surveillance Time[c] (n2[d])**	**Placebo** **N[a]=~~21,096~~20,118** **Cases** **n1[b]** **Surveillance Time[c] (n2[d])**	**Vaccine Efficacy %** **(95% CI[e])**
All participants[f]	77 ~~6.247 (20,712)~~6.092 (19,711)	~~850~~833 ~~6.003 (20,713)~~5.857 (19,741)	~~91.3~~91.1 ~~(89.0, 93.2)~~(88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	~~710~~709 ~~4.654 (15,515)~~4.654 (15,515)	~~90.6~~90.5 ~~(87.9, 92.7)~~(87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
~~65 through 74 years~~	~~6~~ ~~0.994 (3350)~~	~~98~~ ~~0.966 (3379)~~	~~94.1~~ ~~(86.6, 97.9)~~
~~75 years and older~~	~~1~~ ~~0.239 (842)~~	~~26~~ ~~0.237 (847)~~	~~96.2~~ ~~(76.9, 99.9)~~

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY** **N[a]=~~22,166~~21,047** **Cases** **n1[b]** **Surveillance Time[c] (n2[d])**	**Placebo** **N[a]=~~22,320~~21,210** **Cases** **n1[b]** **Surveillance Time[c] (n2[d])**	**Vaccine Efficacy %** **(95% CI[e])**
All participants[f]	81 ~~6.509 (21,642)~~6.340 (20,533)	~~873~~854 ~~6.274 (21,689)~~6.110 (20,595)	~~91.1~~90.9 ~~(88.8, 93.0)~~(88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	~~727~~726 ~~4.879 (16,269)~~4.879 (16,269)	90.2 ~~(87.6, 92.4)~~(87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)
~~65 through 74 years~~	~~6~~ ~~1.021 (3450)~~	~~102~~ ~~0.992 (3468)~~	~~94.3~~ ~~(87.1, 98.0)~~
~~75 years and older~~	~~1~~ ~~0.246 (865)~~	~~26~~ ~~0.240 (858)~~	~~96.2~~ ~~(77.2, 99.9)~~

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

~~f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group (both without and with or without evidence of prior SARS-CoV-2 infection); 16 and 18 in the placebo group (without and with or without evidence of prior SARS-CoV-2 infection, respectively).~~

Subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, geographies, and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

~~The updated subgroup analyses of vaccine efficacy by demographic characteristics are presented in Table 10 and Table 11.~~

~~**Table 10: Vaccine Efficacy - First COVID-19 Occurrence From 7 Days After Dose 2 - Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 by Demographic Characteristics - Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period**~~

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Sex			
Male	42 3.246 (10,637)	399 3.047 (10,433)	90.1 (86.4, 93.0)
Female	35 3.001 (10,075)	451 2.956 (10,280)	92.4 (89.2, 94.7)
Ethnicity			
Hispanic or Latino	29 1.786 (5161)	241 1.711 (5120)	88.5 (83.0, 92.4)
Not Hispanic or Latino	47 4.429 (15,449)	609 4.259 (15,484)	92.6 (90.0, 94.6)
Race			
Black or African American	4 0.545 (1737)	48 0.527 (1737)	91.9 (78.0, 97.9)
White	67 5.208 (17,186)	747 5.026 (17,256)	91.3 (88.9, 93.4)
All others[f]	6 0.494 (1789)	55 0.451 (1720)	90.0 (76.9, 96.5)
Country			
Argentina	15 1.012 (2600)	108 0.986 (2586)	86.5 (76.7, 92.7)
Brazil	12 0.406 (1311)	80 0.374 (1293)	86.2 (74.5, 93.1)
Germany	0 0.047 (236)	1 0.048 (242)	100.0 (3874.2, 100.0)
South Africa	0 0.080 (291)	9 0.074 (276)	100.0 (53.5, 100.0)
Turkey	0 0.027 (228)	5 0.025 (222)	100.0 (0.1, 100.0)
United States	50 4.674 (16,046)	647 4.497 (16,094)	92.6 (90.1, 94.5)

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group.

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

f. All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

Table 11: Vaccine Efficacy - First COVID-19 Occurrence From 7 Days After Dose 2 - Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 by Demographic Characteristics - Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Sex			
Male	44 3.376 (11,103)	411 3.181 (10,920)	89.9 (86.2, 92.8)
Female	37 3.133 (10,539)	462 3.093 (10,769)	92.1 (88.9, 94.5)
Ethnicity			
Hispanic or Latino	32 1.862 (5408)	245 1.794 (5391)	87.4 (81.8, 91.6)
Not Hispanic or Latino	48 4.615 (16,128)	628 4.445 (16,186)	92.6 (90.1, 94.6)
Race			
Black or African American	4 0.611 (1958)	49 0.601 (1985)	92.0 (78.1, 97.9)
White	69 5.379 (17,801)	768 5.191 (17,880)	91.3 (88.9, 93.3)
All others[f]	8 0.519 (1883)	56 0.481 (1824)	86.8 (72.1, 94.5)
Country			
Argentina	16 1.033 (2655)	110 1.017 (2670)	85.7 (75.7, 92.1)
Brazil	14 0.441 (1419)	82 0.408 (1401)	84.2 (71.9, 91.7)
Germany	0 0.047 (237)	1 0.048 (243)	100.0 (3868.6, 100.0)
South Africa	0 0.099 (358)	10 0.096 (358)	100.0 (56.6, 100.0)
Turkey	0 0.029 (238)	6 0.026 (232)	100.0 (22.2, 100.0)
United States	51 4.861 (16,735)	664 4.678 (16,785)	92.6 (90.2, 94.6)

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).
Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group.
* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.
a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
f. All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

The updated subgroup analyses of vaccine efficacy by risk status in participants are presented in Table 12 and Table 13.

Table 12: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First COVID-19 occurrence from 7 days after Dose 2[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
At risk[g]			
Yes	35 2.797 (9167)	401 2.681 (9136)	91.6 (88.2, 94.3)
No	42 3.450 (11,545)	449 3.322 (11,577)	91.0 (87.6, 93.6)
Age group (years) and risk status			
16 through 64 and not at risk	41 2.776 (8887)	385 2.661 (8886)	89.8 (85.9, 92.8)
16 through 64 and at risk	29 2.083 (6632)	325 1.993 (6629)	91.5 (87.5, 94.4)
65 and older and not at risk	1 0.553 (1870)	53 0.546 (1922)	98.1 (89.2, 100.0)
65 and older and at risk	6 0.680 (2322)	71 0.656 (2304)	91.8 (81.4, 97.1)
Obese[h]			

Subgroup	COMIRNATY Na=20,998 Cases n1b Surveillance Time e (n2d)	Placebo Na=21,096 Cases n1b Surveillance Time e (n2d)	Vaccine Efficacy % (95% CI)e
Yes	27 2.103 (6796)	314 2.050 (6875)	91.6 (87.6, 94.6)
No	50 4.143 (13,911)	536 3.952 (13,833)	91.1 (88.1, 93.5)
Age group (years) and obesity status			
16 through 64 and not obese	46 3.178 (10,212)	444 3.028 (10,166)	90.1 (86.6, 92.9)
16 through 64 and obese	24 1.680 (5303)	266 1.624 (5344)	91.3 (86.7, 94.5)
65 and older and not obese	4 0.829 (2821)	79 0.793 (2800)	95.2 (87.1, 98.7)
65 and older and obese	3 0.404 (1370)	45 0.410 (1426)	93.2 (78.9, 98.7)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group.

g. At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age]).

h. Obese is defined as BMI ≥30 kg/m^2. For 12 through 15 years age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY Na=22,166 Cases n1b Surveillance Time e (n2d)	Placebo Na=22,320 Cases n1b Surveillance Time e (n2d)	Vaccine Efficacy % (95% CI)e
First COVID-19 occurrence from 7 days after Dose 2f	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
At riskg			
Yes	36 2.925 (9601)	410 2.807 (9570)	91.6 (88.1, 94.2)
No	45 3.584 (12,041)	463 3.466 (12,119)	90.6 (87.2, 93.2)

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Age group (years) and risk status			
16 through 64 and not at risk	44 2.887 (9254)	397 2.779 (9289)	89.3 (85.4, 92.4)
16 through 64 and at risk	30 2.186 (6964)	330 2.100 (6980)	91.3 (87.3, 94.2)
65 and older and not at risk	1 0.566 (1920)	55 0.559 (1966)	98.2 (89.6, 100.0)
65 and older and at risk	6 0.701 (2395)	73 0.672 (2360)	92.1 (82.0, 97.2)
Obese[h]			
Yes	28 2.207 (7139)	319 2.158 (7235)	91.4 (87.4, 94.4)
No	53 4.301 (14,497)	554 4.114 (14,448)	90.8 (87.9, 93.2)
Age group (years) and obesity status			
16 through 64 and not obese	49 3.303 (10,629)	458 3.158 (10,614)	89.8 (86.2, 92.5)
16 through 64 and obese	25 1.768 (5584)	269 1.719 (5649)	91.0 (86.4, 94.3)
65 and older and not obese	4 0.850 (2899)	82 0.811 (2864)	95.3 (87.6, 98.8)
65 and older and obese	3 0.417 (1415)	46 0.420 (1462)	93.4 (79.5, 98.7)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group.

g. At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age]).

h. Obese is defined as BMI ≥30 kg/m^2. For the 12 through 15 years of age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Efficacy Against Severe COVID-19

Updated efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table ~~14~~7) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table ~~14~~7: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older ~~and~~ With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition ~~After Dose 1 or~~ From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population ~~in~~ During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[cb])	**Placebo Cases n1[a] Surveillance Time[b] (n2[cb])**	**Vaccine Efficacy % (95% CI[de])**
~~After Dose 1~~[d]	~~1 8.439[e] (22,505)~~	~~30 8.288[e] (22,435)~~	~~96.7 (80.3, 99.9)~~
7 days after Dose 2[fd]	1 ~~6.522[ge] (21,649)~~6.353 (20,540)	21 ~~6.404[ge] (21,730)~~6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[cb])	**Placebo Cases n1[a] Surveillance Time[b] (n2[cb])**	**Vaccine Efficacy % (95% CI[de])**
~~After Dose 1~~[d]	~~1 8.427[e] (22,473)~~	~~45 8.269[e] (22,394)~~	~~97.8 (87.2, 99.9)~~
7 days after Dose 2[fd]	0 ~~6.514[ge] (21,620)~~6.345 (20,513)	~~32~~31 ~~6.391[ge] (21,693)~~6.225 (20,593)	100 ~~(88.0, 100.0)~~(87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
de. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
~~d. Efficacy assessed based on the Dose 1 all available efficacy (modified intention-to-treat) population that included all randomized participants who received at least 1 dose of study intervention.~~
~~e. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.~~
fd. ~~Efficacy assessed based on the evaluable efficacy (7 Days) population that included all eligible randomized participants who receive all dose(s) of study intervention as randomized within the predefined window, have no other important protocol deviations as determined by the clinician.~~
ge. ~~Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.~~

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as a 10 mL single-use vial manufactured by Hospira, Inc (NDC 0409-4888-10), or a 2 mL single-use vial manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -80ºC to -60ºC (-112ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

~~There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by calling …..~~

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit ~~www.pfizer.com~~www.comirnatyglobal.com.

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LAB-1448-0.~~2~~3

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Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup
– Blinded Placebo-Controlled Follow-up Period
– Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2
– Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=21047)		Placebo (N[a]=21210)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
First COVID-19 occurrence from 7 days after Dose 2						
Overall	81	6.340 (20533)	854	6.110 (20595)	90.9	(88.5, 92.8)
Age group (years)						
16 to 55	56	3.766 (12088)	584	3.619 (12142)	90.8	(87.9, 93.1)
>55	25	2.573 (8445)	270	2.492 (8453)	91.0	(86.5, 94.3)
≥65	7	1.267 (4315)	128	1.232 (4326)	94.7	(88.7, 97.9)
16 to 17	0	0.065 (365)	11	0.061 (355)	100.0	(62.4, 100.0)
16 to 25	10	0.511 (1734)	84	0.498 (1740)	88.4	(77.6, 94.6)
16 to 64	74	5.073 (16218)	726	4.879 (16269)	90.2	(87.5, 92.4)
18 to 64	74	5.008 (15853)	715	4.817 (15914)	90.0	(87.3, 92.3)
55 to 64	21	1.442 (4563)	158	1.386 (4559)	87.2	(79.8, 92.3)
65 to 74	6	1.021 (3450)	102	0.992 (3468)	94.3	(87.1, 98.0)
≥75	1	0.246 (865)	26	0.240 (858)	96.2	(77.2, 99.9)
75 to 85	1	0.244 (860)	25	0.238 (852)	96.1	(76.2, 99.9)
>85	0	0.001 (5)	1	0.001 (6)	100.0	(-4055.9, 100.0)
Sex						
Male	44	3.289 (10548)	399	3.097 (10354)	89.6	(85.8, 92.6)

Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup
– Blinded Placebo-Controlled Follow-up Period
– Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2
– Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=21047)		Placebo (N[a]=21210)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
Female	37	3.051 (9985)	455	3.013 (10241)	92.0	(88.8, 94.4)
Race						
White	69	5.234 (16846)	749	5.054 (16952)	91.1	(88.6, 93.2)
Black or African American	4	0.602 (1909)	49	0.591 (1928)	92.0	(78.1, 97.9)
American Indian or Alaska Native	0	0.043 (196)	3	0.038 (180)	100.0	(-116.0, 100.0)
Asian	3	0.258 (907)	24	0.247 (896)	88.0	(60.6, 97.7)
Native Hawaiian or other Pacific Islander	0	0.016 (54)	1	0.008 (31)	100.0	(-1947.9, 100.0)
Multiracial	5	0.160 (538)	22	0.140 (503)	80.1	(46.1, 94.1)
Not reported	0	0.027 (83)	6	0.031 (105)	100.0	(1.4, 100.0)
All others[f]	8	0.504 (1778)	56	0.465 (1715)	86.8	(72.2, 94.6)
Ethnicity						
Hispanic/Latino	32	1.841 (5280)	240	1.777 (5266)	87.1	(81.3, 91.4)
Non-Hispanic/non-Latino	48	4.466 (15149)	614	4.300 (15220)	92.5	(89.9, 94.5)
Not reported	1	0.032 (104)	0	0.034 (109)	-∞	(NA, NA)
Country						
Argentina	16	1.033 (2655)	110	1.017 (2670)	85.7	(75.7, 92.1)
Brazil	14	0.441 (1419)	82	0.408 (1401)	84.2	(71.9, 91.7)

Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup
– Blinded Placebo-Controlled Follow-up Period
– Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2
– Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=21047)		Placebo (N[a]=21210)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
Germany	0	0.047 (237)	1	0.048 (243)	100.0	(-3868.6, 100.0)
South Africa	0	0.099 (358)	10	0.096 (358)	100.0	(56.6, 100.0)
Turkey	0	0.029 (238)	6	0.026 (232)	100.0	(22.2, 100.0)
USA	51	4.692 (15626)	645	4.515 (15691)	92.4	(89.9, 94.4)
Prior SARS-CoV-2 Status						
Positive at baseline[g]	3	0.183 (593)	6	0.195 (643)	46.7	(-149.5, 91.4)
Positive N-binding only	2	0.143 (466)	5	0.147 (488)	58.8	(-151.9, 96.1)
Positive NAAT only	0	0.013 (43)	1	0.014 (48)	100.0	(-3922.5, 100.0)
Positive NAAT and N-binding	1	0.027 (84)	0	0.034 (106)	-∞	(NA, NA)
Negative at baseline but positive prior to 7 days after Dose 2[h]	0	0.011 (40)	1	0.013 (50)	100.0	(-4759.2, 100.0)
Negative prior to 7 days after Dose 2[i]	77	6.092 (19711)	833	5.856 (19740)	91.1	(88.8, 93.1)
Unknown	1	0.054 (189)	14	0.046 (162)	93.9	(59.9, 99.9)

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

a. N = number of subjects in the specified group.
b. n1 = Number of subjects meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup
– Blinded Placebo-Controlled Follow-up Period
– Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2
– Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=21047)		Placebo (N[a]=21210)			
Efficacy Endpoint Subgroup	**n1[b]**	**Surveillance Time[c] (n2[d])**	**n1[b]**	**Surveillance Time[c] (n2[d])**	**VE (%)**	**(95% CI[e])**

f. All others = American Indian or Alaska native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.
g. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
h. Negative N-binding antibody result and negative NAAT result at Visit 1, positive NAAT result at Visit 2 or at unscheduled visit, if any, prior to 7 days after Dose 2.
i. Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1 and Visit 2, and negative NAAT result at unscheduled visit, if any, prior to 7 days after Dose 2.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adc19ef Table Generation: 06AUG2021 (08:53)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA_Efficacy_v2/adc19ef_ve_cov_7pd2_sg_eval

Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup
– Blinded Placebo-Controlled Follow-up Period
– Subjects ≥16 Years of Age and Without Evidence of Infection Prior to 7 Days After Dose 2
– Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=19993)		Placebo (N[a]=20118)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
First COVID-19 occurrence from 7 days after Dose 2						
Overall	77	6.092 (19711)	833	5.857 (19741)	91.1	(88.8, 93.1)
Age group (years)						
16 to 55	52	3.593 (11517)	568	3.439 (11533)	91.2	(88.3, 93.5)
>55	25	2.499 (8194)	265	2.417 (8208)	90.9	(86.2, 94.2)
≥65	7	1.233 (4192)	124	1.202 (4226)	94.5	(88.3, 97.8)
16 to 17	0	0.061 (342)	10	0.057 (331)	100.0	(58.2, 100.0)
16 to 25	8	0.482 (1629)	80	0.466 (1622)	90.3	(80.0, 96.0)
16 to 64	70	4.859 (15519)	709	4.654 (15515)	90.5	(87.9, 92.7)
18 to 64	70	4.798 (15177)	699	4.597 (15184)	90.4	(87.7, 92.6)
55 to 64	21	1.399 (4426)	156	1.334 (4388)	87.2	(79.7, 92.3)
65 to 74	6	0.994 (3350)	98	0.966 (3379)	94.1	(86.6, 97.9)
≥75	1	0.239 (842)	26	0.237 (847)	96.2	(76.9, 99.9)
75 to 85	1	0.238 (837)	25	0.235 (841)	96.0	(75.9, 99.9)
>85	0	0.001 (5)	1	0.001 (6)	100.0	(-4055.9, 100.0)
Sex						
Male	42	3.167 (10138)	389	2.972 (9934)	89.9	(86.0, 92.8)

Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup
– Blinded Placebo-Controlled Follow-up Period
– Subjects ≥16 Years of Age and Without Evidence of Infection Prior to 7 Days After Dose 2
– Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=19993)		Placebo (N[a]=20118)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
Female	35	2.926 (9573)	444	2.885 (9807)	92.2	(89.0, 94.7)
Race						
White	67	5.076 (16321)	730	4.902 (16432)	91.1	(88.6, 93.2)
Black or African American	4	0.537 (1697)	48	0.519 (1690)	92.0	(78.0, 97.9)
American Indian or Alaska Native	0	0.040 (183)	3	0.037 (175)	100.0	(-120.7, 100.0)
Asian	3	0.251 (883)	23	0.239 (869)	87.6	(58.9, 97.6)
Native Hawaiian or other Pacific Islander	0	0.015 (51)	1	0.008 (30)	100.0	(-2017.6, 100.0)
Multiracial	3	0.148 (497)	22	0.124 (447)	88.6	(62.1, 97.8)
Not reported	0	0.025 (79)	6	0.029 (98)	100.0	(3.8, 100.0)
All others[f]	6	0.480 (1693)	55	0.436 (1619)	90.1	(77.0, 96.5)
Ethnicity						
Hispanic/Latino	29	1.768 (5052)	236	1.696 (5015)	88.2	(82.6, 92.3)
Non-Hispanic/non-Latino	47	4.293 (14559)	597	4.128 (14620)	92.4	(89.8, 94.5)
Not reported	1	0.031 (100)	0	0.033 (106)	-∞	(NA, NA)
Country						
Argentina	15	1.012 (2600)	108	0.986 (2586)	86.5	(76.7, 92.7)
Brazil	12	0.406 (1311)	80	0.374 (1293)	86.2	(74.5, 93.1)

Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup
– Blinded Placebo-Controlled Follow-up Period
– Subjects ≥16 Years of Age and Without Evidence of Infection Prior to 7 Days After Dose 2
– Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=19993)		Placebo (N[a]=20118)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
Germany	0	0.047 (236)	1	0.048 (242)	100.0	(-3874.2, 100.0)
South Africa	0	0.080 (291)	9	0.074 (276)	100.0	(53.5, 100.0)
Turkey	0	0.027 (228)	5	0.025 (222)	100.0	(-0.1, 100.0)
USA	50	4.519 (15045)	630	4.350 (15122)	92.4	(89.8, 94.4)

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test;
SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.
Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.
a. N = number of subjects in the specified group.
b. n1 = Number of subjects meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
f. All others = American Indian or Alaska native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adc19ef Table Generation: 06AUG2021 (08:52)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA_Efficacy_v2/adc19ef_ve_cov_7pd2_wo_sg_eval

Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC-Definition From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=21047)		Placebo (N[a]=21210)			
Efficacy Endpoint	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
First severe COVID-19 occurrence based on CDC-definition from 7 days after Dose 2	0	6.345 (20513)	31	6.225 (20593)	100.0	(87.6, 100.0)

Abbreviation: VE = vaccine efficacy.

a. N = number of subjects in the specified group.

b. n1 = Number of subjects meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of subjects at risk for the endpoint.

e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:19) Source Data: adc19ef Table Generation: 06AUG2021 (09:21)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA_Efficacy_v2/adc19ef_ve_sev_7pd2_cdc_eval

Vaccine Efficacy – First Severe COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) (N[a]=21047)		Placebo (N[a]=21210)				
Efficacy Endpoint	**n1[b]**	**Surveillance Time[c] (n2[d])**	**n1[b]**	**Surveillance Time[c] (n2[d])**	**VE (%)**	**(95% CI[e])**	**Pr (VE >30% | data)[f]**
First severe COVID-19 occurrence from 7 days after Dose 2	1	6.353 (20540)	21	6.237 (20629)	95.3	(70.9, 99.9)	>0.9999

Abbreviation: VE = vaccine efficacy.

a. N = number of subjects in the specified group.

b. n1 = Number of subjects meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of subjects at risk for the endpoint.

e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:19) Source Data: adc19ef Table Generation: 06AUG2021 (09:07)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA_Efficacy_v2/adc19ef_ve_sev_cov_7pd2_eval

NOTE - expiry format:
EXP: MM/YYYY

Comirnaty 25ct Carton - Kzoo COM25CTKZ 21P August 11, 2021 am

Black PMS 7671 PMS 2162 PMS 7597

Minimum point size - 6pt.

NOTE:
Area around QR Code is a required quiet zone.
Nothing is to print within this space.
Code to scan as:
https://www.comirnatyglobal.com

Comirnaty 25ct Carton COM25CTPUS - Puurs 19P August 11, 2021 am

Black PMS 7671 PMS 2162 PMS 7597

Minimum point size - 7pt.

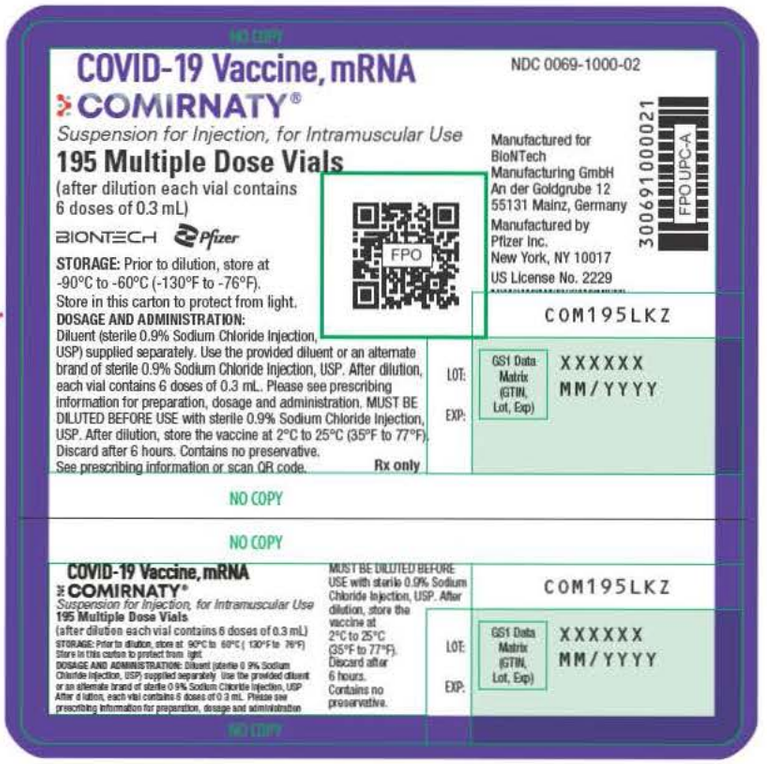
NOTE:
Area around QR Code is a required quiet zone.
Nothing is to print within this space.
Code to scan as:
https://www.comirnatyglobal.com

Comirnaty Carton Label - Kzoo COM195LKZ 20P August 11, 2021 am

Black PMS 7671 PMS 2162 PMS 7597

Minimum point size - 4pt.

NOTE:
Area around QR Code is a required quiet zone.
Nothing is to print within this space.
Code to scan as:
https://www.comirnatyglobal.com



NOTE - expiry format:
EXP: MM/YYYY

GTIN: 00300691000021

Comirnaty Carton Label COM195LPUS - Puurs 19P August 11, 2021 am

Black PMS 7671 PMS 2162 PMS 7597

NOTE - expiry format:
EXP: MM/YYYY

NOTE:
Area around QR Code is a required quiet zone.
Nothing is to print within this space.
Code to scan as:
https://www.comirnatyglobal.com

Comirnaty Label - Kzoo COMVLABKZ 18P August 11, 2021 am

Black PMS 7671

Body text point size - 3.3pt.

NOTE - expiry format:
EXP: MM/YYYY

GS1 DataBar Code Scans as:
(01)10300691000011

Comirnaty Label COMVLABP - Puurs 18P August 11, 2021 am
Black PMS 7671

Body text point size - 3.3pt.

NOTE - expiry format:
EXP: MM/YYYY

GS1 DataBar Code Scans as:
(01)10300691000011

Comirnaty Diluent Label 4P Aug 11, 2021 am

Black PMS 7671 PMS 2162 PMS 7597

(label size: 1.25" x 2.75")

Diluent For Use With

COVID-19 Vaccine, mRNA

COMIRNATY®

Please see the COMIRNATY® prescribing information for preparation, dosage and administration supplied separately.

COMDILRM

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY* (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older (1)

DOSAGE AND ADMINISTRATION

- For intramuscular injection only (2 2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0 3 mL each) 3 weeks apart (2 3)

DOSAGE FORMS AND STRENGTHS

Suspension for injection After preparation, a single dose is 0 3 mL (3)

CONTRAINDICATIONS

Known history of a severe allergic reaction (e g , anaphylaxis) to any component of COMIRNATY (4)

WARNINGS AND PRECAUTIONS

- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose (5 2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY Procedures should be in place to avoid injury from fainting (5 4)

ADVERSE REACTIONS

- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site ~~(88 6%)~~, fatigue ~~(70 1%)~~, headache ~~(64 0%)~~, muscle pain ~~(45 5%)~~, chills ~~(41 5%)~~, joint pain ~~(27 5%)~~, fever ~~(17 8%)~~, and injection site swelling ~~(10 6%)~~ (6 1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site ~~(78 2%)~~, fatigue ~~(56 0%)~~, headache ~~(45 0%)~~, muscle pain ~~(32 5%)~~, chills ~~(24 8%)~~, joint pain ~~(21 5%)~~, injection site swelling ~~(11 8%)~~, fever ~~(11 5%)~~, and injection site redness ~~(10 4%)~~ (6 1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed

Commented [A1]: Pfizer BioNTech Response
The Sponsor proposes to delete this information as we believe it is redundant with the content of the FPI and the purpose of Highlights is to give a succinct overview of the label.

Commented [A2]: PfizerBioNTech response
The Sponsor proposes addition of this heading to be consistent with the updates recently made to the EUA labels that FDA granted a LOA for on 12-Aug-2021.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

Commented [A3]: Pfizer BioNTech comment
The Sponsor accepts insertion of this statement by FDA.

2.1 Preparation for Administration

Prior to Dilution

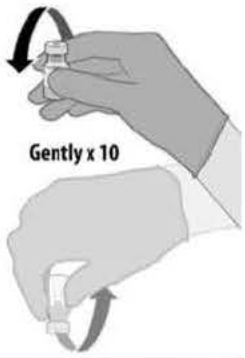
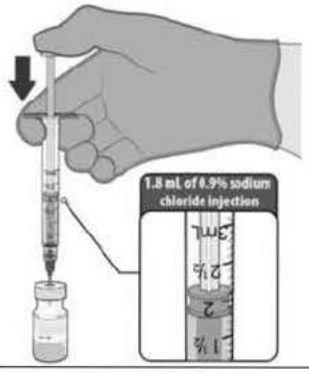
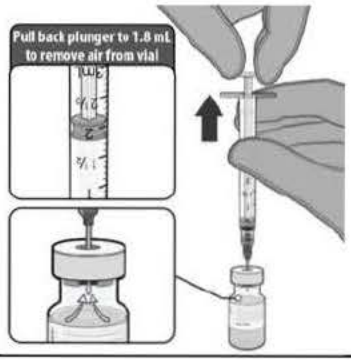
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2°C to 8°C (35°F to 46°F)] or at room temperature [up to 25°C (77°F)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
  - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
  - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
  - Do not use diluent vials to dilute multiple vials of COMIRNATY.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

Commented [A4]: Pfizer BioNTech comment
The Sponsor accepts FDA's proposed revisions to this section.

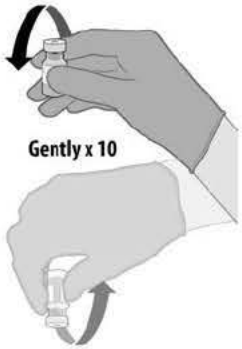
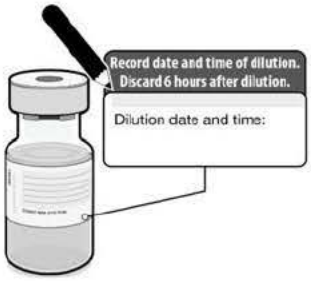
THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2°C to 8°C (35°F to 46°F)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25°C (77°F)] for 30 minutes.

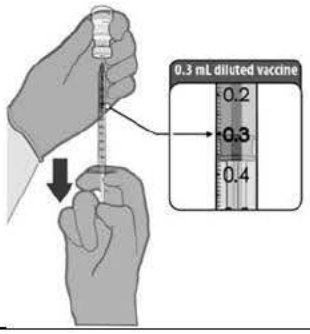
	• Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • Do not shake. • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.
	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.

Commented [A5]: Pfizer BioNTech comment The Sponsor accepts addition of "vaccine."

Commented [A6]: Pfizer BioNTech comment The Sponsor accepts FDA's changes.

Commented [A7]: Pfizer BioNTech comment The Sponsor accepts the addition of "vaccine."

	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

Commented [A8]: Pfizer BioNTech comment The Sponsor accepts FDA's revision to this section.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

Commented [A9]: Pfizer-BioNTech comment The sponsor accepts moving this information from Section 2 2 to Section 2.1.

2.2 Administration Information

Commented [A10]: PfizerBioNTech response
The Sponsor accepts FDA's revisions to this section.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

A third dose of the COMIRNATY (0.3 mL) administered at least 28 days following the first 2 doses of this vaccine is authorized for administration to individuals at least 16 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

Commented [A11]: Pfizer-BioNTech response
The Sponsor proposes addition of this paragraph to section 2.3 to be consistent with the updates recently made to the EUA labels that FDA granted a LOA for on 12-Aug-2021 (expect for the age which has been changed to 16 to reflect the age in BLA).

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

Commented [A12]: FDA Comment
Pfizer,
Please note, we intend to communicate additional comments regarding Section 5 to you next week.

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk has been highest in adolescent and young adult males under 40 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of

symptoms. Information is not yet available about potential long-term sequelae. The CDC has published considerations for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

Commented [A13]: Pfizer BioNTech comment The Sponsor accepts the deletion of the cut-off date.

Commented [A14]:
FDA comment
Pfizer,
Please delete. Our intent is to convey the most commonly reported adverse reactions in this section.

Pfizer-BioNTech response
The Sponsor understands that the most frequently occurring adverse reactions should be presented first, however, we propose rather than deleting this information on less frequently occurring ADRs (<10%) moving it to the end of the section because otherwise certain events that are causally related will completely drop out of the label (i.e., malaise, asthenia, lethargy, hyperhidrosis, nausea, decreased appetite, night sweats) as it's important information for prescribers.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	**Placebo Dose 1 N[a]=2908 n[b] (%)**	**COMIRNATY Dose 2 N[a]=2682 n[b] (%)**	**Placebo Dose 2 N[a]=2684 n[b] (%)**
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm

d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours

f Severity was not collected for use of antipyretic or pain medication

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in participants 56 years of age and older

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, the information was included in the column header

b n = Number of participants with the specified reaction

c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm

d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header

b n = Number of participants with the specified reaction

	COMIRNATY Dose 1 N^a=2008 n^b (%)	Placebo Dose 1 N^a=1989 n^b (%)	COMIRNATY Dose 2 N^a=1860 n^b (%)	Placebo Dose 2 N^a=1833 n^b (%)

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea

f Severity was not collected for use of antipyretic or pain medication

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

In clinical studies, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, in 99 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported in recipients who were followed for 1 month following post Dose 3.

Unsolicited Adverse Events

Overall 51.1% of participants in the COMIRNATY group and 51.4% of participants in the placebo group had follow-up time between >4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 8.1% and 5.9% with >6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

~~Upon issuance of the EUA for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY.~~ Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. At the time of the updated efficacy analysis 54.5% of participants originally randomized to COMIRNATY had >6 months of follow-up from Dose 2 and 47.5% of original placebo participants had follow-up time between >1 month to <2 months after Dose 2 of COMIRNATY. ~~Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began~~

Commented [A15]: FDA comment
Pfizer,
This description is redundant from the overall safety description provided above, so it has been deleted.
To clarify our request: please add a subsection to describe the frequencies of unsolicited non-serious and serious adverse events that occurred from Dose 1 through the March 2021 data cutoff, in the original vaccine recipients that have follow-up for at least 6 months after Dose 2 (n=12,006).

Pfizer-BioNTech response
The Sponsor accepts the deletion of text regarding HIV.

Commented [A16]: Pfizer BioNTech comment The Sponsor proposes to move this text (that was deleted by FDA) from above section 6.1 to the end of this subsection.

Commented [A17]: Pfizer-BioNTech response
The Sponsor proposes addition of this paragraph to be consistent with the updates recently made to the EUA labels that FDA granted a LOA for on 12-Aug-2021.

Commented [A18]: Pfizer BioNTech comment The Sponsor accepts deletion of the text originally included on unblinding and proposes this updated language to clearly represent the data regarding follow-up time for the blinded period and to address FDA's previous request for this information.

Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Table 9.*

~~in a phased manner for participants in the study.~~ Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Adverse events occurred in 28.8% of vaccine recipients who had a follow-up period of at least 6 months after Dose 2; 1.6% of the recipients had serious adverse events.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) ~~at an incidence rate of 2.1 per 100 person-years among~~ COMIRNATY recipients and 117 (0.9%)~~2.4 per 100 person-years among~~ placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported by 165 (1.8%)~~at an incidence rate of 4.9 per 100 person-years among~~ COMIRNATY recipients and 151 (1.7%)~~4.6 per 100 person-years among~~ placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%)~~at an incidence rate of 6.6 per 100 person-years among~~ COMIRNATY recipients and 2 (2%)~~6.9 per 100 person-years among~~ placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4396 (33.8%)~~at an incidence rate of 88.4 per 100 person- years among~~ participants who received COMIRNATY and 2136 (16.4%)~~43.5 per 100 person-years among~~ participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include nonserious adverse events were reported by 2551 (28.6%)~~at an incidence rate of 75.7 per 100 person-years among~~ participants who received COMIRNATY and 1432 (16.1%)~~43.3 per 100 person-years among~~ participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 29 (29%)~~at an incidence rate of 95.8 per 100 person-years among~~ participants who received COMIRNATY and 15 (15%)~~52.0 per 100 person-years among~~ participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse

Commented [A19]: FDA comment
Pfizer,
We do not think that the presentation of these data using incidence rates is helpful for the healthcare provider.

Additionally, we do not agree with the method by which the incidence rates are calculated. It appears that the incidence rate for each event type is based on the number of subjects who reported at least one event divided by the total person-years contributed by all subjects from Dose 1 to unblinding but does not account for the number of events a subject may report, or the timing of these events in deriving the total length of period "at risk." This may be misleading as it under-reports the true incidence rate. In addition, we note that the total lengths of follow-up between arms are within 2% in both age groups (18 through 55, 56 and above), thus differences in follow-up appear to be minor. Therefore, we continue to request the use of proportions to present safety data.

Pfizer BioNTech response
The Sponsor accepts FDA's request to add this subsection and has proposed language accordingly. We believe it's important to include details on both the ≥4 months to <6 ...

Commented [A20]: FDA comment
Pfizer,
This description is redundant from the overall safety description provided above, so it has been deleted.
To clarify our request: please add a subsection to describe the frequencies of unsolicited non-serious and serious adverse events that occurred from Dose 1 through the March 2021 ...

Commented [A21]: Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Table 9.*

Commented [A22]: **Pfizer-BioNTech response**
The Sponsor accepts FDA's request to update the incidence rates to frequencies and therefore has manually calculated the frequencies (n=numbers of participants who had the event / N=total number of participants in the group).

Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-* ...

Commented [A23]: Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Tables 14.179*

Commented [A24]: **Pfizer-BioNTech response**
The Sponsor accepts FDA's request to update the incidence rates to frequencies and therefore has manually calculated the frequencies (n=number of participants who had the event / N=total number of participants in the group).

Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-* ...

Commented [A25]: Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Table 14.179.*

Commented [A26]: Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Table 9.*

events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Comirnaty during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Commented [A27]: FDA comment
Pfizer,
We do not concur because it appears that OTIS is recruiting from a wide variety of sites. We request that you include contact information for the registry in the PI as follows:

"There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting www "

Pfizer-BioNTech response
The Sponsor accepts and has provided an update to this section consistent with FDA's request.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

8.6 Immunocompromised Use

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, safety and effectiveness of a third dose of COMIRNATY have been evaluated in persons that received solid organ transplants. The administration of a third dose of vaccine appears to be only moderately effective in increasing potentially protective antibody titers. Patients should still be counselled to maintain physical precautions to help prevent COVID-19. In addition, close contacts of immunocompromised persons should be vaccinated as appropriate for their health status.

Commented [A28]: Pfizer-BioNTech response
The Sponsor proposes addition of this paragraph to section 8.6 to be consistent with the updates recently made to the EUA labels that FDA granted a LOA for on 12-Aug-2021.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY

contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.35% were male and 48.6% or 49.75% were female, 7579.1% or 7579.21% were 16 through 64 years of age, 20.91% or 20.83% were 65 years of age and older, ~~16.1% or 16.3% were 65 through 74 years of age, 4.0% or 4.0% 75 years of age and~~

Commented [A29]: Pfizer-BioNTech comment The Sponsor accepts FDA's proposed addition.

Commented [A30]: Pfizer-BioNTech comment The Sponsor accepts FDA's proposed revision.

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Commented [A31]: Pfizer-BioNTech comment The Sponsor accepts FDA's proposed revision

Commented [A32]: FDA comment
Pfizer,
Please revise the demographics to describe the efficacy population used for the updated VE analyses in participants 16 years of age and older (please exclude participants 12-15 years of age). Results should be the same as those provided in Shell Table F with STN 126472/0.32.

PfizerBioNTech response
The sponsor accepts FDA's proposal to revise the demographics as requested and has proposed minor modifications to align with Table F.

Source: *Table F Demographics and Other Baseline Characteristics, Participants 16 Years of Age and Older, With or Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy Population (Data Cutoff March 13, 2021)*

~~older, 8281~~.9% or 82.1% were White, ~~9~~8.5% or ~~9~~8.6% were Black or African American, ~~0.9~~1.0% or 0.9% were American Indian or Alaska Native, 4.~~4~~6% or 4.~~3~~5% were Asian, 0.3% or 0.~~1~~2% Native Hawaiian or other Pacific Islander, 2~~5~~4.~~9~~6% or 2~~5~~4.~~4~~6% were Hispanic/Latino, 7~~3~~4.~~6~~9% or 74.1~~8~~% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 4~~4~~6.~~6~~0% or 4~~5~~4.7~~4~~% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 4~~8~~.~~8~~3 or 4~~8~~.~~7~~2~~.~~ years and median age was 5~~1~~0.0 or 5~~1~~0.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

Commented [A33]: Pfizer-BioNTech comment The Sponsor accepts FDA's proposed addition of this text.

~~The vaccine efficacy information is presented in Table 5.~~

~~**Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population**~~

~~First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection[a]~~			
~~Subgroup~~	~~COMIRNATY N[a]=18,198 Cases n1[b] Surveillance Time[c] (n2[d])~~	~~Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])~~	~~Vaccine Efficacy % (95% CI)~~
~~All participants[e]~~	~~8 2,214 (17,411)~~	~~162 2,222 (17,511)~~	~~95.0 (90.3, 97.6)[f]~~
~~16 to 64 years~~	~~7 1,706 (13,549)~~	~~143 1,710 (13,618)~~	~~95.1 (89.6, 98.1)[g]~~
~~65 years and older~~	~~1 508 (3848)~~	~~19 511 (3880)~~	~~94.7 (66.7, 99.9)[g]~~
~~65 to 74 years~~	~~1 406 (3074)~~	~~14 406 (3095)~~	~~92.9 (53.1, 99.8)[g]~~
~~75 years and older~~	~~0 102 (774)~~	~~5 106 (785)~~	~~100.0 (-13.1, 100.0)[g]~~
~~First COVID-19 occurrence from 7 days after Dose 2 in participants with or without[a] evidence of prior SARS-CoV-2 infection~~			
~~Subgroup~~	~~COMIRNATY N[a]=19,965 Cases n1[b] Surveillance Time[c] (n2[d])~~	~~Placebo N[a]=20,172 Cases n1[b] Surveillance Time[c] (n2[d])~~	~~Vaccine Efficacy % (95% CI)~~
~~All participants[e]~~	~~9~~	~~169~~	~~94.6~~

	2,332 (18,559)	2,345 (18,708)	(89.9, 97.3)[f]
16 to 64 years	8 1,802 (14,501)	150 1,814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1 0.530 (4044)	19 0.532 (4067)	94.7 (66.8, 99.9)[g]
65 to 74 years	1 0.424 (3239)	14 0.423 (3255)	92.9 (53.2, 99.8)[g]
75 years and older	0 0.106 (805)	5 0.109 (812)	100.0 (-12.1, 100.0)[g]

Note: Confirmed cases were determined by Reverse Transcription Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever, new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. No confirmed cases were identified in participants 12 to 15 years of age.

f. Two-sided credible interval for vaccine efficacy was calculated using a beta-binomial model with a beta (0.700102, 1) prior for θ=r(1-VE)/(1+r(1-VE)), where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.

g. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0%. The case split was 8 COVID-19 cases in the BNT162b2 group compared to 162 COVID-19 cases in the placebo group. The 95% credible interval for the vaccine efficacy was 90.3% to 97.6%, indicating that the true vaccine efficacy is at least 90.3% with a 97.5% probability, which met the pre-specified success criterion.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

The updated vaccine efficacy information is presented in Table 5~~6~~.

Commented [A34]:
FDA comment
Pfizer:
We continue to request deletion of this Table because the information is redundant with the updated VE analysis that follows with additional confirmed cases. Please insert the text requested below:

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, VE against confirmed COV D-19 occurring at least 7 days after Dose 2 was 95.0%. The case split was 8 COVID-19 cases in the BNT162b2 group compared to 162 COV D-19 cases in the placebo group. The 95% credible interval for the vaccine efficacy was 90 3% to 97.6%, indicating that the true VE is at least 90.3% with a 97.5% probability, which met the pre-specified success criterion.

Pfizer-BioNTech response
The Sponsor accepts the replacement of this of the table with the summary text provided by FDA.

Commented [A35]: **FDA comment**
Pfizer
Revised the language to mirror description of the Safety population.

We note that these numbers were derived from follow-up times, based on the safety population. Please update the information, based on the follow up time after Dose 2 for the efficacy population.

PfizerBioNTech Response
The Sponsor accepts and has updated the information per FDA's request.

See: Supplemental Table *Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population*

Table 56: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI[e])
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI[e])
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

a N = Number of participants in the specified group

b n1 = Number of participants meeting the endpoint definition

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

d n2 = Number of participants at risk for the endpoint

e Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

Subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, geographies, and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior

Commented [A36]: FDA comment
Pfizer,
This general statement is misleading because some of the subgroup analyses were limited by the size of the subgroup and low number of confirmed cases, which limits the interpretation of those analyses. We disagree with this addition and request deletion.

PfizerBioNTech response
Despite the size of the subgroup being limited, the Sponsor proposes retaining this statement as we believe this provides very meaningful information to prescribers about subgroup populations they may be treating.

Commented [A37]: PfizerBioNTech comment The Sponsor accepts the deletion of the word "Updated."

SARS-CoV-2 infection (Table ~~7~~6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table ~~6~~7: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death

a n1 = Number of participants meeting the endpoint definition

b Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

c n2 = Number of participants at risk for the endpoint

d Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

Immunogenicity in Solid Organ Transplant Recipients

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, a single arm study has been conducted in

101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously. A third dose of COMIRNATY was administered to 99 of these individuals approximately 2 months after they had received a second dose. Among the 59 patients who had been seronegative before the third dose, 26 (44%) were seropositive at 4 weeks after the third dose. All 40 patients who had been seropositive before the third dose were still seropositive 4 weeks later. The prevalence of anti-SARS-CoV-2 antibodies was 68% (67 of 99 patients) 4 weeks after the third dose.

Commented [A38]: Pfizer-BioNTech response
The Sponsor proposes addition of this paragraph to section 14 to be consistent with the updates recently made to the EUA labels that FDA granted a LOA for on 12-Aug-2021.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

Commented [A39]: FDA comment:
Pfizer,
Please update this section to include information on the diluent manufactured at the Pfizer Healthcare India site.

Pfizer-BioNTech response
10 mL single-use vial diluent (NDC 0409488810) is registered under NDA 018803 and manufactured in accordance with NDA 018803, including manufacture at both sites in Rocky Mount, NC, USA (site establishment license name "Hospira") and in Andhra Pradesh, India (site establishment license name "Pfizer Healthcare India Pvt. Ltd"). The license holder of NDA 018803 is Hospira, Inc., Lake Forest, Illinois. As such, the proposed USPI is correct as written.

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between ~~80~~90°C to -60°C (~~112°F~~ 130°F to -76°F) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of ~~80~~90°C to -60°C (~~112°F~~ 130°F to -76°F). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

Commented [A40]: Pfizer-BioNTech response
The sponsor has updated the temperature range for ultra cold storage to reflect the long term storage condition filed in the BLA.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90°C to -60°C (-130°F to -76°F). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of ~~80~~90°C to -60°C (~~112°F~~ 130°F to -76°F).

Commented [A41]: Pfizer-BioNTech response
The sponsor has updated the temperature range for ultra cold storage to reflect the long term storage condition filed in the BLA.

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2°C to 8°C (35°F to 46°F)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25°C (77°F)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.
~~calling……~~

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers hhs.gov.

Commented [A42]: FDA comment
Pfizer,
Please see comment in Section 8.1.

PfizerBioNTech response
The Sponsor accepts and has updated this section accordingly.

This product's labeling may have been updated. For the most recent prescribing information, please visit www.comirnatyglobal.com.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.~~3~~4

US Govt. License No. x

Commented [A43]: FDA comment
Pfizer,
Please revise this link to direct to DailyMed.

Pfizer BioNTech response
Pfizer-BioNTech would like to retain the reference to Comimityglobal com in our USPI when referring to a website that contains the most updated version of our labeling. As updates to labeling are typically available more quickly via Comimityglobal com than the posting to Daily Med or http://labels.fda.gov/, referencing the Comimityglobal.com website will ensure that any updates to our labeling will be available to prescribers in the most expedient timeframe.

Commented [A44]: FDA comment
Pfizer,
We acknowledge that two of your labels include CPT codes; however, please delete the CPT code in this label.

Pfizer-BioNTech response
The Sponsor accepts the deletion of the CPT code.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, fever, and injection site swelling. (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, injection site swelling, fever, and injection site redness. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FDA-CBER-2021-5683-0651762

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

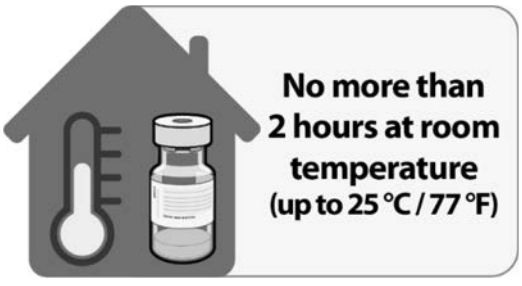
2.1 Preparation for Administration

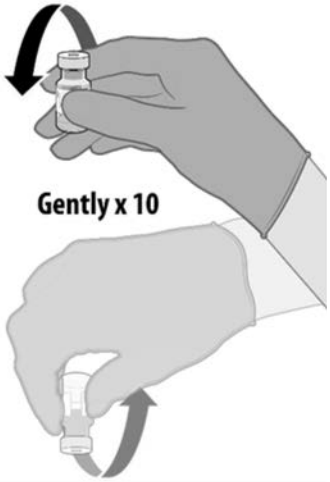
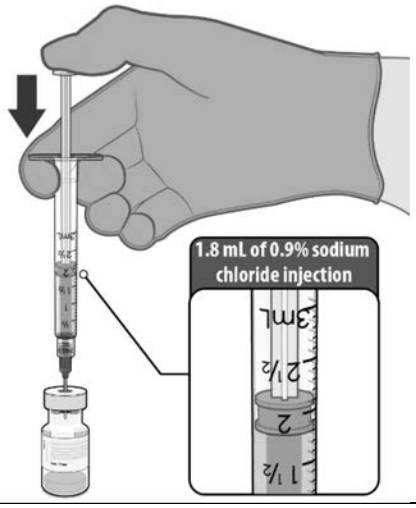
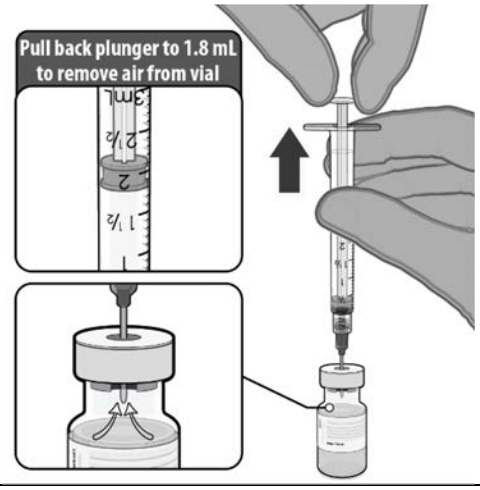
Prior to Dilution

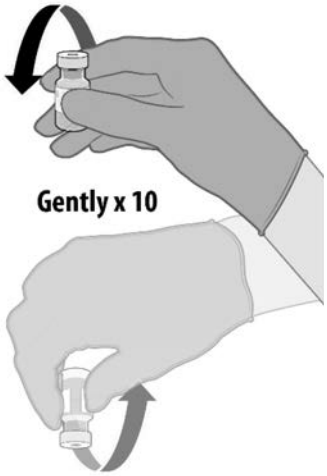
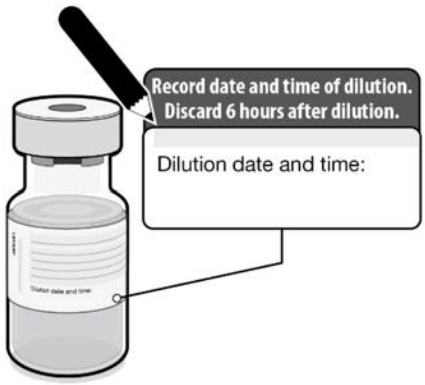
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

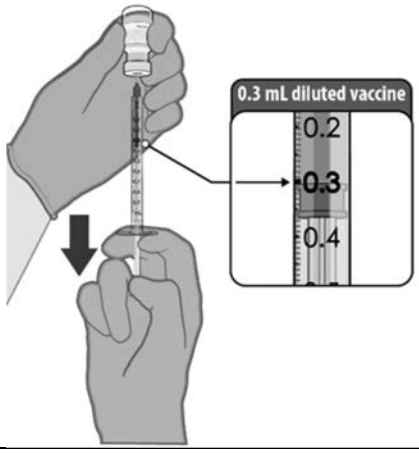
Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not use diluent vials to dilute multiple vials of COMIRNATY.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes.

	• Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.
	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.

	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

A third dose of the COMIRNATY (0.3 mL) administered at least 28 days following the first 2 doses of this vaccine is authorized for administration to individuals at least 16 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk has been highest in adolescent and young adult males under 40 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of

symptoms. Information is not yet available about potential long-term sequelae. The CDC has published considerations for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	**Placebo Dose 1 N[a]=2908 n[b] (%)**	**COMIRNATY Dose 2 N[a]=2682 n[b] (%)**	**Placebo Dose 2 N[a]=2684 n[b] (%)**
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

In clinical studies, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med),* in 99 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported in recipients who were followed for 1 month following post Dose 3.

Unsolicited Adverse Events

Overall 51.1% of participants in the COMIRNATY group and 51.4% of participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 8.1% and 5.9% with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. At the time of the updated efficacy analysis 54.5% of participants originally randomized to COMIRNATY had ≥6 months of follow-up from Dose 2 and 47.5% of original placebo participants had follow-up time between ≥1 month to <2 months after Dose 2 of COMIRNATY. Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Adverse events occurred in 28.8% of vaccine recipients who had a follow-up period of at least 6 months after Dose 2; 1.6% of the recipients had serious adverse events.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant

unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4396 (33.8%) participants who received COMIRNATY and 2136 (16.4%) participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include nonserious adverse events were reported by 2551 (28.6%) participants who received COMIRNATY and 1432 (16.1%) participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 29 (29%) participants who received COMIRNATY and 15 (15%) participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Comirnaty during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

8.6 Immunocompromised Use

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, safety and effectiveness of a third dose of COMIRNATY have been evaluated in persons that received solid organ transplants. The administration of a third dose of vaccine appears to be only moderately effective in increasing potentially protective antibody titers. Patients should still be counselled to maintain physical precautions to help prevent COVID-19. In addition, close contacts of immunocompromised persons should be vaccinated as appropriate for their health status.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials ; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0%. The case split was 8 COVID-19

cases in the BNT162b2 group compared to 162 COVID-19 cases in the placebo group. The 95% credible interval for the vaccine efficacy was 90.3% to 97.6%, indicating that the true vaccine efficacy is at least 90.3% with a 97.5% probability, which met the pre-specified success criterion.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY Na=19,993 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=20,118 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY Na=21,047 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=21,210 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, geographies, and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Immunogenicity in Solid Organ Transplant Recipients

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, a single arm study has been conducted in 101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously. A third dose of COMIRNATY was administered to 99 of these individuals approximately 2 months after they had received a second dose. Among the 59 patients who had been seronegative before the third dose, 26 (44%) were seropositive at 4 weeks after the third dose. All 40 patients who had been seropositive before the third dose were still seropositive 4 weeks later. The prevalence of anti-SARS-CoV-2 antibodies was 68% (67 of 99 patients) 4 weeks after the third dose.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the

re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit www.comirnatyglobal.com.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.4

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

---------- **INDICATIONS AND USAGE** ----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older (1)

---------- **DOSAGE AND ADMINISTRATION** ----------
- For intramuscular injection only (2 2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0 3 mL each) 3 weeks apart (2 3)

---------- **DOSAGE FORMS AND STRENGTHS** ----------
Suspension for injection After preparation, a single dose is 0 3 mL (3)

---------- **CONTRAINDICATIONS** ----------
Known history of a severe allergic reaction (e g , anaphylaxis) to any component of COMIRNATY (4)

---------- **WARNINGS AND PRECAUTIONS** ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose (5 2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY Procedures should be in place to avoid injury from fainting (5 4)

---------- **ADVERSE REACTIONS** ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site ~~(88 6%)~~, fatigue ~~(70 1%)~~, headache ~~(64 9%)~~, muscle pain ~~(45 5%)~~, chills ~~(41 5%)~~, joint pain ~~(27 5%)~~, fever ~~(17 8%)~~, and injection site swelling ~~(10 6%)~~ (6 1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site ~~(78 2%)~~, fatigue ~~(56 9%)~~, headache ~~(45 9%)~~, muscle pain ~~(32 5%)~~, chills ~~(24 8%)~~, joint pain ~~(21 5%)~~, injection site swelling ~~(11 8%)~~, fever ~~(11 5%)~~, and injection site redness ~~(10 4%)~~ (6 1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

2.1 Preparation for Administration

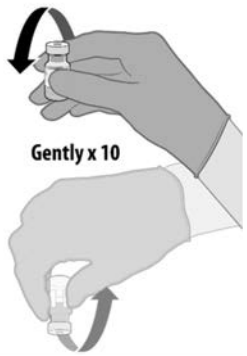
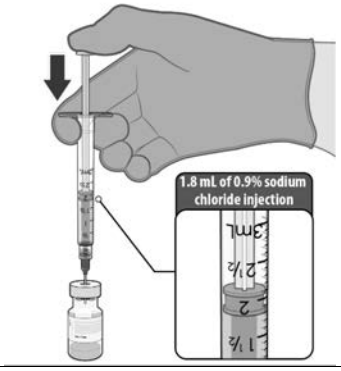
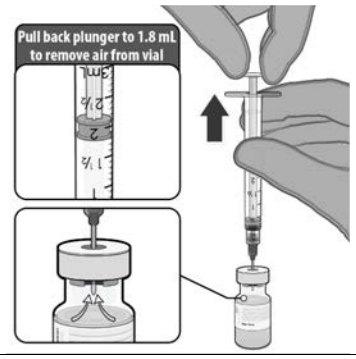
Prior to Dilution

- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

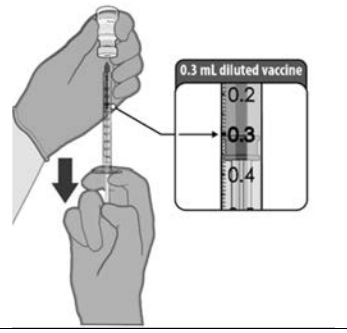
Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not use diluent vials to dilute multiple vials of COMIRNATY.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes.

	• Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.
	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.

	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

A third dose of the COMIRNATY (0.3 mL) administered at least 28 days following the first 2 doses of this vaccine is authorized for administration to individuals at least 16 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk has been highest in adolescent and young adult males under 40 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of

symptoms. Information is not yet available about potential long-term sequelae. The CDC has published considerations for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	**Placebo Dose 1 N[a]=2908 n[b] (%)**	**COMIRNATY Dose 2 N[a]=2682 n[b] (%)**	**Placebo Dose 2 N[a]=2684 n[b] (%)**
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded
a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, this information was included in the column header
b n = Number of participants with the specified reaction
c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm
d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours

f Severity was not collected for use of antipyretic or pain medication

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in participants 56 years of age and older

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, the information was included in the column header

b n = Number of participants with the specified reaction

c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm

d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header

b n = Number of participants with the specified reaction

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea

f Severity was not collected for use of antipyretic or pain medication

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

In clinical studies, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, in 99 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported in recipients who were followed for 1 month following post Dose 3.

Unsolicited Adverse Events

Overall 51.1% of participants in the COMIRNATY group and 51.4% of participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 8.1% and 5.9% with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

~~Upon issuance of the EUA for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY.~~ Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. At the time of the updated efficacy analysis 54.5% of participants originally randomized to COMIRNATY had ≥6 months of follow-up from Dose 2 and 47.5% of original placebo participants had follow-up time between ≥1 month to <2 months after Dose 2 of COMIRNATY. ~~Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began~~

~~in a phased manner for participants in the study.~~ Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Adverse events occurred in 28.8% of vaccine recipients who had a follow-up period of at least 6 months after Dose 2; 1.6% of the recipients had serious adverse events.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) ~~at an incidence rate of 2.1 per 100 person-years among~~ COMIRNATY recipients and 117 (0.9%)~~2.4 per 100 person-years among~~ placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported by 165 (1.8%)~~at an incidence rate of 4.9 per 100 person-years among~~ COMIRNATY recipients and 151 (1.7%)~~4.6 per 100 person-years among~~ placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%)~~at an incidence rate of 6.6 per 100 person-years among~~ COMIRNATY recipients and 2 (2%)~~6.9 per 100 person-years among~~ placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4396 (33.8%)~~at an incidence rate of 88.4 per 100 person- years among~~ participants who received COMIRNATY and 2136 (16.4%)~~43.5 per 100 person-years among~~ participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include nonserious adverse events were reported by 2551 (28.6%)~~at an incidence rate of 75.7 per 100 person-years among~~ participants who received COMIRNATY and 1432 (16.1%)~~43.3 per 100 person-years among~~ participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 29 (29%)~~at an incidence rate of 95.8 per 100 person-years among~~ participants who received COMIRNATY and 15 (15%)~~52.0 per 100 person-years among~~ participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse

events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Comirnaty during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

8.6 Immunocompromised Use

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, safety and effectiveness of a third dose of COMIRNATY have been evaluated in persons that received solid organ transplants. The administration of a third dose of vaccine appears to be only moderately effective in increasing potentially protective antibody titers. Patients should still be counselled to maintain physical precautions to help prevent COVID-19. In addition, close contacts of immunocompromised persons should be vaccinated as appropriate for their health status.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials ; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY

contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

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Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.35% were male and 48.6% or 49.75% were female, ~~75~~79.1% or ~~75~~79.21% were 16 through 64 years of age, 20.91% or 20.83% were 65 years of age and older, ~~16.1% or 16.3% were 65 through 74 years of age, 4.0% or 4.0% 75 years of age and~~

~~older, 82~~81.9% or 82.1% were White, ~~9~~8.5% or ~~9~~8.6% were Black or African American, ~~0.9~~1.0% or 0.9% were American Indian or Alaska Native, 4.~~4~~6% or 4.~~3~~5% were Asian, 0.3% or 0.~~1~~2% Native Hawaiian or other Pacific Islander, 2~~5~~4.~~9~~6% or 2~~5~~4.~~4~~6% were Hispanic/Latino, 7~~3~~4.~~6~~9% or 74.~~1~~8% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 4~~4~~6.~~6~~0% or 4~~5~~4.~~7~~4% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 4~~9~~8.~~8~~3 or 4~~9~~8.~~7~~2 years and median age was 5~~1~~0.0 or 5~~1~~0.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

~~The vaccine efficacy information is presented in Table 5.~~

~~**Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population**~~

~~**First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection***~~			
~~**Subgroup**~~	~~**COMIRNATY N[a]=18,198 Cases n1[b] Surveillance Time[c] (n2[d])**~~	~~**Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])**~~	~~**Vaccine Efficacy % (95% CI)**~~
~~All participants[e]~~	~~8 2.214 (17,411)~~	~~162 2.222 (17,511)~~	~~95.0 (90.3, 97.6)[f]~~
~~16 to 64 years~~	~~7 1.706 (13,549)~~	~~143 1.710 (13,618)~~	~~95.1 (89.6, 98.1)[g]~~
~~65 years and older~~	~~1 0.508 (3848)~~	~~19 0.511 (3880)~~	~~94.7 (66.7, 99.9)[g]~~
~~65 to 74 years~~	~~1 0.406 (3074)~~	~~14 0.406 (3095)~~	~~92.9 (53.1, 99.8)[g]~~
~~75 years and older~~	~~0 0.102 (774)~~	~~5 0.106 (785)~~	~~100.0 (-13.1, 100.0)[g]~~
~~**First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection**~~			
~~**Subgroup**~~	~~**COMIRNATY N[a]=19,965 Cases n1[b] Surveillance Time[c] (n2[d])**~~	~~**Placebo N[a]=20,172 Cases n1[b] Surveillance Time[c] (n2[d])**~~	~~**Vaccine Efficacy % (95% CI)**~~
~~All participants[e]~~	~~9~~	~~169~~	~~94.6~~

	2.332 (18,559)	2.345 (18,708)	(89.9, 97.3)[f]
16 to 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1 0.530 (4044)	19 0.532 (4067)	94.7 (66.8, 99.9)[g]
65 to 74 years	1 0.424 (3239)	14 0.423 (3255)	92.9 (53.2, 99.8)[g]
75 years and older	0 0.106 (805)	5 0.109 (812)	100.0 (12.1, 100.0)[g]

Note: Confirmed cases were determined by Reverse Transcription Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. No confirmed cases were identified in participants 12 to 15 years of age.

f. Two-sided credible interval for vaccine efficacy was calculated using a beta-binomial model with a beta (0.700102, 1) prior for θ=r(1-VE)/(1+r(1-VE)), where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.

g. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0%. The case split was 8 COVID-19 cases in the BNT162b2 group compared to 162 COVID-19 cases in the placebo group. The 95% credible interval for the vaccine efficacy was 90.3% to 97.6%, indicating that the true vaccine efficacy is at least 90.3% with a 97.5% probability, which met the pre-specified success criterion.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

The updated vaccine efficacy information is presented in Table 5~~6~~.

Table 5~~6~~: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY Na=19,993 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=20,118 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
All participantsf	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY Na=21,047 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=21,210 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

a N = Number of participants in the specified group

b n1 = Number of participants meeting the endpoint definition

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

d n2 = Number of participants at risk for the endpoint

e Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

Subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, geographies, and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior

SARS-CoV-2 infection (Table ~~7~~6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table ~~6~~7: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death

a n1 = Number of participants meeting the endpoint definition

b Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

c n2 = Number of participants at risk for the endpoint

d Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

Immunogenicity in Solid Organ Transplant Recipients

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, a single arm study has been conducted in

101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously. A third dose of COMIRNATY was administered to 99 of these individuals approximately 2 months after they had received a second dose. Among the 59 patients who had been seronegative before the third dose, 26 (44%) were seropositive at 4 weeks after the third dose. All 40 patients who had been seropositive before the third dose were still seropositive 4 weeks later. The prevalence of anti-SARS-CoV-2 antibodies was 68% (67 of 99 patients) 4 weeks after the third dose.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -8090ºC to -60ºC (-112ºF 130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -8090ºC to -60ºC (-112ºF 130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -8090ºC to -60ºC (-112ºF 130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.
~~calling …..~~

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit www.comirnatyglobal.com.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.~~3~~4

US Govt. License No. x

Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=21047) n[b] (%)	Placebo (N[a]=21210) n[b] (%)	Total (N[a]=42257) n[b] (%)
Subjects (%) with length of follow-up of:			
Original blinded placebo-controlled follow-up period			
<2 Months	840 (4.0)	910 (4.3)	1750 (4.1)
≥2 Months to <4 months	7411 (35.2)	7851 (37.0)	15262 (36.1)
≥4 Months to <6 months	11031 (52.4)	11158 (52.6)	22189 (52.5)
≥6 Months	1765 (8.4)	1291 (6.1)	3056 (7.2)

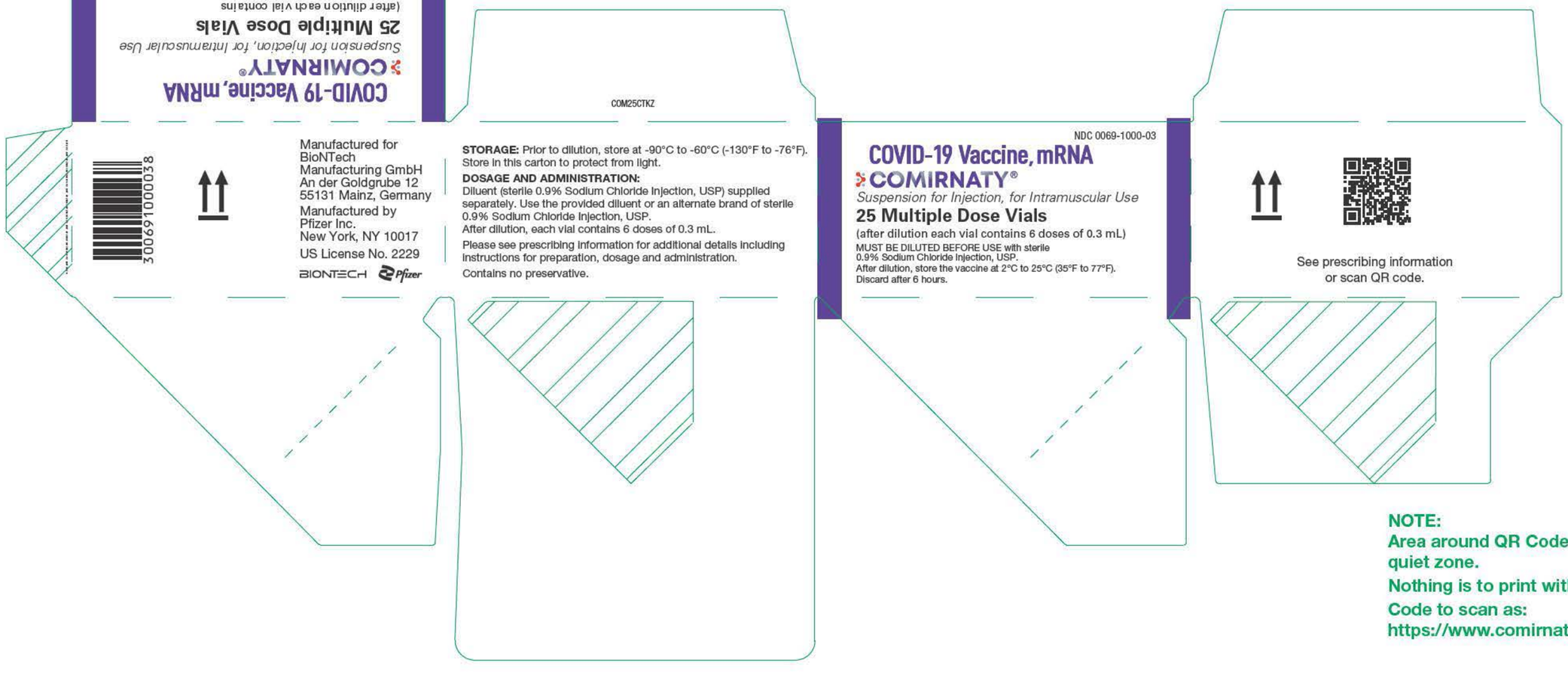
Note: Human immunodeficiency virus (HIV)-positive subjects are not included in this summary.
a. N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.
b. n = Number of subjects with the specified characteristic.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 13AUG2021 (16:37)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA_RR/adsl_fu_d2_p3_nohiv_ge16_eval

NOTE - expiry format:
EXP: MM/YYYY

Comirnaty 25ct Carton - Kzoo COM25CTKZ 22P August 16, 2021 am

Black PMS 7671 PMS 2162 PMS 7597

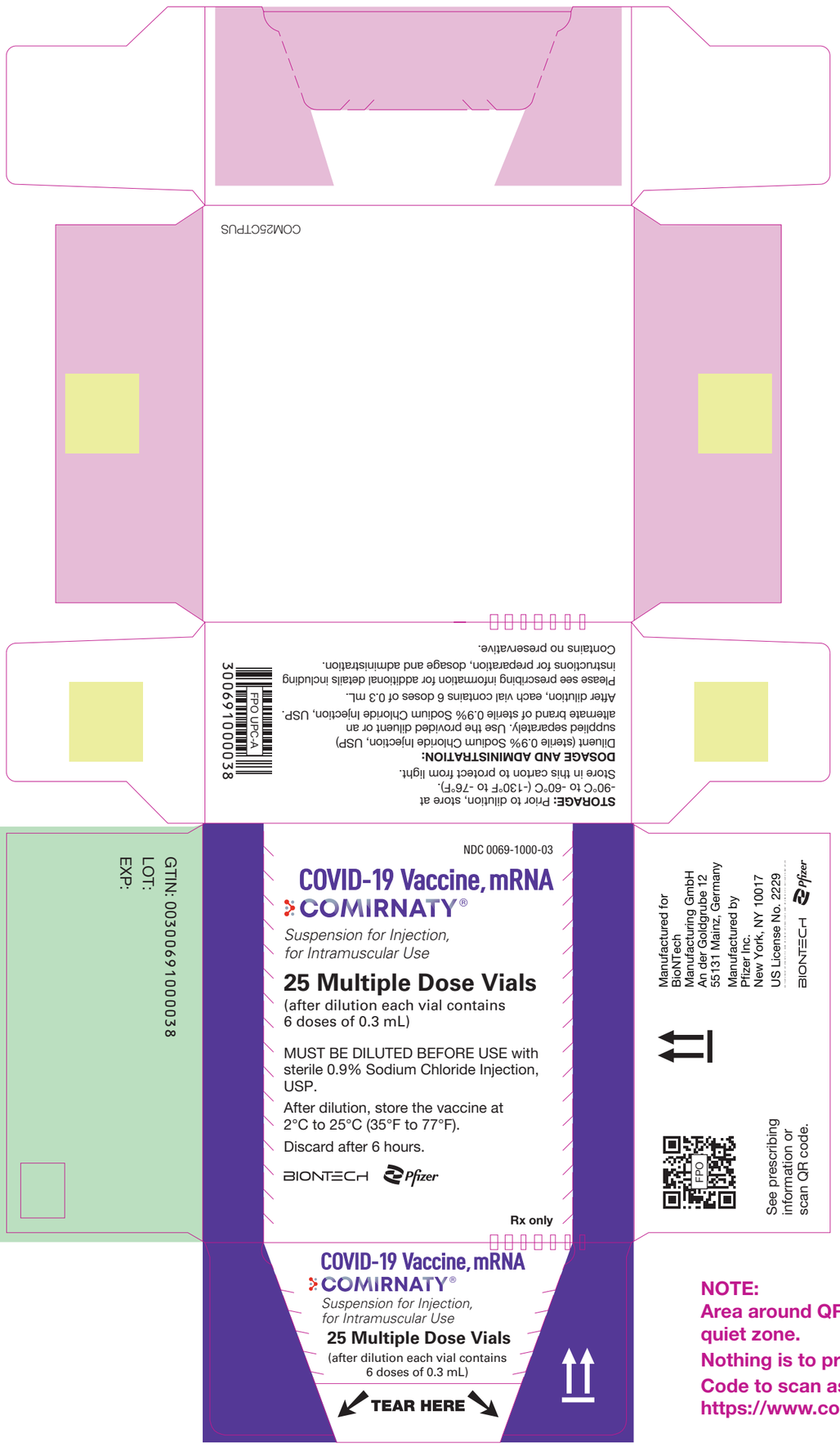
Minimum point size - 6pt.



NOTE:
Area around QR Code is a required quiet zone.
Nothing is to print within this space.
Code to scan as:
https://www.comirnatyglobal.com

Black PMS 7671 PMS 2162 PMS 7597

Minimum point size - 7pt.



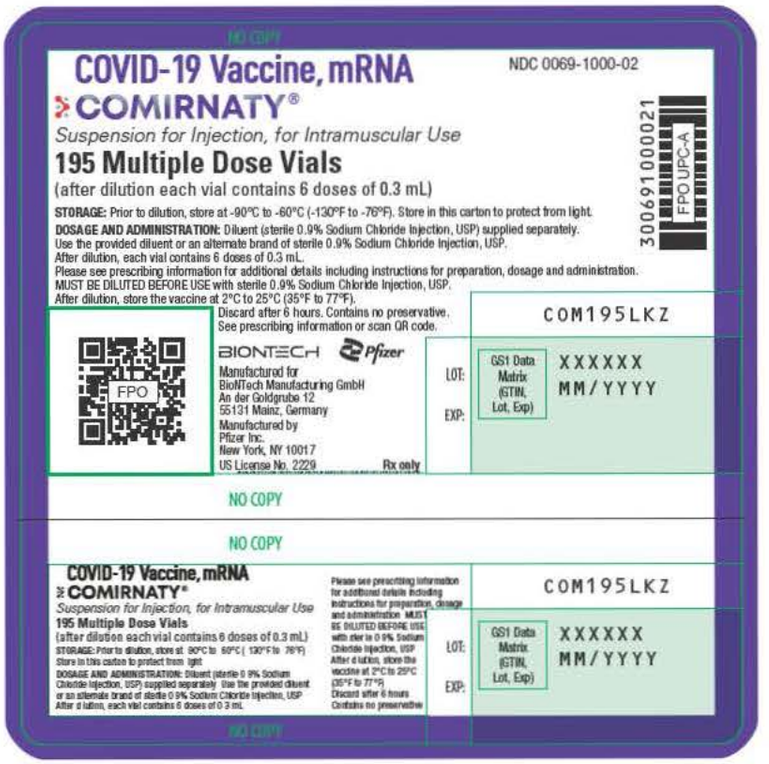
NOTE:
Area around QR Code is a required quiet zone.
Nothing is to print within this space.
Code to scan as:
https://www.comirnatyglobal.com

Comirnaty Carton Label - Kzoo COM195LKZ 21P August 16, 2021 am

Black PMS 7671 PMS 2162 PMS 7597

Minimum point size - 4pt.

NOTE:
Area around QR Code is a required quiet zone.
Nothing is to print within this space.
Code to scan as:
https://www.comirnatyglobal.com

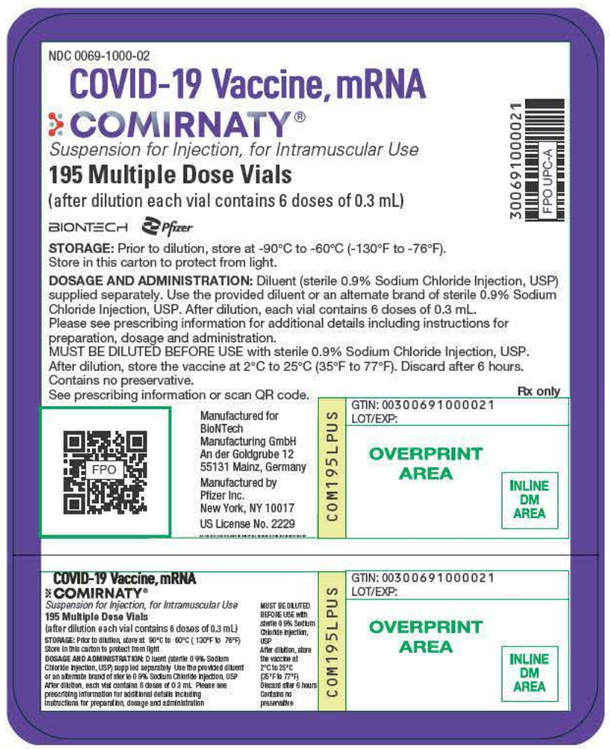


NOTE - expiry format:
EXP: MM/YYYY

GTIN: 00300691000021

Comirnaty Carton Label COM195LPUS - Puurs 20P August 16, 2021 am

Black PMS 7671 PMS 2162 PMS 7597



NOTE - expiry format:
EXP: MM/YYYY

NOTE:
Area around QR Code is a required quiet zone.
Nothing is to print within this space.
Code to scan as:
https://www.comirnatyglobal.com

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY* (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

INDICATIONS AND USAGE
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older (1)

DOSAGE AND ADMINISTRATION
- For intramuscular injection only (2 2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0 3 mL each) 3 weeks apart (2 3)

DOSAGE FORMS AND STRENGTHS
Suspension for injection After preparation, a single dose is 0 3 mL (3)

CONTRAINDICATIONS
Known history of a severe allergic reaction (e g , anaphylaxis) to any component of COMIRNATY (4)

WARNINGS AND PRECAUTIONS
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose (5 2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY Procedures should be in place to avoid injury from fainting (5 4)

ADVERSE REACTIONS
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88 6%), fatigue (70 1%), headache (64 9%), muscle pain (45 5%), chills (41 5%), joint pain (27 5%), fever (17 8%), and injection site swelling (10 6%) (6 1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78 2%), fatigue (56 9%), headache, (45 9%), muscle pain (32 5%), chills (24 8%), joint pain (21 5%), injection site swelling (11 8%), fever (11 5%), and injection site redness (10 4%) (6 1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed

Commented [A1]: FDA Comment
Pfizer,
Please add the percentages as we previously requested. Without the percentages, stating the frequencies ≥10% is misleading.

Commented [A2R1]: Pfizer-BioNTech response
The Sponsor accepts.

Commented [A3]: The Sponsor accepts the deletion of "Immunocompromised Use."

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

2.1 Preparation for Administration

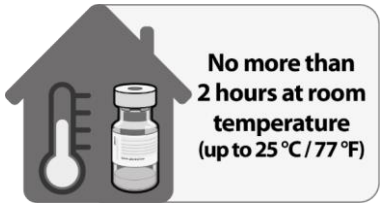
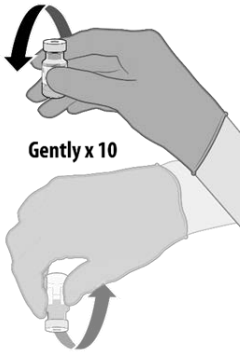
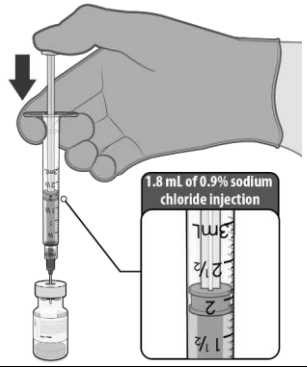
Prior to Dilution

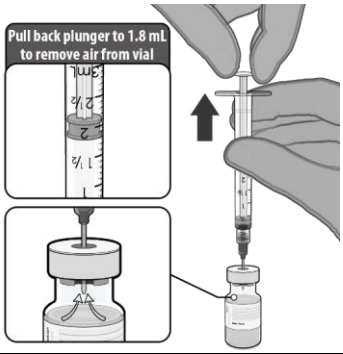
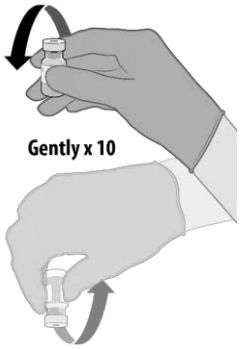
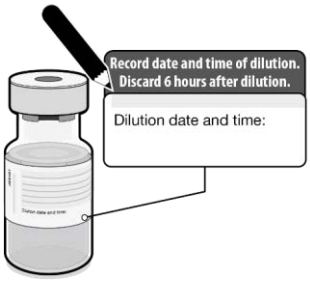
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2°C to 8°C (35°F to 46°F)] or at room temperature [up to 25°C (77°F)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

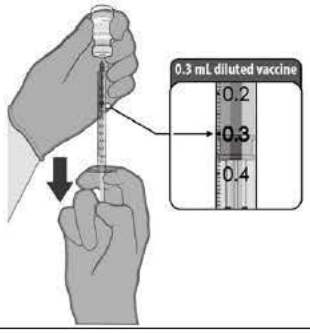
Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

Commented [A4]: Pfizer-BioNTech comment
The Sponsor accepts this revision.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

Commented [A5]: The Sponsor accepts the deletion of text regarding a third dose in immunocompromised individuals.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

Commented [A6]: Pfizer-BioNTech comment
The Sponsor will accept, but disagrees with the characterization of the observed risk as established.

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization ~~EUA~~ (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

Commented [A7]: Pfizer-BioNTech comment
The Sponsor accepts the revisions to this paragraph with a minor editorial change.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm

d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours

f Severity was not collected for use of antipyretic or pain medication

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in participants 56 years of age and older

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, the information was included in the column header

b n = Number of participants with the specified reaction

c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm

d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header

b n = Number of participants with the specified reaction

	COMIRNATY Dose 1 N^a=2008 n^b (%)	Placebo Dose 1 N^a=1989 n^b (%)	COMIRNATY Dose 2 N^a=1860 n^b (%)	Placebo Dose 2 N^a=1833 n^b (%)

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea

f Severity was not collected for use of antipyretic or pain medication

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

In clinical studies, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

Unsolicited adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and

Commented [A8]: FDA comment
Pfizer, This is a mixture of list of solicited and unsolicited adverse reactions. Some of these are captured in the tables above and others that we consider adverse reactions are presented below.

Commented [A9R8]: Pfizer-BioNTech comment
The Sponsor proposes to retain this text. The following adverse vaccine reactions do not appear anywhere else in the label: malaise, asthenia, lethargy, hyperhidrosis, nausea, decreased appetite, night sweats. All of these adverse vaccine reactions appeared in placebo-controlled clinical trials.

Commented [A10]: The Sponsor accepts the deletion of text regarding a third dose in immunocompromised individuals.

Commented [A11]: Pfizer-BioNTech comment
The Sponsor accepts this revision:

Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Table 9.*

Commented [A12]: FDA comment
Pfizer, We agree that presentation of the number of participants who originally received vaccine and had total follow up time for at least 6 months should be displayed.

We disagree with the addition of follow up time for placebo recipients who received vaccine as safety data from the unblinded follow up time is not being displayed.

Commented [A13R12]: Pfizer-BioNTech comment
The Sponsor accepts.

Commented [A14]: Pfizer-BioNTech comment
The Sponsor accepts this revision.

Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Table 9.*

Commented [A15]: Pfizer-BioNTech response
The sponsor accepts this deletion

Commented [A16]: Pfizer-BioNTech response
The Sponsor accepts the revisions to this paragraph.

thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4,396 (33.8%) participants who received COMIRNATY and 2,136 (16.4%) participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), all events, which include nonserious adverse events were reported by 2,551 (28.6%) participants who received COMIRNATY and 1,432 (16.1%) participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 29 (29%) participants who received COMIRNATY and 15 (15%) participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Commented [A17]: Pfizer-BioNTech response
The Sponsor accepts the revisions to this paragraph.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Commented [A18]: Pfizer-BioNTech response
The Sponsor accepts moving this text to the beginning of the section.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on ~~four~~1 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

Commented [A19]: Pfizer-BioNTech response
The Sponsor accepts the deletion of text regarding a third dose in immunocompromised individuals.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

Commented [A20]: Pfizer-BioNTech comment
The Sponsor accepts the revisions to this paragraph.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

Commented [A21]: Pfizer-BioNTech comment
The Sponsor accepts this addition.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI[e])
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI[e])
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

a N = Number of participants in the specified group

b n1 = Number of participants meeting the endpoint definition

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

d n2 = Number of participants at risk for the endpoint

e Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

Subgroup analyses of the primary efficacy endpoint (although some subgroups had limited numbers of participants) showed similar efficacy point estimates across genders, ethnic groups, geographies, and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

Commented [A22]: FDA comment
Pfizer,
We reiterate that this general statement is misleading because some of the subgroup analyses were limited by the size of the subgroup and low number of confirmed cases, which limits the interpretation of those analyses. We disagree with this addition and again request deletion.

Commented [A23R22]: Pfizer-BioNTech comment
The Sponsor believes this paragraph should be retained with a modification to address FDA's concern as it contains accurate and meaningful information for prescribers as indicated by the robust discussion about subgroups at the EUA VRBPAC. In addition, the language regarding similar efficacy across these subgroups is critical to the vaccine uptake especially in minority communities. The clinical trials were developed and executed with the specific goal to have diverse populations with regard to sex, race, ethnicity and comorbidities. Except for a few subgroups (i.e., Turkey Germany) with a small number of cases, the vast majority of the subgroups have a substantial number of cases (e.g., more than 600 cases in both the US and the Non-Hispanic/Non-Latino subgroups) and have high point estimates with 95% confidence intervals that are well above 0.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death

a n1 = Number of participants meeting the endpoint definition

b Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period
c n2 = Number of participants at risk for the endpoint
d Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/ or www.comirnatyglobal.com

Commented [A25]: FDA comment
Pfizer, We do not agree. We continue to request that you revise this link to direct to DailyMed.

Commented [A26R25]: Pfizer-BioNTech comment
The inclusion of this information is consistent with other FDA-approved labels. The Sponsor proposes to include both the DailyMed and Comirnaty Global links.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.5

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HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

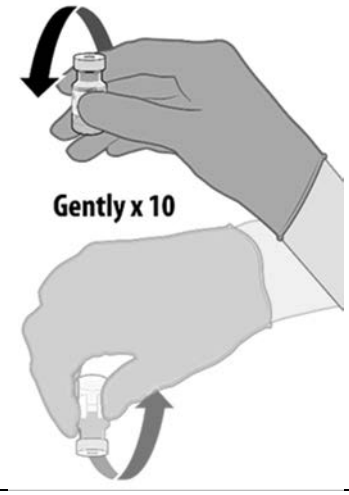
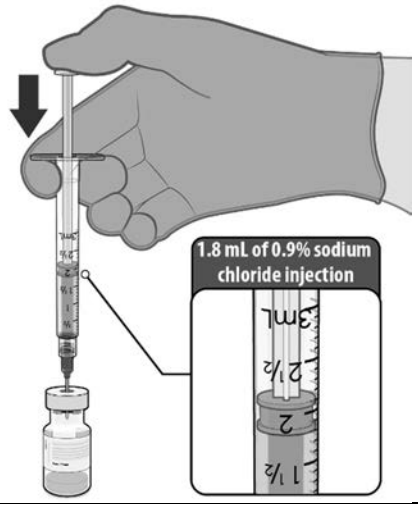
2.1 Preparation for Administration

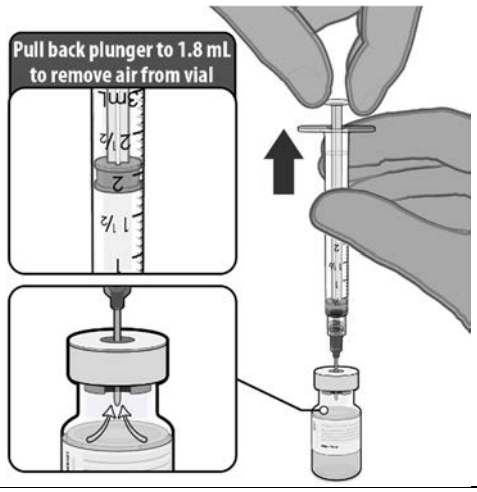
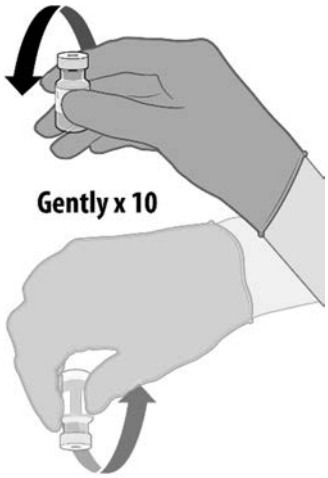
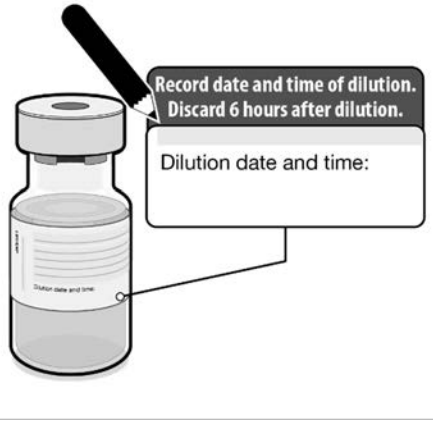
Prior to Dilution

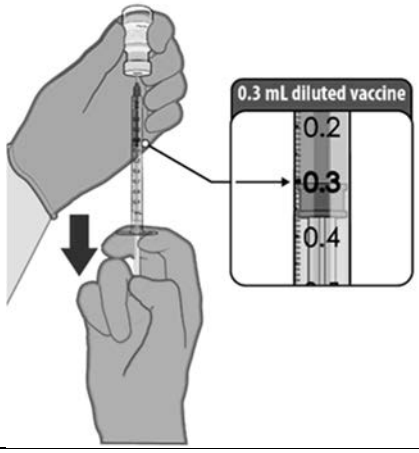
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

In clinical studies, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

Unsolicited adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded

follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4,396 (33.8%) participants who received COMIRNATY and 2,136 (16.4%) participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), all events, which include nonserious adverse events were reported by 2,551 (28.6%) participants who received COMIRNATY and 1,432 (16.1%) participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 29 (29%) participants who received COMIRNATY and 15 (15%) participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were

immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) $\geq$30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for $\geq$4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of the primary efficacy endpoint (although some subgroups had limited numbers of participants) showed similar efficacy point estimates across genders, ethnic groups, geographies, and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior

SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium

Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/ or www.comirnatyglobal.com.

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Manufactured for
BioNTech Manufacturing GmbH
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Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

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US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

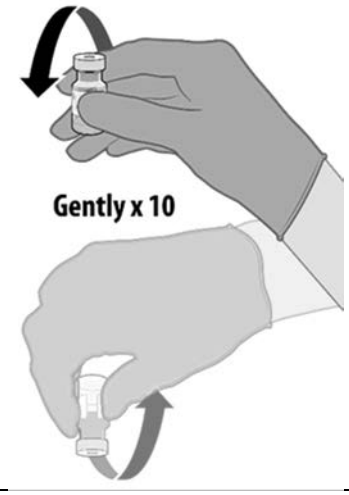
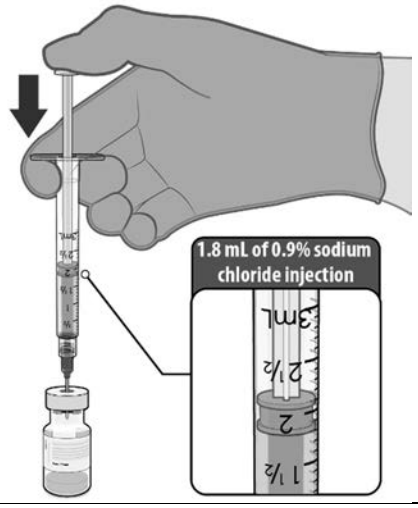
2.1 Preparation for Administration

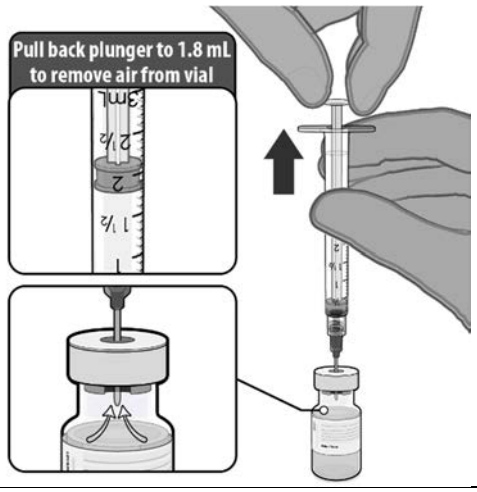
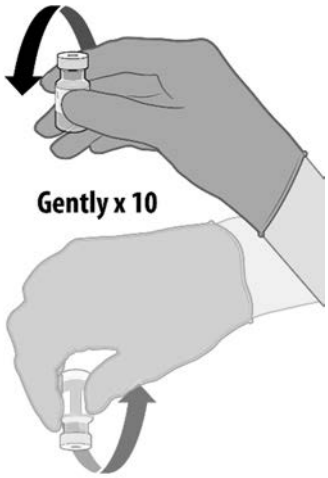
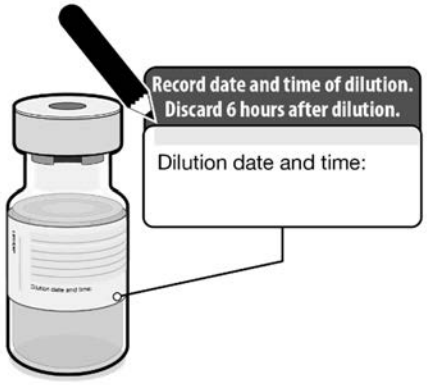
Prior to Dilution

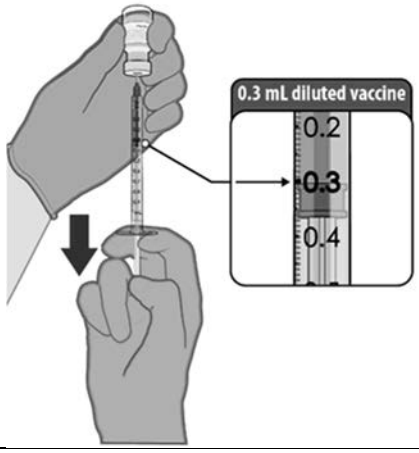
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization ~~EUA~~ (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

In clinical studies, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

Unsolicited adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and

thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4,396 (33.8%) participants who received COMIRNATY and 2,136 (16.4%) participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo- = -8,895), all events, which include nonserious adverse events were reported by 2,551 (28.6%) participants who received COMIRNATY and 1,432 (16.1%) participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 29 (29%) participants who received COMIRNATY and 15 (15%) participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on ~~four~~4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY Na=19,993 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=20,118 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY Na=21,047 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=21,210 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of the primary efficacy endpoint (although some subgroups had limited numbers of participants) showed similar efficacy point estimates across genders, ethnic groups, geographies, and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.

b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/ or www.comirnatyglobal.com.

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Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.5

US Govt. License No. x

NOTE - expiry format:
EXP: MM/YYYY

Comirnaty 25ct Carton - Kzoo COM25CTKZ 22P August 16, 2021 am

Black PMS 7671 PMS 2162 PMS 7597

Minimum point size - 6pt.

LOT/EXP:

GTIN: 30069100003 8

Rx only

BIONTECH Pfizer

MUST BE DILUTED BEFORE USE with
sterile 0.9% Sodium Chloride Injection, USP.
After dilution, store the vaccine at
2°C to 25°C (35°F to 77°F).
Discard after 6 hours.

25 Multiple Dose Vials

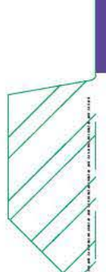
(after dilution each vial contains
6 doses of 0.3 mL)

Suspension for Injection, for Intramuscular Use

COMIRNATY®

COVID-19 Vaccine, mRNA

COM25CTKZ



Manufactured for
BioNTech
Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany
Manufactured by
Pfizer Inc.
New York, NY 10017
US License No. 2229

BIONTECH Pfizer

STORAGE: Prior to dilution, store at -90°C to -60°C (-130°F to -76°F). Store in this carton to protect from light.

DOSAGE AND ADMINISTRATION:
Diluent (sterile 0.9% Sodium Chloride Injection, USP) supplied separately. Use the provided diluent or an alternate brand of sterile 0.9% Sodium Chloride Injection, USP.
After dilution, each vial contains 6 doses of 0.3 mL.

Please see prescribing information for additional details including instructions for preparation, dosage and administration.

Contains no preservative.

NDC 0069-1000-03

COVID-19 Vaccine, mRNA

COMIRNATY®

Suspension for Injection, for Intramuscular Use

25 Multiple Dose Vials

(after dilution each vial contains 6 doses of 0.3 mL)

MUST BE DILUTED BEFORE USE with sterile 0.9% Sodium Chloride Injection, USP.
After dilution, store the vaccine at 2°C to 25°C (35°F to 77°F).
Discard after 6 hours.

See prescribing information or scan QR code.

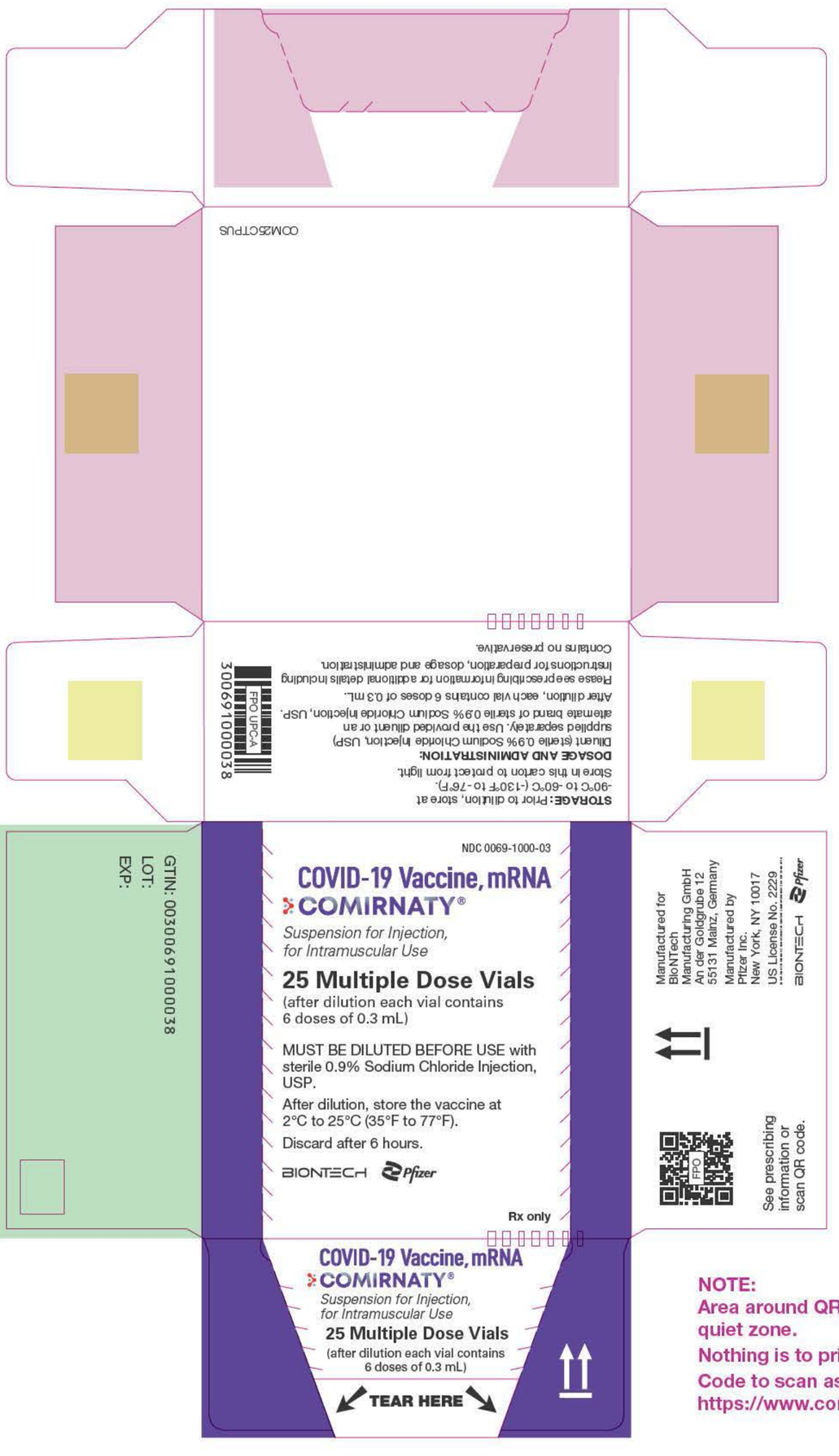
NOTE:
Area around QR Code is a required quiet zone.
Nothing is to print within this space.
Code to scan as:
https://www.comirnatyglobal.com

FDA-CBER-2021-5683-0651873

Comirnaty 25ct Carton COM25CTPUS - Puurs 20P August 16, 2021 am

Black PMS 7671 PMS 2162 PMS 7597

Minimum point size - 7pt.



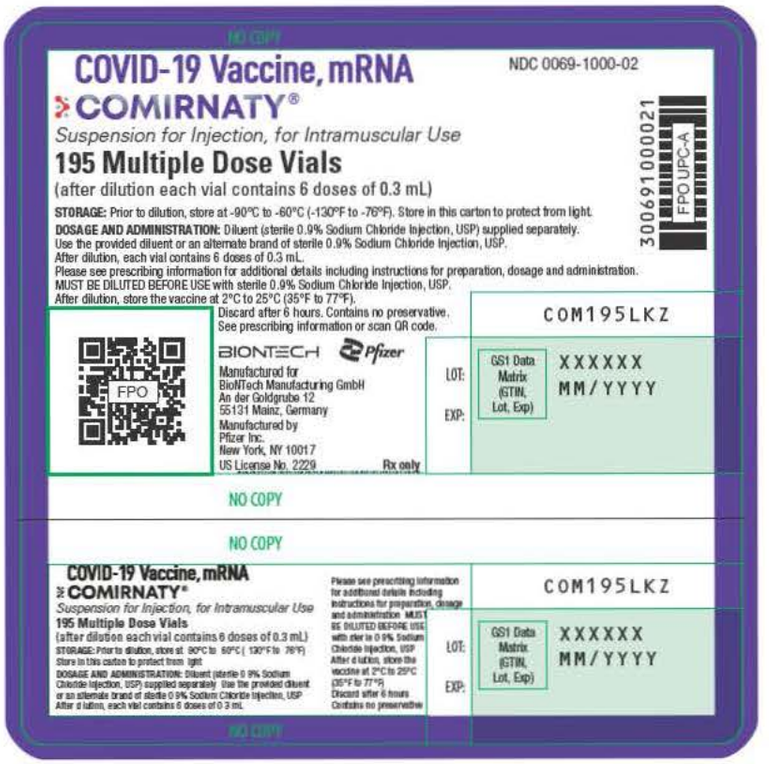
NOTE:
Area around QR Code is a required quiet zone.
Nothing is to print within this space.
Code to scan as:
https://www.comirnatyglobal.com

Comirnaty Carton Label - Kzoo COM195LKZ 21P August 16, 2021 am

Black PMS 7671 PMS 2162 PMS 7597

Minimum point size - 4pt.

NOTE:
Area around QR Code is a required quiet zone.
Nothing is to print within this space.
Code to scan as:
https://www.comirnatyglobal.com



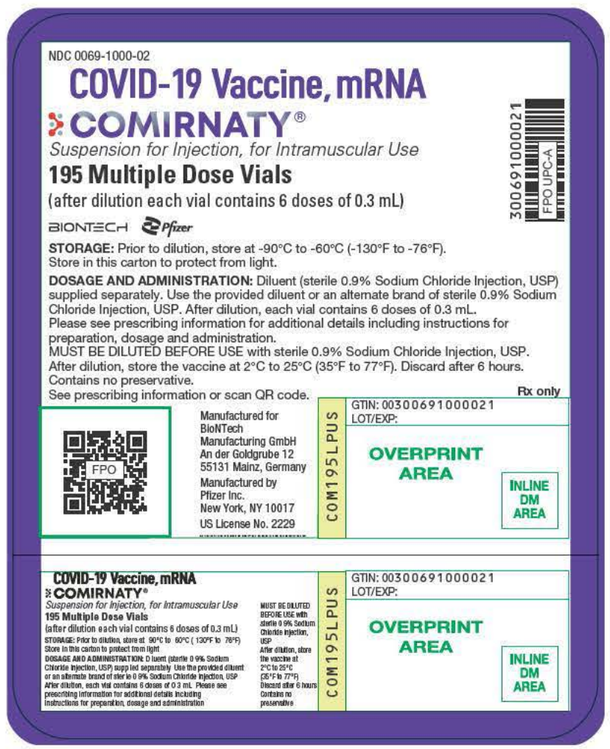
NOTE - expiry format:
EXP: MM/YYYY

GTIN: 00300691000021

090177e197d3482b\Approved\Approved On: 17-Aug-2021 04:36 (GMT)

Comirnaty Carton Label COM195LPUS - Puurs 20P August 16, 2021 am

Black PMS 7671 PMS 2162 PMS 7597



NOTE - expiry format:
EXP: MM/YYYY

NOTE:
Area around QR Code is a required quiet zone.
Nothing is to print within this space.
Code to scan as:
https://www.comirnatyglobal.com

Comirnaty Label - Kzoo COMVLABKZ 18P August 11, 2021 am

Black PMS 7671

Body text point size - 3.3pt.

NOTE - expiry format:
EXP: MM/YYYY

GS1 DataBar Code Scans as:
(01)10300691000011

Comirnaty Label COMVLABP - Puurs 18P August 11, 2021 am
Black PMS 7671

Body text point size - 3.3pt.

NOTE - expiry format:
EXP: MM/YYYY

GS1 DataBar Code Scans as:
(01)10300691000011

Comirnaty Diluent Label 4P Aug 11, 2021 am

Black PMS 7671 PMS 2162 PMS 7597

(label size: 1.25" x 2.75")

Diluent For Use With

COVID-19 Vaccine, mRNA

COMIRNATY®

Please see the COMIRNATY® prescribing information for preparation, dosage and administration supplied separately.

COMDILRM

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only (2 2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0 3 mL each) 3 weeks apart (2 3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection After preparation, a single dose is 0 3 mL (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e g , anaphylaxis) to any component of COMIRNATY (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose (5 2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY Procedures should be in place to avoid injury from fainting (5 4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88 6%), fatigue (70 1%), headache (64 9%), muscle pain (45 5%), chills (41 5%), joint pain (27 5%), fever (17 8%), and injection site swelling (10 6%) (6 1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78 2%), fatigue (56 9%), headache, (45 9%), muscle pain (32 5%), chills (24 8%), joint pain (21 5%), injection site swelling (11 8%), fever (11 5%), and injection site redness (10 4%) (6 1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

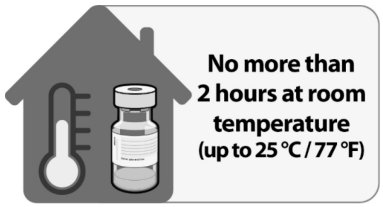
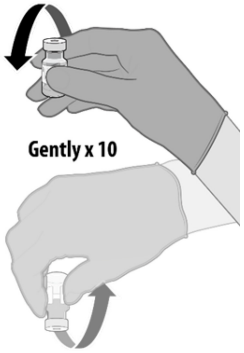
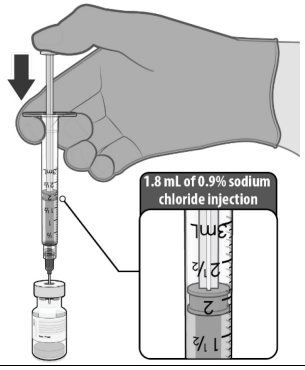
2.1 Preparation for Administration

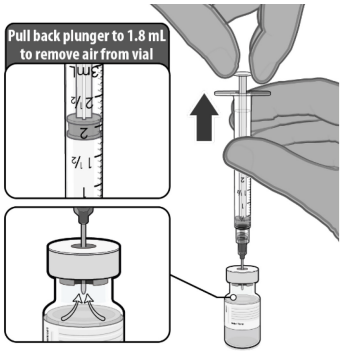
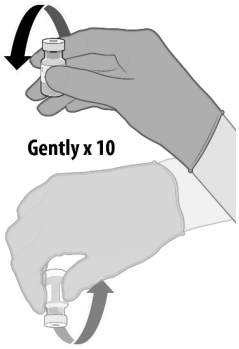
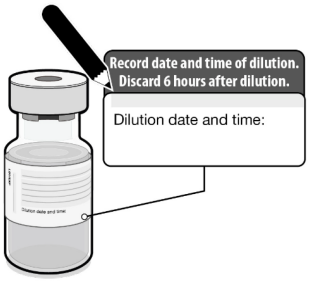
Prior to Dilution

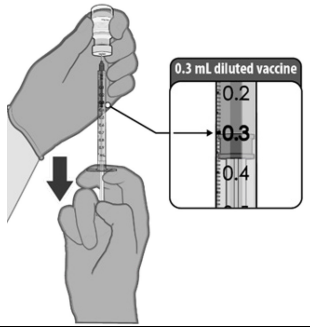
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • Do not shake. • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm

d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours

f Severity was not collected for use of antipyretic or pain medication

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in participants 56 years of age and older

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, the information was included in the column header

b n = Number of participants with the specified reaction

c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm

d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header

b n = Number of participants with the specified reaction

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea

f Severity was not collected for use of antipyretic or pain medication

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

~~In clinical studies, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).~~

~~In clinical studies, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).~~

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

Unsolicited adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded

Commented [A1]: FDA comment

Pfizer, The events not contained in the Tables 1-4 above were not solicited, thus they should be categorized correctly and moved into the discussion of Non-Serious Unsolicited Adverse Events, below, using a format consistent with presentation of those events, by treatment arm and follow-up time period. Events discussed elsewhere should not be included (lymphadenopathy, injection site redness).

Commented [A2R1]:
Pfizer-BioNTech response
The Sponsor accepts and has provided the follow-up period and treatment arm data in the Non Serious Adverse Event section below.

Source:

Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Tables 14.86 and 14.87

follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Among the total participants who received COMIRNATY or placebo 1 month after Dose 2, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were nausea (1.4% or 0.5%), malaise (0.7% or 0.1%), asthenia (0.4% or 0.1%), decreased appetite (0.2% or 0.0%), hyperhidrosis (0.1% or 0.0%), lethargy (0.1% or 0.0%), and night sweats (0.1% or 0.0%).

Among the total participants who received COMIRNATY or placebo 1 month after Dose 2, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0% or 0.3%), malaise (0.5% or 0.1%), asthenia (0.3% or 0.1%), lethargy (0.2% or 0.0%), decreased appetite (0.1% or 0.0%), hyperhidrosis (0.1% or 0.0%), and night sweats (0.1% or 0.0%).

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4,396 (33.8%) participants who received COMIRNATY and 2,136 (16.4%) participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), all events, which include nonserious adverse events were reported by 2,551 (28.6%) participants who received COMIRNATY and 1,432 (16.1%) participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 29 (29%) participants who received COMIRNATY and 15 (15%) participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including

Commented [A3]: FDA comment

Pfizer, The events not contained in the Tables 1-4 above were not solicited, thus they should be categorized correctly and moved into the discussion of Non-Serious Unsolicited Adverse Events, below, using a format consistent with presentation of those events, by treatment arm and follow-up time period. Events discussed elsewhere should not be included (lymphadenopathy, injection site redness).

Pfizer-BioNTech response
The Sponsor accepts and has provided the follow-up period and treatment arm data.

Source:

Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Tables 14.86 and 14.87

under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

a N = Number of participants in the specified group

b n1 = Number of participants meeting the endpoint definition

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

d n2 = Number of participants at risk for the endpoint

e Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, and participants with obesity and medical comorbidities associated with high risk of severe COVID-19.

Commented [A4]: FDA comment

Pfizer,
Please see our revised statement regarding subgroup analyses off vaccine efficacy.

Commented [A5R4]: Pfizer-BioNTech response
The Sponsor accepts the FDA's revision to this paragraph.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death

a n1 = Number of participants meeting the endpoint definition

b Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period
c n2 = Number of participants at risk for the endpoint
d Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed nlm nih.gov/dailymed/.

Commented [A6]: FDA comment

Pfizer,
We continue to request to only provide a link to DailyMed as this is sufficient. Furthermore, the other site may contain elements that are promotional and have not been reviewed by FDA.

Commented [A7R6]: Pfizer-BioNtech response
The Sponsor will comply but we reiterate our concern that there is a delay with labels being posted to DailyMed and we believe that including both websites will allow providers to obtain information about our product as quickly as possible. This is consistent with Pfizer's other approved labels and no objections have been raised. The Sponsor plans to revisit this discussion with the next labeling supplement post-approval.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.6~~5~~

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27 5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21 5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FDA-CBER-2021-5683-0651901

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

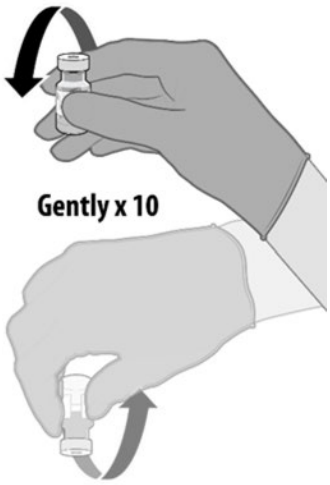
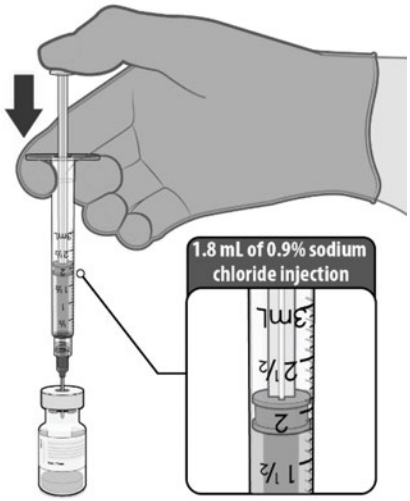
2.1 Preparation for Administration

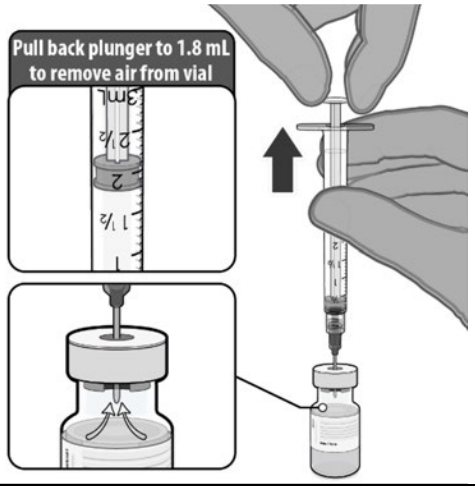
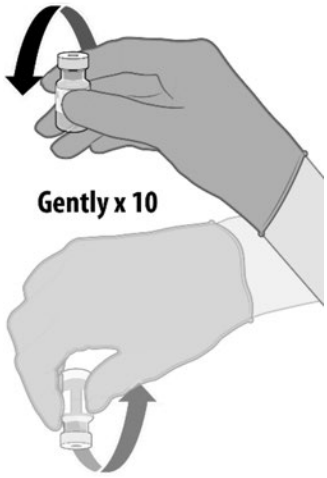
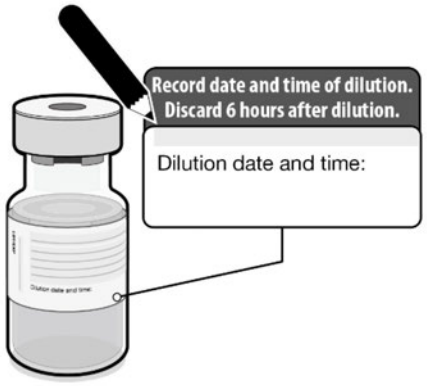
Prior to Dilution

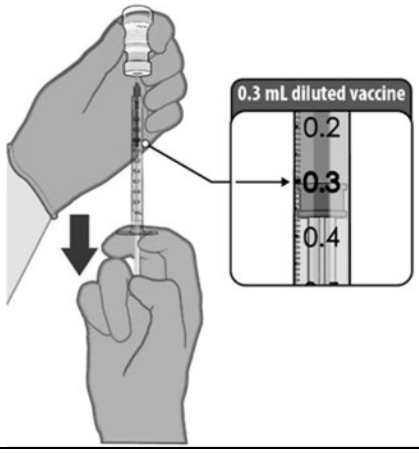
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N^a=2008 n^b (%)	Placebo Dose 1 N^a=1989 n^b (%)	COMIRNATY Dose 2 N^a=1860 n^b (%)	Placebo Dose 2 N^a=1833 n^b (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

Unsolicited adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Among the total participants who received COMIRNATY or placebo 1 month after Dose 2, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were nausea (1.4%

or 0.5%), malaise (0.7% or 0.1%), asthenia (0.4% or 0.1%), decreased appetite (0.2% or 0.0%), hyperhidrosis (0.1% or 0.0%), lethargy (0.1% or 0.0%), and night sweats (0.1% or 0.0%).

Among the total participants who received COMIRNATY or placebo 1 month after Dose 2, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0% or 0.3%), malaise (0.5% or 0.1%), asthenia (0.3% or 0.1%), lethargy (0.2% or 0.0%), decreased appetite (0.1% or 0.0%), hyperhidrosis (0.1% or 0.0%), and night sweats (0.1% or 0.0%).

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4,396 (33.8%) participants who received COMIRNATY and 2,136 (16.4%) participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), all events, which include nonserious adverse events were reported by 2,551 (28.6%) participants who received COMIRNATY and 1,432 (16.1%) participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 29 (29%) participants who received COMIRNATY and 15 (15%) participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY Na=19,993 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=20,118 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
All participantsf	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY Na=21,047 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=21,210 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, and participants with obesity and medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.

b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.6

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27 5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21 5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

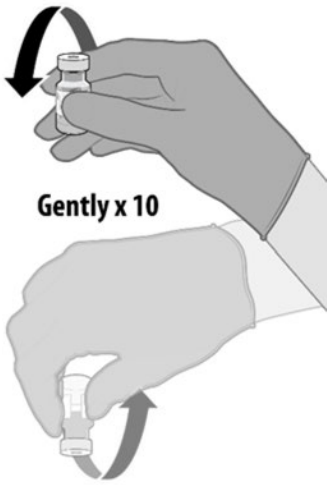
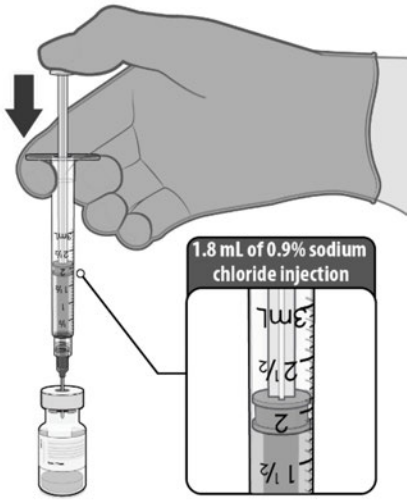
2.1 Preparation for Administration

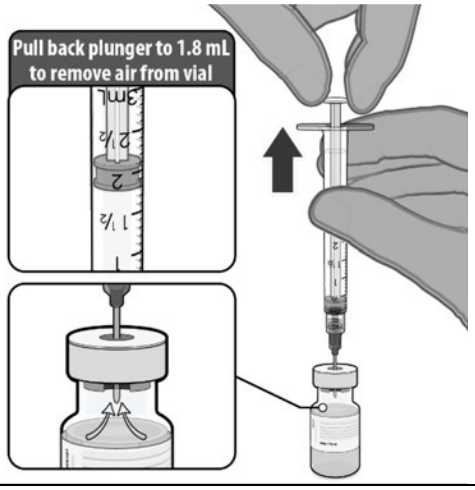
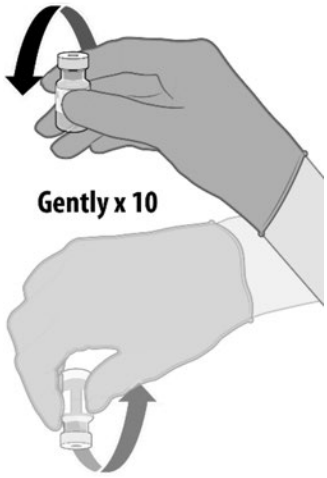
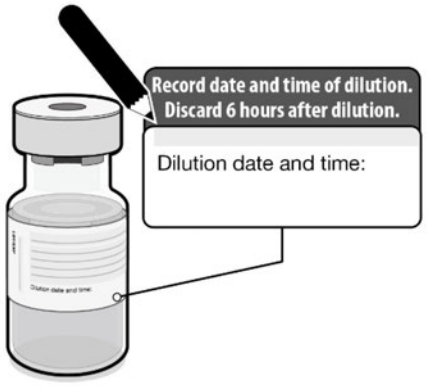
Prior to Dilution

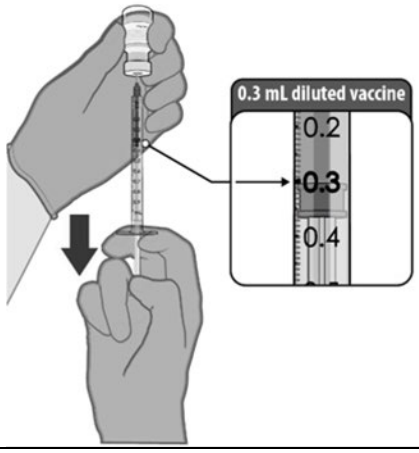
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

~~In clinical studies, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).~~

~~In clinical studies, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).~~

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

Unsolicited adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded

follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Among the total participants who received COMIRNATY or placebo 1 month after Dose 2, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were nausea (1.4% or 0.5%), malaise (0.7% or 0.1%), asthenia (0.4% or 0.1%), decreased appetite (0.2% or 0.0%), hyperhidrosis (0.1% or 0.0%), lethargy (0.1% or 0.0%), and night sweats (0.1% or 0.0%).

Among the total participants who received COMIRNATY or placebo 1 month after Dose 2, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0% or 0.3%), malaise (0.5% or 0.1%), asthenia (0.3% or 0.1%), lethargy (0.2% or 0.0%), decreased appetite (0.1% or 0.0%), hyperhidrosis (0.1% or 0.0%), and night sweats (0.1% or 0.0%).

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4,396 (33.8%) participants who received COMIRNATY and 2,136 (16.4%) participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), all events, which include nonserious adverse events were reported by 2,551 (28.6%) participants who received COMIRNATY and 1,432 (16.1%) participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 29 (29%) participants who received COMIRNATY and 15 (15%) participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including

under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY Na=19,993 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=20,118 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY Na=21,047 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=21,210 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, and participants with obesity and medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.

b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.6~~5~~

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only (2 2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0 3 mL each) 3 weeks apart (2 3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection After preparation, a single dose is 0 3 mL (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e g , anaphylaxis) to any component of COMIRNATY (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose (5 2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY Procedures should be in place to avoid injury from fainting (5 4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88 6%), fatigue (70 1%), headache (64 9%), muscle pain (45 5%), chills (41 5%), joint pain (27 5%), fever (17 8%), and injection site swelling (10 6%) (6 1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78 2%), fatigue (56 9%), headache, (45 9%), muscle pain (32 5%), chills (24 8%), joint pain (21 5%), injection site swelling (11 8%), fever (11 5%), and injection site redness (10 4%) (6 1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

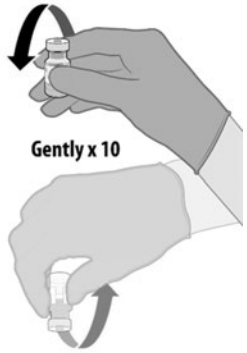
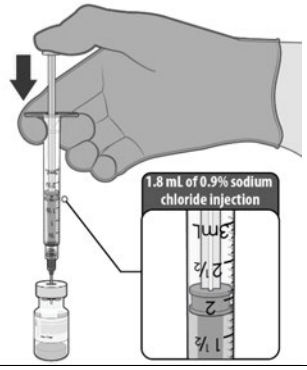
2.1 Preparation for Administration

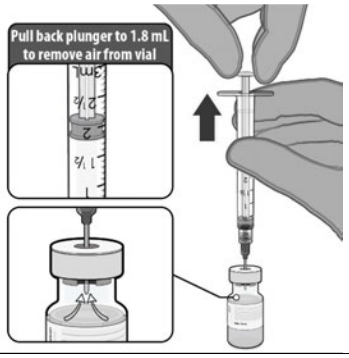
Prior to Dilution

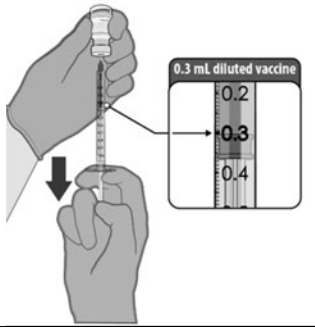
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • Do not shake. • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm

d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours

f Severity was not collected for use of antipyretic or pain medication

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in participants 56 years of age and older

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, the information was included in the column header

b n = Number of participants with the specified reaction

c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm

d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header

b n = Number of participants with the specified reaction

	COMIRNATY Dose 1 N^a=2008 n^b (%)	Placebo Dose 1 N^a=1989 n^b (%)	COMIRNATY Dose 2 N^a=1860 n^b (%)	Placebo Dose 2 N^a=1833 n^b (%)

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea

f Severity was not collected for use of antipyretic or pain medication

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of ~~serious and~~ all adverse events (including serious and non-serious unsolicited adverse events) reported through 1 month after Dose 2 in participants 16 through 55 years of age following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.4% vs. 0.5%), malaise (0.7% vs. 0.1%), asthenia (0.4% vs. 0.1%), decreased appetite (0.2% vs. <0.0~~1~~%), hyperhidrosis (0.1% vs. <0.0~~1~~%), lethargy (0.1% vs. <0.0~~1~~%), and night sweats (0.1% ~~-~~vs. <0.0~~1~~%).

In an analysis of all adverse events (including serious and non-serious unsolicited adverse events) reported through 1 month after Dose 2 in participants 56 years of age and older following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.0% vs. 0.3%), malaise (0.5% vs. 0.1%), asthenia (0.3% vs. 0.1%), lethargy (0.2% vs. <0.0~~1~~%), decreased appetite (0.1% vs. <0.0~~1~~%), hyperhidrosis (0.1% vs. <0.0~~1~~%), and night sweats (0.1% vs. <0.0~~1~~%).

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed

Commented [A1]: Pfizer-BioNTech response

The Sponsor accepts this deletion.

Commented [A2]: Pfizer-BioNTech response

The Sponsor proposes leaving the frequencies as originally proposed as we do not have a source table for non-serious AEs only, but rather any AEs including non-serious.

stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

~~*Non-Serious*~~ *Adverse Events*

In analyses of all events (including serious and non-serious unsolicited adverse events) in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, non-serious unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, non-serious unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection, non-serious unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87, one of which was serious) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Commented [A3]: FDA comment

Pfizer,
Please ensure that the numbers in this paragraph only include the non-serious adverse events.

Commented [A4R3]: Pfizer-BioNTech response

The Sponsor proposes retaining all events in this section as it is consistent with the data provided in the clinical study reports.

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The sponsor accepts the insertion of this text.

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The sponsor accepts this deletion.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

a N = Number of participants in the specified group

b n1 = Number of participants meeting the endpoint definition

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

d n2 = Number of participants at risk for the endpoint

e Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Commented [A7]: Pfizer-BioNTech response

The Sponsor accepts the revisions to this paragraph.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death

a n1 = Number of participants meeting the endpoint definition

b Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period
c n2 = Number of participants at risk for the endpoint
d Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed nlm nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.7~~6~~

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27 5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21 5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

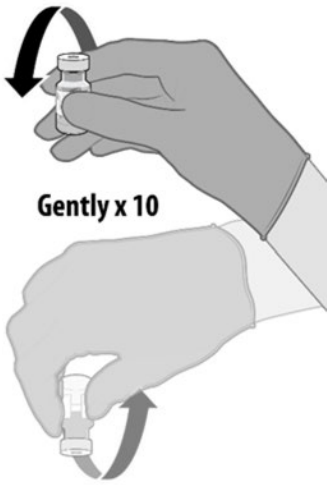
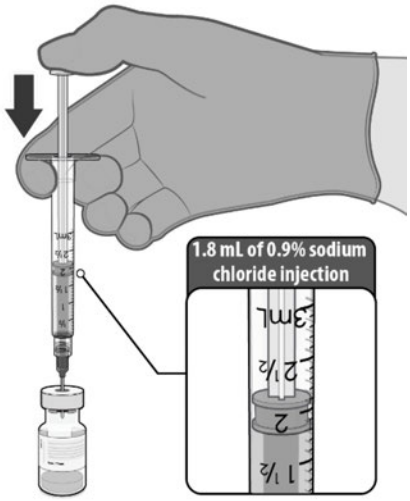
2.1 Preparation for Administration

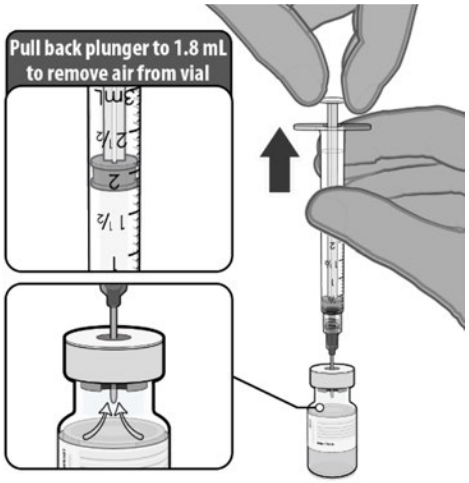
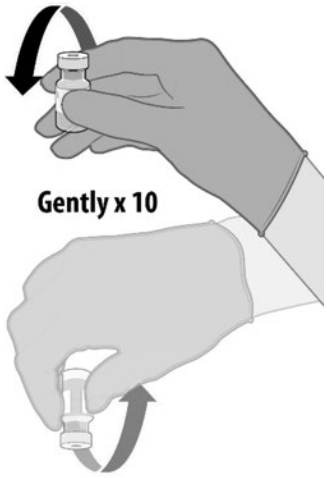
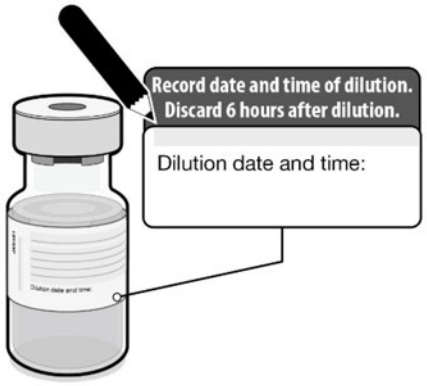
Prior to Dilution

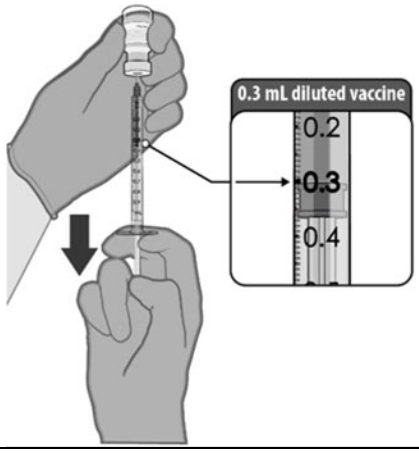
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of all adverse events (including serious and non-serious unsolicited adverse events) reported through 1 month after Dose 2 in participants 16 through 55 years of age following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.4% vs. 0.5%), malaise (0.7% vs. 0.1%), asthenia (0.4% vs. 0.1%), decreased appetite (0.2% vs. <0.0%), hyperhidrosis (0.1% vs. <0.0%), lethargy (0.1% vs. <0.0%), and night sweats (0.1% vs. <0.0%).

In an analysis of all adverse events (including serious and non-serious unsolicited adverse events) reported through 1 month after Dose 2 in participants 56 years of age and older following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.0% vs. 0.3%), malaise (0.5% vs. 0.1%), asthenia (0.3% vs. 0.1%), lethargy (0.2% vs. <0.0%), decreased appetite (0.1% vs. <0.0%), hyperhidrosis (0.1% vs. <0.0%), and night sweats (0.1% vs. <0.0%).

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed

stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

Adverse Events

In analyses of all events (including serious and non-serious unsolicited adverse events) in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, non-serious unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, non-serious unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection, non-serious unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87, one of which was serious) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY Na=19,993 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=20,118 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY Na=21,047 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=21,210 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.

b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.7

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27 5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21 5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

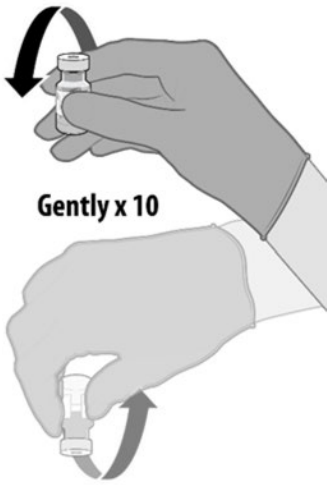
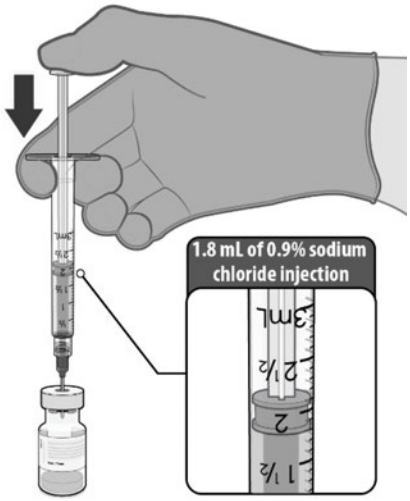
2.1 Preparation for Administration

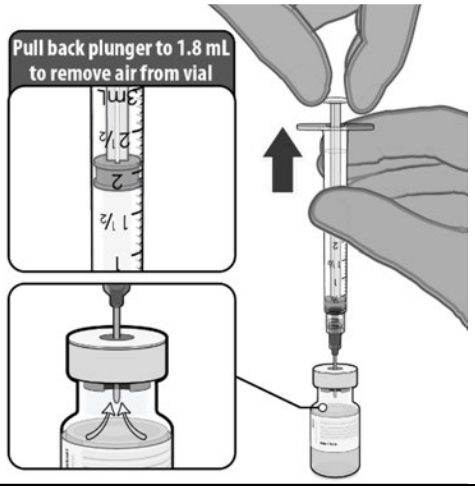
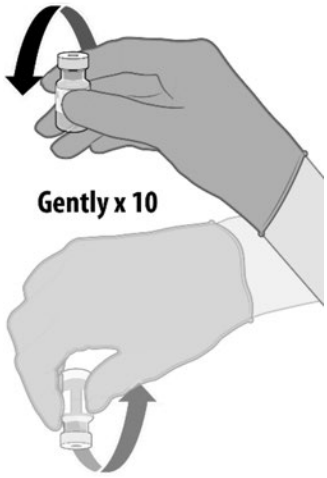
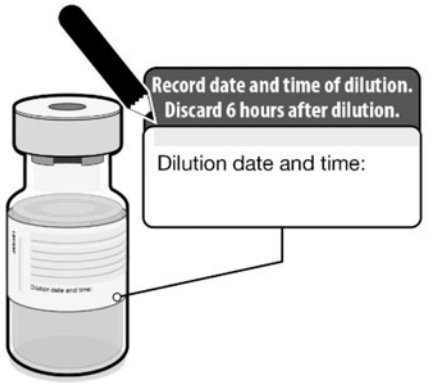
Prior to Dilution

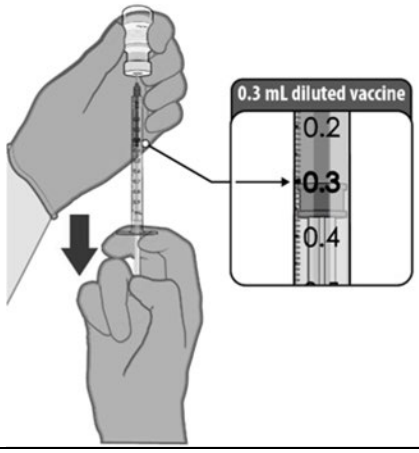
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of ~~serious and~~ all adverse events (including serious and non-serious unsolicited adverse events) reported through 1 month after Dose 2 in participants 16 through 55 years of age following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.4% vs. 0.5%), malaise (0.7% vs. 0.1%), asthenia (0.4% vs. 0.1%), decreased appetite (0.2% vs. <0.0~~1~~%), hyperhidrosis (0.1% vs. <0.0~~1~~%), lethargy (0.1% vs. <0.0~~1~~%), and night sweats (0.1% ~~-~~vs. <0.0~~1~~%).

In an analysis of all adverse events (including serious and non-serious unsolicited adverse events) reported through 1 month after Dose 2 in participants 56 years of age and older following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.0% vs. 0.3%), malaise (0.5% vs. 0.1%), asthenia (0.3% vs. 0.1%), lethargy (0.2% vs. <0.0~~1~~%), decreased appetite (0.1% vs. <0.0~~1~~%), hyperhidrosis (0.1% vs. <0.0~~1~~%), and night sweats (0.1% vs. <0.0~~1~~%).

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931~~,~~; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed

stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

~~*Non-Serious*~~ *Adverse Events*

In analyses of all events (including serious and non-serious unsolicited adverse events) in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, non-serious unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, non-serious unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection, non-serious unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87, one of which was serious) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.

b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.7~~6~~

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only (2 2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0 3 mL each) 3 weeks apart (2 3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection After preparation, a single dose is 0 3 mL (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e g , anaphylaxis) to any component of COMIRNATY (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose (5 2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY Procedures should be in place to avoid injury from fainting (5 4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88 6%), fatigue (70 1%), headache (64 9%), muscle pain (45 5%), chills (41 5%), joint pain (27 5%), fever (17 8%), and injection site swelling (10 6%) (6 1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78 2%), fatigue (56 9%), headache, (45 9%), muscle pain (32 5%), chills (24 8%), joint pain (21 5%), injection site swelling (11 8%), fever (11 5%), and injection site redness (10 4%) (6 1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

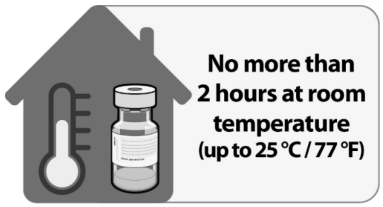
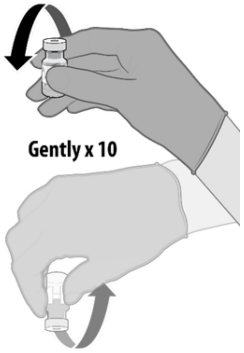
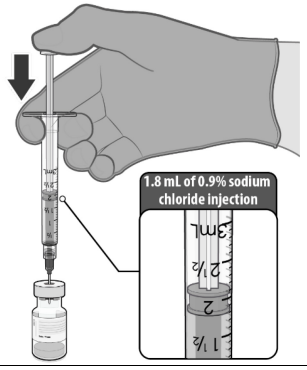
2.1 Preparation for Administration

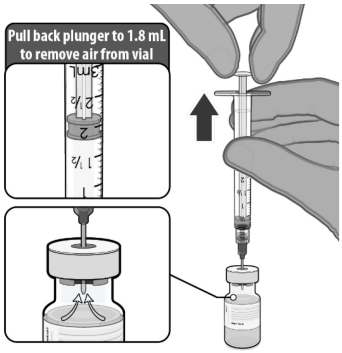
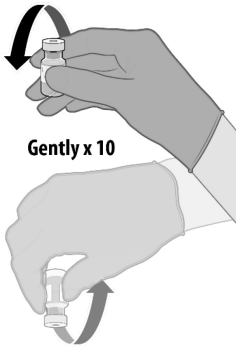
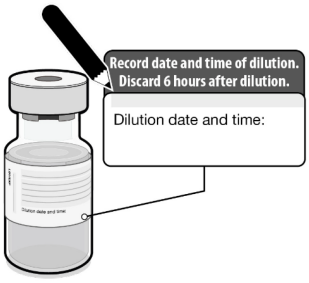
Prior to Dilution

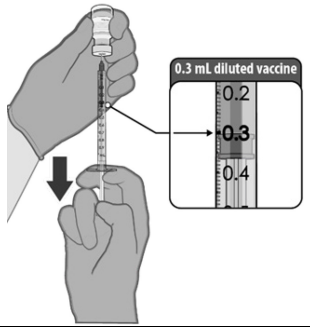
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm

d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours

f Severity was not collected for use of antipyretic or pain medication

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in participants 56 years of age and older

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, the information was included in the column header

b n = Number of participants with the specified reaction

c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm

d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header

b n = Number of participants with the specified reaction

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea

f Severity was not collected for use of antipyretic or pain medication

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

~~In an analysis of all adverse events (including serious and non-serious unsolicited adverse events) reported through 1 month after Dose 2 in participants 16 through 55 years of age following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.4% vs. 0.5%), malaise (0.7% vs. 0.1%), asthenia (0.4% vs. 0.1%), decreased appetite (0.2% vs. <0.01%), hyperhidrosis (0.1% vs. <0.01%), lethargy (0.1% vs. <0.01%), and night sweats (0.1% vs. <0.01%).~~

~~In an analysis of all adverse events (including serious and non-serious unsolicited adverse events) reported through 1 month after Dose 2 in participants 56 years of age and older following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.0% vs. 0.3%), malaise (0.5% vs. 0.1%), asthenia (0.3% vs. 0.1%), lethargy (0.2% vs. <0.01%), decreased appetite (0.1% vs. <0.01%), hyperhidrosis (0.1% vs. <0.01%), and night sweats (0.1% vs. <0.01%).~~

In an analysis of all unsolicited adverse events reported through 1 month after Dose 2 in 43,847 (21,926 COMIRNATY; 21,921 placebo) participants 16 years of age and older following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (274 vs. 87), malaise (130 vs. 22), lymphadenopathy (83 vs. 7), asthenia (76 vs. 25), decreased appetite (39 vs. 9), hyperhidrosis 31 vs. 9), lethargy (25 vs. 6), and night sweats (17 vs. 3).

In analyses of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, non-serious unsolicited adverse events were reported by 4,396 (33.8%)

Commented [A1]: FDA comment

Pfizer,
Instead of presenting percentages for the two age groups separately, report the number of subjects (16 years of age and older) in the vaccine group and the placebo group reporting each event. Please also include lymphadenopathy and delete the sentence pertaining to lymphadenopathy below.

Commented [A2R1]: Pfizer-BioNTech response

The Sponsor accepts and has added the paragraph below.

Source:

Interim Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals (April 2021), Table 30. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

Commented [A3]: Pfizer-BioNTech response

The Sponsor accepts FDA's movement of the Serious Adverse Events paragraphs to end of section.

Commented [A4]: Pfizer-BioNTech response

The Sponsor accepts this revision.

participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, non-serious unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection, non-serious unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Commented [A5]: Pfizer-BioNTech response

The Sponsor accepts this deletion and has included lymphadenopathy above.

Commented [A6]: Pfizer-BioNTech response

The Sponsor accepts the movement of this section from above.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

a N = Number of participants in the specified group

b n1 = Number of participants meeting the endpoint definition

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

d n2 = Number of participants at risk for the endpoint

e Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death

a n1 = Number of participants meeting the endpoint definition

b Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period
c n2 = Number of participants at risk for the endpoint
d Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed nlm nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.87

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27 5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21 5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

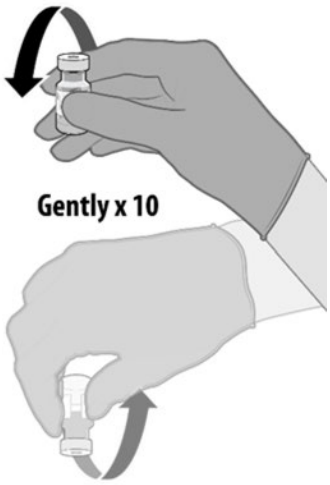
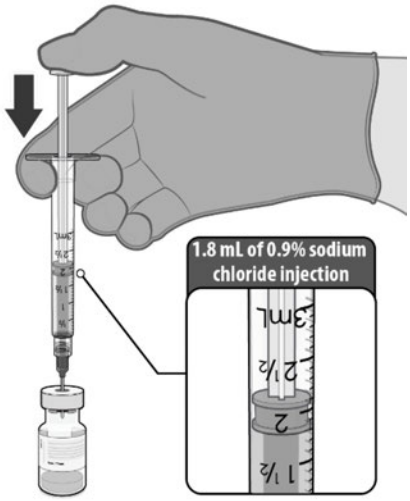
2.1 Preparation for Administration

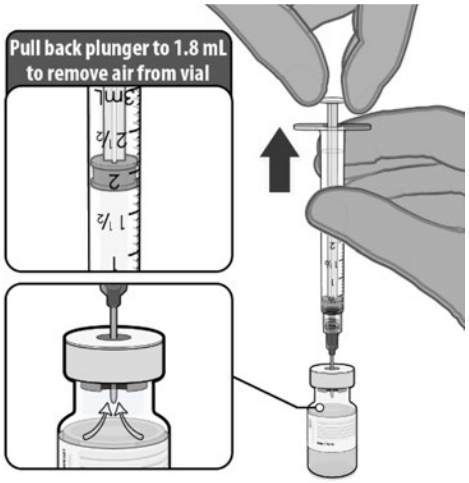
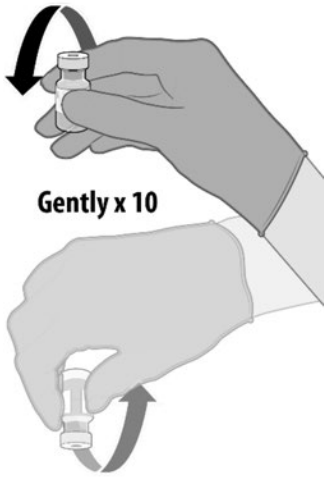
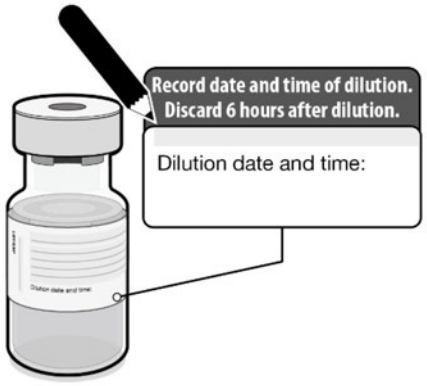
Prior to Dilution

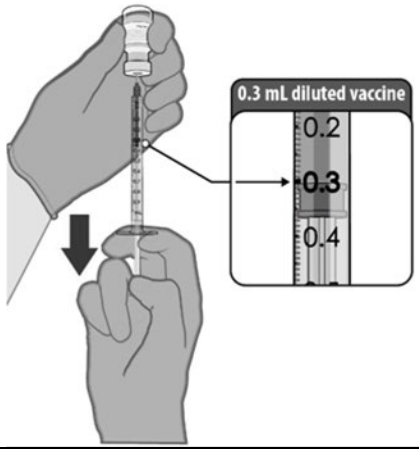
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of all unsolicited adverse events reported through 1 month after Dose 2 in 43,847 (21,926 COMIRNATY; 21,921 placebo) participants 16 years of age and older following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (274 vs. 87), malaise (130 vs. 22), lymphadenopathy (83 vs. 7), asthenia (76 vs. 25), decreased appetite (39 vs. 9), hyperhidrosis 31 vs. 9), lethargy (25 vs. 6), and night sweats (17 vs. 3).

In analyses of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, non-serious unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, non-serious unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection, non-serious unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to

determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to

4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more

comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by

Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.8

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27 5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21 5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

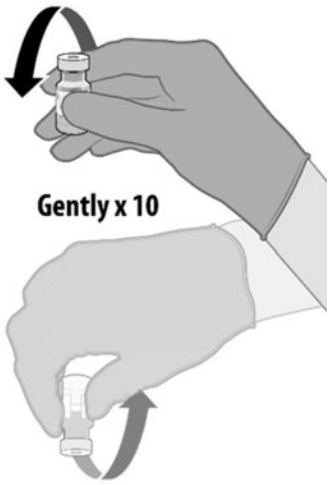
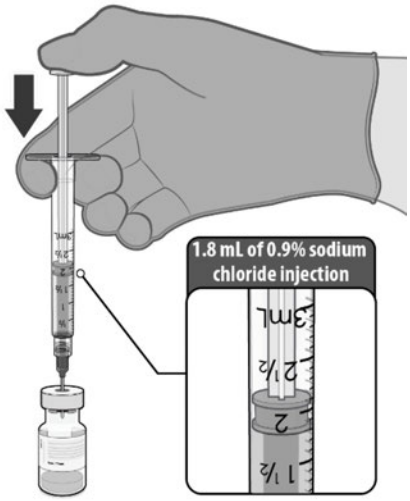
2.1 Preparation for Administration

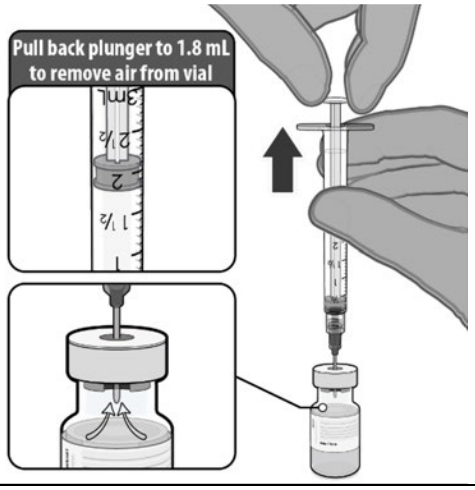
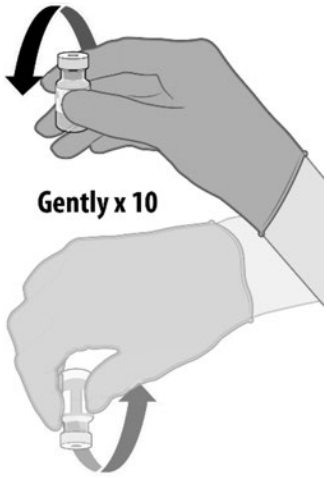
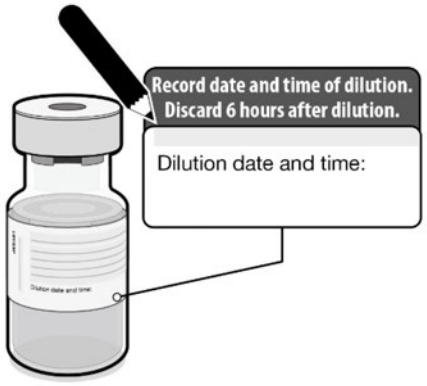
Prior to Dilution

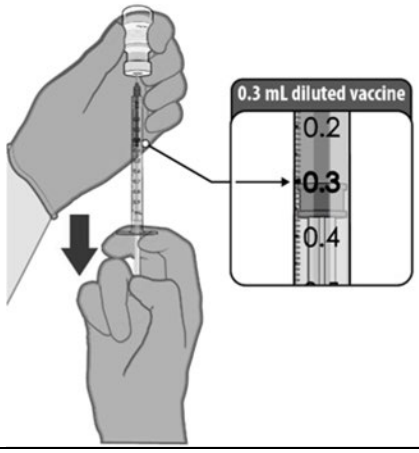
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

~~In an analysis of all adverse events (including serious and non-serious unsolicited adverse events) reported through 1 month after Dose 2 in participants 16 through 55 years of age following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.4% vs. 0.5%), malaise (0.7% vs. 0.1%), asthenia (0.4% vs. 0.1%), decreased appetite (0.2% vs. <0.01%), hyperhidrosis (0.1% vs. <0.01%), lethargy (0.1% vs. <0.01%), and night sweats (0.1% vs. <0.01%).~~

~~In an analysis of all adverse events (including serious and non-serious unsolicited adverse events) reported through 1 month after Dose 2 in participants 56 years of age and older following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.0% vs. 0.3%), malaise (0.5% vs. 0.1%), asthenia (0.3% vs. 0.1%), lethargy (0.2% vs. <0.01%), decreased appetite (0.1% vs. <0.01%), hyperhidrosis (0.1% vs. <0.01%), and night sweats (0.1% vs. <0.01%).~~

In an analysis of all unsolicited adverse events reported through 1 month after Dose 2 in 43,847 (21,926 COMIRNATY; 21,921 placebo) participants 16 years of age and older following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (274 vs. 87), malaise (130 vs. 22), lymphadenopathy (83 vs. 7), asthenia (76 vs. 25), decreased appetite (39 vs. 9), hyperhidrosis 31 vs. 9), lethargy (25 vs. 6), and night sweats (17 vs. 3).

In analyses of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, non-serious unsolicited adverse events were reported by 4,396 (33.8%)

participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, non-serious unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection, non-serious unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.

b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.87

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only (2 2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0 3 mL each) 3 weeks apart (2 3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection After preparation, a single dose is 0 3 mL (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e g , anaphylaxis) to any component of COMIRNATY (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose (5 2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY Procedures should be in place to avoid injury from fainting (5 4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88 6%), fatigue (70 1%), headache (64 9%), muscle pain (45 5%), chills (41 5%), joint pain (27 5%), fever (17 8%), and injection site swelling (10 6%) (6 1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78 2%), fatigue (56 9%), headache, (45 9%), muscle pain (32 5%), chills (24 8%), joint pain (21 5%), injection site swelling (11 8%), fever (11 5%), and injection site redness (10 4%) (6 1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

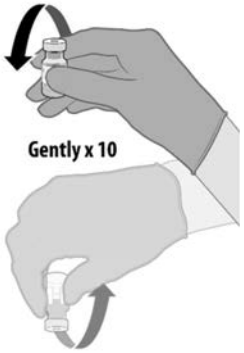
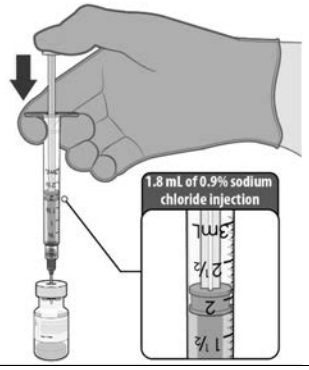
2.1 Preparation for Administration

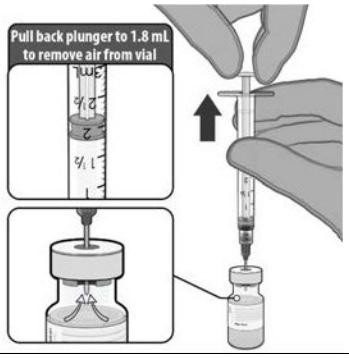
Prior to Dilution

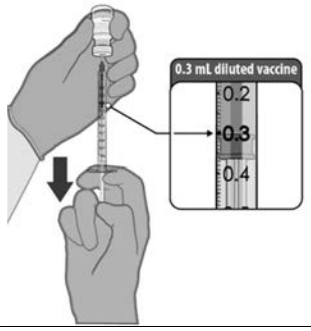
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm

d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header

b n = Number of participants with the specified reaction

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours

f Severity was not collected for use of antipyretic or pain medication

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination
No Grade 4 solicited local reactions were reported in participants 56 years of age and older

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose The N for each reaction was the same, therefore, the information was included in the column header

b n = Number of participants with the specified reaction

c Mild: >2 0 to ≤5 0 cm; Moderate: >5 0 to ≤10 0 cm; Severe: >10 0 cm

d Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention Participants with chronic, stable HIV infection were excluded

a N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header

b n = Number of participants with the specified reaction

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain

d Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting

e Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea

f Severity was not collected for use of antipyretic or pain medication

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of all unsolicited adverse events reported following any dose, through 1 month after Dose 2, in participants 16 years of age and older (N=43,847; 21,926 COMIRNATY group vs. 21,921 placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (274 vs. 87), malaise (130 vs. 22), lymphadenopathy (83 vs. 7), asthenia (76 vs. 25), decreased appetite (39 vs. 9), hyperhidrosis (31 vs. 9), lethargy (25 vs. 6), and night sweats (17 vs. 3).

In analyses of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection that included 100 COMIRNATY recipients and 100 placebo recipients, unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited ~~non-serious~~ adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there

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Sponsor accepts FDA's editorial revision to this sentence.

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Sponsor accepts FDA's editorial revision to this sentence.
Table 14.84

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Sponsor proposes deletion of "non-serious" for consistency.

were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to

4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Specific Populations (8.1)]*.

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Pfizer-BioNTech response
Sponsor accepts FDA's correction of section title.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more

comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

a N = Number of participants in the specified group

b n1 = Number of participants meeting the endpoint definition

c Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

d n2 = Number of participants at risk for the endpoint

e Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting)

* Participants who had no evidence of past SARS-CoV-2 infection (i e , N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death

a n1 = Number of participants meeting the endpoint definition

b Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

c n2 = Number of participants at risk for the endpoint

d Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by

Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed nlm nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.9~~8~~

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27 5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21 5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FDA-CBER-2021-5683-0652088

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

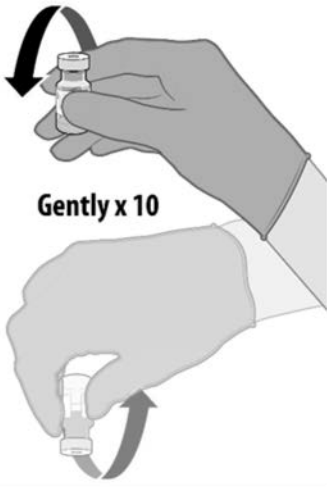
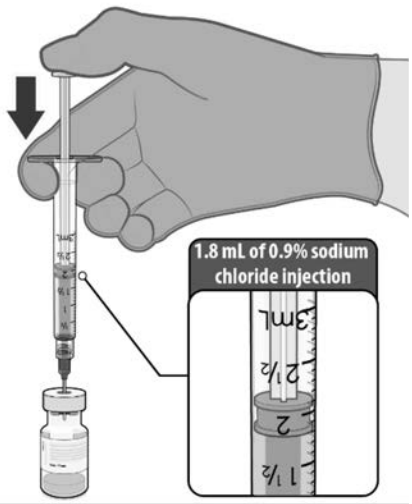
2.1 Preparation for Administration

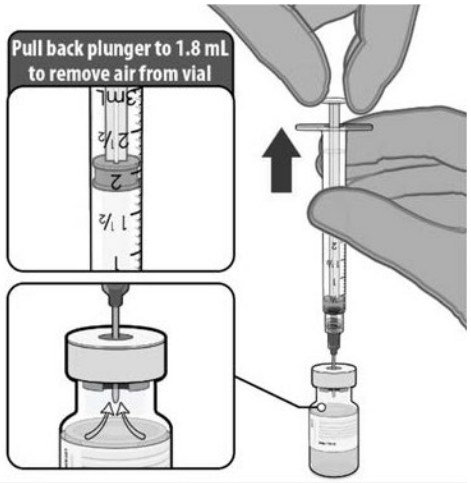
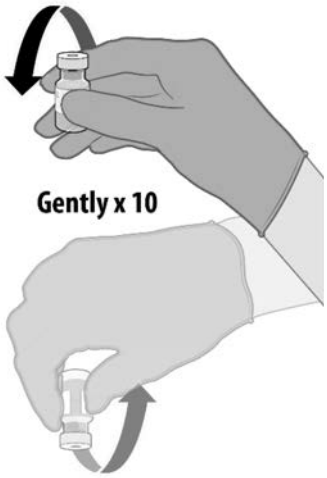
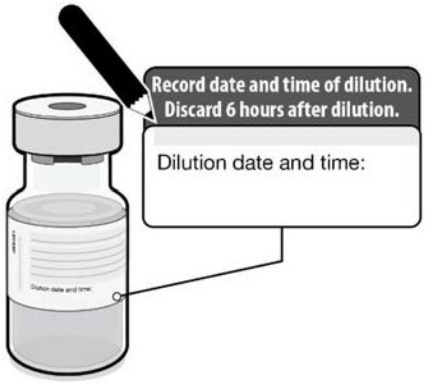
Prior to Dilution

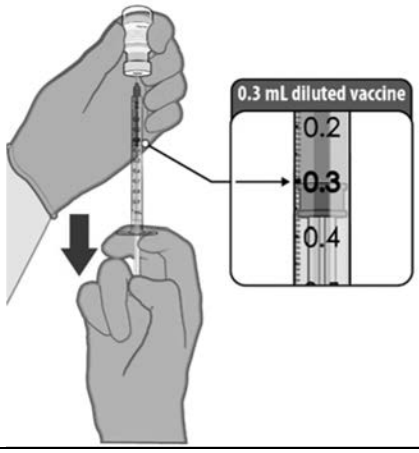
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N^a=2008 n^b (%)	Placebo Dose 1 N^a=1989 n^b (%)	COMIRNATY Dose 2 N^a=1860 n^b (%)	Placebo Dose 2 N^a=1833 n^b (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of all unsolicited adverse events reported following any dose, through 1 month after Dose 2, in participants 16 years of age and older (N=43,847; 21,926 COMIRNATY group vs. 21,921 placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (274 vs. 87), malaise (130 vs. 22), lymphadenopathy (83 vs. 7), asthenia (76 vs. 25), decreased appetite (39 vs. 9), hyperhidrosis (31 vs. 9), lethargy (25 vs. 6), and night sweats (17 vs. 3).

In analyses of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection that included 100 COMIRNATY recipients and 100 placebo recipients, unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there

were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to

4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Specific Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more

comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by

Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.9

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27 5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21 5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FDA-CBER-2021-5683-0652108

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

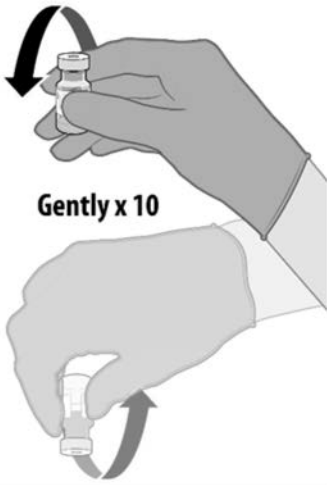
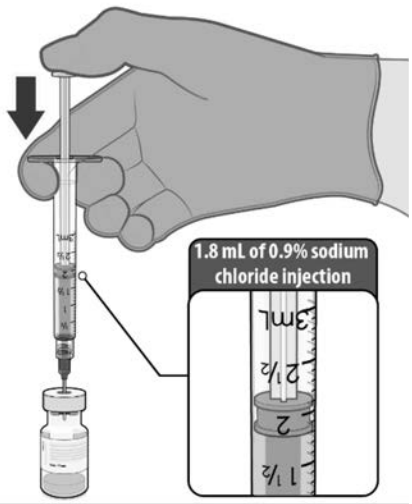
2.1 Preparation for Administration

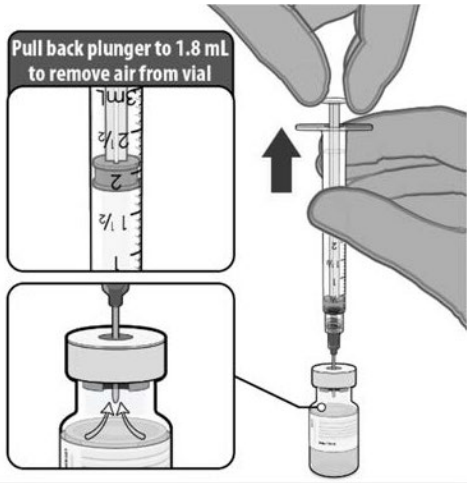
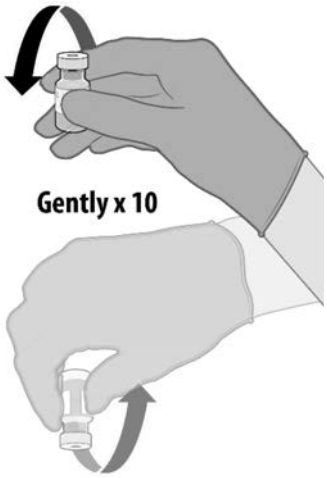
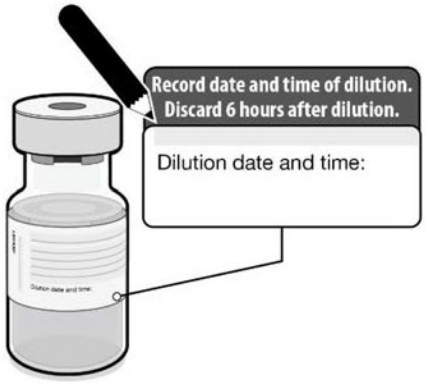
Prior to Dilution

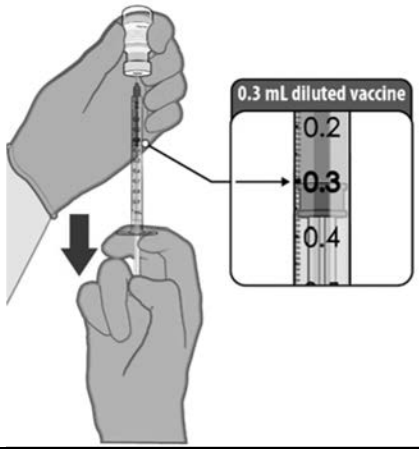
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of all unsolicited adverse events reported following any dose, through 1 month after Dose 2, in participants 16 years of age and older (N=43,847; 21,926 COMIRNATY group vs. 21,921 placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (274 vs. 87), malaise (130 vs. 22), lymphadenopathy (83 vs. 7), asthenia (76 vs. 25), decreased appetite (39 vs. 9), hyperhidrosis (31 vs. 9), lethargy (25 vs. 6), and night sweats (17 vs. 3).

In analyses of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection that included 100 COMIRNATY recipients and 100 placebo recipients, unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited ~~non-serious~~ adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there

were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to

4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Specific Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more

comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by

Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.9~~8~~

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

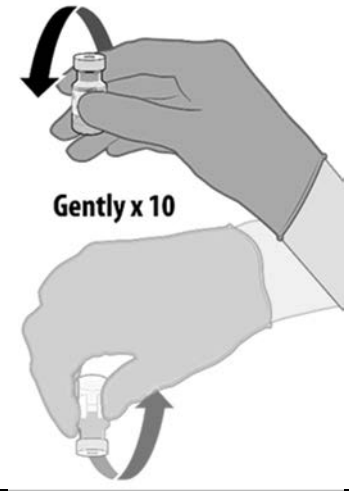
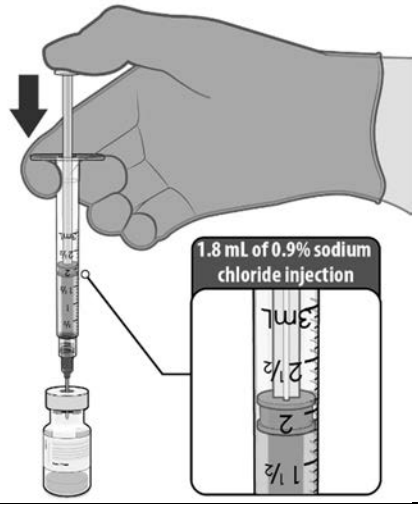
2.1 Preparation for Administration

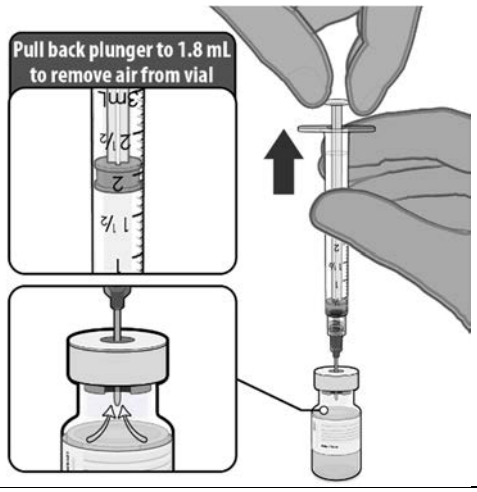
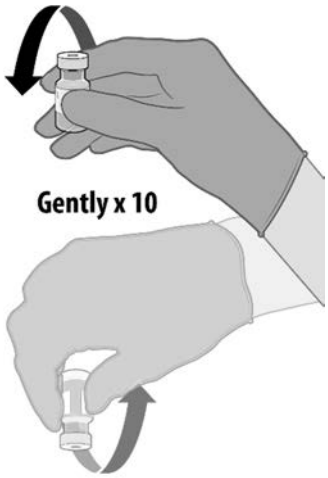
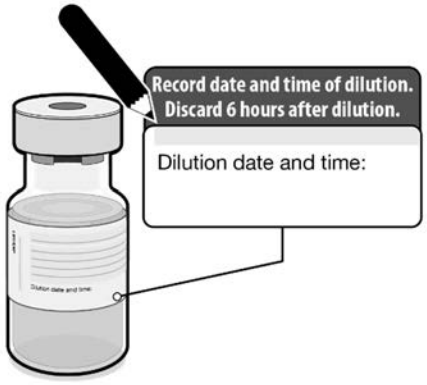
Prior to Dilution

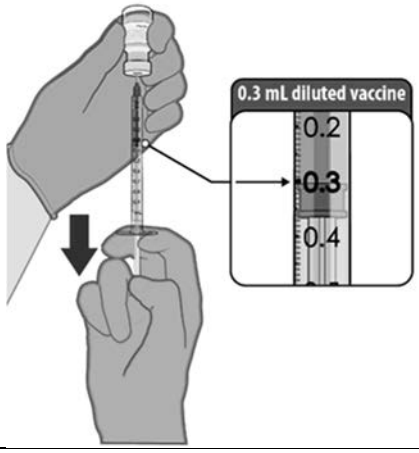
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of all unsolicited adverse events reported following any dose, through 1 month after Dose 2, in participants 16 years of age and older (N=43,847; 21,926 COMIRNATY group vs. 21,921 placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (274 vs. 87), malaise (130 vs. 22), lymphadenopathy (83 vs. 7), asthenia (76 vs. 25), decreased appetite (39 vs. 9), hyperhidrosis (31 vs. 9), lethargy (25 vs. 6), and night sweats (17 vs. 3).

In analyses of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection that included 100 COMIRNATY recipients and 100 placebo recipients, unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there

were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to

4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Specific Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more

comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by

Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-1.0

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FDA-CBER-2021-5683-0652148

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

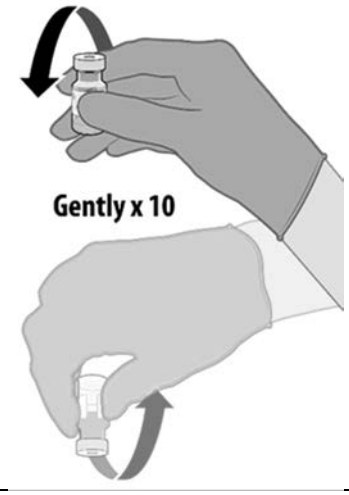
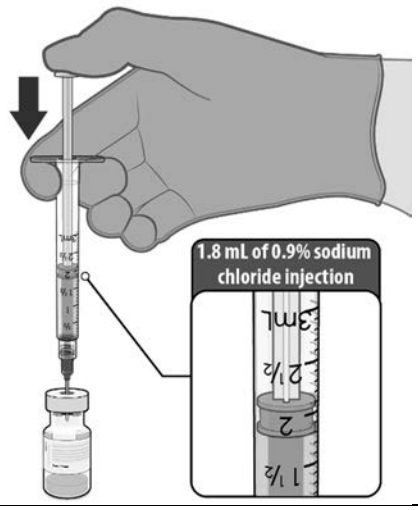
2.1 Preparation for Administration

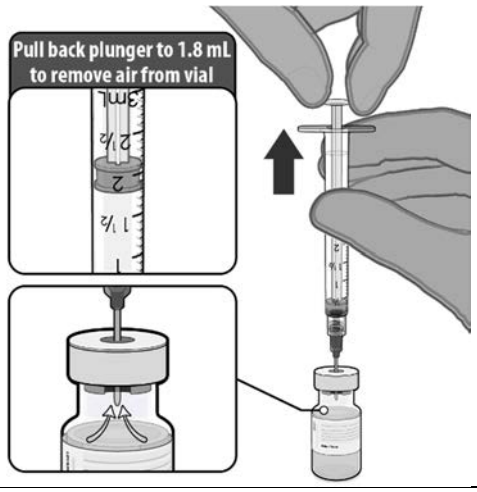
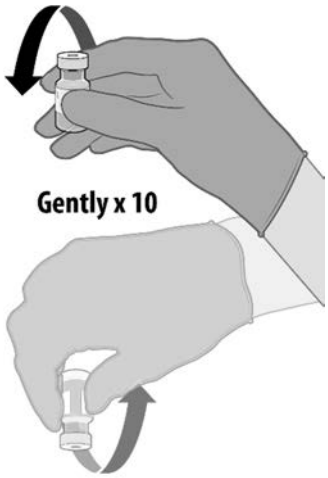
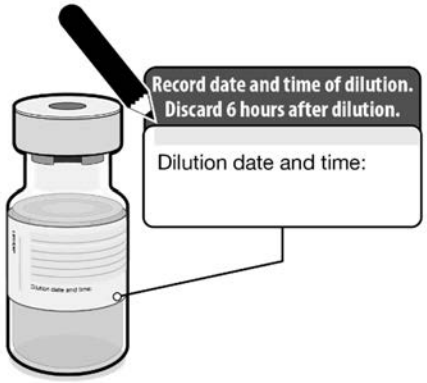
Prior to Dilution

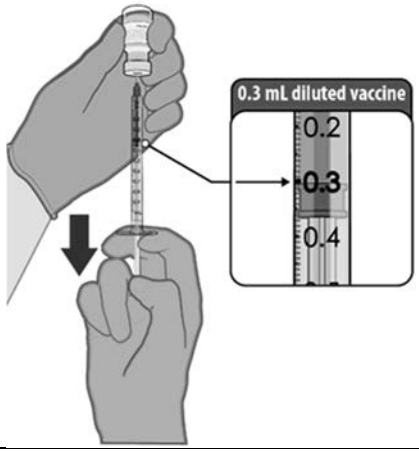
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of all unsolicited adverse events reported following any dose, through 1 month after Dose 2, in participants 16 years of age and older (N=43,847; 21,926 COMIRNATY group vs. 21,921 placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (274 vs. 87), malaise (130 vs. 22), lymphadenopathy (83 vs. 7), asthenia (76 vs. 25), decreased appetite (39 vs. 9), hyperhidrosis (31 vs. 9), lethargy (25 vs. 6), and night sweats (17 vs. 3).

In analyses of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection that included 100 COMIRNATY recipients and 100 placebo recipients, unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there

were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to

4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Specific Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more

comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by

Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-1.0

US Govt. License No. 2229

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing reports of adverse events suggest increased risks of myocarditis and pericarditis, particularly following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
In clinical studies of participants 16 years of age and older, the most commonly reported adverse reactions (>10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, fever, and injection site swelling. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

2.1 Preparation for Administration

Prior to Dilution

- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of 0.9% Sodium Chloride Injection, USP (provided but shipped separately) to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use 0.9% Sodium Chloride Injection, USP as the diluent.
- After dilution, 1 vial contains 6 doses of 0.3 mL.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before use either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.

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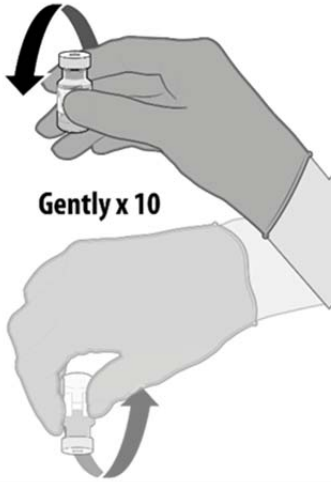
<tr><td> 
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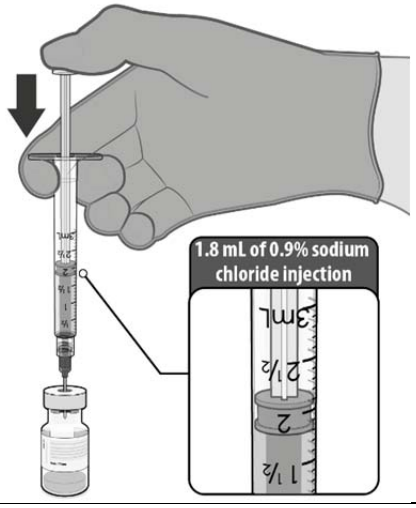
Before dilution invert vaccine vial gently 10 times.
Do not shake.
Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles.
Do not use if liquid is discolored or if other particles are observed.

</td></tr>
<tr><td colspan="2">DILUTION</td></tr>
<tr><td> 
</td><td>

Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent.
Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle).
Cleanse the vaccine vial stopper with a single-use antiseptic swab.
Add 1.8 mL of 0.9% Sodium Chloride Injection, USP into the vaccine vial.

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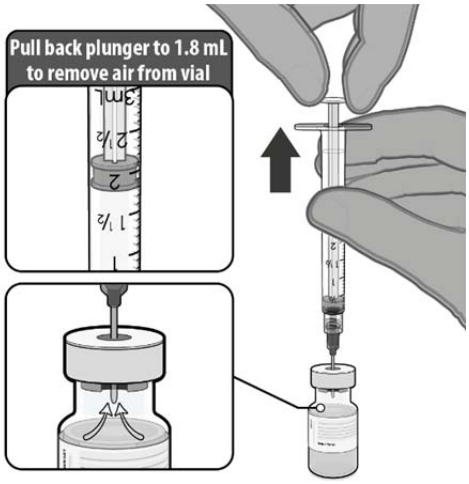
<tr><td> 
</td><td>

Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.

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</table>

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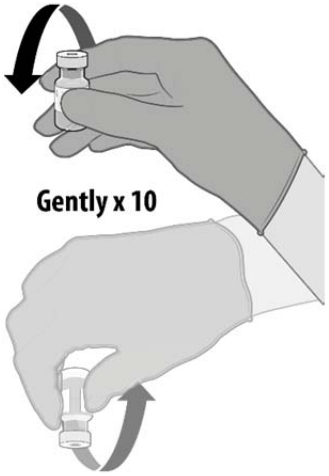
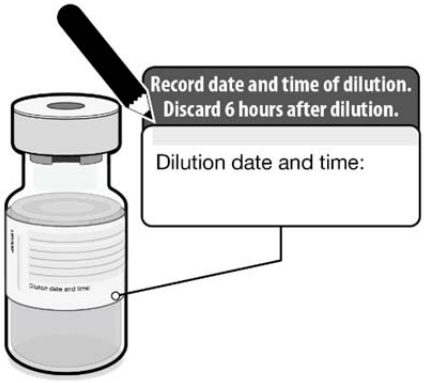
<tr>
<td> 
</td>
<td>

Gently invert the vial containing the COMIRNATY 10 times to mix.
Do not shake.
Inspect the vaccine in the vial.
The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.

</td>
</tr>
<tr>
<td> 
</td>
<td>

Record the date and time of dilution on the COMIRNATY vial label.
Store between 2°C to 25°C (35°F to 77°F).
Discard any unused vaccine 6 hours after dilution.

</td>
</tr>
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<tr>
<th colspan="2">PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY</th>
</tr>
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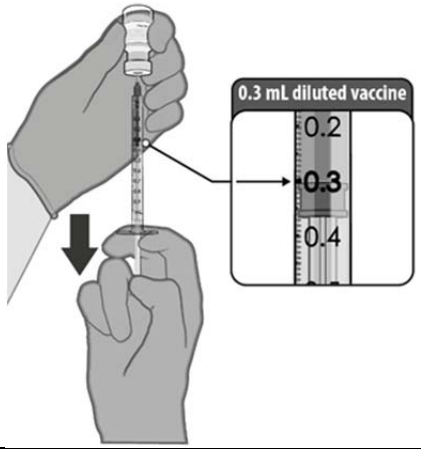
<td> 
</td>
<td>

Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles.
Each dose must contain 0.3 mL of vaccine.
If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
Administer immediately.

</td>
</tr>
</table>

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Visually inspect each dose in the dosing syringe prior to administration. The vaccine will be an off-white suspension. During the visual inspection,

- verify the final dosing volume of 0.3 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

Administer COMIRNATY intramuscularly.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Reports of adverse events following use of COMIRNATY under EUA suggest increased risks of myocarditis and pericarditis, particularly following the second dose. Typically, onset of symptoms has been within a few days following receipt of COMIRNATY. Available data from short-term follow-up suggest that most individuals have had resolution of symptoms, but information is not yet available about potential long-term sequelae. The decision to administer COMIRNATY to an individual with a history of myocarditis or

pericarditis should take into account the individual's clinical circumstances. The CDC has published clinical considerations relevant to myocarditis and pericarditis associated with administration of COMIRNATY (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Concurrent Illness at Time of Vaccination

The administration of COMIRNATY should be postponed in individuals suffering from acute severe febrile illness.

5.4 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.5 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.6 Bleeding Precautions

Individuals receiving anticoagulant therapy or those with a bleeding disorder that would contraindicate intramuscular injection, should not be given the vaccine unless the potential benefit clearly outweighs the risk of administration.

5.7 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies with a data cut-off of March 13, 2021, adverse reactions in participants 16 years of age and older included pain at the injection site (84.3%), fatigue (64.7%), headache (57.1%), muscle pain (40.2%), chills (34.7%), joint pain (25.0%), fever (15.2%), injection site swelling (11.1%), injection site redness (9.9%), nausea (1.2%), malaise (0.6%), lymphadenopathy (0.4%), asthenia (0.3%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

Severe allergic reactions, including anaphylaxis, have been reported following administration of COMIRNATY outside of clinical trials.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 1/2, 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001

(Study 2) is a Phase 1/2/3, multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection (Phase 1) and efficacy (Phase 2/3) study that has enrolled approximately 46,000 participants, 12 years of age or older. Of these, approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) in Phase 2/3 are 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses.

At the time of the analysis of Study 2 for the Emergency Use Authorization (EUA) with a data cut-off of November 14, 2020, there were 37,586 participants (18,801 COMIRNATY and 18,785 placebo) 16 years of age or older followed for a median of 2 months after the second dose of COMIRNATY. At the time of the analysis of Study 2 for the EUA with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

The safety evaluation in Study 2 is ongoing. The safety population includes participants enrolled by October 9, 2020, and includes safety data accrued through March 13, 2021. Participants 16 years and older in the reactogenicity subset are monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male and 49.1% were female, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 to 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.

f. Severity was not collected for use of antipyretic or pain medication.

Table 5 and Table 6 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 16 years of age and older with confirmed stable HIV infection.

Table 5: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – HIV-Positive Participants 16 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Redness[c]				
Any (>2.0 cm)	2 (3.7)	3 (5.4)	4 (6.7)	1 (1.6)
Mild	2 (3.7)	1 (1.8)	3 (5.0)	1 (1.6)
Moderate	0	0	1 (1.7)	0
Severe	0	2 (3.6)	0	0
Swelling[c]				
Any (>2.0 cm)	3 (5.6)	1 (1.8)	5 (8.3)	0
Mild	2 (3.7)	0	2 (3.3)	0
Moderate	1 (1.9)	0	3 (5.0)	0
Severe	0	1 (1.8)	0	0
Pain at the injection site[d]				
Any	34 (63.0)	9 (16.1)	32 (53.3)	5 (8.1)
Mild	26 (48.1)	8 (14.3)	22 (36.7)	5 (8.1)
Moderate	8 (14.8)	1 (1.8)	9 (15.0)	0
Severe	0	0	1 (1.7)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in HIV-positive participants 16 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 6: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – HIV-Positive Participants 16 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Fever				
≥38.0°C	1 (1.9)	4 (7.1)	9 (15.0)	5 (8.1)
≥38.0°C to 38.4°C	1 (1.9)	2 (3.6)	4 (6.7)	5 (8.1)
>38.4°C to 38.9°C	0	0	4 (6.7)	0
>38.9°C to 40.0°C	0	2 (3.6)	1 (1.7)	0
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Fatigue[c]				
Any	22 (40.7)	15 (26.8)	24 (40.0)	12 (19.4)
Mild	15 (27.8)	9 (16.1)	12 (20.0)	5 (8.1)
Moderate	7 (13.0)	5 (8.9)	9 (15.0)	7 (11.3)
Severe	0	1 (1.8)	3 (5.0)	0
Headache[c]				
Any	11 (20.4)	18 (32.1)	18 (30.0)	12 (19.4)
Mild	7 (13.0)	10 (17.9)	8 (13.3)	8 (12.9)
Moderate	4 (7.4)	7 (12.5)	8 (13.3)	4 (6.5)
Severe	0	1 (1.8)	2 (3.3)	0
Chills[c]				
Any	6 (11.1)	5 (8.9)	14 (23.3)	4 (6.5)
Mild	5 (9.3)	4 (7.1)	5 (8.3)	3 (4.8)
Moderate	1 (1.9)	1 (1.8)	8 (13.3)	1 (1.6)
Severe	0	0	1 (1.7)	0
Vomiting[d]				
Any	1 (1.9)	3 (5.4)	2 (3.3)	2 (3.2)
Mild	1 (1.9)	1 (1.8)	1 (1.7)	1 (1.6)
Moderate	0	0	1 (1.7)	1 (1.6)
Severe	0	2 (3.6)	0	0
Diarrhea[e]				
Any	5 (9.3)	8 (14.3)	4 (6.7)	9 (14.5)
Mild	5 (9.3)	6 (10.7)	1 (1.7)	6 (9.7)
Moderate	0	1 (1.8)	2 (3.3)	3 (4.8)
Severe	0	1 (1.8)	1 (1.7)	0
New or worsened muscle pain[c]				
Any	9 (16.7)	10 (17.9)	10 (16.7)	5 (8.1)
Mild	7 (13.0)	7 (12.5)	5 (8.3)	1 (1.6)
Moderate	2 (3.7)	3 (5.4)	5 (8.3)	4 (6.5)
Severe	0	0	0	0
New or worsened joint pain[c]				
Any	5 (9.3)	7 (12.5)	10 (16.7)	5 (8.1)
Mild	5 (9.3)	4 (7.1)	4 (6.7)	1 (1.6)
Moderate	0	3 (5.4)	6 (10.0)	4 (6.5)
Severe	0	0	0	0
Use of antipyretic or pain medication[f]	7 (13.0)	8 (14.3)	16 (26.7)	7 (11.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in HIV-positive participants 16 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each event or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.
f. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

Upon issuance of the EUA for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began in a phased manner for participants in the study. Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 2.1 per 100 person-years among COMIRNATY recipients and 2.4 per 100 person-years among placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported at an incidence rate of 4.9 per 100 person-years among COMIRNATY recipients and 4.6 per 100 person-years among placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 6.6 per 100 person-years among COMIRNATY recipients and 6.9 per 100 person-years among placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 88.4 per 100 person-years among participants who received COMIRNATY and 43.5 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include non-serious adverse events were reported at an incidence rate of 75.7 per 100 person-years among participants who received COMIRNATY and 43.3 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 95.8 per 100 person-years among participants who received COMIRNATY and 52.0 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

6.2 Post Marketing Experience

The following adverse reactions have been identified during post marketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A reproductive and developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions, twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a reproductive and developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY

contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative. The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental and reproductive toxicity study in rats with COMIRNATY, there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

14.1 Efficacy in Participants 16 Years of Age and Older

Study 2 is a multicenter, multinational, Phase 1/2/3, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In the Phase 2/3 portion of Study 2, based on data accrued through November 14, 2020, approximately 44,000 participants 12 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. The efficacy analyses included participants that received their second vaccination within 19 to 42 days after their first vaccination. The majority (93.1%) of vaccine recipients received the second dose 19 days to 23 days after Dose 1. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of

prior infection with SARS-CoV-2 through 7 days after the second dose. Table 7 presents the specific demographic characteristics in the studied population.

Table 7: Demographics (Population For the Primary Efficacy Endpoint)[a]

	COMIRNATY (N=18,242) n (%)	**Placebo (N=18,379) n (%)**
Sex		
Male	9318 (51.1)	9225 (50.2)
Female	8924 (48.9)	9154 (49.8)
Age (years)		
Mean (SD)	50.6 (15.70)	50.4 (15.81)
Median	52.0	52.0
Min, max	(12, 89)	(12, 91)
Age group		
≥12 through 15 years	46 (0.3)	42 (0.2)
≥16 through 64 years	14,216 (77.9)	14,299 (77.8)
≥65 through 74 years	3176 (17.4)	3226 (17.6)
≥75 years	804 (4.4)	812 (4.4)
Race		
White	15,110 (82.8)	15,301 (83.3)
Black or African American	1617 (8.9)	1617 (8.8)
American Indian or Alaska Native	118 (0.6)	106 (0.6)
Asian	815 (4.5)	810 (4.4)
Native Hawaiian or other Pacific Islander	48 (0.3)	29 (0.2)
Other[b]	534 (2.9)	516 (2.8)
Ethnicity		
Hispanic or Latino	4886 (26.8)	4857 (26.4)
Not Hispanic or Latino	13,253 (72.7)	13,412 (73.0)
Not reported	103 (0.6)	110 (0.6)
Comorbidities[c]		
Yes	8432 (46.2)	8450 (46.0)
No	9810 (53.8)	9929 (54.0)

a. All eligible randomized participants who receive all vaccination(s) as randomized within the predefined window, have no other important protocol deviations as determined by the clinician, and have no evidence of SARS-CoV-2 infection prior to 7 days after Dose 2.

b. Includes multiracial and not reported.

c. Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease:
- Chronic lung disease (e.g., emphysema and chronic bronchitis, idiopathic pulmonary fibrosis, and cystic fibrosis) or moderate to severe asthma
- Significant cardiac disease (e.g., heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and pulmonary hypertension)
- Obesity (body mass index ≥30 kg/m^2)
- Diabetes (Type 1, Type 2, or gestational)
- Liver disease
- Human Immunodeficiency Virus (HIV) infection (not included in the efficacy evaluation)

Efficacy Against COVID-19

The population in the primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020.

Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

The vaccine efficacy information is presented in Table 8.

Table 8: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=18,198 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.3, 97.6)[f]
16 to 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)[g]
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)[g]
65 to 74 years	1 0.406 (3074)	14 0.406 (3095)	92.9 (53.1, 99.8)[g]
75 years and older	0 0.102 (774)	5 0.106 (785)	100.0 (-13.1, 100.0)[g]
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=19,965 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,172 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	9 2.332 (18,559)	169 2.345 (18,708)	94.6 (89.9, 97.3)[f]
16 to 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1 0.530 (4044)	19 0.532 (4067)	94.7 (66.8, 99.9)[g]
65 to 74 years	1 0.424 (3239)	14 0.423 (3255)	92.9 (53.2, 99.8)[g]
75 years and older	0 0.106 (805)	5 0.109 (812)	100.0 (-12.1, 100.0)[g]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. No confirmed cases were identified in participants 12 to 15 years of age.
f. Two-sided credible interval for vaccine efficacy was calculated using a beta-binomial model with a beta (0.700102, 1) prior for $\theta=r(1-VE)/(1+r(1-VE))$, where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.
g. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Updated efficacy analyses were performed with additional confirmed COVID-19 cases accrued during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2 for participants in the efficacy population.

The updated vaccine efficacy information is presented in Table 9.

Table 9: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
16 through 64 years	70 4.859 (15,519)	710 4.654 (15,515)	90.6 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
65 through 74 years	6 0.994 (3350)	98 0.966 (3379)	94.1 (86.6, 97.9)
75 years and older	1 0.239 (842)	26 0.237 (847)	96.2 (76.9, 99.9)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
16 through 64 years	74 5.073 (16,218)	727 4.879 (16,269)	90.2 (87.6, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)
65 through 74 years	6 1.021 (3450)	102 0.992 (3468)	94.3 (87.1, 98.0)

75 years and older	1 0.246 (865)	26 0.240 (858)	96.2 (77.2, 99.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group (both without and with or without evidence of prior SARS-CoV-2 infection); 16 and 18 in the placebo group (without and with or without evidence of prior SARS-CoV-2 infection, respectively).

The updated subgroup analyses of vaccine efficacy by demographic characteristics are presented in Table 10 and Table 11.

Table 10: Vaccine Efficacy– First COVID-19 Occurrence From 7 Days After Dose 2 – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 by Demographic Characteristics – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Sex			
Male	42 3.246 (10,637)	399 3.047 (10,433)	90.1 (86.4, 93.0)
Female	35 3.001 (10,075)	451 2.956 (10,280)	92.4 (89.2, 94.7)
Ethnicity			
Hispanic or Latino	29 1.786 (5161)	241 1.711 (5120)	88.5 (83.0, 92.4)
Not Hispanic or Latino	47 4.429 (15,449)	609 4.259 (15,484)	92.6 (90.0, 94.6)
Race			
Black or African American	4 0.545 (1737)	48 0.527 (1737)	91.9 (78.0, 97.9)
White	67 5.208 (17,186)	747 5.026 (17,256)	91.3 (88.9, 93.4)
All others[f]	6 0.494 (1789)	55 0.451 (1720)	90.0 (76.9, 96.5)

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Country			
Argentina	15 1.012 (2600)	108 0.986 (2586)	86.5 (76.7, 92.7)
Brazil	12 0.406 (1311)	80 0.374 (1293)	86.2 (74.5, 93.1)
Germany	0 0.047 (236)	1 0.048 (242)	100.0 (-3874.2, 100.0)
South Africa	0 0.080 (291)	9 0.074 (276)	100.0 (53.5, 100.0)
Turkey	0 0.027 (228)	5 0.025 (222)	100.0 (-0.1, 100.0)
United States	50 4.674 (16,046)	647 4.497 (16,094)	92.6 (90.1, 94.5)

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).
Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group.

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
f. All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

Table 11: Vaccine Efficacy– First COVID-19 Occurrence From 7 Days After Dose 2 – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 by Demographic Characteristics – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Sex			
Male	44 3.376 (11,103)	411 3.181 (10,920)	89.9 (86.2, 92.8)
Female	37 3.133 (10,539)	462 3.093 (10,769)	92.1 (88.9, 94.5)

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Ethnicity			
Hispanic or Latino	32 1.862 (5408)	245 1.794 (5391)	87.4 (81.8, 91.6)
Not Hispanic or Latino	48 4.615 (16,128)	628 4.445 (16,186)	92.6 (90.1, 94.6)
Race			
Black or African American	4 0.611 (1958)	49 0.601 (1985)	92.0 (78.1, 97.9)
White	69 5.379 (17,801)	768 5.191 (17,880)	91.3 (88.9, 93.3)
All others[f]	8 0.519 (1883)	56 0.481 (1824)	86.8 (72.1, 94.5)
Country			
Argentina	16 1.033 (2655)	110 1.017 (2670)	85.7 (75.7, 92.1)
Brazil	14 0.441 (1419)	82 0.408 (1401)	84.2 (71.9, 91.7)
Germany	0 0.047 (237)	1 0.048 (243)	100.0 (-3868.6, 100.0)
South Africa	0 0.099 (358)	10 0.096 (358)	100.0 (56.6, 100.0)
Turkey	0 0.029 (238)	6 0.026 (232)	100.0 (22.2, 100.0)
United States	51 4.861 (16,735)	664 4.678 (16,785)	92.6 (90.2, 94.6)

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group.

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
f. All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

The updated subgroup analyses of vaccine efficacy by risk status in participants are presented in Table 12 and Table 13.

Table 12: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First COVID-19 occurrence from 7 days after Dose 2[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
At risk[g]			
Yes	35 2.797 (9167)	401 2.681 (9136)	91.6 (88.2, 94.3)
No	42 3.450 (11,545)	449 3.322 (11,577)	91.0 (87.6, 93.6)
Age group (years) and risk status			
16 through 64 and not at risk	41 2.776 (8887)	385 2.661 (8886)	89.8 (85.9, 92.8)
16 through 64 and at risk	29 2.083 (6632)	325 1.993 (6629)	91.5 (87.5, 94.4)
65 and older and not at risk	1 0.553 (1870)	53 0.546 (1922)	98.1 (89.2, 100.0)
65 and older and at risk	6 0.680 (2322)	71 0.656 (2304)	91.8 (81.4, 97.1)
Obese[h]			
Yes	27 2.103 (6796)	314 2.050 (6875)	91.6 (87.6, 94.6)
No	50 4.143 (13,911)	536 3.952 (13,833)	91.1 (88.1, 93.5)
Age group (years) and obesity status			
16 through 64 and not obese	46 3.178 (10,212)	444 3.028 (10,166)	90.1 (86.6, 92.9)
16 through 64 and obese	24 1.680 (5303)	266 1.624 (5344)	91.3 (86.7, 94.5)
65 and older and not obese	4 0.829 (2821)	79 0.793 (2800)	95.2 (87.1, 98.7)
65 and older and obese	3 0.404 (1370)	45 0.410 (1426)	93.2 (78.9, 98.7)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group.

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]

g. At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age]).
h. Obese is defined as BMI ≥30 kg/m^2. For 12 through 15 years age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First COVID-19 occurrence from 7 days after Dose 2[f]	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
At risk[g]			
Yes	36 2.925 (9601)	410 2.807 (9570)	91.6 (88.1, 94.2)
No	45 3.584 (12,041)	463 3.466 (12,119)	90.6 (87.2, 93.2)
Age group (years) and risk status			
16 through 64 and not at risk	44 2.887 (9254)	397 2.779 (9289)	89.3 (85.4, 92.4)
16 through 64 and at risk	30 2.186 (6964)	330 2.100 (6980)	91.3 (87.3, 94.2)
65 and older and not at risk	1 0.566 (1920)	55 0.559 (1966)	98.2 (89.6, 100.0)
65 and older and at risk	6 0.701 (2395)	73 0.672 (2360)	92.1 (82.0, 97.2)
Obese[h]			
Yes	28 2.207 (7139)	319 2.158 (7235)	91.4 (87.4, 94.4)
No	53 4.301 (14,497)	554 4.114 (14,448)	90.8 (87.9, 93.2)
Age group (years) and obesity status			
16 through 64 and not obese	49 3.303 (10,629)	458 3.158 (10,614)	89.8 (86.2, 92.5)
16 through 64 and obese	25 1.768 (5584)	269 1.719 (5649)	91.0 (86.4, 94.3)
65 and older and not obese	4 0.850 (2899)	82 0.811 (2864)	95.3 (87.6, 98.8)
65 and older and obese	3 0.417 (1415)	46 0.420 (1462)	93.4 (79.5, 98.7)

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.
f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group.
g. At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age]).
h. Obese is defined as BMI ≥30 kg/m^2. For the 12 through 15 years of age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Efficacy Against Severe COVID-19

Updated efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 14) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 14: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants With or Without* Prior SARS-CoV-2 Infection Based on FDA† or Centers for Disease Control and Prevention (CDC)‡ Definition After Dose 1 or From 7 Days After Dose 2 in the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence Based on FDA Definition			
	COMIRNATY Cases n1[a] Surveillance Time (n2[b])	Placebo Cases n1[a] Surveillance Time (n2[b])	Vaccine Efficacy % (95% CI[c])
After Dose 1[d]	1 8.439[e] (22,505)	30 8.288[e] (22,435)	96.7 (80.3, 99.9)
7 days after Dose 2[f]	1 6.522[g] (21,649)	21 6.404[g] (21,730)	95.3 (70.9, 99.9)

Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time (n2[b])	**Placebo Cases n1[a] Surveillance Time (n2[b])**	**Vaccine Efficacy % (95% CI[c])**
After Dose 1[d]	1 8.427[e] (22,473)	45 8.269[e] (22,394)	97.8 (87.2, 99.9)
7 days after Dose 2[f]	0 6.514[g] (21,620)	32 6.391[g] (21,693)	100 (88.0, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 as defined by FDA is confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. n2 = Number of participants at risk for the endpoint.
c. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
d. Efficacy assessed based on the Dose 1 all available efficacy (modified intention-to-treat) population that included all randomized participants who received at least 1 dose of study intervention.
e. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.
f. Efficacy assessed based on the evaluable efficacy (7 Days) population that included all eligible randomized participants who receive all dose(s) of study intervention as randomized within the predefined window, have no other important protocol deviations as determined by the clinician.
g. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -80ºC to -60ºC (-112ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

For general questions, visit the website or call the telephone number provided below.

Website	Telephone number
www.comirnatyhcp.com	1-877-829-2619 (1-877-VAX-CO19)

This product's labeling may have been updated. For the most recent prescribing information, please visit www.pfizer.com.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.2

US Govt. License No. x

CPT Code x

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ~~TRADENAME~~ COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

---------- INDICATIONS AND USAGE ----------

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------

Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------

Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS----------

- Postmarketing reports of adverse events suggest increased risks of myocarditis and pericarditis, particularly following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS----------

In clinical studies of participants 16 years of age and older, the most commonly reported adverse reactions (>10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, fever, and injection site swelling. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

2.1 Preparation for Administration

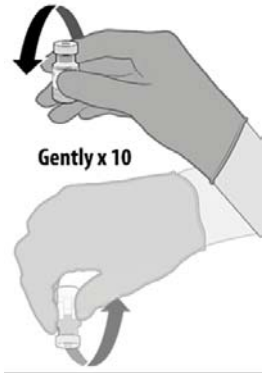
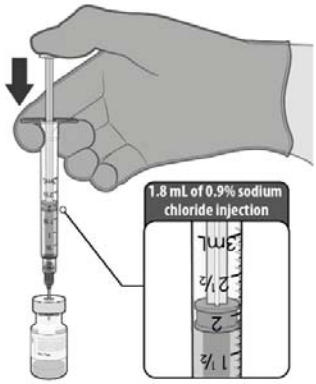
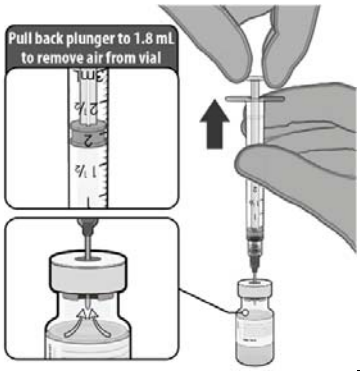
Prior to Dilution

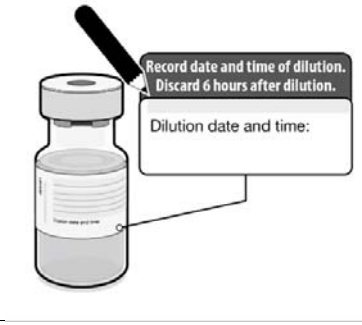
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

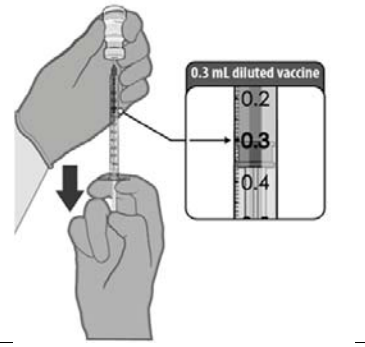
Dilution

- Dilute the vial contents using 1.8 mL of 0.9% Sodium Chloride Injection, USP (provided but shipped separately) to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use 0.9% Sodium Chloride Injection, USP as the diluent.
- After dilution, 1 vial contains 6 doses of 0.3 mL.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before use either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to ~~5 days (120 hours)~~1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.

	• Before dilution invert vaccine vial gently 10 times. • Do not shake. • Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ~~Obtain~~ Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent. • Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Cleanse the vaccine vial stopper with a single-use antiseptic swab. • Add 1.8 mL of 0.9% Sodium Chloride Injection, USP into the vaccine vial.
	• Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.

	• Gently invert the vial containing the COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Visually inspect each dose in the dosing syringe prior to administration. The vaccine will be an off-white suspension. During the visual inspection,

- verify the final dosing volume of 0.3 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

Administer COMIRNATY intramuscularly.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Reports of adverse events following use of COMIRNATY under EUA suggest increased risks of myocarditis and pericarditis, particularly following the second dose. Typically, onset of symptoms has been within a few days following receipt of COMIRNATY. Available data from short-term follow-up suggest that most individuals have had resolution of symptoms, but information is not yet available about potential long-term sequelae. The decision to administer COMIRNATY to an individual with a history of myocarditis or

pericarditis should take into account the individual's clinical circumstances. The CDC has published clinical considerations relevant to myocarditis and pericarditis associated with administration of COMIRNATY (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

~~**5.2 Concurrent Illness at Time of Vaccination**~~

~~The administration of COMIRNATY should be postponed in individuals suffering from acute severe febrile illness.~~

5.3 Concurrent Illness at Time of Vaccination

The administration of COMIRNATY should be postponed in individuals suffering from acute severe febrile illness.

5.~~3~~4 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.~~4~~5 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

~~**5.4 Bleeding Precautions**~~

~~Individuals receiving anticoagulant therapy or those with a bleeding disorder that would contraindicate intramuscular injection, should not be given the vaccine unless the potential benefit clearly outweighs the risk of administration.~~

5.6 Bleeding Precautions

Individuals receiving anticoagulant therapy or those with a bleeding disorder that would contraindicate intramuscular injection, should not be given the vaccine unless the potential benefit clearly outweighs the risk of administration.

5.~~5~~7 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

~~In clinical studies with a data cut-off of March 13, 2021, adverse reactions in participants 16 years of age and older included pain at the injection site (84.3%), fatigue (64.7%), headache (57.1%), muscle pain (40.2%), chills (34.7%), joint pain (25.0%), fever (15.2%), injection site swelling (11.1%), injection site redness (9.9%), nausea (1.2%), malaise (0.6%), lymphadenopathy (0.4%), asthenia (0.3%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).~~

~~Severe allergic reactions, including anaphylaxis, have been reported following administration of COMIRNATY outside of clinical trials.~~

In clinical studies with a data cut-off of March 13, 2021, adverse reactions in participants 16 years of age and older included pain at the injection site (84.3%), fatigue (64.7%), headache (57.1%), muscle pain (40.2%),

chills (34.7%), joint pain (25.0%), fever (15.2%), injection site swelling (11.1%), injection site redness (9.9%), nausea (1.2%), malaise (0.6%), lymphadenopathy (0.4%), asthenia (0.3%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

Severe allergic reactions, including anaphylaxis, have been reported following administration of COMIRNATY outside of clinical trials.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), ~~the~~ United States, Argentina, Brazil, ~~Europe,~~ Turkey, South Africa, and ~~South America~~Germany (Study- 2). Study BNT162-01 (Study 1) was a Phase 1/2, 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3, multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection (Phase 1) and efficacy (Phase 2/3) study that has enrolled approximately 46,000 participants, 12 years of age or older. Of these, approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) in Phase 2/3 are 16 years of age or older (including 378 and 376 participants~~adolescents~~ 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses.

At the time of the analysis of Study 2 for the Emergency Use Authorization (EUA) with a data cut-off of November 14, 2020, there were 37,586 participants (18,801 COMIRNATY and 18,785 placebo) 16 years of age or older followed for a median of 2 months after the second dose of COMIRNATY. At the time of the analysis of Study 2 for the EUA with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031- COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

The safety evaluation in Study 2 is ongoing. The safety population includes participants enrolled by October 9, 2020, and includes safety data accrued through March 13, 2021. Participants 16 years and older in the reactogenicity subset are monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male and 49.1% were female, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants

16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 to 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	**Placebo Dose 1 N[a]=2908 n[b] (%)**	**COMIRNATY Dose 2 N[a]=2682 n[b] (%)**	**Placebo Dose 2 N[a]=2684 n[b] (%)**
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.
No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.
f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

each dose.
The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

Table 5 and Table 6 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 16 years of age and older with confirmed stable HIV infection.

Table 5: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – HIV-Positive Participants 16 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Redness[c]				
Any (>2.0 cm)	2 (3.7)	3 (5.4)	4 (6.7)	1 (1.6)
Mild	2 (3.7)	1 (1.8)	3 (5.0)	1 (1.6)
Moderate	0	0	1 (1.7)	0
Severe	0	2 (3.6)	0	0
Swelling[c]				
Any (>2.0 cm)	3 (5.6)	1 (1.8)	5 (8.3)	0
Mild	2 (3.7)	0	2 (3.3)	0
Moderate	1 (1.9)	0	3 (5.0)	0
Severe	0	1 (1.8)	0	0

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Pain at the injection site[d]				
Any	34 (63.0)	9 (16.1)	32 (53.3)	5 (8.1)
Mild	26 (48.1)	8 (14.3)	22 (36.7)	5 (8.1)
Moderate	8 (14.8)	1 (1.8)	9 (15.0)	0
Severe	0	0	1 (1.7)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in HIV-positive participants 16 years of age and older.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 6: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – HIV-Positive Participants 16 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Fever				
≥38.0°C	1 (1.9)	4 (7.1)	9 (15.0)	5 (8.1)
≥38.0°C to 38.4°C	1 (1.9)	2 (3.6)	4 (6.7)	5 (8.1)
>38.4°C to 38.9°C	0	0	4 (6.7)	0
>38.9°C to 40.0°C	0	2 (3.6)	1 (1.7)	0
>40.0°C	0	0	0	0
Fatigue[c]				
Any	22 (40.7)	15 (26.8)	24 (40.0)	12 (19.4)
Mild	15 (27.8)	9 (16.1)	12 (20.0)	5 (8.1)
Moderate	7 (13.0)	5 (8.9)	9 (15.0)	7 (11.3)
Severe	0	1 (1.8)	3 (5.0)	0
Headache[c]				
Any	11 (20.4)	18 (32.1)	18 (30.0)	12 (19.4)
Mild	7 (13.0)	10 (17.9)	8 (13.3)	8 (12.9)
Moderate	4 (7.4)	7 (12.5)	8 (13.3)	4 (6.5)
Severe	0	1 (1.8)	2 (3.3)	0
Chills[c]				
Any	6 (11.1)	5 (8.9)	14 (23.3)	4 (6.5)
Mild	5 (9.3)	4 (7.1)	5 (8.3)	3 (4.8)
Moderate	1 (1.9)	1 (1.8)	8 (13.3)	1 (1.6)
Severe	0	0	1 (1.7)	0

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Vomiting[d]				
Any	1 (1.9)	3 (5.4)	2 (3.3)	2 (3.2)
Mild	1 (1.9)	1 (1.8)	1 (1.7)	1 (1.6)
Moderate	0	0	1 (1.7)	1 (1.6)
Severe	0	2 (3.6)	0	0
Diarrhea[e]				
Any	5 (9.3)	8 (14.3)	4 (6.7)	9 (14.5)
Mild	5 (9.3)	6 (10.7)	1 (1.7)	6 (9.7)
Moderate	0	1 (1.8)	2 (3.3)	3 (4.8)
Severe	0	1 (1.8)	1 (1.7)	0
New or worsened muscle pain[c]				
Any	9 (16.7)	10 (17.9)	10 (16.7)	5 (8.1)
Mild	7 (13.0)	7 (12.5)	5 (8.3)	1 (1.6)
Moderate	2 (3.7)	3 (5.4)	5 (8.3)	4 (6.5)
Severe	0	0	0	0
New or worsened joint pain[c]				
Any	5 (9.3)	7 (12.5)	10 (16.7)	5 (8.1)
Mild	5 (9.3)	4 (7.1)	4 (6.7)	1 (1.6)
Moderate	0	3 (5.4)	6 (10.0)	4 (6.5)
Severe	0	0	0	0
Use of antipyretic or pain medication[f]	7 (13.0)	8 (14.3)	16 (26.7)	7 (11.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in HIV-positive participants 16 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each event or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

Upon issuance of the EUA for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began in a phased manner for participants in the study. Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 2.1 per 100 person-years among

COMIRNATY recipients and 2.4 per 100 person-years among placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported at an incidence rate of 4.9 per 100 person-years among COMIRNATY recipients and 4.6 per 100 person-years among placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 6.6 per 100 person-years among COMIRNATY recipients and 6.9 per 100 person-years among placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 88.4 per 100 person-years among participants who received COMIRNATY and 43.5 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include non-serious adverse events were reported at an incidence rate of 75.7 per 100 person-years among participants who received COMIRNATY and 43.3 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 95.8 per 100 person-years among participants who received COMIRNATY and 52.0 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

6.2 Post Marketing Experience

The following adverse reactions have been identified during post marketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
~~Gastrointestinal Disorders: diarrhea, vomiting~~
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A reproductive and developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions, twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

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Data

Animal Data

In a reproductive and developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative. The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In ~~studies~~ a developmental and reproductive toxicity study in rats with COMIRNATY, there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

14.1 Efficacy in Participants 16 Years of Age and Older

Study 2 is a multicenter, multinational, Phase 1/2/3, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or

hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In the Phase 2/3 portion of Study 2, based on data accrued through November 14, 2020, approximately 44,000 participants 12 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. The efficacy analyses included participants that received their second vaccination within 19 to 42 days after their first vaccination. The majority (93.1%) of vaccine recipients received the second dose 19 days to 23 days after Dose 1. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. Table 7 presents the specific demographic characteristics in the studied population.

Table 7: Demographics (Population For the Primary Efficacy Endpoint)[a]

	COMIRNATY (N=18,242) n (%)	**Placebo (N=18,379) n (%)**
Sex		
Male	9318 (51.1)	9225 (50.2)
Female	8924 (48.9)	9154 (49.8)
Age (years)		
Mean (SD)	50.6 (15.70)	50.4 (15.81)
Median	52.0	52.0
Min, max	(12, 89)	(12, 91)
Age group		
≥12 through 15 years	46 (0.3)	42 (0.2)
≥16 through 64 years	14,216 (77.9)	14,299 (77.8)
≥65 through 74 years	3176 (17.4)	3226 (17.6)
≥75 years	804 (4.4)	812 (4.4)
Race		
White	15,110 (82.8)	15,301 (83.3)
Black or African American	1617 (8.9)	1617 (8.8)
American Indian or Alaska Native	118 (0.6)	106 (0.6)
Asian	815 (4.5)	810 (4.4)
Native Hawaiian or other Pacific Islander	48 (0.3)	29 (0.2)
Other[b]	534 (2.9)	516 (2.8)
Ethnicity		
Hispanic or Latino	4886 (26.8)	4857 (26.4)
Not Hispanic or Latino	13,253 (72.7)	13,412 (73.0)
Not reported	103 (0.6)	110 (0.6)
Comorbidities[c]		
Yes	8432 (46.2)	8450 (46.0)
No	9810 (53.8)	9929 (54.0)

a. All eligible randomized participants who receive all vaccination(s) as randomized within the predefined window, have no other important protocol deviations as determined by the clinician, and have no evidence of SARS-CoV-2 infection prior to 7 days after Dose 2.
b. Includes multiracial and not reported.
c. Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease:

- Chronic lung disease (e.g., emphysema and chronic bronchitis, idiopathic pulmonary fibrosis, and cystic fibrosis) or moderate to severe asthma
- Significant cardiac disease (e.g., heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and pulmonary hypertension)
- Obesity (body mass index ≥30 kg/m^2)
- Diabetes (Type 1, Type 2, or gestational)
- Liver disease
- Human Immunodeficiency Virus (HIV) infection (not included in the efficacy evaluation)

Efficacy Against COVID-19

The population in the primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

The vaccine efficacy information is presented in Table 8.

Table 8: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=18,198 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.3, 97.6)[f]
16 to 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)[g]
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)[g]
65 to 74 years	1 0.406 (3074)	14 0.406 (3095)	92.9 (53.1, 99.8)[g]
75 years and older	0 0.102 (774)	5 0.106 (785)	100.0 (-13.1, 100.0)[g]
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=19,965 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,172 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	9 2.332 (18,559)	169 2.345 (18,708)	94.6 (89.9, 97.3)[f]
16 to 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1	19	94.7

	0.530 (4044)	0.532 (4067)	(66.8, 99.9)[g]
65 to 74 years	1 0.424 (3239)	14 0.423 (3255)	92.9 (53.2, 99.8)[g]
75 years and older	0 0.106 (805)	5 0.109 (812)	100.0 (-12.1, 100.0)[g]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. No confirmed cases were identified in participants 12 to 15 years of age.
f. Two-sided credible interval for vaccine efficacy was calculated using a beta-binomial model with a beta (0.700102, 1) prior for $\theta=r(1-VE)/(1+r(1-VE))$, where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.
g. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Updated efficacy analyses were performed with additional confirmed COVID-19 cases accrued during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2 for participants in the efficacy population.

The updated vaccine efficacy information is presented in Table 9.

Table 9: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
16 through 64 years	70 4.859 (15,519)	710 4.654 (15,515)	90.6 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
65 through 74 years	6 0.994 (3350)	98 0.966 (3379)	94.1 (86.6, 97.9)
75 years and older	1 0.239 (842)	26 0.237 (847)	96.2 (76.9, 99.9)

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
16 through 64 years	74 5.073 (16,218)	727 4.879 (16,269)	90.2 (87.6, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)
65 through 74 years	6 1.021 (3450)	102 0.992 (3468)	94.3 (87.1, 98.0)
75 years and older	1 0.246 (865)	26 0.240 (858)	96.2 (77.2, 99.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group (both without and with or without evidence of prior SARS-CoV-2 infection); 16 and 18 in the placebo group (without and with or without evidence of prior SARS-CoV-2 infection, respectively).

The updated subgroup analyses of vaccine efficacy by demographic characteristics are presented in Table 10 and Table 11.

Table 10: Vaccine Efficacy– First COVID-19 Occurrence From 7 Days After Dose 2 – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 by Demographic Characteristics – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	**COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)[e]**
Sex			
Male	42 3.246 (10,637)	399 3.047 (10,433)	90.1 (86.4, 93.0)
Female	35 3.001 (10,075)	451 2.956 (10,280)	92.4 (89.2, 94.7)
Ethnicity			

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Hispanic or Latino	29 1.786 (5161)	241 1.711 (5120)	88.5 (83.0, 92.4)
Not Hispanic or Latino	47 4.429 (15,449)	609 4.259 (15,484)	92.6 (90.0, 94.6)
Race			
Black or African American	4 0.545 (1737)	48 0.527 (1737)	91.9 (78.0, 97.9)
White	67 5.208 (17,186)	747 5.026 (17,256)	91.3 (88.9, 93.4)
All others[f]	6 0.494 (1789)	55 0.451 (1720)	90.0 (76.9, 96.5)
Country			
Argentina	15 1.012 (2600)	108 0.986 (2586)	86.5 (76.7, 92.7)
Brazil	12 0.406 (1311)	80 0.374 (1293)	86.2 (74.5, 93.1)
Germany	0 0.047 (236)	1 0.048 (242)	100.0 (-3874.2, 100.0)
South Africa	0 0.080 (291)	9 0.074 (276)	100.0 (53.5, 100.0)
Turkey	0 0.027 (228)	5 0.025 (222)	100.0 (-0.1, 100.0)
United States	50 4.674 (16,046)	647 4.497 (16,094)	92.6 (90.1, 94.5)

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).
Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group.

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
f. All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

Table 11: Vaccine Efficacy– First COVID-19 Occurrence From 7 Days After Dose 2 – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 by Demographic Characteristics – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Sex			
Male	44 3.376 (11,103)	411 3.181 (10,920)	89.9 (86.2, 92.8)
Female	37 3.133 (10,539)	462 3.093 (10,769)	92.1 (88.9, 94.5)
Ethnicity			
Hispanic or Latino	32 1.862 (5408)	245 1.794 (5391)	87.4 (81.8, 91.6)
Not Hispanic or Latino	48 4.615 (16,128)	628 4.445 (16,186)	92.6 (90.1, 94.6)
Race			
Black or African American	4 0.611 (1958)	49 0.601 (1985)	92.0 (78.1, 97.9)
White	69 5.379 (17,801)	768 5.191 (17,880)	91.3 (88.9, 93.3)
All others[f]	8 0.519 (1883)	56 0.481 (1824)	86.8 (72.1, 94.5)
Country			
Argentina	16 1.033 (2655)	110 1.017 (2670)	85.7 (75.7, 92.1)
Brazil	14 0.441 (1419)	82 0.408 (1401)	84.2 (71.9, 91.7)
Germany	0 0.047 (237)	1 0.048 (243)	100.0 (-3868.6, 100.0)
South Africa	0 0.099 (358)	10 0.096 (358)	100.0 (56.6, 100.0)
Turkey	0 0.029 (238)	6 0.026 (232)	100.0 (22.2, 100.0)
United States	51 4.861 (16,735)	664 4.678 (16,785)	92.6 (90.2, 94.6)

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group.

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
f. All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

The updated subgroup analyses of vaccine efficacy by risk status in participants are presented in Table 12 and Table 13.

Table 12: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First COVID-19 occurrence from 7 days after Dose 2[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
At risk[g]			
Yes	35 2.797 (9167)	401 2.681 (9136)	91.6 (88.2, 94.3)
No	42 3.450 (11,545)	449 3.322 (11,577)	91.0 (87.6, 93.6)
Age group (years) and risk status			
16 through 64 and not at risk	41 2.776 (8887)	385 2.661 (8886)	89.8 (85.9, 92.8)
16 through 64 and at risk	29 2.083 (6632)	325 1.993 (6629)	91.5 (87.5, 94.4)
65 and older and not at risk	1 0.553 (1870)	53 0.546 (1922)	98.1 (89.2, 100.0)
65 and older and at risk	6 0.680 (2322)	71 0.656 (2304)	91.8 (81.4, 97.1)
Obese[h]			
Yes	27 2.103 (6796)	314 2.050 (6875)	91.6 (87.6, 94.6)
No	50 4.143 (13,911)	536 3.952 (13,833)	91.1 (88.1, 93.5)
Age group (years) and obesity status			
16 through 64 and not obese	46 3.178 (10,212)	444 3.028 (10,166)	90.1 (86.6, 92.9)
16 through 64 and obese	24 1.680 (5303)	266 1.624 (5344)	91.3 (86.7, 94.5)
65 and older and not obese	4 0.829 (2821)	79 0.793 (2800)	95.2 (87.1, 98.7)
65 and older and obese	3 0.404 (1370)	45 0.410 (1426)	93.2 (78.9, 98.7)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint.

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]

Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group.

g. At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age]).

h. Obese is defined as BMI ≥30 kg/m^2. For 12 through 15 years age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First COVID-19 occurrence from 7 days after Dose 2[f]	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
At risk[g]			
Yes	36 2.925 (9601)	410 2.807 (9570)	91.6 (88.1, 94.2)
No	45 3.584 (12,041)	463 3.466 (12,119)	90.6 (87.2, 93.2)
Age group (years) and risk status			
16 through 64 and not at risk	44 2.887 (9254)	397 2.779 (9289)	89.3 (85.4, 92.4)
16 through 64 and at risk	30 2.186 (6964)	330 2.100 (6980)	91.3 (87.3, 94.2)
65 and older and not at risk	1 0.566 (1920)	55 0.559 (1966)	98.2 (89.6, 100.0)
65 and older and at risk	6 0.701 (2395)	73 0.672 (2360)	92.1 (82.0, 97.2)
Obese[h]			
Yes	28 2.207 (7139)	319 2.158 (7235)	91.4 (87.4, 94.4)
No	53 4.301 (14,497)	554 4.114 (14,448)	90.8 (87.9, 93.2)
Age group (years) and obesity status			
16 through 64 and not obese	49 3.303 (10,629)	458 3.158 (10,614)	89.8 (86.2, 92.5)
16 through 64 and obese	25 1.768 (5584)	269 1.719 (5649)	91.0 (86.4, 94.3)
65 and older and not obese	4 0.850 (2899)	82 0.811 (2864)	95.3 (87.6, 98.8)

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
65 and older and obese	3 0.417 (1415)	46 0.420 (1462)	93.4 (79.5, 98.7)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.
f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group.
g. At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age]).
h. Obese is defined as BMI ≥30 kg/m^2. For the 12 through 15 years of age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Efficacy Against Severe COVID-19

Updated efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 14) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 14: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants With or Without* Prior SARS-CoV-2 Infection Based on FDA[†] or Centers for Disease Control and Prevention (CDC)[‡] Definition After Dose 1 or From 7 Days After Dose 2 in the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence Based on FDA Definition			
	COMIRNATY Cases n1[a] Surveillance Time (n2[b])	Placebo Cases n1[a] Surveillance Time (n2[b])	Vaccine Efficacy % (95% CI[c])
After Dose 1[d]	1 8.439[e] (22,505)	30 8.288[e] (22,435)	96.7 (80.3, 99.9)
7 days after Dose 2[f]	1 6.522[g] (21,649)	21 6.404[g] (21,730)	95.3 (70.9, 99.9)

Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time (n2[b])	**Placebo Cases n1[a] Surveillance Time (n2[b])**	**Vaccine Efficacy % (95% CI[c])**
After Dose 1[d]	1 8.427[e] (22,473)	45 8.269[e] (22,394)	97.8 (87.2, 99.9)
7 days after Dose 2[f]	0 6.514[g] (21,620)	32 6.391[g] (21,693)	100 (88.0, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 as defined by FDA is confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. n2 = Number of participants at risk for the endpoint.
c. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
d. Efficacy assessed based on the Dose 1 all available efficacy (modified intention-to-treat) population that included all randomized participants who received at least 1 dose of study intervention.
e. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.
f. Efficacy assessed based on the evaluable efficacy (7 Days) population that included all eligible randomized participants who receive all dose(s) of study intervention as randomized within the predefined window, have no other important protocol deviations as determined by the clinician.
g. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -80ºC to -60ºC (-112ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage ~~within this temperature range~~of the vials between -96°C to -60°C (-141°F to -76°F)~~.~~ is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to ~~5 days (120 hours)~~1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours. ~~Any hours used for transport at 2°C to 8°C (35°F to 46°F) count against the 120-hour limit for storage at 2°C to 8°C (35°F to 46°F).~~

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

~~For general questions, visit the website or call the telephone number provided below.~~

~~Website~~	~~Telephone number~~
~~www.cvdvaccine.com~~	~~1-877-829-2619 (1-877-VAX-CO19)~~

For general questions, visit the website or call the telephone number provided below.

Website	Telephone number
www.comirnatyhcp.com	1-877-829-2619 (1-877-VAX-CO19)

This product's labeling may have been updated. For the most recent prescribing information, please visit www.pfizer.com.

Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.~~1~~2

US Govt. License No. x

~~CPT Code x~~CPT Code x

6.284 (20356)	6.048 (20395)	(88.8, 93.0)
1 0.015 (50)	0 0.015 (46)	-∞ (NA, NA)
1 0.030 (101)	1 0.037 (130)	-24.7 (-9685.9, 98.4)
80 6.293 (20376)	849 6.061 (20423)	90.9 (88.6, 92.9)
0 0.017 (56)	4 0.013 (42)	100.0 (-11.3, 100.0)

(58)	(71)	
3	5	36.0
0.169	0.181	(-228.7, 90.1)
(550)	(594)	
78	847	91.1
6.147	5.910	(88.8, 93.1)
(19896)	(19927)	
0	2	100.0
0.023	0.019	(-348.8, 100.0)
(87)	(74)	

eoprotein–binding; NA = Not applicable; NP = nasopharyngeal;
ain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2;

oup.

6.422 (20836)	6.144 (20697)	(88.9, 93.1)
1 0.016 (51)	0 0.016 (49)	-∞ (NA, NA)
1 0.031 (105)	1 0.038 (131)	-22.3 (-9503.8, 98.4)
81 6.431 (20857)	865 6.156 (20723)	91.0 (88.7, 93.0)
0 0.017 (57)	4 0.013 (47)	100.0 (-16.4, 100.0)

(61)	(72)	
3	5	35.8
0.173	0.185	(-229.9, 90.0)
(563)	(608)	
79	863	91.3
6.283	6.002	(89.0, 93.1)
(20367)	(20218)	
0	2	100.0
0.023	0.019	(-344.1, 100.0)
(89)	(75)	

eoprotein–binding; NA = Not applicable; NP = nasopharyngeal;
ain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2;

oup.

lack of PI oversight	21 (0.1)	22 (0.1)	43 (0.1)
	21648 (98.0)	21624 (97.9)	43272 (98.0)
to 7 days after Dose 2	20536 (93.0)	20487 (92.8)	41023 (92.9)
ficacy population	437 (2.0)	456 (2.1)	893 (2.0)
	374 (1.7)	430 (1.9)	804 (1.8)
lack of PI oversight	21 (0.1)	22 (0.1)	43 (0.1)
	44 (0.2)	11 (0.0)	55 (0.1)
	21136 (95.7)	21300 (96.5)	42436 (96.1)
to 7 days after Dose 2	20064 (90.8)	20197 (91.5)	40261 (91.2)
ays) population	949 (4.3)	780 (3.5)	1729 (3.9)

characteristic.
percentage calculations.
e than 1 reason.

(10, 89)	(10, 91)	(10, 91)
370 (1.8)	362 (1.7)	732 (1.7)
12120 (57.3)	12252 (57.5)	24372 (57.4)
8646 (40.9)	8686 (40.8)	17332 (40.8)
4407 (20.9)	4429 (20.8)	8836 (20.8)
204 (1.0)	190 (0.9)	394 (0.9)
929 (4.4)	924 (4.3)	1853 (4.4)
2009 (9.5)	2036 (9.6)	4045 (9.5)
der	56 (0.3)	32 (0.2)	88 (0.2)
17304 (81.9)	17487 (82.1)	34791 (82.0)
545 (2.6)	519 (2.4)	1064 (2.5)
89 (0.4)	112 (0.5)	201 (0.5)
5403 (25.6)	5409 (25.4)	10812 (25.5)

ction: Negative[f]	20365 (96.4)	20511 (96.3)	40876 (96.3)
ction: Positive[e]	627 (3.0)	669 (3.1)	1296 (3.1)
ction: Missing	144 (0.7)	120 (0.6)	264 (0.6)
	2686 (12.7)	2710 (12.7)	5396 (12.7)
	1437 (6.8)	1432 (6.7)	2869 (6.8)
	240 (1.1)	243 (1.1)	483 (1.1)
	391 (1.8)	392 (1.8)	783 (1.8)
	241 (1.1)	238 (1.1)	479 (1.1)
	16141 (76.4)	16285 (76.5)	32426 (76.4)

piratory syndrome coronavirus 2.
s summary but not included in the analyses of the overall study objectives.
oup, or the total sample. This value is the denominator for the percentage calculations.
characteristic.

97)	(9955)		
	48	93.7	NA
80	0.983	(80.6, 98.8)	
00)	(7543)		

eoprotein–binding; NAAT = nucleic acid amplification test;
ome coronavirus 2; VE = vaccine efficacy.
ogical evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding
-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any
were included in the analysis.
oup.
oint definition.
rs for the given endpoint across all subjects within each group at risk for the endpoint. Time period for
se 2 to the end of the surveillance period.
dpoint.
based on the Clopper and Pearson method adjusted for surveillance time.

(11517)	(11533)	
25	265	90.9
2.499	2.417	(86.2, 94.2)
(8194)	(8208)	

eoprotein–binding; NAAT = nucleic acid amplification test;
me coronavirus 2; VE = vaccine efficacy.
gical evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding
-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any
ere included in the analysis.
up.
oint definition.
rs for the given endpoint across all subjects within each group at risk for the endpoint. Time period for
se 2 to the end of the surveillance period.
dpoint.
based on the Clopper and Pearson method adjusted for surveillance time.

(12088)	(12142)	
25	270	91.0
2.573	2.492	(86.5, 94.3)
(8445)	(8453)	

spiratory syndrome coronavirus 2; VE = vaccine efficacy.
oup.
oint definition.
rs for the given endpoint across all subjects within each group at risk for the endpoint. Time period for
se 2 to the end of the surveillance period.
dpoint.
based on the Clopper and Pearson method adjusted for surveillance time.

0 0.065 (365)	11 0.061 (355)	100.0 (62.4, 100.0)
74 5.008 (15853)	715 4.817 (15914)	90.0 (87.3, 92.3)
7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)
6 1.021 (3450)	102 0.992 (3468)	94.3 (87.1, 98.0)
1 0.246 (865)	26 0.240 (858)	96.2 (77.2, 99.9)
36	402	91.4

44 2.887 (9254)	397 2.779 (9289)	89.3 (85.4, 92.4)
30 2.186 (6964)	329 2.100 (6980)	91.2 (87.3, 94.2)
1 0.566 (1920)	55 0.559 (1966)	98.2 (89.6, 100.0)
6 0.701 (2395)	73 0.672 (2360)	92.1 (82.0, 97.2)
28 2.185 (6999)	314 2.139 (7111)	91.3 (87.1, 94.3)
53	540	90.6

25 1.768 (5584)	268 1.719 (5649)	90.9 (86.3, 94.2)
4 0.850 (2899)	82 0.811 (2864)	95.3 (87.6, 98.8)
3 0.417 (1415)	46 0.420 (1462)	93.4 (79.5, 98.7)
37 3.051 (9985)	455 3.013 (10241)	92.0 (88.8, 94.4)
44 3.289 (10548)	399 3.097 (10354)	89.6 (85.8, 92.6)
32	240	87.1

	1	0	-∞
	0.032	0.034	(NA, NA)
	(104)	(109)	
	0	3	100.0
	0.043	0.038	(-116.0, 100.0)
	(196)	(180)	
	3	24	88.0
	0.258	0.247	(60.6, 97.7)
	(907)	(896)	
	4	49	92.0
	0.602	0.591	(78.1, 97.9)
	(1909)	(1928)	
r	0	1	100.0
	0.016	0.008	(-1947.9, 100.0)
	(54)	(31)	
	69	749	91.1

0 0.027 (83)	6 0.031 (105)	100.0 (1.4, 100.0)
3 0.183 (593)	6 0.195 (643)	46.7 (-149.5, 91.4)
77 6.119 (19805)	846 5.883 (19838)	91.2 (88.9, 93.2)
1 0.038 (135)	2 0.033 (114)	56.9 (-728.5, 99.3)
16 1.033 (2655)	110 1.017 (2670)	85.7 (75.7, 92.1)
14	82	84.2

0	10	100.0
0.099	0.096	(56.6, 100.0)
(358)	(358)	
0	6	100.0
0.029	0.026	(22.2, 100.0)
(238)	(232)	
51	645	92.4
4.692	4.515	(89.9, 94.4)
(15626)	(15691)	

eoprotein–binding; NAAT = nucleic acid amplification test;
me coronavirus 2; VE = vaccine efficacy.
oup.
oint definition.
rs for the given endpoint across all subjects within each group at risk for the endpoint. Time period for
se 2 to the end of the surveillance period.
dpoint.
based on the Clopper and Pearson method adjusted for surveillance time.

	7 (9.1)	124 (14.9)	131 (14.4)
	6 (7.8)	98 (11.8)	104 (11.4)
	1 (1.3)	26 (3.1)	27 (3.0)
	0	3 (0.4)	3 (0.3)
	3 (3.9)	23 (2.8)	26 (2.9)
	4 (5.2)	48 (5.8)	52 (5.7)
der	0	1 (0.1)	1 (0.1)
	67 (87.0)	730 (87.6)	797 (87.6)
	3 (3.9)	22 (2.6)	25 (2.7)
	0	6 (0.7)	6 (0.7)
	35 (45.5)	444 (53.3)	479 (52.6)
	42 (54.5)	389 (46.7)	431 (47.4)
	29 (37.7)	236 (28.3)	265 (29.1)

15 (19.5)	108 (13.0)	123 (13.5)
12 (15.6)	80 (9.6)	92 (10.1)
0	1 (0.1)	1 (0.1)
0	9 (1.1)	9 (1.0)
0	5 (0.6)	5 (0.5)
50 (64.9)	630 (75.6)	680 (74.7)

oup, or the total sample. This value is the denominator for the percentage calculations.
characteristic.
omorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of
MI $\geq$30 kg/m^2.

6.092 (19711)	5.857 (19741)	(88.8, 93.1)
42 3.329 (10757)	438 3.207 (10808)	90.8 (87.3, 93.4)
35 2.763 (8954)	395 2.650 (8933)	91.5 (88.0, 94.2)
3 0.228 (770)	27 0.213 (747)	89.6 (66.3, 98.0)
3 0.172 (584)	22 0.159 (555)	87.4 (58.1, 97.6)
8	66	88.7

27 2.083 (6673)	310 2.034 (6770)	91.5 (87.4, 94.5)
15 1.481 (4900)	190 1.427 (4895)	92.4 (87.1, 95.8)
9 0.468 (1537)	62 0.447 (1527)	86.1 (71.9, 93.9)

eoprotein–binding; NAAT = nucleic acid amplification test;
me coronavirus 2; VE = vaccine efficacy.
gical evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding
-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any
ere included in the analysis.
up.
oint definition.

ome coronavirus 2; VE = vaccine efficacy.
gical evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding
-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any
ere included in the analysis.
oup.
oint definition.
rs for the given endpoint across all subjects within each group at risk for the endpoint. Time period for
se 2 to the end of the surveillance period.
dpoint.
based on the Clopper and Pearson method adjusted for surveillance time.

0	1	100.0
0.403	0.402	(-3783.8, 100.0)
(21056)	(20962)	
1	23	95.8
6.493	6.337	(73.9, 99.9)
(21029)	(20940)	

oup.
oint definition.
rs for the given endpoint across all subjects within each group at risk for the endpoint. Time period for
nd of the surveillance period.
dpoint.
based on the Clopper and Pearson method adjusted for surveillance time.

3	30	90.0
0.403	0.401	(68.0, 98.1)
(21049)	(20952)	
82	870	91.0
6.479	6.207	(88.7, 92.9)
(21019)	(20901)	

oup.
oint definition.
rs for the given endpoint across all subjects within each group at risk for the endpoint. Time period for
nd of the surveillance period.
dpoint.
based on the Clopper and Pearson method adjusted for surveillance time.

Table.B Study Disposition of Phase 2/3 Randomized Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N^a=22085) n^b (%)	**Placebo (N^a=22080) n^b (%)**	**Total (N^a=44165) n^b (%)**
Randomized	22085 (100.0)	22080 (100.0)	44165 (100.0)
Not vaccinated	55 (0.2)	50 (0.2)	105 (0.2)
Original blinded placebo-controlled follow-up period			
Vaccinated	22030 (99.8)	22030 (99.8)	44060 (99.8)
Dose 1	22030 (99.8)	22030 (99.8)	44060 (99.8)
Dose 2	21675 (98.1)	21650 (98.1)	43325 (98.1)
Discontinued from original blinded placebo-controlled vaccination period[c]	352 (1.6)	528 (2.4)	880 (2.0)
Reason for discontinuation			
Lost to follow-up	151 (0.7)	153 (0.7)	304 (0.7)
Withdrawal by subject	109 (0.5)	181 (0.8)	290 (0.7)
No longer meets eligibility criteria	26 (0.1)	120 (0.5)	146 (0.3)
Adverse event	27 (0.1)	26 (0.1)	53 (0.1)
Physician decision	5 (0.0)	8 (0.0)	13 (0.0)
Pregnancy	6 (0.0)	6 (0.0)	12 (0.0)
Protocol deviation	3 (0.0)	8 (0.0)	11 (0.0)
Death	3 (0.0)	4 (0.0)	7 (0.0)
Medication error without associated adverse event	3 (0.0)	2 (0.0)	5 (0.0)
Withdrawal by parent/guardian	1 (0.0)	0	1 (0.0)
Other	18 (0.1)	20 (0.1)	38 (0.1)
Unblinded before 1-month post–Dose 2 visit	253 (1.1)	240 (1.1)	493 (1.1)

Table.B Study Disposition of Phase 2/3 Randomized Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N^a=22085) n^b (%)	**Placebo (N^a=22080) n^b (%)**	**Total (N^a=44165) n^b (%)**
Completed 1-month post–Dose 2 visit	21382 (96.8)	21293 (96.4)	42675 (96.6)
Withdrawn from the study	343 (1.6)	484 (2.2)	827 (1.9)
Withdrawn after Dose 1 and before Dose 2	176 (0.8)	211 (1.0)	387 (0.9)
Withdrawn after Dose 2 and before 1-month post–Dose 2 visit	100 (0.5)	139 (0.6)	239 (0.5)
Withdrawn after 1-month post–Dose 2 visit	67 (0.3)	134 (0.6)	201 (0.5)
Reason for withdrawal from the study			
Lost to follow-up	174 (0.8)	191 (0.9)	365 (0.8)
Withdrawal by subject	122 (0.6)	226 (1.0)	348 (0.8)
Protocol deviation	11 (0.0)	24 (0.1)	35 (0.1)
Death	16 (0.1)	15 (0.1)	31 (0.1)
Adverse event	9 (0.0)	8 (0.0)	17 (0.0)
Physician decision	3 (0.0)	6 (0.0)	9 (0.0)
No longer meets eligibility criteria	1 (0.0)	4 (0.0)	5 (0.0)
Pregnancy	0	1 (0.0)	1 (0.0)
Medication error without associated adverse event	1 (0.0)	0	1 (0.0)
Withdrawal by parent/guardian	1 (0.0)	0	1 (0.0)
Other	5 (0.0)	9 (0.0)	14 (0.0)
Open-label follow-up period			
Originally randomized to BNT162b2	20404 (92.4)		
Received Dose 2/unplanned dose	87 (0.4)		
Completed 1-month post–Dose 2 visit	210 (1.0)		

Table.B Study Disposition of Phase 2/3 Randomized Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=22085) n[b] (%)	**Placebo (N[a]=22080) n[b] (%)**	**Total (N[a]=44165) n[b] (%)**
Completed 6-month post–Dose 2 visit	6414 (29.0)		
Withdrawn from the study	105 (0.5)		
Withdrawn before 6-month post–Dose 2 visit	103 (0.5)		
Withdrawn after 6-month post–Dose 2 visit	2 (0.0)		
Reason for withdrawal from the study			
Withdrawal by subject	56 (0.3)		
Protocol deviation	35 (0.2)		
Lost to follow-up	4 (0.0)		
Death	3 (0.0)		
Physician decision	2 (0.0)		
Adverse event	1 (0.0)		
No longer meets eligibility criteria	1 (0.0)		
Other	3 (0.0)		
Originally randomized to placebo		20948 (94.9)	
Completed 6-month post–Dose 2 visit		153 (0.7)	
Withdrawn from the study after unblinding and before Dose 3		497 (2.3)	
Received Dose 3 (first dose of BNT162b2 [30 µg])		19612 (88.8)	
Received Dose 4 (second dose of BNT162b2 [30 µg])		15986 (72.4)	
Discontinued from open-label vaccination period[d]		24 (0.1)	
Reason for discontinuation from open-label vaccination period			
Protocol deviation		6 (0.0)	

Table.B Study Disposition of Phase 2/3 Randomized Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=22085) n[b] (%)	Placebo (N[a]=22080) n[b] (%)	Total (N[a]=44165) n[b] (%)
Adverse event		5 (0.0)	
Withdrawal by subject		5 (0.0)	
Pregnancy		4 (0.0)	
Death		2 (0.0)	
Lost to follow-up		2 (0.0)	
Completed 1-month post–Dose 4 visit		7209 (32.6)	
Withdrawn from the study		14 (0.1)	
Withdrawn after Dose 3 and before Dose 4		11 (0.0)	
Withdrawn after Dose 4 and before 1-month post–Dose 4 visit		2 (0.0)	
Withdrawn after 1-month post–Dose 4 visit		1 (0.0)	
Reason for withdrawal from the study			
Withdrawal by subject		7 (0.0)	
Protocol deviation		3 (0.0)	
Death		2 (0.0)	
Adverse event		1 (0.0)	
Lost to follow-up		1 (0.0)	

Note: Human immunodeficiency virus (HIV)-positive subjects are included in this summary but analyzed and reported separately.
Note: Subjects randomized but did not sign informed consent or had a significant quality event due to lack of PI oversight are not included in any analysis population.
Note: Because of a dosing error, Subjects C4591001 1081 10811053, C4591001 1088 10881077, C4591001 1177 11771089 and C4591001 1231 12311057 received an additional dose of BNT162b2 (30 µg) at an unscheduled visit after receiving 1 dose of BNT162b2 (30 µg) and 1 dose of placebo.
a. N = number of randomized subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.

Table.B Study Disposition of Phase 2/3 Randomized Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N^a=22085) n^b (%)	**Placebo (N^a=22080) n^b (%)**	**Total (N^a=44165) n^b (%)**

b. n = Number of subjects with the specified characteristic.
c. Original blinded placebo-controlled vaccination period is defined as the time period from Dose 1 to 1 month post–Dose 2.
d. Open-label vaccination period is defined as the time period from Dose 3 (first dose of BNT162b2 [30 µg]) to 1 month post–Dose 4 (second dose of BNT162b2 [30 µg]).

Table.C Disposition of Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13 2021, Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=22026) n[b] (%)	Placebo (N[a]=22021) n[b] (%)	Total (N[a]=44050) n[b] (%)
Randomized			44165
Not vaccinated			105
Vaccinated	22026 (100.0)	22021 (100.0)	44050 (100.0)
Completed 1 dose	22026 (100.0)	22021 (100.0)	44050 (100.0)
Completed 2 doses	21674 (98.4)	21645 (98.3)	43319 (98.3)
Safety population	22026 (100.0)	22021 (100.0)	44050 (100.0)
Reactogenicity subset	5033 (22.9)	5032 (22.9)	10068 (22.9)
HIV-positive	100 (0.5)	100 (0.5)	200 (0.5)
Indeterminate vaccine			3 (0.0)
Participants excluded from safety population			115 (0.3)
Reason for exclusion			
Participant did not receive study vaccine			105 (0.2)
Unreliable data due to lack of PI oversight			10 (0.0)
Completed at least 6 months follow-up after Dose 2 in blinded placebo-controlled follow-up period	1778 (8.1)	1304 (5.9)	3082 (7.0)
Completed at least 6 months follow-up after Dose 2 in blinded and open-label follow-up period	12006 (54.5)		
Completed 1-month post–Dose 2 visit (vaccination period)	21378 (97.1)	21291 (96.7)	42669 (96.9)
Discontinued from vaccination period but continued in the study up to 1-month post–Dose 2 visit	350 (1.6)	520 (2.4)	873 (2.0)

Table.C Disposition of Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13 2021, Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N^a=22026) n^b (%)	**Placebo (N^a=22021) n^b (%)**	**Total (N^a=44050) n^b (%)**
Discontinued after Dose 1 and before Dose 2	233 (1.1)	359 (1.6)	595 (1.4)
Discontinued after Dose 2 and before 1-month post–Dose 2 visit	117 (0.5)	161 (0.7)	278 (0.6)
Reason for discontinuation from vaccination period			
Lost to follow-up	151 (0.7)	149 (0.7)	300 (0.7)
Withdrawal by subject	108 (0.5)	181 (0.8)	289 (0.7)
No longer meets eligibility criteria	25 (0.1)	120 (0.5)	145 (0.3)
Adverse event	27 (0.1)	26 (0.1)	53 (0.1)
Physician decision	5 (0.0)	7 (0.0)	12 (0.0)
Pregnancy	6 (0.0)	6 (0.0)	12 (0.0)
Protocol deviation	3 (0.0)	8 (0.0)	11 (0.0)
Death	3 (0.0)	4 (0.0)	7 (0.0)
Medication error without associated adverse event	2 (0.0)	0	5 (0.0)
Withdrawal by parent/guardian	1 (0.0)	0	1 (0.0)
Other	19 (0.1)	19 (0.1)	38 (0.1)
Withdrawn from study before 1-month post–Dose 2 visit	273 (1.2)	344 (1.6)	617 (1.4)
Withdrawn after Dose 1 and before Dose 2	173 (0.8)	205 (0.9)	378 (0.9)
Withdrawn after Dose 2 and before 1-month post–Dose 2 visit	100 (0.5)	139 (0.6)	239 (0.5)
Reason for withdrawal			
Lost to follow-up	151 (0.7)	153 (0.7)	304 (0.7)
Withdrawal by subject	101 (0.5)	168 (0.8)	269 (0.6)
Adverse event	9 (0.0)	7 (0.0)	16 (0.0)

Table.C Disposition of Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13 2021, Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N^a=22026) n^b (%)	**Placebo (N^a=22021) n^b (%)**	**Total (N^a=44050) n^b (%)**
Physician decision	3 (0.0)	5 (0.0)	8 (0.0)
Death	3 (0.0)	4 (0.0)	7 (0.0)
Protocol deviation	0	1 (0.0)	1 (0.0)
Medication error without associated adverse event	1 (0.0)	0	1 (0.0)
No longer meets eligibility criteria	0	1 (0.0)	1 (0.0)
Withdrawal by parent/guardian	1 (0.0)	0	1 (0.0)
Other	4 (0.0)	5 (0.0)	9 (0.0)

Note: Human immunodeficiency virus (HIV)-positive subjects are included in this summary but not included in the analyses of the overall study objectives.
Note: Subjects randomized but did not sign informed consent or had a significant quality event due to lack of PI oversight are not included in any analysis population.
Note: Because of a dosing error, Subjects C4591001 1081 10811053, C4591001 1088 10881077, C4591001 1177 11771089 and C4591001 1231 12311057 received an additional dose of BNT162b2 (30 µg) at an unscheduled visit after receiving 1 dose of BNT162b2 (30 µg) and 1 dose of placebo.
Note: "Indeterminate vaccine" refers to subjects whose vaccine group (as administered) could not be determined. These subjects were included in the number of subjects for "Total" column. These subjects were not included in the safety analysis but their safety data is listed separately.
a. N = number of randomized subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.
b. n = Number of subjects with the specified characteristic.

Table.E Demographics and Other Baseline Characteristics, Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021, Safety Population

Characteristic	Vaccine Group (as Administered) BNT162b2 (30 µg) (N[a]=22026) n[b] (%)	Placebo (N[a]=22021) n[b] (%)	Total (N[a]=44047) n[b] (%)
Sex: Female	10704 (48.6)	10923 (49.6)	21627 (49.1)
Sex: Male	11322 (51.4)	11098 (50.4)	22420 (50.9)
Age at Vaccination: Mean years (SD)	49.7 (15.99)	49.6 (16.05)	49.7 (16.02)
Age at Vaccination: Median (years)	51.0	51.0	51.0
Age at Vaccination: Min, max (years)	(16, 89)	(16, 91)	(16, 91)
Age Group: 16 to <18 years	378 (1.7)	376 (1.7)	754 (1.7)
Age Group: 18 to 55 years	12691 (57.6)	12719 (57.8)	25410 (57.7)
Age Group: >55 years	8957 (40.7)	8926 (40.5)	17883 (40.6)
Age Group: ≥65 years	4552 (20.7)	4545 (20.6)	9097 (20.7)
Race: American Indian or Alaska Native	221 (1.0)	217 (1.0)	438 (1.0)
Race: Asian	952 (4.3)	942 (4.3)	1894 (4.3)
Race: Black or African American	2098 (9.5)	2118 (9.6)	4216 (9.6)
Race: Native Hawaiian or Other Pacific Islander	58 (0.3)	32 (0.1)	90 (0.2)
Race: White	18056 (82.0)	18064 (82.0)	36120 (82.0)
Race: Multiracial	550 (2.5)	533 (2.4)	1083 (2.5)
Race: Not reported	91 (0.4)	115 (0.5)	206 (0.5)
Ethnicity: Hispanic or Latino	5704 (25.9)	5695 (25.9)	11399 (25.9)
Ethnicity: Not Hispanic or Latino	16211 (73.6)	16212 (73.6)	32423 (73.6)

Table.E Demographics and Other Baseline Characteristics, Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021, Safety Population

Characteristic	Vaccine Group (as Administered) BNT162b2 (30 µg) (N[a]=22026) n[b] (%)	Placebo (N[a]=22021) n[b] (%)	Total (N[a]=44047) n[b] (%)
Ethnicity: Not reported	111 (0.5)	114 (0.5)	225 (0.5)
Obesity: Yes[c]	7543 (34.2)	7629 (34.6)	15172 (34.4)
Obesity: No	14483 (65.8)	14392 (65.4)	28875 (65.6)
Comorbidities: Yes[d]	10119 (45.9)	10071 (45.7)	20190 (45.8)
Comorbidities: No	11907 (54.1)	11950 (54.3)	23857 (54.2)
Baseline evidence of prior SARS-CoV-2 infection: Negative[f]	21185 (96.2)	21180 (96.2)	42365 (96.2)
Baseline evidence of prior SARS-CoV-2 infection: Positive[e]	689 (3.1)	716 (3.3)	1405 (3.2)
Baseline evidence of prior SARS-CoV-2 infection: Missing	152 (0.7)	125 (0.6)	277 (0.6)
Country: Argentina	2883 (13.1)	2881 (13.1)	5764 (13.1)
Country: Brazil	1452 (6.6)	1448 (6.6)	2900 (6.6)
Country: Germany	249 (1.1)	250 (1.1)	499 (1.1)
Country: South Africa	401 (1.8)	399 (1.8)	800 (1.8)
Country: Turkey	249 (1.1)	249 (1.1)	498 (1.1)
Country: United States of America	16792 (76.2)	16794 (76.3)	33586 (76.3)

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: HIV-positive subjects are included in this summary but not included in the analyses of the overall study objectives.
a. N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.
b. n = Number of subjects with the specified characteristic.
c. Subjects who had BMI ≥30 kg/m^2.
d. Number of subjects who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or BMI ≥30 kg/m^2.
e. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.

Table.E Demographics and Other Baseline Characteristics, Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021, Safety Population

Characteristic	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=22026) n[b] (%)	Placebo (N[a]=22021) n[b] (%)	Total (N[a]=44047) n[b] (%)

f. Negative N-binding antibody result and negative NAAT result at Visit 1 and no medical history of COVID-19.

Table.P Safety Overview, Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021, Safety Population

	BNT162b2 (30 µg) n/N (%)	Placebo n/N (%)
Immediate unsolicited AE within 30 minutes after vaccination		
Dose1	105/21926 (0.5)	81/21921 (0.4)
Dose2	71/21571 (0.3)	54/21549 (0.3)
Solicited injection site reaction within 7 days		
Dose1	3877/4907 (79.0)	639/4897 (13.0)
Dose2	3351/4542 (73.8)	483/4517 (10.7)
Solicited systemic AE within 7 days		
Dose1	2963/4907 (60.4)	2308/4897 (47.1)
Dose2	3237/4542 (71.3)	1542/4517 (34.1)
From Dose 1 through 1 month after Dose 2		
Unsolicited non-serious AE	6557/21926 (29.9)	2996/21921 (13.7)
SAE	127/21926 (0.6)	116/21921 (0.5)
Dose 1 to Data Cutoff March 13 2021 /Participant Unblinding (whichever is Earlier)		
SAE	268/21926 (1.2)	268/21921 (1.2)
Withdrawal due to AEs	45/21926 (0.2)	51/21921 (0.2)
Deaths	15/21926 (<0.1)	14/21921 (<0.1)

Note: MedDRA (v23.1) coding dictionary applied.
Note: Immediate AE refers to an AE reported in the 30-minute observation period after vaccination.

Table.Q Characteristics of Solicited Local and Systemic Adverse Reactions, Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021, Safety Population

	Vaccine Group (as Administered)			
Event	**BNT162b2 (30 µg)/Dose 1 n/N**	**BNT162b2 (30 µg)/Dose 2 n/N**	**Placebo/Dose 1 n/N**	**Placebo/Dose 2 n/N**
Redness				
Day of onset: Median (range)	2.0 (1, 7)	2.0 (1, 6)	1.0 (1, 5)	2.0 (1, 6)
Duration: Median (range)	2.0 (1, 20)	2.0 (1, 34)	1.0 (1, 10)	1.0 (1, 7)
Persisted beyond 7 days	8/4907	8/4542	1/4897	0
Swelling				
Day of onset: Median (range)	2.0 (1, 5)	2.0 (1, 5)	1.0 (1, 5)	1.0 (1, 5)
Duration: Median (range)	1.0 (1, 12)	2.0 (1, 34)	1.0 (1, 11)	1.5 (1, 5)
Persisted beyond 7 days	1/4907	6/4542	2/4897	0
Pain at injection site				
Day of onset: Median (range)	1.0 (1, 7)	1.0 (1, 7)	1.0 (1, 7)	1.0 (1, 7)
Duration: Median (range)	2.0 (1, 22)	2.0 (1, 70)	1.0 (1, 19)	1.0 (1, 35)
Persisted beyond 7 days	32/4907	35/4542	10/4897	4/4517
Any solicited local reaction				
Day of onset: Median (range)	2.0 (1, 7)	1.0 (1, 7)	1.0 (1, 7)	1.0 (1, 7)
Duration: Median (range)	2.0 (1, 22)	2.0 (1, 70)	1.0 (1, 19)	1.0 (1, 35)
Persisted beyond 7 days	41/4907	40/4542	11/4897	4/4517
Chills				
Day of onset: Median (range)	2.0 (1, 7)	2.0 (1, 7)	2.0 (1, 7)	2.0 (1, 7)
Duration: Median (range)	1.0 (1, 11)	1.0 (1, 11)	1.0 (1, 31)	1.0 (1, 16)
Persisted beyond 7 days	7/4907	2/4542	6/4897	6/4517

Table.Q Characteristics of Solicited Local and Systemic Adverse Reactions, Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021, Safety Population

	Vaccine Group (as Administered)			
Event	**BNT162b2 (30 µg)/Dose 1 n/N**	**BNT162b2 (30 µg)/Dose 2 n/N**	**Placebo/Dose 1 n/N**	**Placebo/Dose 2 n/N**
Diarrhea				
Day of onset: Median (range)	3.0 (1, 7)	3.0 (1, 7)	3.0 (1, 7)	3.0 (1, 7)
Duration: Median (range)	1.0 (1, 39)	1.0 (1, 31)	1.0 (1, 23)	1.0 (1, 33)
Persisted beyond 7 days	7/4907	6/4542	12/4897	5/4517
Fatigue				
Day of onset: Median (range)	2.0 (1, 7)	2.0 (1, 7)	2.0 (1, 7)	2.0 (1, 7)
Duration: Median (range)	1.0 (1, 34)	1.0 (1, 35)	1.0 (1, 23)	1.0 (1, 69)
Persisted beyond 7 days	84/4907	61/4542	93/4897	45/4517
Fever				
Day of onset: Median (range)	2.0 (1, 7)	2.0 (1, 7)	4.0 (1, 7)	4.0 (1, 7)
Duration: Median (range)	1.0 (1, 7)	1.0 (1, 8)	1.0 (1, 8)	1.0 (1, 6)
Persisted beyond 7 days	0	1/4542	1/4897	0
Joint pain				
Day of onset: Median (range)	2.0 (1, 7)	2.0 (1, 7)	3.0 (1, 7)	3.0 (1, 7)
Duration: Median (range)	1.0 (1, 36)	1.0 (1, 32)	1.0 (1, 17)	1.0 (1, 16)
Persisted beyond 7 days	7/4907	13/4542	8/4897	9/4517
Muscle pain				
Day of onset: Median (range)	2.0 (1, 7)	2.0 (1, 7)	3.0 (1, 7)	2.0 (1, 7)
Duration: Median (range)	1.0 (1, 17)	1.0 (1, 23)	1.0 (1, 31)	1.0 (1, 27)
Persisted beyond 7 days	11/4907	7/4542	15/4897	12/4517
Vomiting				

Table.Q Characteristics of Solicited Local and Systemic Adverse Reactions, Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021, Safety Population

	Vaccine Group (as Administered)			
Event	**BNT162b2 (30 µg)/Dose 1 n/N**	**BNT162b2 (30 µg)/Dose 2 n/N**	**Placebo/Dose 1 n/N**	**Placebo/Dose 2 n/N**
Day of onset: Median (range)	3.0 (1, 7)	2.0 (1, 7)	4.0 (1, 7)	4.0 (1, 7)
Duration: Median (range)	1.0 (1, 6)	1.0 (1, 37)	1.0 (1, 4)	1.0 (1, 6)
Persisted beyond 7 days	0	3/4542	0	0
Headache				
Day of onset: Median (range)	2.0 (1, 7)	2.0 (1, 7)	2.0 (1, 7)	2.0 (1, 7)
Duration: Median (range)	1.0 (1, 25)	1.0 (1, 25)	1.0 (1, 22)	1.0 (1, 35)
Persisted beyond 7 days	50/4907	30/4542	61/4897	32/4517
Any solicited systemic reaction				
Day of onset: Median (range)	2.0 (1, 7)	2.0 (1, 7)	2.0 (1, 7)	2.0 (1, 7)
Duration: Median (range)	1.0 (1, 39)	1.0 (1, 37)	1.0 (1, 31)	1.0 (1, 69)
Persisted beyond 7 days	138/4907	94/4542	139/4897	74/4517

Table.R Frequency of Unsolicited AEs with Occurrence in ≥1% of Phase 2/3 Participants in Any Treatment Group From Dose 1 to 1 Month After Dose 2, 16 Years of Age and Older, Safety Population

	BNT162b2 (30 µg) (N=21926)		Placebo (N=21921)	
SYSTEM ORGAN CLASS and Preferred Term	**Any n (%)**	**Severe n (%)**	**Any n (%)**	**Severe n (%)**
GASTROINTESTINAL DISORDERS				
Diarrhoea	248(1.1)	4 (0.0)	188(0.9)	5 (0.0)
Nausea	274(1.2)	1 (0.0)	87(0.4)	2 (0.0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
Chills	1365(6.2)	18 (0.1)	120(0.5)	0 (0.0)
Fatigue	1463(6.7)	24 (0.1)	379(1.7)	2 (0.0)
Injection site pain	2915(13.3)	19 (0.1)	397(1.8)	0 (0.0)
Pain	628(2.9)	9 (0.0)	61(0.3)	0 (0.0)
Pyrexia	1517(6.9)	38 (0.2)	77(0.4)	1 (0.0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS				
Arthralgia	268(1.2)	4 (0.0)	102(0.5)	6 (0.0)
Myalgia	1239(5.7)	21 (0.1)	168(0.8)	3 (0.0)
NERVOUS SYSTEM DISORDERS				
Headache	1339(6.1)	25 (0.1)	424(1.9)	10 (0.0)

MedDRA v23.1 coding dictionary applied.

Table.R.1 Frequency of Unsolicited AEs with Occurrence in ≥1% of Phase 2/3 Participants in Any Treatment Group From Dose 1 to Data Cutoff March 13 2021 /Unblinding (whichever is Earlier), 16 Years of Age and Older, Safety Population

	BNT162b2 (30 µg) (N=21926)		Placebo (N=21921)	
SYSTEM ORGAN CLASS and Preferred Term	**Any n (%)**	**Severe n (%)**	**Any n (%)**	**Severe n (%)**
GASTROINTESTINAL DISORDERS				
Diarrhoea	255(1.2)	4 (0.0)	189(0.9)	5 (0.0)
Nausea	277(1.3)	1 (0.0)	88(0.4)	2 (0.0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
Chills	1368(6.2)	18 (0.1)	121(0.6)	0 (0.0)
Fatigue	1466(6.7)	24 (0.1)	379(1.7)	2 (0.0)
Injection site pain	2917(13.3)	19 (0.1)	399(1.8)	0 (0.0)
Pain	628(2.9)	9 (0.0)	62(0.3)	0 (0.0)
Pyrexia	1520(6.9)	38 (0.2)	78(0.4)	1 (0.0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS				
Arthralgia	281(1.3)	5 (0.0)	122(0.6)	7 (0.0)
Myalgia	1245(5.7)	21 (0.1)	170(0.8)	3 (0.0)
NERVOUS SYSTEM DISORDERS				
Headache	1348(6.1)	25 (0.1)	429(2.0)	12 (0.1)

MedDRA v23.1 coding dictionary applied.

Table.R.2 Frequency of Unsolicited AEs with Occurrence in ≥1% of Phase 2/3 Participants From Unblinding Date to Cutoff Date (13MAR2021)
– Open-Label Follow-up Period– Participants Who Originally Received BNT162b2 – 16 Years of Age and Older, Safety Population

Table not created

No subject meets the reporting criteria

MedDRA v23.1 coding dictionary applied.

Table.R.3 Frequency of Unsolicited AEs with Occurrence in ≥1% of Phase 2/3 Participants From Dose 3 to Cutoff Date (13MAR2021) – Open-Label Follow-up Period – Participants Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – 16 Years of Age and Older, Safety Population

	BNT162b2 (30 µg) (N=19525)	
SYSTEM ORGAN CLASS and Preferred Term	**Any n (%)**	**Severe n (%)**
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS		
Chills	994(5.1)	15 (0.1)
Fatigue	1379(7.1)	23 (0.1)
Injection site pain	2944(15.1)	19 (0.1)
Pain	394(2.0)	5 (0.0)
Pyrexia	906(4.6)	18 (0.1)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS		
Myalgia	925(4.7)	15 (0.1)
NERVOUS SYSTEM DISORDERS		
Headache	1108(5.7)	18 (0.1)

Note: Dose 3 = First dose of BNT162b2 (30 µg).
MedDRA v23.1 coding dictionary applied.

Table.S Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Participants ≥16 Years of Age – Safety Population (Data Cutoff March 13, 2021)

		Vaccine Group (as Administered)	
		BNT162b2 (30 µg) (N[a]=21926)	Placebo (N[a]=21921)
SMQ	Overall SMQ System Organ Class Preferred Term	n[b] (%)	n[b] (%)
	Subjects with any unsolicited adverse events within SMQ	224 (1.02)	217 (0.99)
Angioedema (SMQ)	Any unsolicited adverse events within Angioedema (SMQ)	30 (0.14)	29 (0.13)
	Eye disorders	2 (0.01)	2 (0.01)
	Conjunctival oedema	0	1 (0.00)
	Eye swelling	0	1 (0.00)
	Eyelid oedema	1 (0.00)	0
	Swelling of eyelid	1 (0.00)	0
	Gastrointestinal disorders	6 (0.03)	3 (0.01)
	Gingival swelling	0	1 (0.00)
	Lip oedema	1 (0.00)	0
	Lip swelling	2 (0.01)	1 (0.00)
	Swollen tongue	2 (0.01)	1 (0.00)
	Tongue oedema	1 (0.00)	0
	General disorders and administration site conditions	4 (0.02)	7 (0.03)
	Face oedema	2 (0.01)	0
	Swelling face	2 (0.01)	7 (0.03)
	Respiratory, thoracic and mediastinal disorders	1 (0.00)	3 (0.01)

Table.S Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Participants ≥16 Years of Age – Safety Population (Data Cutoff March 13, 2021)

		Vaccine Group (as Administered)	
		BNT162b2 (30 µg) (N[a]=21926)	Placebo (N[a]=21921)
SMQ	Overall SMQ System Organ Class Preferred Term	n[b] (%)	n[b] (%)
	Pharyngeal swelling	1 (0.00)	3 (0.01)
	Skin and subcutaneous tissue disorders	21 (0.10)	18 (0.08)
	Angioedema	3 (0.01)	2 (0.01)
	Urticaria	18 (0.08)	15 (0.07)
	Urticaria papular	0	1 (0.00)
Arthritis (SMQ)	Any unsolicited adverse events within Arthritis (SMQ)	35 (0.16)	48 (0.22)
	Infections and infestations	1 (0.00)	0
	Arthritis bacterial	1 (0.00)	0
	Metabolism and nutrition disorders	5 (0.02)	3 (0.01)
	Gout	5 (0.02)	3 (0.01)
	Musculoskeletal and connective tissue disorders	29 (0.13)	45 (0.21)
	Arthritis	6 (0.03)	6 (0.03)
	Arthritis reactive	1 (0.00)	0
	Osteoarthritis	15 (0.07)	23 (0.10)
	Patellofemoral pain syndrome	0	1 (0.00)
	Periarthritis	4 (0.02)	1 (0.00)
	Polyarthritis	0	1 (0.00)
	Rheumatoid arthritis	0	2 (0.01)

Table.S Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Participants ≥16 Years of Age – Safety Population (Data Cutoff March 13, 2021)

SMQ	Overall SMQ System Organ Class Preferred Term	Vaccine Group (as Administered) BNT162b2 (30 µg) (N[a]=21926) n[b] (%)	Vaccine Group (as Administered) Placebo (N[a]=21921) n[b] (%)
	Spinal osteoarthritis	2 (0.01)	4 (0.02)
	Spondylitis	1 (0.00)	1 (0.00)
	Synovitis	0	2 (0.01)
	Temporomandibular joint syndrome	1 (0.00)	4 (0.02)
Convulsions (SMQ)	Any unsolicited adverse events within Convulsions (SMQ)	2 (0.01)	2 (0.01)
	Nervous system disorders	2 (0.01)	2 (0.01)
	Generalised tonic-clonic seizure	0	1 (0.00)
	Seizure	2 (0.01)	1 (0.00)
Demyelination (SMQ)	Any unsolicited adverse events within Demyelination (SMQ)	2 (0.01)	1 (0.00)
	Nervous system disorders	2 (0.01)	1 (0.00)
	Guillain-Barre syndrome	0	1 (0.00)
	Optic neuritis	2 (0.01)	0
Hypersensitivity (SMQ)	Any unsolicited adverse events within Hypersensitivity (SMQ)	182 (0.83)	161 (0.73)
	Ear and labyrinth disorders	0	1 (0.00)
	Allergic otitis media	0	1 (0.00)
	Eye disorders	5 (0.02)	5 (0.02)
	Conjunctival oedema	0	1 (0.00)
	Conjunctivitis allergic	3 (0.01)	2 (0.01)

Table.S Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Participants ≥16 Years of Age – Safety Population (Data Cutoff March 13, 2021)

		Vaccine Group (as Administered)	
		BNT162b2 (30 µg) (N[a]=21926)	Placebo (N[a]=21921)
SMQ	Overall SMQ System Organ Class Preferred Term	n[b] (%)	n[b] (%)
	Eye allergy	0	1 (0.00)
	Eye swelling	0	1 (0.00)
	Eyelid oedema	1 (0.00)	0
	Swelling of eyelid	1 (0.00)	0
	Gastrointestinal disorders	6 (0.03)	3 (0.01)
	Gingival swelling	0	1 (0.00)
	Lip oedema	1 (0.00)	0
	Lip swelling	2 (0.01)	1 (0.00)
	Swollen tongue	2 (0.01)	1 (0.00)
	Tongue oedema	1 (0.00)	0
	General disorders and administration site conditions	8 (0.04)	9 (0.04)
	Application site rash	0	1 (0.00)
	Face oedema	2 (0.01)	0
	Injection site dermatitis	1 (0.00)	0
	Injection site rash	2 (0.01)	1 (0.00)
	Injection site urticaria	1 (0.00)	0
	Swelling face	2 (0.01)	7 (0.03)
	Immune system disorders	10 (0.05)	13 (0.06)

Table.S Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Participants ≥16 Years of Age – Safety Population (Data Cutoff March 13, 2021)

		Vaccine Group (as Administered)	
		BNT162b2 (30 µg) (N[a]=21926)	Placebo (N[a]=21921)
SMQ	Overall SMQ System Organ Class Preferred Term	n[b] (%)	n[b] (%)
	Anaphylactic reaction	1 (0.00)	0
	Anaphylactic shock	0	1 (0.00)
	Drug hypersensitivity	7 (0.03)	7 (0.03)
	Hypersensitivity	2 (0.01)	5 (0.02)
	Infections and infestations	5 (0.02)	1 (0.00)
	Dermatitis infected	0	1 (0.00)
	Pustule	3 (0.01)	0
	Rash pustular	2 (0.01)	0
	Injury, poisoning and procedural complications	3 (0.01)	0
	Administration related reaction	2 (0.01)	0
	Stoma site rash	1 (0.00)	0
	Investigations	1 (0.00)	0
	Blood immunoglobulin E increased	1 (0.00)	0
	Respiratory, thoracic and mediastinal disorders	19 (0.09)	21 (0.10)
	Allergic respiratory disease	0	1 (0.00)
	Allergic sinusitis	2 (0.01)	0
	Bronchospasm	3 (0.01)	3 (0.01)
	Pharyngeal swelling	1 (0.00)	3 (0.01)

Table.S Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Participants ≥16 Years of Age – Safety Population (Data Cutoff March 13, 2021)

		Vaccine Group (as Administered)	
		BNT162b2 (30 µg) (N[a]=21926)	Placebo (N[a]=21921)
SMQ	Overall SMQ System Organ Class Preferred Term	n[b] (%)	n[b] (%)
	Rhinitis allergic	13 (0.06)	14 (0.06)
	Skin and subcutaneous tissue disorders	134 (0.61)	119 (0.54)
	Angioedema	3 (0.01)	2 (0.01)
	Dermatitis	5 (0.02)	4 (0.02)
	Dermatitis acneiform	1 (0.00)	0
	Dermatitis allergic	3 (0.01)	5 (0.02)
	Dermatitis atopic	0	1 (0.00)
	Dermatitis bullous	0	1 (0.00)
	Dermatitis contact	14 (0.06)	21 (0.10)
	Dermatitis exfoliative	1 (0.00)	0
	Drug eruption	0	2 (0.01)
	Eczema	7 (0.03)	3 (0.01)
	Erythema nodosum	1 (0.00)	0
	Fixed eruption	1 (0.00)	0
	Hand dermatitis	2 (0.01)	2 (0.01)
	Perioral dermatitis	0	1 (0.00)
	Pruritus allergic	0	2 (0.01)
	Rash	62 (0.28)	52 (0.24)

Table.S Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Participants ≥16 Years of Age – Safety Population (Data Cutoff March 13, 2021)

		Vaccine Group (as Administered)	
		BNT162b2 (30 µg) (N[a]=21926)	Placebo (N[a]=21921)
SMQ	Overall SMQ System Organ Class Preferred Term	n[b] (%)	n[b] (%)
	Rash erythematous	2 (0.01)	3 (0.01)
	Rash maculo-papular	7 (0.03)	4 (0.02)
	Rash papular	1 (0.00)	0
	Rash pruritic	8 (0.04)	6 (0.03)
	Urticaria	18 (0.08)	15 (0.07)
	Urticaria contact	0	1 (0.00)
	Urticaria papular	0	1 (0.00)
Peripheral neuropathy (SMQ)	Any unsolicited adverse events within Peripheral neuropathy (SMQ)	3 (0.01)	6 (0.03)
	Nervous system disorders	3 (0.01)	6 (0.03)
	Guillain-Barre syndrome	0	1 (0.00)
	Neuralgia	1 (0.00)	1 (0.00)
	Neuritis	0	1 (0.00)
	Neuropathy peripheral	1 (0.00)	3 (0.01)
	Peripheral sensory neuropathy	1 (0.00)	0

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event," n = the number of subjects reporting at least 1 occurrence of any event.

Table.T SAEs considered related by Investigator – Phase 2/3 Participants 16 Years of Age and Older, Safety Population (Data Cutoff March 13, 2021)

Product (Vaccine or Placebo)	SAE	Dose/Rel Day[a]	Demographics: Age/Sex/Risk Factors from Charlson Index	Resolution	Related per Investigator
BNT162b2	Shoulder injury related to vaccine administration	2/1	30 F; no relevant medical history	Resolved	Yes
BNT162b2	Paraesthesia	2/47	53 F; no relevant medical history	Resolving	Yes
BNT162b2	Ventricular arrhythmia	2/1	71 F; Any malignancy	Resolved	Yes
BNT162b2	Lymphadenopathy	1/13	48 F; no relevant medical history	Resolved	Yes
BNT162b2	Myocardial infarction	2/71#	41 M; no relevant medical history	Resolved	Yes
Placebo	Psoriatic arthropathy	2/38	25 M; no relevant medical history	Not Resolved	Yes
Placebo crossover to BNT162b2	Anaphylactoid reaction	3/3#	17 F; Chronic pulmonary disease	Resolved	Yes

Note: MedDRA (v23.1) coding dictionary applied.
Note: # = SAE occurring on or after unblinding.
a. Relative day (Rel Day) = date of SAE - date of last vaccination + 1.

Table.U Deaths, Phase 2/3 Participants 16 Years of Age and Older, Safety Population, (Data Cutoff March 13, 2021)

Product - Number of doses received	Subject Number	Dose/Rel Day[a]	Primary Cause of Death	Positive COVID-19 test (Y/N)	Age/Sex/ Race/Ethnicity	Demographics: Risk Factors from Charlson Index
BNT162b2 - 2	C4591001 1007 10071101∞	2/63	Cardiac arrest	N	56/F/White/Not Hispanic or Latino	Chronic pulmonary disease
BNT162b2 - 2	C4591001 1021 10211127∞	2/88	Cardiac failure congestive	Y	54/M/Black or African American/Not Hispanic or Latino	Chronic pulmonary disease, Congestive heart failure
BNT162b2 - 2	C4591001 1036 10361140∞#	2/91	Road traffic accident	N	64/M/White/Not Hispanic or Latino	
BNT162b2 - 2	C4591001 1039 10391010∞	2/71	Arteriosclerosis	N	84/M/White/Not Hispanic or Latino	Cerebrovascular disease
BNT162b2 - 2	C4591001 1084 10841266∞	2/121	Sepsis	N	77/M/White/Hispanic or Latino	Congestive heart failure, Diabetes without chronic complication, Peripheral vascular disease
BNT162b2 - 2	C4591001 1088 10881139∞#	2/143	Metastases to lung	N	82/M/White/Not Hispanic or Latino	Chronic pulmonary disease
BNT162b2 - 2	C4591001 1089 10891073∞	2/70	Chronic obstructive pulmonary disease	N	63/F/White/Not Hispanic or Latino	Any malignancy, Chronic pulmonary disease, Diabetes with chronic complication, Diabetes without chronic complication, Myocardial infarction
BNT162b2 - 2	C4591001 1097 10971023∞	2/98	Septic shock	N	86/F/White/Not Hispanic or Latino	
BNT162b2 - 2	C4591001 1114 11141050∞	2/42	Unevaluable event	N	63/F/White/Not Hispanic or Latino	Rheumatic disease
BNT162b2	C4591001 1120	2/73	Cardiac arrest	N	58/F/White/Not Hispanic or	Diabetes without chronic complication

Table.U Deaths, Phase 2/3 Participants 16 Years of Age and Older, Safety Population, (Data Cutoff March 13, 2021)

Product - Number of doses received	Subject Number	Dose/Rel Day[a]	Primary Cause of Death	Positive COVID-19 test (Y/N)	Age/Sex/ Race/Ethnicity	Demographics: Risk Factors from Charlson Index
- 2	11201050∞				Latino	
BNT162b2 - 2	C4591001 1120 11201266∞	2/113	Lung cancer metastatic	N	51/M/White/Not Hispanic or Latino	
BNT162b2 - 2	C4591001 1127 11271112∞	2/86	Cardio-respiratory arrest	N	53/M/Multiple/Not Hispanic or Latino	Chronic pulmonary disease, Myocardial infarction
BNT162b2 - 2	C4591001 1129 11291166∞#	2/129	Myocardial infarction	N	78/F/White/Not Hispanic or Latino	
BNT162b2 - 2	C4591001 1136 11361102∞	2/31	Cardiac arrest	N	76/M/White/Not Hispanic or Latino	
BNT162b2 - 2	C4591001 1140 11401117∞	2/117	Cardiac arrest	N	58/M/White/Not Hispanic or Latino	
BNT162b2 - 1	C4591001 1152 11521497∞	1/36	Shigella sepsis	N	72/M/White/Hispanic or Latino	Diabetes without chronic complication
BNT162b2 - 2	C4591001 1156 11561160∞†	2/74	Road traffic accident	N	62/F/Black or African American/Not Hispanic or Latino	AIDS/HIV, Chronic pulmonary disease
BNT162b2 - 1	C4591001 1162 11621327∞	1/4	Arteriosclerosis	Y	60/M/White/Not Hispanic or Latino	
BNT162b2 - 2	C4591001 1252 12521010∞	2/110	COVID-19 pneumonia	N	80/M/White/Not Hispanic or Latino	
Placebo - 2	C4591001 1019 10191146	2/87	Metastases to liver	N	67/M/White/Not Hispanic or Latino	Chronic pulmonary disease
Placebo - 2	C4591001 1027 10271191#	2/135	Respiratory failure	Y	68/F/Black or African American/Not Hispanic or	Any malignancy, Chronic pulmonary disease

Table.U Deaths, Phase 2/3 Participants 16 Years of Age and Older, Safety Population, (Data Cutoff March 13, 2021)

Product - Number of doses received	Subject Number	Dose/Rel Day[a]	Primary Cause of Death	Positive COVID-19 test (Y/N)	Age/Sex/ Race/Ethnicity	Demographics: Risk Factors from Charlson Index
					Latino	
Placebo - 1	C4591001 1066 10661350	1/16	Myocardial infarction	N	58/M/White/Not Hispanic or Latino	Congestive heart failure, Myocardial infarction
Placebo - 2	C4591001 1081 10811194	2/37	Myocardial infarction	N	51/F/White/Not Hispanic or Latino	Chronic pulmonary disease
Placebo - 2	C4591001 1084 10841470	2/83	Multiple organ dysfunction syndrome	N	65/M/White/Hispanic or Latino	Chronic pulmonary disease
Placebo - 2	C4591001 1088 10881126	2/70	Cardiac arrest	Y	65/M/White/Not Hispanic or Latino	
Placebo - 2	C4591001 1089 10891088	2/125	Dementia	N	82/F/White/Not Hispanic or Latino	Dementia
Placebo - 2	C4591001 1094 10941112	2/81	Acute respiratory failure	N	57/F/White/Hispanic or Latino	Chronic pulmonary disease, Diabetes without chronic complication
Placebo - 2	C4591001 1128 11281009	2/102	Pneumonia	N	66/M/White/Not Hispanic or Latino	Diabetes without chronic complication, Myocardial infarction
Placebo - 2	C4591001 1131 11311204*#	3/26	Cardio-respiratory arrest	N	84/M/White/Not Hispanic or Latino	Cerebrovascular disease, Peripheral vascular disease
Placebo - 2	C4591001 1135 11351033*#	3/5		N	67/M/White/Not Hispanic or Latino	
Placebo - 1	C4591001 1152 11521085	1/8	Death	N	42/F/White/Not Hispanic or Latino	Any malignancy
Placebo - 2	C4591001 1156 11561124	2/32	Overdose	N	53/M/White/Not Hispanic or Latino	

Table.U Deaths, Phase 2/3 Participants 16 Years of Age and Older, Safety Population, (Data Cutoff March 13, 2021)

Product - Number of doses received	Subject Number	Dose/Rel Day[a]	Primary Cause of Death	Positive COVID-19 test (Y/N)	Age/Sex/ Race/Ethnicity	Demographics: Risk Factors from Charlson Index
Placebo - 2	C4591001 1168 11681083	2/65	Aortic rupture	N	64/M/White/Not Hispanic or Latino	
Placebo - 2	C4591001 1207 12071055#	2/76	Pneumonia bacterial	N	65/M/White/Not Hispanic or Latino	Diabetes without chronic complication, Mild liver disease
Placebo - 2	C4591001 1229 12291083†	2/76	COVID-19 pneumonia	N	55/F/Black or African American/Not Hispanic or Latino	AIDS/HIV, Chronic pulmonary disease
Placebo - 2	C4591001 1231 12313972	2/16	Haemorrhagic stroke	N	61/F/White/Hispanic or Latino	
Placebo - 2	C4591001 1231 12314987	2/82	Cardio-respiratory arrest	N	47/M/White/Hispanic or Latino	
Placebo - 2	C4591001 1231 12315324	2/136	Multiple organ dysfunction syndrome	Y	58/F/White/Hispanic or Latino	

Note: MedDRA (v23.1) coding dictionary applied.
Note: † = Human immunodeficiency virus (HIV)-positive subject, # = death occurring on or after unblinding, * = subjects who originally received placebo and then received BNT162b2 after unblinding, ∞ = subjects who originally received BNT162b2.
a. Relative day (Rel Day)= date of death - date of last vaccination + 1.

Table V. Clinical Trials Submitted in Support of Safety and Effectiveness of the Pfizer-BioNTech COVID-19 Vaccine

Study Number/ Country	Study Description	Number of BNT162b2 (30 µg) subjects (N)	Number of placebo subjects (N)	Study Status
C4591001 Phase 1	A Phase 1/2/3 Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Individuals	24	6	Ongoing
C4591001 Phase 2/3		22085	22080	Ongoing
Argentina		2887	2889	
Brazil		1452	1448	
Germany		250	250	
South Africa		401	399	
Turkey		251	249	
USA		16844	16845	
BNT162-01 Phase 1/2 Germany (BNT162b2 30 µg)	A multi-site, Phase I/II, 2-part, dose escalation trial investigating the safety and immunogenicity of four prophylactic SARS-CoV-2 RNA vaccines against COVID-19 using different dosing regimens in healthy adults	24	0	Ongoing

N= total number of randomized participants 16 years of age and older, as of March 13, 2021.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

---------- INDICATIONS AND USAGE ----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection ~~administration~~ only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS----------
- In clinical studies of participants 16 through 55 years of age ~~and older~~, the most commonly reported adverse reactions (~~>~~≥10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, fever, and injection site swelling. (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, injection site swelling, fever, and injection site redness. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

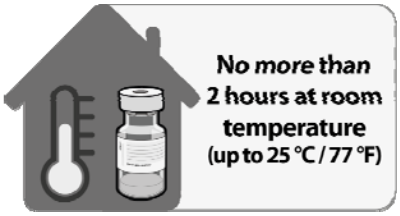
2.1 Preparation for Administration

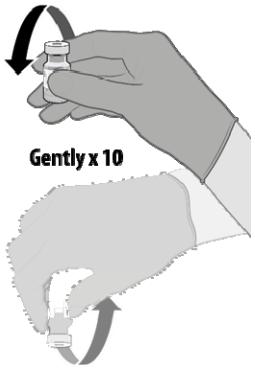
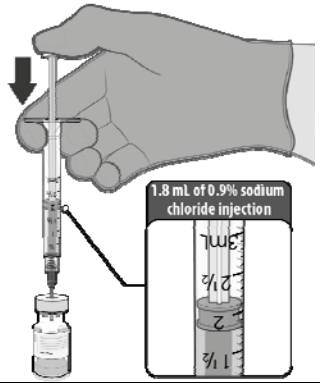
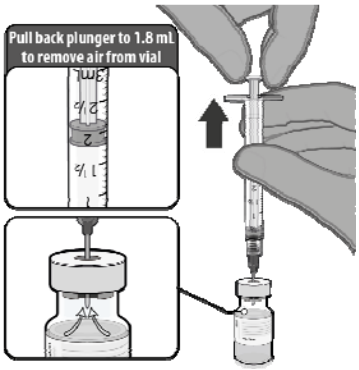
Prior to Dilution

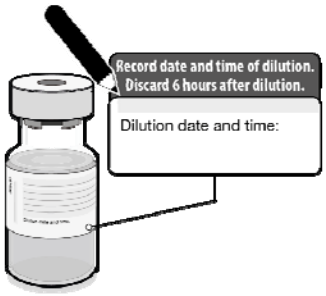
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

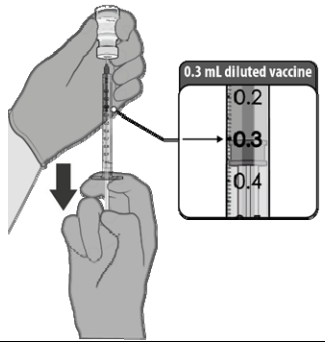
Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or an alternate brand of sterile 0.9% Sodium Chloride Injection, USP as the diluent.
- Provided diluent vials are single-use only and should be discarded after 1.8 mL is withdrawn. Do not use provided diluent vials to dilute multiple vials of COMIRNATY.
- After dilution, 1 vial contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.

	• Before dilution invert vaccine vial gently 10 times. • Do not shake. • Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Cleanse the vaccine vial stopper with a single-use antiseptic swab. • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.
	• Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.

	• Gently invert the vial containing the COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

2.2 Administration Information

For intramuscular injection only.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Visually inspect each dose in the dosing syringe prior to administration. The vaccine will be an off-white suspension. During the visual inspection,

- verify the final dosing volume of 0.3 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk has been highest in adolescent and young adult males under 40 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of symptoms. Information is not yet available about potential long-term sequelae. The CDC has published

considerations for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies with a data cut-off of March 13, 2021, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies with a data cut-off of March 13, 2021, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

In clinical studies with a data cut-off of March 13, 2021, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies with a data cut-off of March 13, 2021, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine

candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 ~~TRADENAME~~COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection~~disease~~ was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were ≥65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 ~~to~~ through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

~~Table 5 and Table 6 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 16 years of age and older with confirmed stable HIV infection.~~

In participants with chronic, stable HIV infection after receiving Dose 2, local reactions and systemic events were similar to those observed for all participants 16 years of age and older by severity, onset day, and median duration. The frequency of pain at the injection site was similar after Dose 1 compared with Dose 2 of COMIRNATY (63.0% versus 53.3%). The frequency of redness and swelling was similar after Dose 1 compared with Dose 2 of COMIRNATY (redness: 3.7% versus 6.7%; swelling: 5.6% versus 8.3%, respectively). There was 1 (1.7%) severe reaction (pain at the injection site) reported after Dose 2 of COMIRNATY and no Grade 4 local reactions were reported. Fever, headache, chills, and joint pain increased in frequency from Dose 1 to Dose 2 while fatigue, vomiting, diarrhea, and muscle pain were similar after each dose of COMIRNATY. There were no severe systemic events after Dose 1 of COMIRNATY but after Dose 2, there was 1 (1.7%) severe fever (>38.9°C to 40.0°C), 3 (5.0%) participants with severe fatigue, 2 (3.3%) participants with severe headache, 1 (1.7%) participant with severe chills, and 1 (1.7%) participant with severe diarrhea. There were no Grade 4 systemic events reported after either dose.

~~**Table 5: Study 2 Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose HIV-Positive Participants 16 Years of Age and Older Reactogenicity Subset of the Safety Population***~~

	~~COMIRNATY Dose 1 N[a]=54 n[b] (%)~~	~~Placebo Dose 1 N[a]=56 n[b] (%)~~	~~COMIRNATY Dose 2 N[a]=60 n[b] (%)~~	~~Placebo Dose 2 N[a]=62 n[b] (%)~~
~~Redness[e]~~				
~~Any (>2.0 cm)~~	~~2 (3.7)~~	~~3 (5.4)~~	~~4 (6.7)~~	~~1 (1.6)~~
~~Mild~~	~~2 (3.7)~~	~~1 (1.8)~~	~~3 (5.0)~~	~~1 (1.6)~~
~~Moderate~~	~~0~~	~~0~~	~~1 (1.7)~~	~~0~~
~~Severe~~	~~0~~	~~2 (3.6)~~	~~0~~	~~0~~
~~Swelling[e]~~				
~~Any (>2.0 cm)~~	~~3 (5.6)~~	~~1 (1.8)~~	~~5 (8.3)~~	~~0~~
~~Mild~~	~~2 (3.7)~~	~~0~~	~~2 (3.3)~~	~~0~~
~~Moderate~~	~~1 (1.9)~~	~~0~~	~~3 (5.0)~~	~~0~~
~~Severe~~	~~0~~	~~1 (1.8)~~	~~0~~	~~0~~

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Pain at the injection site[d]				
Any	34 (63.0)	9 (16.1)	32 (53.3)	5 (8.1)
Mild	26 (48.1)	8 (14.3)	22 (36.7)	5 (8.1)
Moderate	8 (14.8)	1 (1.8)	9 (15.0)	0
Severe	0	0	1 (1.7)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in HIV-positive participants 16 years of age and older.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 6: Study 2 Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose HIV-Positive Participants 16 Years of Age and Older Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Fever				
≥38.0°C	1 (1.9)	4 (7.1)	9 (15.0)	5 (8.1)
≥38.0°C to 38.4°C	1 (1.9)	2 (3.6)	4 (6.7)	5 (8.1)
>38.4°C to 38.9°C	0	0	4 (6.7)	0
>38.9°C to 40.0°C	0	2 (3.6)	1 (1.7)	0
>40.0°C	0	0	0	0
Fatigue[e]				
Any	22 (40.7)	15 (26.8)	24 (40.0)	12 (19.4)
Mild	15 (27.8)	9 (16.1)	12 (20.0)	5 (8.1)
Moderate	7 (13.0)	5 (8.9)	9 (15.0)	7 (11.3)
Severe	0	1 (1.8)	3 (5.0)	0
Headache[e]				
Any	11 (20.4)	18 (32.1)	18 (30.0)	12 (19.4)
Mild	7 (13.0)	10 (17.9)	8 (13.3)	8 (12.9)
Moderate	4 (7.4)	7 (12.5)	8 (13.3)	4 (6.5)
Severe	0	1 (1.8)	2 (3.3)	0
Chills[e]				
Any	6 (11.1)	5 (8.9)	14 (23.3)	4 (6.5)
Mild	5 (9.3)	4 (7.1)	5 (8.3)	3 (4.8)
Moderate	1 (1.9)	1 (1.8)	8 (13.3)	1 (1.6)
Severe	0	0	1 (1.7)	0

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Vomiting[d]				
Any	1 (1.9)	3 (5.4)	2 (3.3)	2 (3.2)
Mild	1 (1.9)	1 (1.8)	1 (1.7)	1 (1.6)
Moderate	0	0	1 (1.7)	1 (1.6)
Severe	0	2 (3.6)	0	0
Diarrhea[e]				
Any	5 (9.3)	8 (14.3)	4 (6.7)	9 (14.5)
Mild	5 (9.3)	6 (10.7)	1 (1.7)	6 (9.7)
Moderate	0	1 (1.8)	2 (3.3)	3 (4.8)
Severe	0	1 (1.8)	1 (1.7)	0
New or worsened muscle pain[e]				
Any	9 (16.7)	10 (17.9)	10 (16.7)	5 (8.1)
Mild	7 (13.0)	7 (12.5)	5 (8.3)	1 (1.6)
Moderate	2 (3.7)	3 (5.4)	5 (8.3)	4 (6.5)
Severe	0	0	0	0
New or worsened joint pain[e]				
Any	5 (9.3)	7 (12.5)	10 (16.7)	5 (8.1)
Mild	5 (9.3)	4 (7.1)	4 (6.7)	1 (1.6)
Moderate	0	3 (5.4)	6 (10.0)	4 (6.5)
Severe	0	0	0	0
Use of antipyretic or pain medication[f]	7 (13.0)	8 (14.3)	16 (26.7)	7 (11.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in HIV-positive participants 16 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each event or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

Upon issuance of the EUA for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Unblinded participants originally randomized to COMIRNATY and placebo recipients administered COMIRNATY continued to be followed for unsolicited adverse events including serious adverse events, throughout the study [from Dose 1 of COMIRNATY through 1 month (all unsolicited adverse events) and 6 months (serious adverse events) after the last vaccination]. Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began in a phased manner for participants in the study. Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 2.1 per 100 person-years among COMIRNATY recipients and 2.4 per 100 person-years among placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported at an incidence rate of 4.9 per 100 person-years among COMIRNATY recipients and 4.6 per 100 person-years among placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 6.6 per 100 person-years among COMIRNATY recipients and 6.9 per 100 person-years among placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 88.4 per 100 person-years among participants who received COMIRNATY and 43.5 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include non-serious adverse events were reported at an incidence rate of 75.7 per 100 person-years among participants who received COMIRNATY and 43.3 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 95.8 per 100 person-years among participants who received COMIRNATY and 52.0 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-marketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions, twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL

of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY~~,~~ ~~t~~There were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is a multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of

prior infection with SARS-CoV-2 through 7 days after the second dose. Table 7 presents the specific demographic characteristics in the studied population. Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.5% were male and 48.6% or 49.5% were female, 4.8% or 4.6% were 12 through 15 years of age, 75.1% or 75.1% were 16 through 64 years of age, 20.1% or 20.3% were 65 years of age and older, 16.1% or 16.3% were 65 through 74 years of age, 4.0% or 4.0% ≥75 years of age and older, 82.9% or 83.1% were White, 8.5% or 8.6% were Black or African American, 0.9% or 0.9% were American Indian or Alaska Native, 4.6% or 4.5% were Asian, 0.3% or 0.1% Native Hawaiian or other Pacific Islander, 24.9% or 24.6% were Hispanic/Latino, 74.6% or 74.8% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 44.6% or 44.4% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2 (16 years of age and older) or BMI ≥95th percentile (12 through 15 years of age)], respectively. The mean age at vaccination was 48.3 or 48.2 years and median age was 50.0 or 50.0 in participants who received COMIRNATY or placebo, respectively.

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Table 7: Demographics (Population For the Primary Efficacy Endpoint)[a]

	COMIRNATY (N=18,242) n (%)	Placebo (N=18,379) n (%)
Sex		
Male	9318 (51.1)	9225 (50.2)
Female	8924 (48.9)	9154 (49.8)
Age (years)		
Mean (SD)	50.6 (15.70)	50.4 (15.81)
Median	52.0	52.0
Min, max	(12, 89)	(12, 91)
Age group		
≥12 through 15 years	46 (0.3)	42 (0.2)
≥16 through 64 years	14,216 (77.9)	14,299 (77.8)
≥65 through 74 years	3176 (17.4)	3226 (17.6)
≥75 years	804 (4.4)	812 (4.4)
Race		
White	15,110 (82.8)	15,301 (83.3)
Black or African American	1617 (8.9)	1617 (8.8)
American Indian or Alaska Native	118 (0.6)	106 (0.6)
Asian	815 (4.5)	810 (4.4)
Native Hawaiian or other Pacific Islander	48 (0.3)	29 (0.2)
Other[b]	534 (2.9)	516 (2.8)
Ethnicity		
Hispanic or Latino	4886 (26.8)	4857 (26.4)
Not Hispanic or Latino	13,253 (72.7)	13,412 (73.0)
Not reported	103 (0.6)	110 (0.6)
Comorbidities[c]		
Yes	8432 (46.2)	8450 (46.0)
No	9810 (53.8)	9929 (54.0)

a. All eligible randomized participants who receive all vaccination(s) as randomized within the predefined window, have no other important protocol deviations as determined by the clinician, and have no evidence of SARS-CoV-2 infection prior to 7 days after Dose 2.

b. Includes multiracial and not reported.

c. Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease:

- Chronic lung disease (e.g., emphysema and chronic bronchitis, idiopathic pulmonary fibrosis, and cystic fibrosis) or moderate

~~to severe asthma~~

- ~~Significant cardiac disease (e.g., heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and pulmonary hypertension)~~
- ~~Obesity (body mass index ≥30 kg/m^2)~~
- ~~Diabetes (Type 1, Type 2, or gestational)~~
- ~~Liver disease~~
- ~~Human Immunodeficiency Virus (HIV) infection (not included in the efficacy evaluation)~~

Efficacy Against COVID-19

The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

The vaccine efficacy information is presented in Table ~~8~~5.

Table ~~5~~8: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=18,198 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.3, 97.6)[f]
16 to 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)[g]
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)[g]
65 to 74 years	1 0.406 (3074)	14 0.406 (3095)	92.9 (53.1, 99.8)[g]
75 years and older	0 0.102 (774)	5 0.106 (785)	100.0 (-13.1, 100.0)[g]
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=19,965 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,172 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	9 2.332 (18,559)	169 2.345 (18,708)	94.6 (89.9, 97.3)[f]
16 to 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1 0.530 (4044)	19 0.532 (4067)	94.7 (66.8, 99.9)[g]

65 to 74 years	1 0.424 (3239)	14 0.423 (3255)	92.9 (53.2, 99.8)[g]
75 years and older	0 0.106 (805)	5 0.109 (812)	100.0 (-12.1, 100.0)[g]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. No confirmed cases were identified in participants 12 to 15 years of age.
f. Two-sided credible interval for vaccine efficacy was calculated using a beta-binomial model with a beta (0.700102, 1) prior for θ=r(1-VE)/(1+r(1-VE)), where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.
g. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021~~0~~, representing up to 6 months of follow-up after Dose 2. Overall, 59.2% of participants in the COMIRNATY group and 57.3% of participants in the placebo group had ≥4 months of follow-up time after Dose 2 in the blinded placebo-controlled follow-up period.
~~Updated efficacy analyses were performed with additional confirmed COVID-19 cases accrued during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2 for participants in the efficacy population.~~

The updated vaccine efficacy information is presented in Table ~~9~~6.

Table ~~9~~6: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY** **N[a]=~~20,998~~19,993** **Cases n1[b]** **Surveillance Time[c] (n2[d])**	**Placebo** **N[a]=~~21,096~~20,118** **Cases n1[b]** **Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 ~~6.247 (20,712)~~6.092 (19,711)	~~850~~833 ~~6.003 (20,713)~~5.857 (19,741)	~~91.3~~91.1 ~~(89.0, 93.2)~~(88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	~~710~~709 ~~4.654 (15,515)~~4.654 (15,515)	~~90.6~~90.5 ~~(87.9, 92.7)~~(87.9, 92.7)
65 years and older	7	124	94.5

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	1.233 (4192)	1.202 (4226)	(88.3, 97.8)
~~65 through 74 years~~	~~6~~ ~~0.994 (3350)~~	~~98~~ ~~0.966 (3379)~~	~~94.1~~ ~~(86.6, 97.9)~~
~~75 years and older~~	~~1~~ ~~0.239 (842)~~	~~26~~ ~~0.237 (847)~~	~~96.2~~ ~~(76.9, 99.9)~~
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY** **N[a]=~~22,166~~21,047** **Cases** **n1[b]** **Surveillance Time[c] (n2[d])**	**Placebo** **N[a]=~~22,320~~21,210** **Cases** **n1[b]** **Surveillance Time[c] (n2[d])**	**Vaccine Efficacy %** **(95% CI[e])**
All participants[~~f~~]	81 ~~6.509 (21,642)~~6.340 (20,533)	~~873~~854 ~~6.274 (21,689)~~6.110 (20,595)	~~91.1~~90.9 ~~(88.8, 93.0)~~(88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	~~727~~726 ~~4.879 (16,269)~~4.879 (16,269)	90.2 ~~(87.6, 92.4)~~(87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)
~~65 through 74 years~~	~~6~~ ~~1.021 (3450)~~	~~102~~ ~~0.992 (3468)~~	~~94.3~~ ~~(87.1, 98.0)~~
~~75 years and older~~	~~1~~ ~~0.246 (865)~~	~~26~~ ~~0.240 (858)~~	~~96.2~~ ~~(77.2, 99.9)~~

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

~~f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group (both without and with or without evidence of prior SARS-CoV-2 infection); 16 and 18 in the placebo group (without and with or without evidence of prior SARS-CoV-2 infection, respectively).~~

Subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, geographies, and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

~~The updated subgroup analyses of vaccine efficacy by demographic characteristics are presented in Table 10 and Table 11.~~

~~**Table 10: Vaccine Efficacy - First COVID-19 Occurrence From 7 Days After Dose 2 - Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 by Demographic Characteristics - Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period**~~

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Sex			
Male	42 3.246 (10,637)	399 3.047 (10,433)	90.1 (86.4, 93.0)
Female	35 3.001 (10,075)	451 2.956 (10,280)	92.4 (89.2, 94.7)
Ethnicity			
Hispanic or Latino	29 1.786 (5161)	241 1.711 (5120)	88.5 (83.0, 92.4)
Not Hispanic or Latino	47 4.429 (15,449)	609 4.259 (15,484)	92.6 (90.0, 94.6)
Race			
Black or African American	4 0.545 (1737)	48 0.527 (1737)	91.9 (78.0, 97.9)
White	67 5.208 (17,186)	747 5.026 (17,256)	91.3 (88.9, 93.4)
All others[f]	6 0.494 (1789)	55 0.451 (1720)	90.0 (76.9, 96.5)
Country			
Argentina	15 1.012 (2600)	108 0.986 (2586)	86.5 (76.7, 92.7)
Brazil	12 0.406 (1311)	80 0.374 (1293)	86.2 (74.5, 93.1)
Germany	0 0.047 (236)	1 0.048 (242)	100.0 (-3874.2, 100.0)
South Africa	0 0.080 (291)	9 0.074 (276)	100.0 (53.5, 100.0)
Turkey	0 0.027 (228)	5 0.025 (222)	100.0 (-0.1, 100.0)
United States	50 4.674 (16,046)	647 4.497 (16,094)	92.6 (90.1, 94.5)

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group.

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

f. All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

Table 11: Vaccine Efficacy - First COVID-19 Occurrence From 7 Days After Dose 2 - Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 by Demographic Characteristics - Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Sex			
Male	44 3,376 (11,103)	411 3,181 (10,920)	89.9 (86.2, 92.8)
Female	37 3,133 (10,539)	462 3,093 (10,769)	92.1 (88.9, 94.5)
Ethnicity			
Hispanic or Latino	32 1,862 (5408)	245 1,794 (5391)	87.4 (81.8, 91.6)
Not Hispanic or Latino	48 4,615 (16,128)	628 4,445 (16,186)	92.6 (90.1, 94.6)
Race			
Black or African American	4 611 (1958)	49 601 (1985)	92.0 (78.1, 97.9)
White	69 5,379 (17,801)	768 5,191 (17,880)	91.3 (88.9, 93.3)
All others[f]	8 519 (1883)	56 481 (1824)	86.8 (72.1, 94.5)
Country			
Argentina	16 1,033 (2655)	110 1,017 (2670)	85.7 (75.7, 92.1)
Brazil	14 441 (1419)	82 408 (1401)	84.2 (71.9, 91.7)
Germany	0 47 (237)	1 48 (243)	100.0 (-3868.6, 100.0)
South Africa	0 99 (358)	10 96 (358)	100.0 (56.6, 100.0)
Turkey	0 29 (238)	6 26 (232)	100.0 (22.2, 100.0)
United States	51 4,861 (16,735)	664 4,678 (16,785)	92.6 (90.2, 94.6)

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group.

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

f. All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

The updated subgroup analyses of vaccine efficacy by risk status in participants are presented in Table 12 and Table 13.

Table 12: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First COVID-19 occurrence from 7 days after Dose 2[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
At risk[g]			
Yes	35 2.797 (9167)	401 2.681 (9136)	91.6 (88.2, 94.3)
No	42 3.450 (11,545)	449 3.322 (11,577)	91.0 (87.6, 93.6)
Age group (years) and risk status			
16 through 64 and not at risk	41 2.776 (8887)	385 2.661 (8886)	89.8 (85.9, 92.8)
16 through 64 and at risk	29 2.083 (6632)	325 1.993 (6629)	91.5 (87.5, 94.4)
65 and older and not at risk	1 0.553 (1870)	53 0.546 (1922)	98.1 (89.2, 100.0)
65 and older and at risk	6 0.680 (2322)	71 0.656 (2304)	91.8 (81.4, 97.1)
Obese[h]			

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Yes	27 2.103 (6796)	314 2.050 (6875)	91.6 (87.6, 94.6)
No	50 4.143 (13,911)	536 3.952 (13,833)	91.1 (88.1, 93.5)
Age group (years) and obesity status			
16 through 64 and not obese	46 3.178 (10,212)	444 3.028 (10,166)	90.1 (86.6, 92.9)
16 through 64 and obese	24 1.680 (5303)	266 1.624 (5344)	91.3 (86.7, 94.5)
65 and older and not obese	4 0.829 (2821)	79 0.793 (2800)	95.2 (87.1, 98.7)
65 and older and obese	3 0.404 (1370)	45 0.410 (1426)	93.2 (78.9, 98.7)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group.

g. At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age]).

h. Obese is defined as BMI ≥30 kg/m^2. For 12 through 15 years age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First COVID-19 occurrence from 7 days after Dose 2[f]	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
At risk[g]			
Yes	36 2.925 (9601)	410 2.807 (9570)	91.6 (88.1, 94.2)
No	45 3.584 (12,041)	463 3.466 (12,119)	90.6 (87.2, 93.2)

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Age group (years) and risk status			
16 through 64 and not at risk	44 2.887 (9254)	397 2.779 (9289)	89.3 (85.4, 92.4)
16 through 64 and at risk	30 2.186 (6964)	330 2.100 (6980)	91.3 (87.3, 94.2)
65 and older and not at risk	1 0.566 (1920)	55 0.559 (1966)	98.2 (89.6, 100.0)
65 and older and at risk	6 0.701 (2395)	73 0.672 (2360)	92.1 (82.0, 97.2)
Obese[h]			
Yes	28 2.207 (7139)	319 2.158 (7235)	91.4 (87.4, 94.4)
No	53 4.301 (14,497)	554 4.114 (14,448)	90.8 (87.9, 93.2)
Age group (years) and obesity status			
16 through 64 and not obese	49 3.303 (10,629)	458 3.158 (10,614)	89.8 (86.2, 92.5)
16 through 64 and obese	25 1.768 (5584)	269 1.719 (5649)	91.0 (86.4, 94.3)
65 and older and not obese	4 0.850 (2899)	82 0.811 (2864)	95.3 (87.6, 98.8)
65 and older and obese	3 0.417 (1415)	46 0.420 (1462)	93.4 (79.5, 98.7)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.
f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group.
g. At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age]).
h. Obese is defined as BMI ≥30 kg/m^2. For the 12 through 15 years of age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Efficacy Against Severe COVID-19

Updated efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table ~~14~~7) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table ~~14~~7: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older ~~and~~ With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition ~~After Dose 1 or~~ From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population ~~in~~ During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[cb])	**Placebo Cases n1[a] Surveillance Time[b] (n2[cb])**	**Vaccine Efficacy % (95% CI[de])**
~~After Dose 1[d]~~	~~1 8.439[e] (22,505)~~	~~30 8.288[e] (22,435)~~	~~96.7 (80.3, 99.9)~~
7 days after Dose 2[fd]	1 ~~6.522[ge] (21,649)~~6.353 (20,540)	21 ~~6.404[ge] (21,730)~~6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[cb])	**Placebo Cases n1[a] Surveillance Time[b] (n2[cb])**	**Vaccine Efficacy % (95% CI[de])**
~~After Dose 1[d]~~	~~1 8.427[e] (22,473)~~	~~45 8.269[e] (22,394)~~	~~97.8 (87.2, 99.9)~~
7 days after Dose 2[fd]	0 ~~6.514[ge] (21,620)~~6.345 (20,513)	~~32~~31 ~~6.391[ge] (21,693)~~6.225 (20,593)	100 ~~(88.0, 100.0)~~(87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;

- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
de. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
~~d. Efficacy assessed based on the Dose 1 all available efficacy (modified intention-to-treat) population that included all randomized participants who received at least 1 dose of study intervention.~~
~~e. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.~~
~~f~~d. ~~Efficacy assessed based on the evaluable efficacy (7 Days) population that included all eligible randomized participants who receive all dose(s) of study intervention as randomized within the predefined window, have no other important protocol deviations as determined by the clinician.~~
~~g~~e. ~~Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.~~

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as a 10 mL single-use vial manufactured by Hospira, Inc (NDC 0409-4888-10), or a 2 mL single-use vial manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -80ºC to -60ºC (-112ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

~~There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by calling …..~~

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit ~~www.pfizer.com~~www.comirnatyglobal.com.

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BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.~~2~~3

US Govt. License No. x

CPT Code x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

---------- INDICATIONS AND USAGE ----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection ~~administration~~ only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS----------
- In clinical studies of participants 16 through 55 years of age ~~and older~~, the most commonly reported adverse reactions (~~>~~≥10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, fever, and injection site swelling. (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, injection site swelling, fever, and injection site redness. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

Comment [A2]: Pfizer-BioNTech accepts FDA revision.

Comment [A3]: FDA comment:
Pfizer,
Please see section 6 for a statement to include in highlights.

Pfizer-BioNTech response:
The Sponsor accepts and has included the listing of adverse reactions occurring at >10% in participants 16-55 years of age and 56 years of age and older.

Comment [A1]: Pfizer-BioNTech proposes to revise for consistency with FPI.

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Comment [A4]: FDA comment:
Pfizer,
Please make table of contents consistent with Full PI.

Pfizer-BioNTech response:
The Sponsor accepts and has revised the table of contents consistent with the Full Prescribing Information.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

Comment [A5]: Pfizer-BioNTech accepts FDA revisions to this section.

2.1 Preparation for Administration

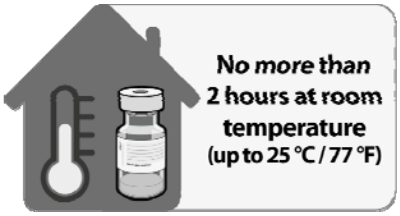
Prior to Dilution

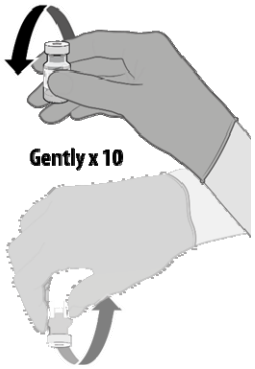
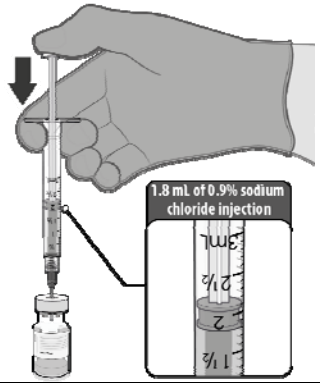
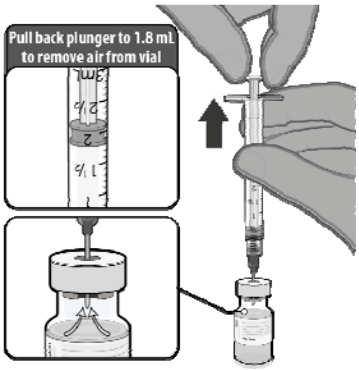
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

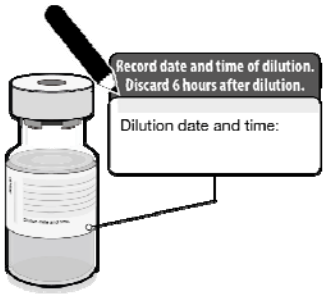
Dilution

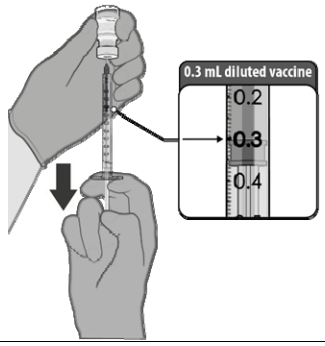
- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or an alternate brand of sterile 0.9% Sodium Chloride Injection, USP as the diluent.
- Provided diluent vials are single-use only and should be discarded after 1.8 mL is withdrawn. Do not use provided diluent vials to dilute multiple vials of COMIRNATY.
- After dilution, 1 vial contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

Comment [A6]: Pfizer BioNTech proposes to add this information to address the query received separately from CBER related to the number of uses of provided diluent vials.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.

	• Before dilution invert vaccine vial gently 10 times. • Do not shake. • Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Cleanse the vaccine vial stopper with a single-use antiseptic swab. • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.
	• Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.

	• Gently invert the vial containing the COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

2.2 Administration Information

For intramuscular injection only.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Visually inspect each dose in the dosing syringe prior to administration. The vaccine will be an off-white suspension. During the visual inspection,

- verify the final dosing volume of 0.3 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Comment [A7]: Pfizer-BioNTech accepts FDA revisions to this subsection.

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk has been highest in adolescent and young adult males under 40 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of symptoms. Information is not yet available about potential long-term sequelae. The CDC has published

considerations for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies with a data cut-off of March 13, 2021, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies with a data cut-off of March 13, 2021, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

In clinical studies with a data cut-off of March 13, 2021, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies with a data cut-off of March 13, 2021, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine

Comment [A8]: Pfizer-BioNTech accepts FDA deletion of this information "In clinical studies with a data cut-off of March 13, 2021, adverse reactions in participants 16 years of age and older included pain at the injection site (84.3%), fatigue (64.7%), headache (57.1%), muscle pain (40.2%), chills (34.7%), joint pain (25.0%), fever (15.2%), injection site swelling (11.1%), injection site redness (9.9%), nausea (1.2%), malaise (0.6%), lymphadenopathy (0.4%), asthenia (0.3%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).
Severe allergic reactions, including anaphylaxis, have been reported following administration of COMIRNATY outside of clinical trials." and has provided updated proposal below.

Comment [A9]: FDA comment:
Pfizer,
Please complete the sentences and include in the Highlights.

Pfizer-BioNTech response:
The Sponsor accepts and has updated the text as requested in section 6 of the Full Prescribing Information and in the Highlights page. The Sponsor has revised the FDA proposed text to list the adverse reactions by "≥" 10%. The Sponsor has also included the adverse reactions reported <10% by participants 16 to 55 years of age and 56 years of age and older.

candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 ~~TRADENAME~~COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection~~disease~~ was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were ~~≥~~65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 ~~to~~ through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Comment [A10]: Pfizer BioNTech agrees with the minor FDA revisions to this section with one modification to update TRADENAME to Comirnaty.

Comment [A11]: Pfizer BioNTech proposes to modify for consistency throughout the label.

Comment [A12]: Pfizer BioNTech accepts FDA addition of this statement.

Comment [A13]: Pfizer BioNTech agrees with FDA deletion of the following statement "At the time of the analysis of Study 2 for the Emergency Use Authorization (EUA) with a data cut-off of November 14, 2020, there were 37,586 participants (18,801 COMIRNATY and 18,785 placebo) 16 years of age or older followed for a median of 2 months after the second dose of COMIRNATY." as well as the minor modifications to this paragraph.

Comment [A14]: Pfizer BioNTech agrees with FDA deletion of the following statement "The safety evaluation in Study 2 is ongoing. The safety population includes participants enrolled by October 9, 2020, and includes safety data accrued through March 13, 2021."

Comment [A15]: FDA comment:
Pfizer: Please also include the age demographics for percentages of participants who are 16 through 64 years and ≥65 years of age.

Pfizer-BioNTech response:
Pfizer has updated the label as per FDA request.
Source: Table E Demographics and Other Baseline Characteristics, Phase 2/3 Participants 16 Years of Age and Older, Through Data Cutoff March 13, 2021, Safety Population in label bundle, age group >=65 years row.

Comment [A16]: Pfizer BioNTech proposes to modify for consistency throughout the label.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

Comment [A17]: Pfizer: Please add footnotes to Tables 1-4, that participants with chronic, stable HIV disease were excluded.

Pfizer-BioNTech response:
The Sponsor accepts and has added the footnote to Tables 1-4.

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N^a=2008 n^b (%)	Placebo Dose 1 N^a=1989 n^b (%)	COMIRNATY Dose 2 N^a=1860 n^b (%)	Placebo Dose 2 N^a=1833 n^b (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

~~Table 5 and Table 6 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 16 years of age and older with confirmed stable HIV infection.~~

In participants with chronic, stable HIV infection after receiving Dose 2, local reactions and systemic events were similar to those observed for all participants 16 years of age and older by severity, onset day, and median duration. The frequency of pain at the injection site was similar after Dose 1 compared with Dose 2 of COMIRNATY (63.0% versus 53.3%). The frequency of redness and swelling was similar after Dose 1 compared with Dose 2 of COMIRNATY (redness: 3.7% versus 6.7%; swelling: 5.6% versus 8.3%, respectively). There was 1 (1.7%) severe reaction (pain at the injection site) reported after Dose 2 of COMIRNATY and no Grade 4 local reactions were reported. Fever, headache, chills, and joint pain increased in frequency from Dose 1 to Dose 2 while fatigue, vomiting, diarrhea, and muscle pain were similar after each dose of COMIRNATY. There were no severe systemic events after Dose 1 of COMIRNATY but after Dose 2, there was 1 (1.7%) severe fever (>38.9°C to 40.0°C), 3 (5.0%) participants with severe fatigue, 2 (3.3%) participants with severe headache, 1 (1.7%) participant with severe chills, and 1 (1.7%) participant with severe diarrhea. There were no Grade 4 systemic events reported after either dose.

Comment [A18]: Pfizer: Please describe local and systemic reactogenicity for the stable, chronic HIV+ participants in text to indicate that the frequencies of local and solicited reactions were generally the same or less frequent as compared to the overall safety population described in Tables 1-4.

Pfizer-BioNTech response:
The Sponsor accepts deletion of the 2 HIV tables and has proposed summary text.

~~**Table 5: Study 2 Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose HIV-Positive Participants 16 Years of Age and Older Reactogenicity Subset of the Safety Population***~~

	~~COMIRNATY Dose 1 N^a=54 n^b (%)~~	~~Placebo Dose 1 N^a=56 n^b (%)~~	~~COMIRNATY Dose 2 N^a=60 n^b (%)~~	~~Placebo Dose 2 N^a=62 n^b (%)~~
~~Redness[e]~~				
~~Any (>2.0 cm)~~	~~2 (3.7)~~	~~3 (5.4)~~	~~4 (6.7)~~	~~1 (1.6)~~
~~Mild~~	~~2 (3.7)~~	~~1 (1.8)~~	~~3 (5.0)~~	~~1 (1.6)~~
~~Moderate~~	~~0~~	~~0~~	~~1 (1.7)~~	~~0~~
~~Severe~~	~~0~~	~~2 (3.6)~~	~~0~~	~~0~~
~~Swelling[e]~~				
~~Any (>2.0 cm)~~	~~3 (5.6)~~	~~1 (1.8)~~	~~5 (8.3)~~	~~0~~
~~Mild~~	~~2 (3.7)~~	~~0~~	~~2 (3.3)~~	~~0~~
~~Moderate~~	~~1 (1.9)~~	~~0~~	~~3 (5.0)~~	~~0~~
~~Severe~~	~~0~~	~~1 (1.8)~~	~~0~~	~~0~~

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Pain at the injection site[d]				
Any	34 (63.0)	9 (16.1)	32 (53.3)	5 (8.1)
Mild	26 (48.1)	8 (14.3)	22 (36.7)	5 (8.1)
Moderate	8 (14.8)	1 (1.8)	9 (15.0)	0
Severe	0	0	1 (1.7)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in HIV-positive participants 16 years of age and older.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 6: Study 2 Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose HIV-Positive Participants 16 Years of Age and Older Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Fever				
≥38.0°C	1 (1.9)	4 (7.1)	9 (15.0)	5 (8.1)
≥38.0°C to 38.4°C	1 (1.9)	2 (3.6)	4 (6.7)	5 (8.1)
>38.4°C to 38.9°C	0	0	4 (6.7)	0
>38.9°C to 40.0°C	0	2 (3.6)	1 (1.7)	0
>40.0°C	0	0	0	0
Fatigue[e]				
Any	22 (40.7)	15 (26.8)	24 (40.0)	12 (19.4)
Mild	15 (27.8)	9 (16.1)	12 (20.0)	5 (8.1)
Moderate	7 (13.0)	5 (8.9)	9 (15.0)	7 (11.3)
Severe	0	1 (1.8)	3 (5.0)	0
Headache[e]				
Any	11 (20.4)	18 (32.1)	18 (30.0)	12 (19.4)
Mild	7 (13.0)	10 (17.9)	8 (13.3)	8 (12.9)
Moderate	4 (7.4)	7 (12.5)	8 (13.3)	4 (6.5)
Severe	0	1 (1.8)	2 (3.3)	0
Chills[e]				
Any	6 (11.1)	5 (8.9)	14 (23.3)	4 (6.5)
Mild	5 (9.3)	4 (7.1)	5 (8.3)	3 (4.8)
Moderate	1 (1.9)	1 (1.8)	8 (13.3)	1 (1.6)
Severe	0	0	1 (1.7)	0

	COMIRNATY Dose 1 N[a]=54 n[b] (%)	Placebo Dose 1 N[a]=56 n[b] (%)	COMIRNATY Dose 2 N[a]=60 n[b] (%)	Placebo Dose 2 N[a]=62 n[b] (%)
Vomiting[d]				
Any	1 (1.9)	3 (5.4)	2 (3.3)	2 (3.2)
Mild	1 (1.9)	1 (1.8)	1 (1.7)	1 (1.6)
Moderate	0	0	1 (1.7)	1 (1.6)
Severe	0	2 (3.6)	0	0
Diarrhea[e]				
Any	5 (9.3)	8 (14.3)	4 (6.7)	9 (14.5)
Mild	5 (9.3)	6 (10.7)	1 (1.7)	6 (9.7)
Moderate	0	1 (1.8)	2 (3.3)	3 (4.8)
Severe	0	1 (1.8)	1 (1.7)	0
New or worsened muscle pain[e]				
Any	9 (16.7)	10 (17.9)	10 (16.7)	5 (8.1)
Mild	7 (13.0)	7 (12.5)	5 (8.3)	1 (1.6)
Moderate	2 (3.7)	3 (5.4)	5 (8.3)	4 (6.5)
Severe	0	0	0	0
New or worsened joint pain[e]				
Any	5 (9.3)	7 (12.5)	10 (16.7)	5 (8.1)
Mild	5 (9.3)	4 (7.1)	4 (6.7)	1 (1.6)
Moderate	0	3 (5.4)	6 (10.0)	4 (6.5)
Severe	0	0	0	0
Use of antipyretic or pain medication[f]	7 (13.0)	8 (14.3)	16 (26.7)	7 (11.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in HIV-positive participants 16 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each event or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

Upon issuance of the EUA for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Unblinded participants originally randomized to COMIRNATY and placebo recipients administered COMIRNATY continued to be followed for unsolicited adverse events including serious adverse events, throughout the study [from Dose 1 of COMIRNATY through 1 month (all unsolicited adverse events) and 6 months (serious adverse events) after the last vaccination]. Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began in a phased manner for participants in the study. Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 2.1 per 100 person-years among COMIRNATY recipients and 2.4 per 100 person-years among placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported at an incidence rate of 4.9 per 100 person-years among COMIRNATY recipients and 4.6 per 100 person-years among placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 6.6 per 100 person-years among COMIRNATY recipients and 6.9 per 100 person-years among placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

Comment [A19]: FDA comment:
Pfizer: Please add a subsection to provide a description of the safety evaluation for the original BNT162b2 recipients who have at least 6 months of follow up post dose 2, through blinded and unblinded time periods.

Pfizer-BioNTech response:
The Sponsor accepts and has provided the requested text.

Comment [A20]: FDA comment:
Pfizer: Please delete this sentence and revise this introduction to describe the variable exposure caused by the unblinding that occurred in a phased manner, to include the actual difference in duration of follow up between groups. We will then report the following events as frequencies n/N (%) rather than incidence rates, as revised below.

Pfizer-BioNTech response:
The Sponsor is not in agreement with FDA request and the FDA proposed revisions to the SAE and AE paragraphs. Proportion is more appropriate to summarize adverse events over a specified period of time for all participants. In this study however, participants had differential follow-up time due to the phased manner for unblinding, with approximately 42% of subjects with <4 months of follow up and approximately 58% with >+4 months follow-up. Pfizer therefore proposes to report incidence rates for safety events accounting for the differential follow-up time as a more accurate statistical summary of the safety results.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 88.4 per 100 person-years among participants who received COMIRNATY and 43.5 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include non-serious adverse events were reported at an incidence rate of 75.7 per 100 person-years among participants who received COMIRNATY and 43.3 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 95.8 per 100 person-years among participants who received COMIRNATY and 52.0 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-marketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Comment [A21]: **Pfizer BioNTech** accepts FDA addition of the statement "From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8)."

Comment [A22]: FDA comment:
Pfizer,
This subsection should focus on adverse reactions not observed in clinical trials. Please provide a rationale for inclusion of diarrhea, vomiting and pain in extremity (arm).

Pfizer-BioNTech response:
The Sponsor identified Diarrhea, Vomiting and Pain in extremity (arm) as adverse reactions caused by the vaccine in the post-authorization setting, not the clinical study setting. In the clinical study, there was not differentiation in the frequency of these events between the placebo vs vaccine groups. Please refer to the Clinical Overview submitted with this response for a complete justification of these terms.

Comment [A23]: FDA comment:
Pfizer,
Please add the PTs for "Dizziness" and "Dyspnea" and their corresponding SOCs to section 6.2

Pfizer-BioNTech response:
The Sponsor is not in agreement with the FDA request. The Sponsor does not consider Dizziness and Dyspnea as adverse reactions independent of potential symptoms of a Vaccination stress-related response due to the vaccination process.

Comment [A24]: FDA comment:
Pfizer,
Please include information regarding Pregnancy Exposure Registry for COMIRNATY to monitor pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Please list the telephone number for the health care providers to call and register women who receive COMIRNATY during pregnancy.

Pfizer-BioNTech response:
The Sponsor is not in agreement with the inclusion of the Pregnancy Exposure Registry. The study registry is performed by the University of California San Diego (UCSD) with a limited enrollment of vaccinated pregnant women with COMIRNATY. The recruitment is handled by UCSD using their established registry procedures.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions, twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Comment [A25]: Pfizer-BioNTech accepts deletion of "reproductive and" from this sentence.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

Comment [A26]: Pfizer-BioNTech accepts deletion of "reproductive and" from this sentence.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

Comment [A27]: Pfizer-BioNTech accepts FDA editorial revisions to this section.

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL

of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY~~.~~, ~~t~~There were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

Comment [A28]: Pfizer-BioNTech accepts deletion of "and reproductive" from this sentence.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is a multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Comment [A29]: Pfizer BioNTech agrees with FDA deletion of the following statement "The efficacy analyses included participants that received their second vaccination within 19 to 42 days after their first vaccination. The majority (93.1%) of vaccine recipients received the second dose 19 days to 23 days after Dose 1." as well as the other edits within this paragraph.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of

prior infection with SARS-CoV-2 through 7 days after the second dose. ~~Table 7 presents the specific demographic characteristics in the studied population.~~ Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.5% were male and 48.6% or 49.5% were female, 4.8% or 4.6% were 12 through 15 years of age, 75.1% or 75.1% were 16 through 64 years of age, 20.1% or 20.3% were 65 years of age and older, 16.1% or 16.3% were 65 through 74 years of age, 4.0% or 4.0% ≥75 years of age and older, 82.9% or 83.1% were White, 8.5% or 8.6% were Black or African American, 0.9% or 0.9% were American Indian or Alaska Native, 4.6% or 4.5% were Asian, 0.3% or 0.1% Native Hawaiian or other Pacific Islander, 24.9% or 24.6% were Hispanic/Latino, 74.6% or 74.8% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 44.6% or 44.4% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2 (16 years of age and older) or BMI ≥95th percentile (12 through 15 years of age)], respectively. The mean age at vaccination was 48.3 or 48.2 years and median age was 50.0 or 50.0 in participants who received COMIRNATY or placebo, respectively.

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~~Table 7: Demographics (Population For the Primary Efficacy Endpoint)~~[a]

	~~COMIRNATY (N=18,242) n (%)~~	~~Placebo (N=18,379) n (%)~~
~~Sex~~		
~~Male~~	~~9318 (51.1)~~	~~9225 (50.2)~~
~~Female~~	~~8924 (48.9)~~	~~9154 (49.8)~~
~~Age (years)~~		
~~Mean (SD)~~	~~50.6 (15.70)~~	~~50.4 (15.81)~~
~~Median~~	~~52.0~~	~~52.0~~
~~Min, max~~	~~(12, 89)~~	~~(12, 91)~~
~~Age group~~		
~~≥12 through 15 years~~	~~46 (0.3)~~	~~42 (0.2)~~
~~≥16 through 64 years~~	~~14,216 (77.9)~~	~~14,299 (77.8)~~
~~≥65 through 74 years~~	~~3176 (17.4)~~	~~3226 (17.6)~~
~~≥75 years~~	~~804 (4.4)~~	~~812 (4.4)~~
~~Race~~		
~~White~~	~~15,110 (82.8)~~	~~15,301 (83.3)~~
~~Black or African American~~	~~1617 (8.9)~~	~~1617 (8.8)~~
~~American Indian or Alaska Native~~	~~118 (0.6)~~	~~106 (0.6)~~
~~Asian~~	~~815 (4.5)~~	~~810 (4.4)~~
~~Native Hawaiian or other Pacific Islander~~	~~48 (0.3)~~	~~29 (0.2)~~
~~Other~~[b]	~~534 (2.9)~~	~~516 (2.8)~~
~~Ethnicity~~		
~~Hispanic or Latino~~	~~4886 (26.8)~~	~~4857 (26.4)~~
~~Not Hispanic or Latino~~	~~13,253 (72.7)~~	~~13,412 (73.0)~~
~~Not reported~~	~~103 (0.6)~~	~~110 (0.6)~~
~~Comorbidities~~[c]		
~~Yes~~	~~8432 (46.2)~~	~~8450 (46.0)~~
~~No~~	~~9810 (53.8)~~	~~9929 (54.0)~~

~~a. All eligible randomized participants who receive all vaccination(s) as randomized within the predefined window, have no other important protocol deviations as determined by the clinician, and have no evidence of SARS-CoV-2 infection prior to 7 days after Dose 2.~~

~~b. Includes multiracial and not reported.~~

~~c. Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease:~~

- ~~Chronic lung disease (e.g., emphysema and chronic bronchitis, idiopathic pulmonary fibrosis, and cystic fibrosis) or moderate~~

Comment [A30]: FDA Comment:
Pfizer: Please delete this table and describe demographics of the efficacy population using the March 2021 data cutoff, to also include percentages of the participants in the age group ≥65 years, and those with comorbidities (with a definition).

Pfizer-BioNTech response:
Pfizer-BioNTech has updated the label as per FDA request.

~~to severe asthma~~

- ~~Significant cardiac disease (e.g., heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and pulmonary hypertension)~~
- ~~Obesity (body mass index ≥30 kg/m^2)~~
- ~~Diabetes (Type 1, Type 2, or gestational)~~
- ~~Liver disease~~
- ~~Human Immunodeficiency Virus (HIV) infection (not included in the efficacy evaluation)~~

Efficacy Against COVID-19

The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

The vaccine efficacy information is presented in Table ~~8~~5.

Table ~~5~~8: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=18,198 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.3, 97.6)[f]
16 to 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)[g]
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)[g]
65 to 74 years	1 0.406 (3074)	14 0.406 (3095)	92.9 (53.1, 99.8)[g]
75 years and older	0 0.102 (774)	5 0.106 (785)	100.0 (-13.1, 100.0)[g]
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=19,965 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,172 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All participants[e]	9 2.332 (18,559)	169 2.345 (18,708)	94.6 (89.9, 97.3)[f]
16 to 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1 0.530 (4044)	19 0.532 (4067)	94.7 (66.8, 99.9)[g]

Comment [A31]: Pfizer BioNTech agrees with FDA addition of this information.

Comment [A32]: FDA comment:
Pfizer: Please describe the primary efficacy analysis in text as outlined below and remove Table 8.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0%. The case split was 8 COVID-19 cases in the BNT162b2 group compared to 162 COVID-19 cases in the placebo group. The 95% credible interval for the vaccine efficacy was 90.3% to 97.6%, indicating that the true VE is at least 90.3% with a 97.5% probability, which met the pre-specified success criterion.

Pfizer-BioNTech response:
The Sponsor proposes to retain the information as presented in the table as it is more informative and clearer for the healthcare provider.

65 to 74 years	1 0.424 (3239)	14 0.423 (3255)	92.9 (53.2, 99.8)[g]
75 years and older	0 0.106 (805)	5 0.109 (812)	100.0 (-12.1, 100.0)[g]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. No confirmed cases were identified in participants 12 to 15 years of age.
f. Two-sided credible interval for vaccine efficacy was calculated using a beta-binomial model with a beta (0.700102, 1) prior for θ=r(1-VE)/(1+r(1-VE)), where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.
g. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021~~0~~, representing up to 6 months of follow-up after Dose 2. Overall, 59.2% of participants in the COMIRNATY group and 57.3% of participants in the placebo group had ≥4 months of follow-up time after Dose 2 in the blinded placebo-controlled follow-up period.

~~Updated efficacy analyses were performed with additional confirmed COVID-19 cases accrued during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2 for participants in the efficacy population.~~

The updated vaccine efficacy information is presented in Table ~~9~~6.

Table ~~9~~6: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	COMIRNATY N[a]=~~20,998~~19,993 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=~~21,096~~20,118 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI[e])
All participants[f]	77 ~~6.247 (20,712)~~6.092 (19,711)	~~850~~833 ~~6.003 (20,713)~~5.857 (19,741)	~~91.3~~91.1 ~~(89.0, 93.2)~~(88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	~~710~~709 ~~4.654 (15,515)~~4.654 (15,515)	~~90.6~~90.5 ~~(87.9, 92.7)~~(87.9, 92.7)
65 years and older	7	124	94.5

Comment [A33]: FDA comment:
Pfizer: Please insert a sentence describing the percentage of participants with blinded placebo-controlled follow up ≥4months, to mirror the description of the Safety population.

Pfizer-BioNTech response:
Pfizer-BioNTech has updated the label as per FDA request.

Comment [A34]: FDA comment:
Pfizer: Please revise Updated VE tables to display VE for participants 16 years of age and older (exclude participants 12-15 years of age) for only confirmed cases that we agree upon (exclude participant 10031167 from all analyses, as previously communicated).

Please also delete the last 2 rows of each portion of the table: 65 through 74 years and 75 years and older.

Pfizer-BioNTech response:
Pfizer has updated the table as per FDA request.
Source: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup– Blinded Placebo-Controlled Follow-up Period– Subjects ≥16 Years of Age and Without Evidence of Infection Prior to 7 Days After Dose 2– Evaluable Efficacy (7 Days) Population

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	1.233 (4192)	1.202 (4226)	(88.3, 97.8)
~~65 through 74 years~~	~~6~~ ~~0.994 (3350)~~	~~98~~ ~~0.966 (3379)~~	~~94.1~~ ~~(86.6, 97.9)~~
~~75 years and older~~	~~1~~ ~~0.239 (842)~~	~~26~~ ~~0.237 (847)~~	~~96.2~~ ~~(76.9, 99.9)~~

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection

Subgroup	COMIRNATY N[a]=~~22,166~~21,047 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=~~22,320~~21,210 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI[e])
All participants[f]	81 ~~6.509 (21,642)~~6.340 (20,533)	~~873~~854 ~~6.274 (21,689)~~6.110 (20,595)	~~91.1~~90.9 ~~(88.8, 93.0)~~(88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	~~727~~726 ~~4.879 (16,269)~~4.879 (16,269)	90.2 ~~(87.6, 92.4)~~(87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)
~~65 through 74 years~~	~~6~~ ~~1.021 (3450)~~	~~102~~ ~~0.992 (3468)~~	~~94.3~~ ~~(87.1, 98.0)~~
~~75 years and older~~	~~1~~ ~~0.246 (865)~~	~~26~~ ~~0.240 (858)~~	~~96.2~~ ~~(77.2, 99.9)~~

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

~~f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group (both without and with or without evidence of prior SARS-CoV-2 infection); 16 and 18 in the placebo group (without and with or without evidence of prior SARS-CoV-2 infection, respectively).~~

Subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, geographies, and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

~~The updated subgroup analyses of vaccine efficacy by demographic characteristics are presented in Table 10 and Table 11.~~

~~**Table 10: Vaccine Efficacy - First COVID-19 Occurrence From 7 Days After Dose 2 - Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 by Demographic Characteristics - Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period**~~

Comment [A35]: Pfizer BioNTech accepts deletion of the 65 through 74 years and 75 years and older rows.

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Comment [A36]: **Pfizer BioNTech** accepts deletion of the 65 through 74 years and 75 years and older rows.

Comment [A37]: **FDA comment:** Pfizer: This footnote should be removed based on our comment above to exclude all participants 12-15 years of age from this analysis.

Pfizer-BioNTech: The Sponsor accepts and has deleted the footnote.

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Comment [A38]: **FDA comment:** Pfizer: Please delete Table 10-13.

Pfizer-BioNTech: The Sponsor accepts and has deleted Tables 10-13 and proposes a summary statement of the vaccine efficacy.

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Sex			
Male	42 3.246 (10,637)	399 3.047 (10,433)	90.1 (86.4, 93.0)
Female	35 3.001 (10,075)	451 2.956 (10,280)	92.4 (89.2, 94.7)
Ethnicity			
Hispanic or Latino	29 1.786 (5161)	241 1.711 (5120)	88.5 (83.0, 92.4)
Not Hispanic or Latino	47 4.429 (15,449)	609 4.259 (15,484)	92.6 (90.0, 94.6)
Race			
Black or African American	4 0.545 (1737)	48 0.527 (1737)	91.9 (78.0, 97.9)
White	67 5.208 (17,186)	747 5.026 (17,256)	91.3 (88.9, 93.4)
All others[f]	6 0.494 (1789)	55 0.451 (1720)	90.0 (76.9, 96.5)
Country			
Argentina	15 1.012 (2600)	108 0.986 (2586)	86.5 (76.7, 92.7)
Brazil	12 0.406 (1311)	80 0.374 (1293)	86.2 (74.5, 93.1)
Germany	0 0.047 (236)	1 0.048 (242)	100.0 (-3874.2, 100.0)
South Africa	0 0.080 (291)	9 0.074 (276)	100.0 (53.5, 100.0)
Turkey	0 0.027 (228)	5 0.025 (222)	100.0 (-0.1, 100.0)
United States	50 4.674 (16,046)	647 4.497 (16,094)	92.6 (90.1, 94.5)

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).
Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group.
* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.
a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
f. All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

Table 11: Vaccine Efficacy - First COVID-19 Occurrence From 7 Days After Dose 2 - Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 by Demographic Characteristics - Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Sex			
Male	44 3.376 (11,103)	411 3.181 (10,920)	89.9 (86.2, 92.8)
Female	37 3.133 (10,539)	462 3.093 (10,769)	92.1 (88.9, 94.5)
Ethnicity			
Hispanic or Latino	32 1.862 (5408)	245 1.794 (5391)	87.4 (81.8, 91.6)
Not Hispanic or Latino	48 4.615 (16,128)	628 4.445 (16,186)	92.6 (90.1, 94.6)
Race			
Black or African American	4 0.611 (1958)	49 0.601 (1985)	92.0 (78.1, 97.9)
White	69 5.379 (17,801)	768 5.191 (17,880)	91.3 (88.9, 93.3)
All others[f]	8 0.519 (1883)	56 0.481 (1824)	86.8 (72.1, 94.5)
Country			
Argentina	16 1.033 (2655)	110 1.017 (2670)	85.7 (75.7, 92.1)
Brazil	14 0.441 (1419)	82 0.408 (1401)	84.2 (71.9, 91.7)
Germany	0 0.047 (237)	1 0.048 (243)	100.0 (-3868.6, 100.0)
South Africa	0 0.099 (358)	10 0.096 (358)	100.0 (56.6, 100.0)
Turkey	0 0.029 (238)	6 0.026 (232)	100.0 (22.2, 100.0)
United States	51 4.861 (16,735)	664 4.678 (16,785)	92.6 (90.2, 94.6)

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]

Notes: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group.

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

f. All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

The updated subgroup analyses of vaccine efficacy by risk status in participants are presented in Table 12 and Table 13.

Table 12: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First COVID-19 occurrence from 7 days after Dose 2[f]	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
At risk[g]			
Yes	35 2.797 (9167)	401 2.681 (9136)	91.6 (88.2, 94.3)
No	42 3.450 (11,545)	449 3.322 (11,577)	91.0 (87.6, 93.6)
Age group (years) and risk status			
16 through 64 and not at risk	41 2.776 (8887)	385 2.661 (8886)	89.8 (85.9, 92.8)
16 through 64 and at risk	29 2.083 (6632)	325 1.993 (6629)	91.5 (87.5, 94.4)
65 and older and not at risk	1 0.553 (1870)	53 0.546 (1922)	98.1 (89.2, 100.0)
65 and older and at risk	6 0.680 (2322)	71 0.656 (2304)	91.8 (81.4, 97.1)
Obese[h]			

Subgroup	COMIRNATY N[a]=20,998 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,096 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Yes	27 2.103 (6796)	314 2.050 (6875)	91.6 (87.6, 94.6)
No	50 4.143 (13,911)	536 3.952 (13,833)	91.1 (88.1, 93.5)
Age group (years) and obesity status			
16 through 64 and not obese	46 3.178 (10,212)	444 3.028 (10,166)	90.1 (86.6, 92.9)
16 through 64 and obese	24 1.680 (5303)	266 1.624 (5344)	91.3 (86.7, 94.5)
65 and older and not obese	4 0.829 (2821)	79 0.793 (2800)	95.2 (87.1, 98.7)
65 and older and obese	3 0.404 (1370)	45 0.410 (1426)	93.2 (78.9, 98.7)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.
f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 16 in the placebo group.
g. At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age]).
h. Obese is defined as BMI ≥30 kg/m^2. For 12 through 15 years age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
First COVID-19 occurrence from 7 days after Dose 2[f]	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
At risk[g]			
Yes	36 2.925 (9601)	410 2.807 (9570)	91.6 (88.1, 94.2)
No	45 3.584 (12,041)	463 3.466 (12,119)	90.6 (87.2, 93.2)

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	COMIRNATY N[a]=22,166 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=22,320 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Age group (years) and risk status			
16 through 64 and not at risk	44 2.887 (9254)	397 2.779 (9289)	89.3 (85.4, 92.4)
16 through 64 and at risk	30 2.186 (6964)	330 2.100 (6980)	91.3 (87.3, 94.2)
65 and older and not at risk	1 0.566 (1920)	55 0.559 (1966)	98.2 (89.6, 100.0)
65 and older and at risk	6 0.701 (2395)	73 0.672 (2360)	92.1 (82.0, 97.2)
Obese[h]			
Yes	28 2.207 (7139)	319 2.158 (7235)	91.4 (87.4, 94.4)
No	53 4.301 (14,497)	554 4.114 (14,448)	90.8 (87.9, 93.2)
Age group (years) and obesity status			
16 through 64 and not obese	49 3.303 (10,629)	458 3.158 (10,614)	89.8 (86.2, 92.5)
16 through 64 and obese	25 1.768 (5584)	269 1.719 (5649)	91.0 (86.4, 94.3)
65 and older and not obese	4 0.850 (2899)	82 0.811 (2864)	95.3 (87.6, 98.8)
65 and older and obese	3 0.417 (1415)	46 0.420 (1462)	93.4 (79.5, 98.7)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

f. Included confirmed cases in participants 12 through 15 years of age: 0 in the COMIRNATY group; 18 in the placebo group.

g. At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 or BMI ≥95th percentile [12 through 15 years of age]).

h. Obese is defined as BMI ≥30 kg/m^2. For the 12 through 15 years of age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Efficacy Against Severe COVID-19

Updated efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table ~~14~~7) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table ~~14~~7: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older ~~and~~ With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition ~~After Dose 1 or~~ From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population ~~in~~ During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[cb])	**Placebo Cases n1[a] Surveillance Time[b] (n2[cb])**	**Vaccine Efficacy % (95% CI[de])**
~~After Dose 1[d]~~	~~1 8.439[e] (22,505)~~	~~30 8.288[e] (22,435)~~	~~96.7 (80.3, 99.9)~~
7 days after Dose 2[fd]	1 ~~6.522[ge] (21,649)~~6.353 (20,540)	21 ~~6.404[ge] (21,730)~~6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[cb])	**Placebo Cases n1[a] Surveillance Time[b] (n2[cb])**	**Vaccine Efficacy % (95% CI[de])**
~~After Dose 1[d]~~	~~1 8.427[e] (22,473)~~	~~45 8.269[e] (22,394)~~	~~97.8 (87.2, 99.9)~~
7 days after Dose 2[fd]	0 ~~6.514[ge] (21,620)~~6.345 (20,513)	~~32~~31 ~~6.391[ge] (21,693)~~6.225 (20,593)	100 ~~(88.0, 100.0)~~(87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;

Comment [A39]: FDA comment:
Pfizer: Please revise this table as follows:
1.Remove the rows for severe cases after Dose 1
2.Remove the specification of the FDA Definition of Severe Disease, as revised.

Pfizer-BioNTech response:
The Sponsor accepts the FDA requests. The original table presented results for all participants 12 years of age or older. To be consistent with other updated VE analyses in the label, e.g. Table 6, 7 days after Dose 2 results were updated for participants 16 years of age or older. Pfizer BioNTech also proposes to add population to table title and rearranged footnote to be consistent with Table 6.

Comment [A40]: Pfizer BioNTech accepts the replacement of "FDA" with "Protocol" in the table title and footnotes.

Comment [A41]: Source: Vaccine Efficacy – First Severe COVID-19 Occurrence From 7 Days After Dose 2– Blinded Placebo-Controlled Follow-up Period– Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2– Evaluable Efficacy (7 Days) Population

Comment [A42]: Source: Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC-Definition From 7 Days After Dose 2– Blinded Placebo-Controlled Follow-up Period – Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2– Evaluable Efficacy (7 Days) Population

- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
de. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
~~d. Efficacy assessed based on the Dose 1 all available efficacy (modified intention-to-treat) population that included all randomized participants who received at least 1 dose of study intervention.~~
~~e. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.~~
~~f~~d. ~~Efficacy assessed based on the evaluable efficacy (7 Days) population that included all eligible randomized participants who receive all dose(s) of study intervention as randomized within the predefined window, have no other important protocol deviations as determined by the clinician.~~
~~g~~e. ~~Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.~~

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as a 10 mL single-use vial manufactured by Hospira, Inc (NDC 0409-4888-10), or a 2 mL single-use vial manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

Comment [A43]: FDA comment:
Pfizer,
Please include a description of the vials from each of the two suppliers and include NDC numbers for cartons and containers of diluent from each of the manufacturers.

Pfizer-BioNTech response:
Pfizer-BioNTech has updated the label as per FDA request.

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -80ºC to -60ºC (-112ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -80ºC to -60ºC (-112ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

~~There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by calling …..~~

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

Comment [A44]: Pfizer-BioNTech comment:
The Sponsor is not in agreement with the inclusion of the Pregnancy Exposure Registry. The study registry is performed by the USD with a limited enrollment of vaccinated pregnant women with COMIRNATY. The recruitment will be handled by the UCSD procedures.

Comment [A45]: FDA comment:
Pfizer,
We do not concur; please delete.

Pfizer-BioNTech response:
The Sponsor accepts deletion of the website and telephone number for general questions.

This product's labeling may have been updated. For the most recent prescribing information, please visit ~~www.pfizer.com~~www.comirnatyglobal.com.

Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.~~2~~3

US Govt. License No. x

CPT Code x

Comment [A46]: Pfizer BioNTech proposes to update the website link.

Formatted: Underline

Comment [A47]: FDA comment:
Pfizer,
CPT codes are not typically included in labeling. Please provide a rationale for inclusion.

Pfizer-BioNTech response:
The Sponsor proposes to retain the CPT code in the label for consistency with other Pfizer Vaccine label such as Trumenba and Prevnar 13.

ctions or subsections omitted from the full prescribing information are
isted.

ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC
g (16)].
.

9% Sodium Chloride Injection, USP to form
diluent.
on, USP as the diluent. Do not use bacteriostatic 0.9%

USP are provided but shipped separately. Use the
.9% Sodium Chloride Injection, USP as the diluent.
ould be discarded after 1.8 mL is withdrawn. Do not use
COMIRNATY.
each.
as in the panels below.

l(s) of COMIRNATY before dilution either ing vial(s) to thaw in the refrigerator [2ºC (35ºF to 46ºF)]. A carton of vials may take 3 hours to thaw, and thawed vials can be in the refrigerator for up to 1 month. ing vial(s) to sit at room temperature [up to (77ºF)] for 30 minutes. her thawing method, vials must reach room ure before dilution and must be diluted hours.

2

se sterile 0.9% Sodium Chloride Injection,
ne diluent.
eptic technique, withdraw 1.8 mL of diluent
nsfer syringe (21-gauge or narrower

he vaccine vial stopper with a single-use
swab.
mL of sterile 0.9% Sodium Chloride
USP into the vaccine vial.

vial pressure before removing the needle
vial by withdrawing 1.8 mL air into the
uent syringe.

ne date and time of dilution on the
NATY vial label.
ween 2°C to 25°C (35°F to 77°F).
ny unused vaccine 6 hours after dilution.

OF COMIRNATY

eptic technique, cleanse the vial stopper
ngle-use antiseptic swab, and withdraw
f COMIRNATY preferentially using low
ume syringes and/or needles.
e must contain 0.3 mL of vaccine.
ount of vaccine remaining in a single vial
ovide a full dose of 0.3 mL, discard the
ny excess volume.
er immediately.

4

es of 2 doses (0.3 mL each) 3 weeks apart.

OMIRNATY with other COVID-19 vaccines to complete
ose of COMIRNATY should receive a second dose of

ration, a single dose is 0.3 mL.

own history of a severe allergic reaction (e.g.,
ee Description (11)].

te allergic reactions must be immediately available in
g administration of COMIRNATY.

arditis and pericarditis, particularly within 7 days
ighest in adolescent and young adult males under
up suggest that most individuals have had resolution of
al long-term sequelae. The CDC has published

5

the most commonly reported (≥10%) adverse reactions
dose were pain at the injection site (88.6%), fatigue
(41.5%), joint pain (27.5%), fever (17.8%), and

the most commonly reported (≥10%) adverse reactions
ose were pain at the injection site (78.2%), fatigue
(24.8%), joint pain (21.5%), injection site swelling
%).

the adverse reactions occurring in <10% of participants
ction site redness (9.5%), nausea (1.4%),
%), decreased appetite (0.2%), hyperhidrosis (0.1%),

the adverse reactions occurring in <10% of participants
ea (1.0%), malaise (0.5%), asthenia (0.3%),
petite (0.1%), hyperhidrosis (0.1%), and night sweats

ng conditions, adverse reaction rates observed in the
o rates in the clinical trials of another vaccine and may

nts 16 years of age and older in 2 clinical studies
na, Brazil, Turkey, South Africa, and Germany
art, dose-escalation trial that enrolled 60 participants,
gh 85 years of age. Study C4591001 (Study 2) is a
ontrolled, observer-blind, dose-finding, vaccine

imilar with regard to age, gender, race, and ethnicity
se who received placebo. Overall, among the total
bo, 50.9% were male, 49.1% were female, 79.3% were
and older, 82.0% were White, 9.6% were Black or
ere Asian, and 1.0% were American Indian or Alaska

Study 2

f reported solicited local and systemic reactions,
IRNATY and placebo in the subset of participants
tion who were monitored for reactogenicity with an

f reported solicited local and systemic reactions,
Y and placebo for participants 56 years of age and

g Dose 2, the mean duration of pain at the injection site
range 1 to 9 days), and for swelling 2.1 days (range 1 to
participants 56 years of age and older after receiving
as 2.4 days (range 1 to 36 days), for redness 3.0 days
to 34 days) for participants in the COMIRNATY group.

14 (14.2)	2101 (78.3)	312 (11.6)
91 (13.4)	1274 (47.5)	284 (10.6)
20 (0.7)	788 (29.4)	28 (1.0)
3 (0.1)	39 (1.5)	0

m Day 1 to Day 7 after vaccination.
6 through 55 years of age.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
n the column header.

.0 cm.
activity; Severe: prevents daily activity.

articipants with Solicited Systemic Reactions, by Each Dose – Participants 16 Through 55 Years of Population*

lacebo Dose 1 N^a=2908 n^b (%)	**COMIRNATY Dose 2 N^a=2682 n^b (%)**	**Placebo Dose 2 N^a=2684 n^b (%)**
5 (0.9)	440 (16.4)	11 (0.4)
6 (0.6)	254 (9.5)	5 (0.2)
5 (0.2)	146 (5.4)	4 (0.1)
4 (0.1)	39 (1.5)	2 (0.1)
0	1 (0.0)	0
0 (33.0)	1649 (61.5)	614 (22.9)
0 (19.6)	558 (20.8)	317 (11.8)
2 (12.8)	949 (35.4)	283 (10.5)
8 (0.6)	142 (5.3)	14 (0.5)

5 (0.2)	12 (0.4)	10 (0.4)
1 (0.0)	4 (0.1)	0
3 (11.1)	269 (10.0)	205 (7.6)
64 (9.1)	219 (8.2)	169 (6.3)
8 (2.0)	44 (1.6)	35 (1.3)
1 (0.0)	6 (0.2)	1 (0.0)
9 (11.3)	1055 (39.3)	237 (8.8)
81 (7.9)	441 (16.4)	150 (5.6)
6 (3.3)	552 (20.6)	84 (3.1)
2 (0.1)	62 (2.3)	3 (0.1)
68 (5.8)	638 (23.8)	147 (5.5)
12 (3.9)	291 (10.9)	82 (3.1)
5 (1.9)	320 (11.9)	61 (2.3)
1 (0.0)	27 (1.0)	4 (0.1)
8 (13.7)	1213 (45.2)	320 (11.9)

lected in the electronic diary (e-diary) from Day 1 to Day 7 after

ts 16 through 55 years of age.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
herefore, this information was included in the column header.

ce with activity; Severe: prevents daily activity.
Severe: requires intravenous hydration.
ls in 24 hours; Severe: 6 or more loose stools in 24 hours.
on.

185 (9.3)	1230 (66.1)	143 (7.8)
177 (8.9)	873 (46.9)	138 (7.5)
8 (0.4)	347 (18.7)	5 (0.3)
0	10 (0.5)	0

m Day 1 to Day 7 after vaccination.
6 years of age and older.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
n the column header.

.0 cm.
activity; Severe: prevents daily activity.

articipants with Solicited Systemic Reactions, by Each Dose – Participants 56 Years of Age and y Population*

Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
8 (0.4)	219 (11.8)	4 (0.2)
3 (0.2)	158 (8.5)	2 (0.1)
3 (0.2)	54 (2.9)	1 (0.1)
2 (0.1)	7 (0.4)	1 (0.1)
0	0	0

0

49 (2.5)	229 (12.3)	45 (2.5)
19 (1.0)	185 (9.9)	12 (0.7)
1 (0.1)	21 (1.1)	0
9 (0.5)	13 (0.7)	5 (0.3)
9 (0.5)	10 (0.5)	5 (0.3)
0	1 (0.1)	0
0	2 (0.1)	0
130 (6.5)	152 (8.2)	102 (5.6)
109 (5.5)	125 (6.7)	76 (4.1)
20 (1.0)	25 (1.3)	22 (1.2)
1 (0.1)	2 (0.1)	4 (0.2)
165 (8.3)	537 (28.9)	99 (5.4)
111 (5.6)	229 (12.3)	65 (3.5)
51 (2.6)	288 (15.5)	33 (1.8)
3 (0.2)	20 (1.1)	1 (0.1)
124 (6.2)	353 (19.0)	72 (3.9)
78 (3.9)	183 (9.8)	44 (2.4)
45 (2.3)	161 (8.7)	27 (1.5)
1 (0.1)	9 (0.5)	1 (0.1)
224 (11.3)	688 (37.0)	170 (9.3)

lected in the electronic diary (e-diary) from Day 1 to Day 7 after

s 56 years of age and older was fatigue.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. N for each
herefore was included in the column header.

at the injection site) reported after Dose 2 of
orted. Fever, headache, chills, and joint pain increased in
g, diarrhea, and muscle pain were similar after each
events after Dose 1 of COMIRNATY but after Dose 2,
5.0%) participants with severe fatigue, 2 (3.3%)
with severe chills, and 1 (1.7%) participant with severe
d after either dose.

8931, placebo = 8895), serious adverse events were
among COMIRNATY recipients and 4.6 per
d at least 1 dose of COMIRNATY or placebo,
nts had at least 4 months of follow-up after Dose 2.
serious adverse events from Dose 1 up to the
eported at an incidence rate of 6.6 per 100 person-years
-years among placebo recipients.

s for specific categories of serious adverse events
otic events) that would suggest a causal relationship to

vents among COMIRNATY recipients (inclusive of
s primarily attributed to local and systemic adverse
se of vaccine that are consistent with adverse reactions
and presented in Table 3 and Table 4.

ts of lymphadenopathy were imbalanced with notably
placebo group (8).

od to date, Bell's palsy (facial paralysis) was reported
cipants in the placebo group. Onset of facial paralysis
se 2) and Days 3, 9, and 48 after Dose 2. In the placebo
102. Currently available information is insufficient to
were no other notable patterns or numerical imbalances
serious adverse events (including other neurologic or
suggest a causal relationship to COMIRNATY.

ring postmarketing use of COMIRNATY, including
ctions are reported voluntarily from a population of
ate their frequency or establish a causal relationship to

uding anaphylaxis, and other hypersensitivity reactions

in extremity (arm)

le rats by the intramuscular route on 4 occasions: 21
20. No vaccine-related adverse effects on female
re reported in the study.

man milk. Data are not available to assess the effects of
tion/excretion. The developmental and health benefits
ther's clinical need for COMIRNATY and any
MIRNATY or from the underlying maternal condition.
on is susceptibility to disease prevented by the vaccine.

s 16 through 17 years of age is based on safety and
lverse Reactions (6) and Clinical Studies (14.1)].

duals younger than 16 years of age have not been

y 2 as of March 13, 2021 (N = 22,026),
2% (n = 925) were 75 years of age and older *[see*
or effectiveness were observed between these

e suspension for injection for intramuscular use.
ltiple dose vials; each vial must be diluted with 1.8 mL

rmulated in lipid particles, which enable delivery of the
CoV-2 S antigen. The vaccine elicits an immune
D-19.

rtility

o cause carcinogenicity, genotoxicity, or impairment of
with COMIRNATY. There were no vaccine-related
ns (8.1)].

cebo-controlled, observer-blind, dose-finding, vaccine
2 years of age and older. Randomization was stratified
of age, or 56 years of age and older, with a minimum of
xcluded participants who were immunocompromised
diagnosis of COVID-19. Participants with preexisting
nt change in therapy or hospitalization for worsening
uded as were participants with known stable infection
HBV).

21, approximately 44,000 participants 16 years of age
of COMIRNATY or placebo. Participants are planned
afety and efficacy against COVID-19.

ndpoint included, 36,621 participants 12 years of age
9 in the placebo group) who did not have evidence of

age and 56 years of age and older began enrollment
rollment from September 16, 2020, and 12 through
0.

.

rence From 7 Days After Dose 2, by Age Subgroup – n and Participants With or Without Evidence of valuable Efficacy (7 Days) Population

Dose 2 in participants without evidence of prior -2 infection*	
Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])	**Vaccine Efficacy % (95% CI)**
162 2.222 (17,511)	95.0 (90.3, 97.6)[f]
143 1.710 (13,618)	95.1 (89.6, 98.1)[g]
19 0.511 (3880)	94.7 (66.7, 99.9)[g]
14 0.406 (3095)	92.9 (53.1, 99.8)[g]
5 0.106 (785)	100.0 (-13.1, 100.0)[g]

Polymerase Chain Reaction (RT-PCR) and at least 1 symptom
eased cough; new or increased shortness of breath; chills; new or
ea; vomiting).
n (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-
d had negative NAAT (nasal swab) at any unscheduled visit prior

oint across all participants within each group at risk for the endpoint.
se 2 to the end of the surveillance period.

s of age.
using a beta-binomial model with a beta (0.700102, 1) prior for
in the active vaccine group over that in the placebo group.
ed based on the Clopper and Pearson method adjusted to the

included participants 16 years of age and older who
the development of COVID-19 during blinded
epresenting up to 6 months of follow-up after Dose 2.
up and 57.3% of participants in the placebo group had
placebo-controlled follow-up period.

Table 6.

2 in participants with or without* evidence of prior -2 infection

	Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI[e])
n2[d])		
	854 6.110 (20,595)	90.9 (88.5, 92.8)
	726 4.879 (16,269)	90.2 (87.5, 92.4)
	128 1.232 (4326)	94.7 (88.7, 97.9)

Polymerase Chain Reaction (RT-PCR) and at least 1 symptom
eased cough; new or increased shortness of breath; chills; new or
hea; vomiting).
n (i.e., N-binding antibody [serum] negative at Visit 1 and
d 2), and had negative NAAT (nasal swab) at any unscheduled visit

oint across all participants within each group at risk for the endpoint.
se 2 to the end of the surveillance period.

ed based on the Clopper and Pearson method adjusted to the

wed similar efficacy point estimates across genders,
al comorbidities and obesity associated with high risk of

nts supported benefit of COMIRNATY in preventing
VID-19 is presented only for participants with or without

	Cases n1[a] Surveillance Time[b] (n2[c])	Vaccine Efficacy % (95% CI[d])
n2[c])		
	31 6.225 (20,593)	100 (87.6, 100.0)

Polymerase Chain Reaction (RT-PCR) and at least 1 symptom
eased cough; new or increased shortness of breath; chills; new or
hea; vomiting).
n (i.e., N-binding antibody [serum] negative at Visit 1 and
d 2), and had negative NAAT (nasal swab) at any unscheduled visit

med COVID-19 and presence of at least 1 of the following:
respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per
l, or ratio of arterial oxygen partial pressure to fractional inspired

noninvasive ventilation, mechanical ventilation or extracorporeal

astolic blood pressure <60 mm Hg, or requiring vasopressors);

OVID-19 and presence of at least 1 of the following:

oint across all participants within each group at risk for the endpoint.
se 2 to the end of the surveillance period.

l based on the Clopper and Pearson method adjusted to the

Multiple Dose Vials are supplied in a carton containing
tiple dose vials (NDC 0069-1000-02). A 0.9% Sodium

0

s. Vials must be kept frozen and protected from light, in
5°C to -15°C (-13°F to 5°F) for up to 2 weeks may be
f -80ºC to -60ºC (-112ºF to -76ºF). Total cumulative
) should be tracked and should not exceed 2 weeks.

hermal container in which COMIRNATY arrives may
to the top of the container with dry ice. Refer to the
ner for instructions regarding the use of the thermal
maintains a temperature range of -90ºC to -60ºC (-130ºF
141°F to -76°F) is not considered an excursion from

ng vials cannot be transported at -90°C to -60°C
15°C (-13°F to 5°F). Any hours used for transport at
limit for storage at -25°C to -15°C (-13°F to 5°F).
) may be returned 1 time to the recommended storage

ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of
tively, to thaw in the refrigerator, whereas a fewer

ature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials

1

g the two dose vaccination series.

their healthcare provider or to the Vaccine Adverse
aers.hhs.gov.

most recent prescribing information, please visit

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

---------- INDICATIONS AND USAGE ----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site ~~(88.6%)~~, fatigue ~~(70.1%)~~, headache ~~(64.9%)~~, muscle pain ~~(45.5%)~~, chills ~~(41.5%)~~, joint pain ~~(27.5%)~~, fever ~~(17.8%)~~, and injection site swelling ~~(10.6%)~~. (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site ~~(78.2%)~~, fatigue ~~(56.9%)~~, headache ~~(45.9%)~~, muscle pain ~~(32.5%)~~, chills ~~(24.8%)~~, joint pain ~~(21.5%)~~, injection site swelling ~~(11.8%)~~, fever ~~(11.5%)~~, and injection site redness ~~(10.4%)~~. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

2.1 Preparation for Administration

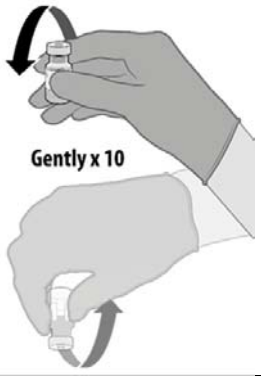
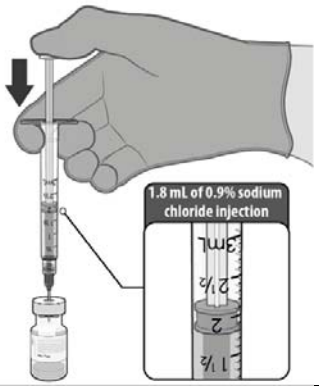
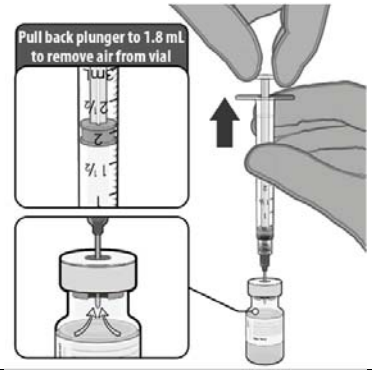
Prior to Dilution

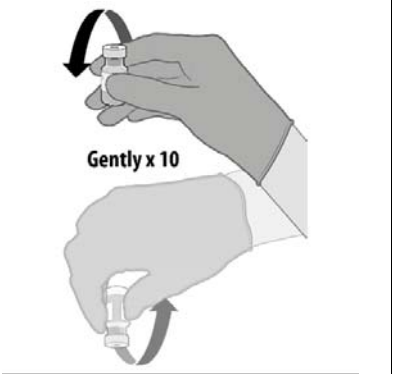
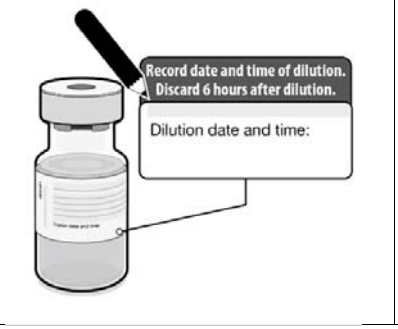
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

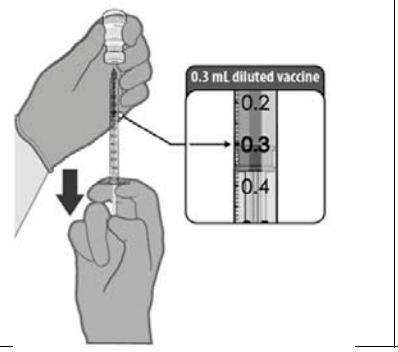
Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not use diluent vials to dilute multiple vials of COMIRNATY.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted

	within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.
	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.

	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

A third dose of the COMIRNATY (0.3 mL) administered at least 28 days following the first 2 doses of this vaccine is authorized for administration to individuals at least 16 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk has been highest in adolescent and young adult males under 40 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of

symptoms. Information is not yet available about potential long-term sequelae. The CDC has published considerations for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	**Placebo Dose 1 N[a]=2908 n[b] (%)**	**COMIRNATY Dose 2 N[a]=2682 n[b] (%)**	**Placebo Dose 2 N[a]=2684 n[b] (%)**
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N^a=2008 n^b (%)	Placebo Dose 1 N^a=1989 n^b (%)	COMIRNATY Dose 2 N^a=1860 n^b (%)	Placebo Dose 2 N^a=1833 n^b (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

In clinical studies, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, in 99 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported in recipients who were followed for 1 month following post Dose 3.

Unsolicited Adverse Events

Overall 51.1% of participants in the COMIRNATY group and 51.4% of participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 8.1% and 5.9% with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

~~Upon issuance of the EUA for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY.~~ Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. At the time of the updated efficacy analysis 54.5% of participants originally randomized to COMIRNATY had ≥6 months of follow-up from Dose 2 and 47.5% of original placebo participants had follow-up time between ≥1 month to <2 months after Dose 2 of COMIRNATY. ~~Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began in a phased manner for participants in the study.~~ Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Adverse events occurred in 28.8% of vaccine recipients who had a follow-up period of at least 6 months after Dose 2; 1.6% of the recipients had serious adverse events.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) ~~at an incidence rate of 2.1 per 100 person-years among~~ COMIRNATY recipients and 117 (0.9%)~~2.4 per 100 person-years among~~ placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported by 165 (1.8%)~~at an incidence rate of 4.9 per 100 person-years among~~ COMIRNATY recipients and 151 (1.7%)~~4.6 per 100 person-years among~~ placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%)~~at an incidence rate of 6.6 per 100 person-years among~~ COMIRNATY recipients and 2 (2%)~~6.9 per 100 person-years among~~ placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4396 (33.8%)~~at an incidence rate of 88.4 per 100 person- years among~~ participants who received COMIRNATY and 2136 (16.4%)~~43.5 per 100 person-years among~~ participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include nonserious adverse events were reported by 2551 (28.6%)~~at an incidence rate of 75.7 per 100 person-years among~~ participants who received COMIRNATY and 1432 (16.1%)~~43.3 per 100 person-years among~~ participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the

participant unblinding date in ongoing follow-up were reported by 29 (29%)~~at an incidence rate of 95.8 per 100 person-years among~~ participants who received COMIRNATY and 15 (15%)~~52.0 per 100 person-years among~~ participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Comirnaty during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

8.6 Immunocompromised Use

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, safety and effectiveness of a third dose of COMIRNATY have been evaluated in persons that received solid organ transplants. The administration of a third dose of vaccine appears to be only moderately effective in increasing potentially protective antibody titers. Patients should still be counselled to maintain physical precautions to help prevent COVID-19. In addition, close contacts of immunocompromised persons should be vaccinated as appropriate for their health status.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials ; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

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Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.35% were male and 48.6% or 49.75% were female, 7579.1% or 7579.21% were 16 through 64 years of age, 20.91% or 20.83% were 65 years of age and older, ~~16.1% or 16.3% were 65 through 74 years of age, 4.0% or 4.0% 75 years of age and older, 82~~81.9% or 82.1% were White, 98.5% or 98.6% were Black or African American, ~~0.9~~1.0% or 0.9% were American Indian or Alaska Native, 4.46% or 4.35% were Asian, 0.3% or 0.12% Native Hawaiian or other Pacific Islander, 254.96% or 254.46% were Hispanic/Latino, 734.69% or 74.18% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 446.60% or 454.74% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 498.83 or 498.72 years and median age was 510.0 or 510.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

~~The vaccine efficacy information is presented in Table 5.~~

~~Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population~~

~~First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*~~			
~~Subgroup~~	**~~COMIRNATY N[a]=18,198 Cases n1[b] Surveillance Time[c] (n2[d])~~**	**~~Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])~~**	**~~Vaccine Efficacy % (95% CI)~~**
~~All participants[e]~~	~~8 2.214 (17,411)~~	~~162 2.222 (17,511)~~	~~95.0 (90.3, 97.6)[f]~~
~~16 to 64 years~~	~~7 1.706 (13,549)~~	~~143 1.710 (13,618)~~	~~95.1 (89.6, 98.1)[g]~~
~~65 years and older~~	~~1 0.508 (3848)~~	~~19 0.511 (3880)~~	~~94.7 (66.7, 99.9)[g]~~
~~65 to 74 years~~	~~1 0.406 (3074)~~	~~14 0.406 (3095)~~	~~92.9 (53.1, 99.8)[g]~~
~~75 years and older~~	~~0 0.102 (774)~~	~~5 0.106 (785)~~	~~100.0 (-13.1, 100.0)[g]~~
~~First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection~~			
~~Subgroup~~	**~~COMIRNATY N[a]=19,965~~**	**~~Placebo N[a]=20,172~~**	**~~Vaccine Efficacy % (95% CI)~~**

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	~~Cases n1[b] Surveillance Time[c] (n2[d])~~	~~Cases n1[b] Surveillance Time[c] (n2[d])~~	
~~All participants[e]~~	~~9 2.332 (18,559)~~	~~169 2.345 (18,708)~~	~~94.6 (89.9, 97.3)[f]~~
~~16 to 64 years~~	~~8 1.802 (14,501)~~	~~150 1.814 (14,627)~~	~~94.6 (89.1, 97.7)[g]~~
~~65 years and older~~	~~1 0.530 (4044)~~	~~19 0.532 (4067)~~	~~94.7 (66.8, 99.9)[g]~~
~~65 to 74 years~~	~~1 0.424 (3239)~~	~~14 0.423 (3255)~~	~~92.9 (53.2, 99.8)[g]~~
~~75 years and older~~	~~0 0.106 (805)~~	~~5 0.109 (812)~~	~~100.0 (-12.1, 100.0)[g]~~

~~Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).~~

~~* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.~~

~~a. N = Number of participants in the specified group.~~

~~b. n1 = Number of participants meeting the endpoint definition.~~

~~c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.~~

~~d. n2 = Number of participants at risk for the endpoint.~~

~~e. No confirmed cases were identified in participants 12 to 15 years of age.~~

~~f. Two-sided credible interval for vaccine efficacy was calculated using a beta-binomial model with a beta (0.700102, 1) prior for θ=r(1-VE)/(1+r(1-VE)), where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.~~

~~g. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.~~

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0%. The case split was 8 COVID-19 cases in the BNT162b2 group compared to 162 COVID-19 cases in the placebo group. The 95% credible interval for the vaccine efficacy was 90.3% to 97.6%, indicating that the true vaccine efficacy is at least 90.3% with a 97.5% probability, which met the pre-specified success criterion.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

The updated vaccine efficacy information is presented in Table 5~~6~~.

Table 56: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, geographies, and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior

SARS-CoV-2 infection (Table ~~7~~6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table ~~6~~7: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Immunogenicity in Solid Organ Transplant Recipients

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, a single arm study has been conducted in

101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously. A third dose of COMIRNATY was administered to 99 of these individuals approximately 2 months after they had received a second dose. Among the 59 patients who had been seronegative before the third dose, 26 (44%) were seropositive at 4 weeks after the third dose. All 40 patients who had been seropositive before the third dose were still seropositive 4 weeks later. The prevalence of anti-SARS-CoV-2 antibodies was 68% (67 of 99 patients) 4 weeks after the third dose.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -8090ºC to -60ºC (-112ºF 130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -8090ºC to -60ºC (-112ºF 130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -8090ºC to -60ºC (-112ºF 130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.
~~calling …..~~

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit www.comirnatyglobal.com.

Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.~~3~~4

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

---------- INDICATIONS AND USAGE ----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

----------ADVERSE REACTIONS----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site ~~(88.6%)~~, fatigue ~~(70.1%)~~, headache ~~(64.9%)~~, muscle pain ~~(45.5%)~~, chills ~~(41.5%)~~, joint pain ~~(27.5%)~~, fever ~~(17.8%)~~, and injection site swelling ~~(10.6%)~~. (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site ~~(78.2%)~~, fatigue ~~(56.9%)~~, headache ~~(45.9%)~~, muscle pain ~~(32.5%)~~, chills ~~(24.8%)~~, joint pain ~~(21.5%)~~, injection site swelling ~~(11.8%)~~, fever ~~(11.5%)~~, and injection site redness ~~(10.4%)~~. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

Comment [A1]: Pfizer BioNTech Response: The Sponsor proposes to delete this information as we believe it is redundant with the content of the FPI and the purpose of Highlights is to give a succinct overview of the label.

Comment [A2]: PfizerBioNTech response: The Sponsor proposes addition of this heading to be consistent with the updates recently made to the EUA labels that FDA granted a LOA for on 12-Aug-2021.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

Comment [A3]: Pfizer BioNTech comment: The Sponsor accepts insertion of this statement by FDA.

2.1 Preparation for Administration

Prior to Dilution

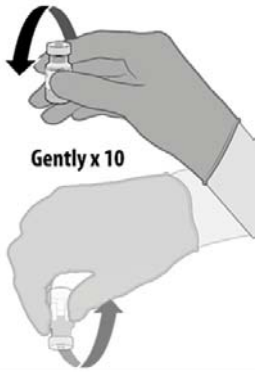
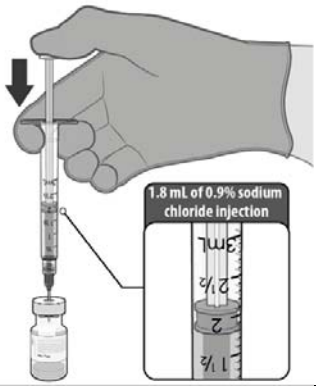
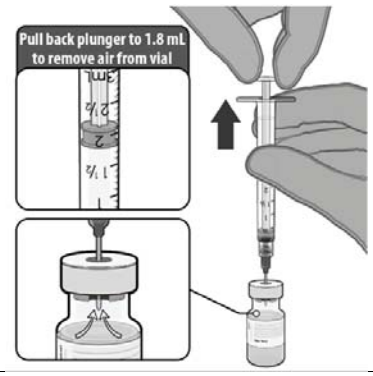
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not use diluent vials to dilute multiple vials of COMIRNATY.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

Comment [A4]: Pfizer BioNTech comment: The Sponsor accepts FDA's proposed revisions to this section.

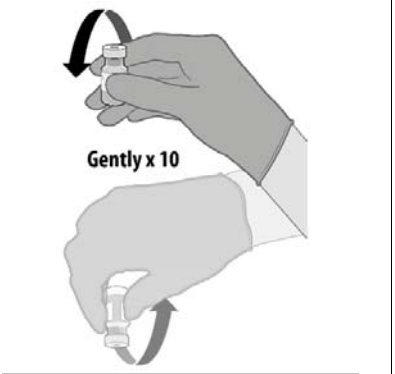
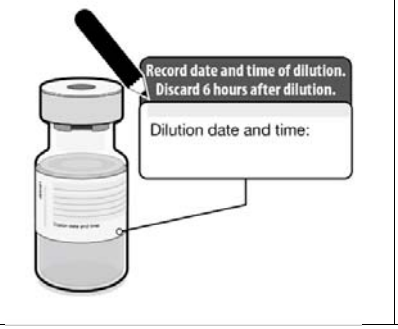
THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted

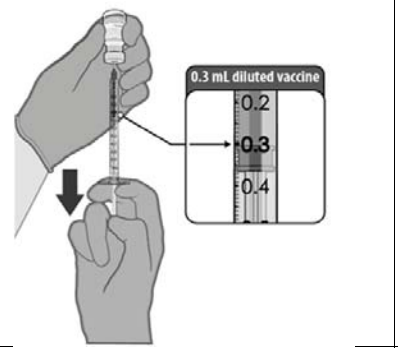
	within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • Do not shake. • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.
	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.

Comment [A5]: Pfizer BioNTech comment: The Sponsor accepts addition of "vaccine."

Comment [A6]: Pfizer BioNTech comment: The Sponsor accepts FDA's changes.

Comment [A7]: Pfizer BioNTech comment: The Sponsor accepts the addition of "vaccine."

	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

Comment [A8]: Pfizer BioNTech comment: The Sponsor accepts FDA's revision to this section.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

Comment [A9]: Pfizer-BioNTech comment: The sponsor accepts moving this information from Section 2.2 to Section 2.1.

2.2 Administration Information

Comment [A10]: PfizerBioNTech response: The Sponsor accepts FDA's revisions to this section.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

A third dose of the COMIRNATY (0.3 mL) administered at least 28 days following the first 2 doses of this vaccine is authorized for administration to individuals at least 16 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

Comment [A11]: Pfizer-BioNTech response: The Sponsor proposes addition of this paragraph to section 2.3 to be consistent with the updates recently made to the EUA labels that FDA granted a LOA for on 12-Aug-2021 (expect for the age which has been changed to 16 to reflect the age in BLA).

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

Comment [A12]: FDA Comment: Pfizer,
Please note, we intend to communicate additional comments regarding Section 5 to you next week.

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk has been highest in adolescent and young adult males under 40 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of

symptoms. Information is not yet available about potential long-term sequelae. The CDC has published considerations for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

Comment [A13]: Pfizer BioNTech comment: The Sponsor accepts the deletion of the cut-off date.

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

Comment [A14]:
FDA comment:
Pfizer,
Please delete. Our intent is to convey the most commonly reported adverse reactions in this section.

Pfizer-BioNTech response:
The Sponsor understands that the most frequently occurring adverse reactions should be presented first, however, we propose rather than deleting this information on less frequently occurring ADRs (<10%) moving it to the end of the section because otherwise certain events that are causally related will completely drop out of the label (i.e., malaise, asthenia, lethargy, hyperhidrosis, nausea, decreased appetite, night sweats) as it's important information for prescribers.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	**Placebo Dose 1 N[a]=2908 n[b] (%)**	**COMIRNATY Dose 2 N[a]=2682 n[b] (%)**	**Placebo Dose 2 N[a]=2684 n[b] (%)**
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N^a=2008 n^b (%)	Placebo Dose 1 N^a=1989 n^b (%)	COMIRNATY Dose 2 N^a=1860 n^b (%)	Placebo Dose 2 N^a=1833 n^b (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

In clinical studies, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, in 99 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported in recipients who were followed for 1 month following post Dose 3.

Comment [A15]: FDA comment:
Pfizer,
This description is redundant from the overall safety description provided above, so it has been deleted.
To clarify our request: please add a subsection to describe the frequencies of unsolicited non-serious and serious adverse events that occurred from Dose 1 through the March 2021 data cutoff, in the original vaccine recipients that have follow-up for at least 6 months after Dose 2 (n=12,006).

Pfizer-BioNTech response:
The Sponsor accepts the deletion of text regarding HIV.

Comment [A16]: Pfizer BioNTech comment: The Sponsor proposes to move this text (that was deleted by FDA) from above section 6.1 to the end of this subsection.

Comment [A17]: Pfizer-BioNTech response:
The Sponsor proposes addition of this paragraph to be consistent with the updates recently made to the EUA labels that FDA granted a LOA for on 12-Aug-2021.

Unsolicited Adverse Events

Overall 51.1% of participants in the COMIRNATY group and 51.4% of participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 8.1% and 5.9% with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

~~Upon issuance of the EUA for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY.~~ Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. At the time of the updated efficacy analysis 54.5% of participants originally randomized to COMIRNATY had ≥6 months of follow-up from Dose 2 and 47.5% of original placebo participants had follow-up time between ≥1 month to <2 months after Dose 2 of COMIRNATY. ~~Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began in a phased manner for participants in the study.~~ Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Adverse events occurred in 28.8% of vaccine recipients who had a follow-up period of at least 6 months after Dose 2; 1.6% of the recipients had serious adverse events.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) ~~at an incidence rate of 2.1 per 100 person-years among~~ COMIRNATY recipients and 117 (0.9%)~~2.4 per 100 person-years among~~ placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported by 165 (1.8%)~~at an incidence rate of 4.9 per 100 person-years among~~ COMIRNATY recipients and 151 (1.7%)~~4.6 per 100 person-years among~~ placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%)~~at an incidence rate of 6.6 per 100 person-years among~~ COMIRNATY recipients and 2 (2%)~~6.9 per 100 person-years among~~ placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4396 (33.8%)~~at an incidence rate of 88.4 per 100 person-years among~~ participants who received COMIRNATY and 2136 (16.4%)~~43.5 per 100 person-years among~~ participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include nonserious adverse events were reported by 2551 (28.6%)~~at an incidence rate of 75.7 per 100 person-years among~~ participants who received COMIRNATY and 1432 (16.1%)~~43.3 per 100 person-years among~~ participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the

Comment [A18]: Pfizer BioNTech comment: The Sponsor accepts deletion of the text originally included on unblinding and proposes this updated language to clearly represent the data regarding follow-up time for the blinded period and to address FDA's previous request for this information.

Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Table 9.*

Comment [A19]: FDA comment:
Pfizer,
We do not think that the presentation of these data using incidence rates is helpful for the healthcare provider.

Additionally, we do not agree with the method by which the incidence rates are calculated. It appears that the incidence rate for each event type is based on the number of subjects who reported at least one event divided by the total person-years contributed by all subjects from Dose 1 to unblinding but does not account for the number of events a subject may report, or the timing of these events in deriving the total length of period "at risk." This may be misleading as it under-reports the true incidence rate. In addition, we note that the total lengths of follow-up between arms are within 2% in ... [1]

Comment [A20]: FDA comment:
Pfizer,
This description is redundant from the overall safety description provided above, so it has been deleted.
To clarify our request: please add a subsection to describe the frequencies of unsolicited non-serious and serious adverse events that occurred from Dose 1 through the March 2021 data cutoff, in the original vaccine recipien ... [2]

Comment [A21]: Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Table 9.*

Comment [A22]: Pfizer-BioNTech response:
The Sponsor accepts FDA's request to update the incidence rates to frequencies and therefore has manually calculated the frequencies (n=numbers of participants who had the event / N=total number of participants in the group).

Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Findi* ... [3]

Comment [A23]: Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Tables 14.179*

participant unblinding date in ongoing follow-up were reported by 29 (29%)~~at an incidence rate of 95.8 per 100 person-years among~~ participants who received COMIRNATY and 15 (15%)~~52.0 per 100 person-years among~~ participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Comment [A24]: Pfizer-BioNTech response:
The Sponsor accepts FDA's request to update the incidence rates to frequencies and therefore has manually calculated the frequencies (n=number of participants who had the event / N=total number of participants in the group).

Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Tables 14.120 and 14.121*

Comment [A25]: Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Table 14.179.*

Comment [A26]: Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Table 9.*

Comment [A27]: FDA comment:
Pfizer,
We do not concur because it appears that OTIS is recruiting from a wide variety of sites. We request that you include contact information for the registry in the PI as follows:

"There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting www…"

Pfizer-BioNTech response:
The Sponsor accepts and has provided an update to this section consistent with FDA's request.

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Comirnaty during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

8.6 Immunocompromised Use

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, safety and effectiveness of a third dose of COMIRNATY have been evaluated in persons that received solid organ transplants. The administration of a third dose of vaccine appears to be only moderately effective in increasing potentially protective antibody titers. Patients should still be counselled to maintain physical precautions to help prevent COVID-19. In addition, close contacts of immunocompromised persons should be vaccinated as appropriate for their health status.

Comment [A28]: Pfizer-BioNTech response:
The Sponsor proposes addition of this paragraph to section 8.6 to be consistent with the updates recently made to the EUA labels that FDA granted a LOA for on 12-Aug-2021.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials ; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Comment [A29]: Pfizer-BioNTech comment: The Sponsor accepts FDA's proposed addition.

Comment [A30]: Pfizer-BioNTech comment: The Sponsor accepts FDA's proposed revision.

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Comment [A31]: Pfizer-BioNTech comment: The Sponsor accepts FDA's proposed revision

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.35% were male and 48.6% or 49.75% were female, 7579.1% or 7579.21% were 16 through 64 years of age, 20.91% or 20.83% were 65 years of age and older, ~~16.1% or 16.3% were 65 through 74 years of age, 4.0% or 4.0% 75 years of age and older, 82~~81.9% or 82.1% were White, 98.5% or 98.6% were Black or African American, ~~0.9~~1.0% or 0.9% were American Indian or Alaska Native, 4.46% or 4.35% were Asian, 0.3% or 0.12% Native Hawaiian or other Pacific Islander, 254.96% or 254.46% were Hispanic/Latino, 734.69% or 74.18% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 446.60% or 454.74% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 498.83 or 498.72 years and median age was 510.0 or 510.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

~~The vaccine efficacy information is presented in Table 5.~~

~~Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population~~

~~First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*~~			
~~Subgroup~~	**~~COMIRNATY N[a]=18,198 Cases n1[b] Surveillance Time[c] (n2[d])~~**	**~~Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])~~**	**~~Vaccine Efficacy % (95% CI)~~**
~~All participants[e]~~	~~8 2.214 (17,411)~~	~~162 2.222 (17,511)~~	~~95.0 (90.3, 97.6)[f]~~
~~16 to 64 years~~	~~7 1.706 (13,549)~~	~~143 1.710 (13,618)~~	~~95.1 (89.6, 98.1)[g]~~
~~65 years and older~~	~~1 0.508 (3848)~~	~~19 0.511 (3880)~~	~~94.7 (66.7, 99.9)[g]~~
~~65 to 74 years~~	~~1 0.406 (3074)~~	~~14 0.406 (3095)~~	~~92.9 (53.1, 99.8)[g]~~
~~75 years and older~~	~~0 0.102 (774)~~	~~5 0.106 (785)~~	~~100.0 (-13.1, 100.0)[g]~~
~~First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection~~			
~~Subgroup~~	**~~COMIRNATY N[a]=19,965~~**	**~~Placebo N[a]=20,172~~**	**~~Vaccine Efficacy % (95% CI)~~**

Comment [A32]: FDA comment:
Pfizer,
Please revise the demographics to describe the efficacy population used for the updated VE analyses in participants 16 years of age and older (please exclude participants 12-15 years of age). Results should be the same as those provided in Shell Table F with STN 126472/0.32.

PfizerBioNTech response:
The sponsor accepts FDA's proposal to revise the demographics as requested and has proposed minor modifications to align with Table F.

Source: *Table F Demographics and Other Baseline Characteristics, Participants 16 Years of Age and Older, With or Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy Population (Data Cutoff March 13, 2021)*

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Comment [A33]: Pfizer-BioNTech comment: The Sponsor accepts FDA's proposed addition of this text.

	~~Cases n1[b] Surveillance Time[c] (n2[d])~~	~~Cases n1[b] Surveillance Time[c] (n2[d])~~	
~~All participants[e]~~	~~9 2.332 (18,559)~~	~~169 2.345 (18,708)~~	~~94.6 (89.9, 97.3)[f]~~
~~16 to 64 years~~	~~8 1.802 (14,501)~~	~~150 1.814 (14,627)~~	~~94.6 (89.1, 97.7)[g]~~
~~65 years and older~~	~~1 0.530 (4044)~~	~~19 0.532 (4067)~~	~~94.7 (66.8, 99.9)[g]~~
~~65 to 74 years~~	~~1 0.424 (3239)~~	~~14 0.423 (3255)~~	~~92.9 (53.2, 99.8)[g]~~
~~75 years and older~~	~~0 0.106 (805)~~	~~5 0.109 (812)~~	~~100.0 (-12.1, 100.0)[g]~~

~~Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).~~

~~* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.~~

~~a. N = Number of participants in the specified group.~~

~~b. n1 = Number of participants meeting the endpoint definition.~~

~~c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.~~

~~d. n2 = Number of participants at risk for the endpoint.~~

~~e. No confirmed cases were identified in participants 12 to 15 years of age.~~

~~f. Two-sided credible interval for vaccine efficacy was calculated using a beta-binomial model with a beta (0.700102, 1) prior for θ=r(1-VE)/(1+r(1-VE)), where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.~~

~~g. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.~~

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0%. The case split was 8 COVID-19 cases in the BNT162b2 group compared to 162 COVID-19 cases in the placebo group. The 95% credible interval for the vaccine efficacy was 90.3% to 97.6%, indicating that the true vaccine efficacy is at least 90.3% with a 97.5% probability, which met the pre-specified success criterion.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

The updated vaccine efficacy information is presented in Table 5~~6~~.

Comment [A34]:
FDA comment:
Pfizer:
We continue to request deletion of this Table because the information is redundant with the updated VE analysis that follows with additional confirmed cases. Please insert the text requested below:

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0%. The case split was 8 COVID-19 cases in the BNT162b2 group compared to 162 COVID-19 cases in the placebo group. The 95% credible interval for the vaccine efficacy was 90.3% to 97.6%, indicating that the true VE is at least 90.3% with a 97.5% probability, which met the pre-specified success criterion.

Pfizer-BioNTech response:
The Sponsor accepts the replacement of this of the table with the summary text provided by FDA.

Comment [A35]: FDA comment:
Pfizer,
Revised the language to mirror description of the Safety population.

We note that these numbers were derived from follow-up times, based on the safety population. Please update the information, based on the follow up time after Dose 2 for the efficacy population.

PfizerBioNTech Response:
The Sponsor accepts and has updated the information per FDA's request.

See: Supplemental Table *Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population*

Table 56: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, geographies, and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior

Comment [A36]: FDA comment:
Pfizer,
This general statement is misleading because some of the subgroup analyses were limited by the size of the subgroup and low number of confirmed cases, which limits the interpretation of those analyses. We disagree with this addition and request deletion.

PfizerBioNTech response:
Despite the size of the subgroup being limited, the Sponsor proposes retaining this statement as we believe this provides very meaningful information to prescribers about subgroup populations they may be treating.

Comment [A37]: PfizerBioNTech comment:
The Sponsor accepts the deletion of the word "Updated."

SARS-CoV-2 infection (Table ~~7~~6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table ~~6~~7: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Immunogenicity in Solid Organ Transplant Recipients

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, a single arm study has been conducted in

101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously. A third dose of COMIRNATY was administered to 99 of these individuals approximately 2 months after they had received a second dose. Among the 59 patients who had been seronegative before the third dose, 26 (44%) were seropositive at 4 weeks after the third dose. All 40 patients who had been seropositive before the third dose were still seropositive 4 weeks later. The prevalence of anti-SARS-CoV-2 antibodies was 68% (67 of 99 patients) 4 weeks after the third dose.

Comment [A38]: Pfizer-BioNTech response:
The Sponsor proposes addition of this paragraph to section 14 to be consistent with the updates recently made to the EUA labels that FDA granted a LOA for on 12-Aug-2021.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

Comment [A39]: FDA comment:
Pfizer,
Please update this section to include information on the diluent manufactured at the Pfizer Healthcare India site.

Pfizer-BioNTech response:
10 mL single-use vial diluent (NDC 0409488810) is registered under NDA 018803 and manufactured in accordance with NDA 018803, including manufacture at both sites in Rocky Mount, NC, USA (site establishment license name "Hospira") and in Andhra Pradesh, India (site establishment license name "Pfizer Healthcare India Pvt. Ltd"). The license holder of NDA 018803 is Hospira, Inc., Lake Forest, Illinois. As such, the proposed USPI is correct as written.

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between ~~-80~~90ºC to -60ºC (~~-112ºF~~ 130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of ~~-80~~90ºC to -60ºC (~~-112ºF~~ 130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

Comment [A40]: Pfizer-BioNTech response:
The sponsor has updated the temperature range for ultra cold storage to reflect the long term storage condition filed in the BLA.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of ~~-80~~90ºC to -60ºC (~~-112ºF~~ 130ºF to -76ºF).

Comment [A41]: Pfizer-BioNTech response:
The sponsor has updated the temperature range for ultra cold storage to reflect the long term storage condition filed in the BLA.

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.
~~calling …..~~

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

Comment [A42]: FDA comment:
Pfizer,
Please see comment in Section 8.1.

PfizerBioNTech response:
The Sponsor accepts and has updated this section accordingly.

This product's labeling may have been updated. For the most recent prescribing information, please visit www.comirnatyglobal.com.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.~~3~~4

US Govt. License No. x

Comment [A43]: FDA comment:
Pfizer,
Please revise this link to direct to DailyMed.

Pfizer BioNTech response:
Pfizer-BioNTech would like to retain the reference to Comirnityglobal.com in our USPI when referring to a website that contains the most updated version of our labeling. As updates to labeling are typically available more quickly via Comirnityglobal.com than the posting to Daily Med or http://labels.fda.gov/, referencing the Comirnityglobal.com website will ensure that any updates to our labeling will be available to prescribers in the most expedient timeframe.

Comment [A44]: FDA comment:
Pfizer,
We acknowledge that two of your labels include CPT codes; however, please delete the CPT code in this label.

Pfizer-BioNTech response:
The Sponsor accepts the deletion of the CPT code.

Page 13: [1] Comment [A19] **Author**

FDA comment:
Pfizer,
We do not think that the presentation of these data using incidence rates is helpful for the healthcare provider.

Additionally, we do not agree with the method by which the incidence rates are calculated. It appears that the incidence rate for each event type is based on the number of subjects who reported at least one event divided by the total person-years contributed by all subjects from Dose 1 to unblinding but does not account for the number of events a subject may report, or the timing of these events in deriving the total length of period "at risk." This may be misleading as it under-reports the true incidence rate. In addition, we note that the total lengths of follow-up between arms are within 2% in both age groups (18 through 55, 56 and above), thus differences in follow-up appear to be minor. Therefore, we continue to request the use of proportions to present safety data.

Pfizer BioNTech response:
The Sponsor accepts FDA's request to add this subsection and has proposed language accordingly. We believe it's important to include details on both the ≥4 months to <6 months after Dose 2 and ≥ 6 months after Dose 2 for transparency to prescribers. In addition, the Sponsor accepts the deletion of the incidence rate per 100 person years per FDA's request.

Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Table 9 and Table 14.29*

Page 13: [2] Comment [A20] **Author**

FDA comment:
Pfizer,
This description is redundant from the overall safety description provided above, so it has been deleted.
To clarify our request: please add a subsection to describe the frequencies of unsolicited non-serious and serious adverse events that occurred from Dose 1 through the March 2021 data cutoff, in the original vaccine recipients that have follow-up for at least 6 months after Dose 2 (n=12,006).

Pfizer-BioNTech response:
The Sponsor agrees and has added information regarding the frequency of serious adverse events and all adverse events (including non-serious AEs), which is consistent with the presentation of the data in the section below.

Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Tables 33.

Page 13: [3] Comment [A22] **Author**

Pfizer-BioNTech response:

The Sponsor accepts FDA's request to update the incidence rates to frequencies and therefore has manually calculated the frequencies (n=numbers of participants who had the event / N=total number of participants in the group).

Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Tables 14.167 and 14.168*

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, fever, and injection site swelling. (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, injection site swelling, fever, and injection site redness. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

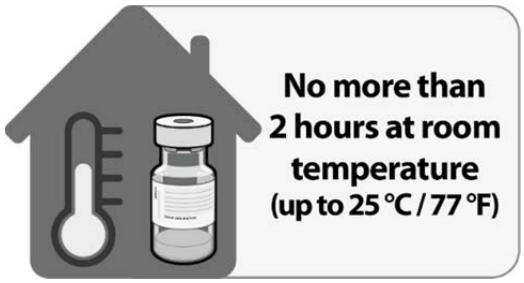
2.1 Preparation for Administration

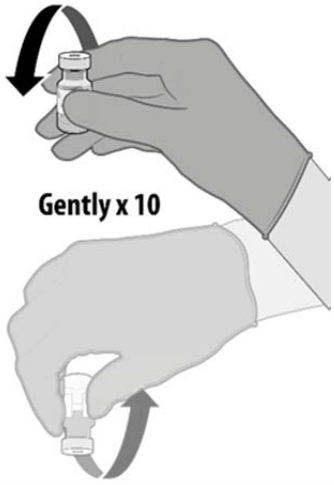
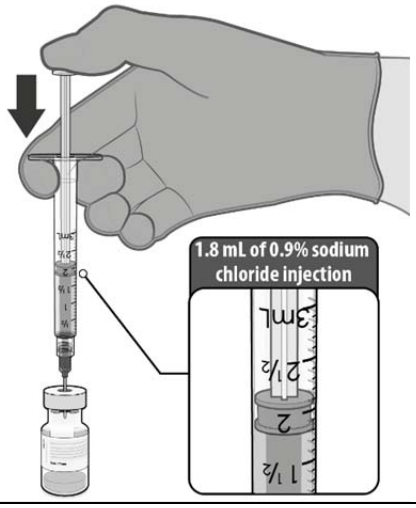
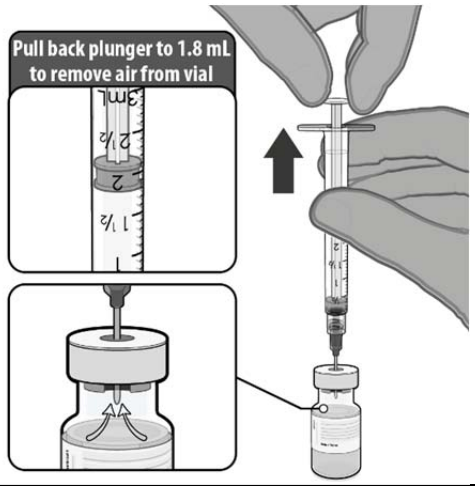
Prior to Dilution

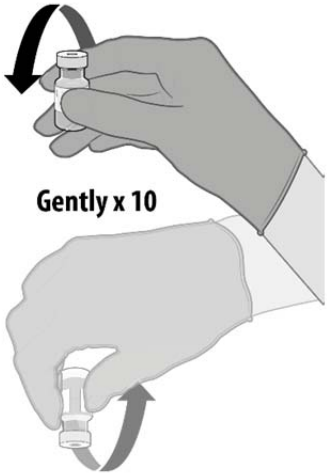
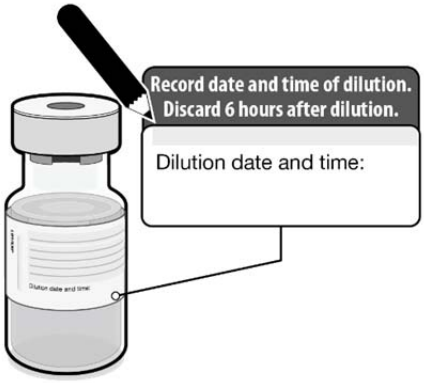
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

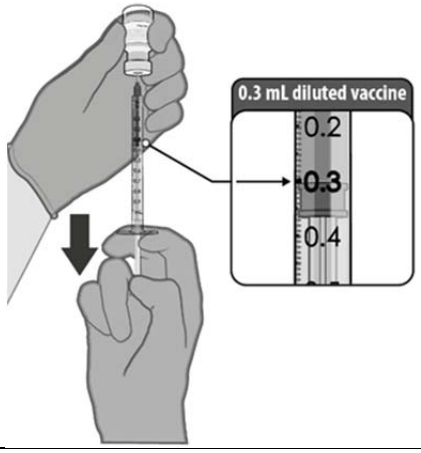
Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not use diluent vials to dilute multiple vials of COMIRNATY.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted

	within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.
	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.

	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

A third dose of the COMIRNATY (0.3 mL) administered at least 28 days following the first 2 doses of this vaccine is authorized for administration to individuals at least 16 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk has been highest in adolescent and young adult males under 40 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of

symptoms. Information is not yet available about potential long-term sequelae. The CDC has published considerations for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	**Placebo Dose 1 N[a]=2908 n[b] (%)**	**COMIRNATY Dose 2 N[a]=2682 n[b] (%)**	**Placebo Dose 2 N[a]=2684 n[b] (%)**
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

In clinical studies, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, in 99 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported in recipients who were followed for 1 month following post Dose 3.

Unsolicited Adverse Events

Overall 51.1% of participants in the COMIRNATY group and 51.4% of participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 8.1% and 5.9% with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. At the time of the updated efficacy analysis 54.5% of participants originally randomized to COMIRNATY had ≥6 months of follow-up from Dose 2 and 47.5% of original placebo participants had follow-up time between ≥1 month to <2 months after Dose 2 of COMIRNATY. Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Adverse events occurred in 28.8% of vaccine recipients who had a follow-up period of at least 6 months after Dose 2; 1.6% of the recipients had serious adverse events.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant

unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4396 (33.8%) participants who received COMIRNATY and 2136 (16.4%) participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include nonserious adverse events were reported by 2551 (28.6%) participants who received COMIRNATY and 1432 (16.1%) participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 29 (29%) participants who received COMIRNATY and 15 (15%) participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on four occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Comirnaty during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

8.6 Immunocompromised Use

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, safety and effectiveness of a third dose of COMIRNATY have been evaluated in persons that received solid organ transplants. The administration of a third dose of vaccine appears to be only moderately effective in increasing potentially protective antibody titers. Patients should still be counselled to maintain physical precautions to help prevent COVID-19. In addition, close contacts of immunocompromised persons should be vaccinated as appropriate for their health status.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials ; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0%. The case split was 8 COVID-19

cases in the BNT162b2 group compared to 162 COVID-19 cases in the placebo group. The 95% credible interval for the vaccine efficacy was 90.3% to 97.6%, indicating that the true vaccine efficacy is at least 90.3% with a 97.5% probability, which met the pre-specified success criterion.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint.

Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, geographies, and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;

- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Immunogenicity in Solid Organ Transplant Recipients

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, a single arm study has been conducted in 101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously. A third dose of COMIRNATY was administered to 99 of these individuals approximately 2 months after they had received a second dose. Among the 59 patients who had been seronegative before the third dose, 26 (44%) were seropositive at 4 weeks after the third dose. All 40 patients who had been seropositive before the third dose were still seropositive 4 weeks later. The prevalence of anti-SARS-CoV-2 antibodies was 68% (67 of 99 patients) 4 weeks after the third dose.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF

to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit www.comirnatyglobal.com.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.4

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

---------- INDICATIONS AND USAGE ----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

----------ADVERSE REACTIONS----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

Comment [A1]: FDA Comment:
Pfizer,
Please add the percentages as we previously requested. Without the percentages, stating the frequencies ≥10% is misleading.

Comment [A2]: Pfizer-BioNTech response:
The Sponsor accepts.

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

Comment [A3]: The Sponsor accepts the deletion of "Immunocompromised Use."

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

2.1 Preparation for Administration

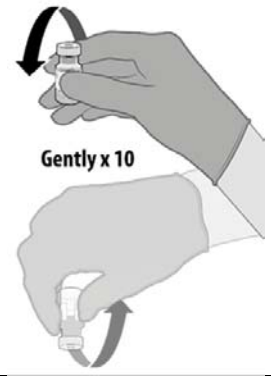
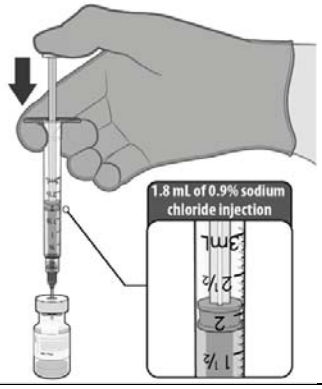
Prior to Dilution

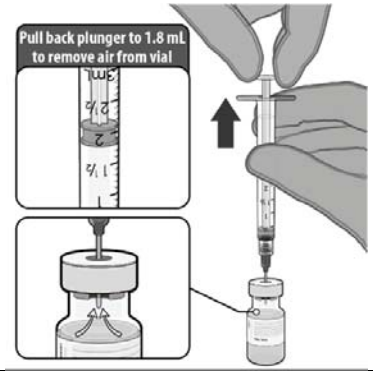
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

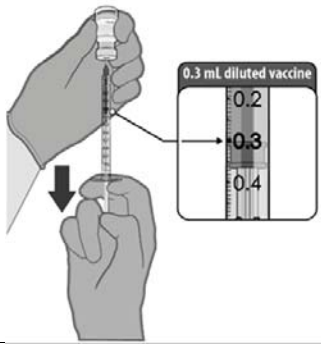
Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

Comment [A4]: Pfizer-BioNTech comment: The Sponsor accepts this revision.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • <u>Do not shake</u>. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

Comment [A5]: The Sponsor accepts the deletion of text regarding a third dose in immunocompromised individuals.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

Comment [A6]: Pfizer-BioNTech comment: The Sponsor will accept, but disagrees with the characterization of the observed risk as established.

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization ~~EUA~~ (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

Comment [A7]: Pfizer-BioNTech comment: The Sponsor accepts the revisions to this paragraph with a minor editorial change.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

In clinical studies, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

Unsolicited adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and

Comment [A8]: FDA comment:
Pfizer, This is a mixture of list of solicited and unsolicited adverse reactions. Some of these are captured in the tables above and others that we consider adverse reactions are presented below.

Comment [A9]: Pfizer-BioNTech comment:
The Sponsor proposes to retain this text. The following adverse vaccine reactions do not appear anywhere else in the label: malaise, asthenia, lethargy, hyperhidrosis, nausea, decreased appetite, night sweats. All of these adverse vaccine reactions appeared in placebo-controlled clinical trials.

Comment [A10]: The Sponsor accepts the deletion of text regarding a third dose in immunocompromised individuals.

Comment [A11]: Pfizer-BioNTech comment:
The Sponsor accepts this revision:

Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Table 9.*

Comment [A12]: FDA comment:
Pfizer, We agree that presentation of the number of participants who originally received vaccine and had total follow up time for at least 6 months should be displayed.

We disagree with the addition of follow up time for placebo recipients who received vaccine as safety data from the unblinded follow up time is not being displayed.

Comment [A13]: Pfizer-BioNTech comment:
The Sponsor accepts.

Comment [A14]: Pfizer-BioNTech comment:
The Sponsor accepts this revision.

Source: *Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Table 9.*

Comment [A15]: Pfizer-BioNTech response:
The sponsor accepts this deletion

Comment [A16]: Pfizer-BioNTech response:
The Sponsor accepts the revisions to this paragraph.

thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4,396 (33.8%) participants who received COMIRNATY and 2,136 (16.4%) participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), all events, which include nonserious adverse events were reported by 2,551 (28.6%) participants who received COMIRNATY and 1,432 (16.1%) participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 29 (29%) participants who received COMIRNATY and 15 (15%) participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Comment [A17]: Pfizer-BioNTech response:
The Sponsor accepts the revisions to this paragraph.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Comment [A18]: Pfizer-BioNTech response:
The Sponsor accepts moving this text to the beginning of the section.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on ~~four~~4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

Comment [A19]: Pfizer-BioNTech response:
The Sponsor accepts the deletion of text regarding a third dose in immunocompromised individuals.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

Comment [A20]: Pfizer-BioNTech comment:
The Sponsor accepts the revisions to this paragraph.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

Comment [A21]: Pfizer-BioNTech comment:
The Sponsor accepts this addition.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of the primary efficacy endpoint (although some subgroups had limited numbers of participants) showed similar efficacy point estimates across genders, ethnic groups, geographies, and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.

b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint.

Comment [A22]: FDA comment:
Pfizer,
We reiterate that this general statement is misleading because some of the subgroup analyses were limited by the size of the subgroup and low number of confirmed cases, which limits the interpretation of those analyses. We disagree with this addition and again request deletion.

Comment [A23]: Pfizer-BioNTech comment:
The Sponsor believes this paragraph should be retained with a modification to address FDA's concern as it contains accurate and meaningful information for prescribers as indicated by the robust discussion about subgroups at the EUA VRBPAC. In addition, the language regarding similar efficacy across these subgroups is critical to the vaccine uptake especially in minority communities. The clinical trials were developed and executed with the specific goal to have diverse populations with regard to sex, race, ethnicity and comorbidities. Except for a few subgroups (i.e., Turkey Germany) with a small number of cases, the vast majority of the subgroups have a substantial number of cases (e.g., more than 600 cases in both the US and the Non-Hispanic/Non-Latino subgroups) and have high point estimates with 95% confidence intervals that are well above 0.

Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

c. n2 = Number of participants at risk for the endpoint.

d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/ or www.comirnatyglobal.com.

Comment [A25]: FDA comment:
Pfizer, We do not agree. We continue to request that you revise this link to direct to DailyMed.

Comment [A26]: Pfizer-BioNTech comment:
The inclusion of this information is consistent with other FDA-approved labels. The Sponsor proposes to include both the DailyMed and Comirnaty Global links.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.5

US Govt. License No. x

ctions or subsections omitted from the full prescribing information are
isted.

thawed and diluted prior to administration.
ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC
g (16)].
.

9% Sodium Chloride Injection, USP to form
diluent.
on, USP as the diluent. Do not use bacteriostatic 0.9%

USP are provided but shipped separately. Use the
Chloride Injection, USP as the diluent.
; discard after 1.8 mL is withdrawn.
njection, USP is used as the diluent, discard after

NATY using the same diluent vial.
6 doses of 0.3 mL each.
as in the panels below.

2

ake.
e liquid in the vaccine vial prior to
The liquid is a white to off-white
n and may contain white to off-white
morphous particles.
e if liquid is discolored or if other particles
ved.

se sterile 0.9% Sodium Chloride Injection,
e diluent.
1.8 mL of diluent into a transfer syringe
e or narrower needle).
mL of sterile 0.9% Sodium Chloride
USP into the vaccine vial.

vert the vial containing COMIRNATY
to mix.
ake.
e vaccine in the vial.
ine will be an off-white suspension. Do not
cine is discolored or contains particulate

e date and time of dilution on the
NATY vial label.
ween 2°C to 25°C (35°F to 77°F).
ny unused vaccine 6 hours after dilution.

4

. If standard syringes and needles are used, there may
ngle vial. Irrespective of the type of syringe and needle,

mnot provide a full dose of 0.3 mL, discard the vial and

r particulate matter and discoloration prior to
The vaccine will be an off-white suspension. Do not
e matter.

muscularly.

es of 2 doses (0.3 mL each) 3 weeks apart.

OMIRNATY with other COVID-19 vaccines to complete
ose of COMIRNATY should receive a second dose of

ration, a single dose is 0.3 mL.

own history of a severe allergic reaction (e.g.,
ee Description (11)].

5

istration of injectable vaccines, including
njury from fainting.

eiving immunosuppressant therapy, may have a

adverse reactions in participants 16 through 55 years of
8.6%), fatigue (70.1%), headache (64.9%), muscle pain
%), and injection site swelling (10.6%).

adverse reactions in participants 56 years of age and
78.2%), fatigue (56.9%), headache, (45.9%), muscle
n site swelling (11.8%), fever (11.5%), and injection

ng conditions, adverse reaction rates observed in the
o rates in the clinical trials of another vaccine and may

5

12,620 placebo) 16 years of age and older followed for

set were monitored for solicited local and systemic
ccination in an electronic diary. Participants are being
ous adverse events, throughout the study [from Dose 1
nths (serious adverse events) after the last vaccination].

imilar with regard to age, gender, race, and ethnicity
se who received placebo. Overall, among the total
bo, 50.9% were male, 49.1% were female, 79.3% were
and older, 82.0% were White, 9.6% were Black or
ere Asian, and 1.0% were American Indian or Alaska

Study 2

f reported solicited local and systemic reactions,
IRNATY and placebo in the subset of participants
tion who were monitored for reactogenicity with an

f reported solicited local and systemic reactions,
Y and placebo for participants 56 years of age and

g Dose 2, the mean duration of pain at the injection site
range 1 to 9 days), and for swelling 2.1 days (range 1 to
participants 56 years of age and older after receiving
as 2.4 days (range 1 to 36 days), for redness 3.0 days
to 34 days) for participants in the COMIRNATY group.

14 (14.2)	2101 (78.3)	312 (11.6)
91 (13.4)	1274 (47.5)	284 (10.6)
20 (0.7)	788 (29.4)	28 (1.0)
3 (0.1)	39 (1.5)	0

m Day 1 to Day 7 after vaccination.
6 through 55 years of age.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
n the column header.

.0 cm.
activity; Severe: prevents daily activity.

articipants with Solicited Systemic Reactions, by Each Dose – Participants 16 Through 55 Years of Population*

lacebo Dose 1 N^a=2908 n^b (%)	**COMIRNATY Dose 2 N^a=2682 n^b (%)**	**Placebo Dose 2 N^a=2684 n^b (%)**
5 (0.9)	440 (16.4)	11 (0.4)
6 (0.6)	254 (9.5)	5 (0.2)
5 (0.2)	146 (5.4)	4 (0.1)
4 (0.1)	39 (1.5)	2 (0.1)
0	1 (0.0)	0
0 (33.0)	1649 (61.5)	614 (22.9)
0 (19.6)	558 (20.8)	317 (11.8)
2 (12.8)	949 (35.4)	283 (10.5)
8 (0.6)	142 (5.3)	14 (0.5)

5 (0.2)	12 (0.4)	10 (0.4)
1 (0.0)	4 (0.1)	0
3 (11.1)	269 (10.0)	205 (7.6)
64 (9.1)	219 (8.2)	169 (6.3)
8 (2.0)	44 (1.6)	35 (1.3)
1 (0.0)	6 (0.2)	1 (0.0)
9 (11.3)	1055 (39.3)	237 (8.8)
81 (7.9)	441 (16.4)	150 (5.6)
6 (3.3)	552 (20.6)	84 (3.1)
2 (0.1)	62 (2.3)	3 (0.1)
68 (5.8)	638 (23.8)	147 (5.5)
12 (3.9)	291 (10.9)	82 (3.1)
5 (1.9)	320 (11.9)	61 (2.3)
1 (0.0)	27 (1.0)	4 (0.1)
8 (13.7)	1213 (45.2)	320 (11.9)

lected in the electronic diary (e-diary) from Day 1 to Day 7 after

ts 16 through 55 years of age.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
herefore, this information was included in the column header.

ce with activity; Severe: prevents daily activity.
Severe: requires intravenous hydration.
ls in 24 hours; Severe: 6 or more loose stools in 24 hours.
on.

185 (9.3)	1230 (66.1)	143 (7.8)
177 (8.9)	873 (46.9)	138 (7.5)
8 (0.4)	347 (18.7)	5 (0.3)
0	10 (0.5)	0

m Day 1 to Day 7 after vaccination.
6 years of age and older.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
n the column header.

.0 cm.
activity; Severe: prevents daily activity.

articipants with Solicited Systemic Reactions, by Each Dose – Participants 56 Years of Age and y Population*

Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
8 (0.4)	219 (11.8)	4 (0.2)
3 (0.2)	158 (8.5)	2 (0.1)
3 (0.2)	54 (2.9)	1 (0.1)
2 (0.1)	7 (0.4)	1 (0.1)
0	0	0

0

49 (2.5)	229 (12.3)	45 (2.5)
19 (1.0)	185 (9.9)	12 (0.7)
1 (0.1)	21 (1.1)	0
9 (0.5)	13 (0.7)	5 (0.3)
9 (0.5)	10 (0.5)	5 (0.3)
0	1 (0.1)	0
0	2 (0.1)	0
130 (6.5)	152 (8.2)	102 (5.6)
109 (5.5)	125 (6.7)	76 (4.1)
20 (1.0)	25 (1.3)	22 (1.2)
1 (0.1)	2 (0.1)	4 (0.2)
165 (8.3)	537 (28.9)	99 (5.4)
111 (5.6)	229 (12.3)	65 (3.5)
51 (2.6)	288 (15.5)	33 (1.8)
3 (0.2)	20 (1.1)	1 (0.1)
124 (6.2)	353 (19.0)	72 (3.9)
78 (3.9)	183 (9.8)	44 (2.4)
45 (2.3)	161 (8.7)	27 (1.5)
1 (0.1)	9 (0.5)	1 (0.1)
224 (11.3)	688 (37.0)	170 (9.3)

lected in the electronic diary (e-diary) from Day 1 to Day 7 after

s 56 years of age and older was fatigue.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. N for each
herefore was included in the column header.

, lethargy (0.1%), and night sweats (0.1%).

0% of participants 56 years of age and older following
0.3%), lymphadenopathy (0.2%), lethargy (0.2%),
ght sweats (0.1%).

Y group and 11,316 (51.4%) participants in the
<6 months after Dose 2 in the blinded
,778 (8.1%) and 1,304 (5.9%) with ≥6 months of
o groups, respectively.

ts 16 years of age and older are for the
rticipants' unblinding dates.

ized to COMIRNATY had ≥6 months total (blinded

ge who had received at least 1 dose of vaccine or
rious adverse events from Dose 1 up to the participant
103 (0.8%) COMIRNATY recipients and 117 (0.9%)
56 years of age and older (COMIRNATY = 8,931,
by 165 (1.8%) COMIRNATY recipients and 151 (1.7%)
RNATY or placebo, respectively. In these analyses,
ow-up after Dose 2. Among participants with confirmed
up to the participant unblinding date in ongoing
ients and 2 (2%) placebo recipients.

there were no notable patterns between treatment
including neurologic, neuro-inflammatory, and

2

st 4 months of follow-up after Dose 2. The higher
vents among COMIRNATY recipients (inclusive of
s primarily attributed to local and systemic adverse
se of vaccine that are consistent with adverse reactions
and presented in Table 3 and Table 4.

ts of lymphadenopathy were imbalanced with notably
placebo group (8).

od to date, Bell's palsy (facial paralysis) was reported
cipants in the placebo group. Onset of facial paralysis
se 2) and Days 3, 9, and 48 after Dose 2. In the placebo
102. Currently available information is insufficient to
analysis of blinded, placebo-controlled follow-up, there
between treatment groups for specific categories of
r neuro-inflammatory, and thrombotic events) that
the analysis of unblinded follow-up, there were no
verse events that would suggest a causal relationship to

ring postmarketing use of COMIRNATY, including
ctions are reported voluntarily from a population of
ate their frequency or establish a causal relationship to

scarriage in clinically recognized pregnancies is 2% to
OMIRNATY administered to pregnant women are
ncy.

emale rats administered the equivalent of a single
e prior to mating and twice during gestation. These
the vaccine *(see Animal Data)*.

formulation containing the same quantity of
A) (30 mcg) and other ingredients included in a single
le rats by the intramuscular route on 4 occasions: 21
20. No vaccine-related adverse effects on female
ere reported in the study.

man milk. Data are not available to assess the effects of
tion/excretion. The developmental and health benefits
other's clinical need for COMIRNATY and any
MIRNATY or from the underlying maternal condition.
on is susceptibility to disease prevented by the vaccine.

e suspension for injection for intramuscular use.
ltiple dose vials; each vial must be diluted with 1.8 mL
use to form the vaccine. Each dose of COMIRNATY
NA (mRNA) encoding the viral spike (S) glycoprotein

e following ingredients: lipids (0.43 mg
exyldecanoate), 0.05 mg 2-(polyethylene
stearoyl-sn-glycero-3-phosphocholine, and 0.2 mg
basic potassium phosphate, 0.36 mg sodium chloride,
sucrose. The diluent (0.9% Sodium Chloride Injection,
per dose.

rmulated in lipid particles, which enable delivery of the
CoV-2 S antigen. The vaccine elicits an immune
D-19.

rtility

o cause carcinogenicity, genotoxicity, or impairment of
with COMIRNATY there were no vaccine-related
ns (8.1)].

5

IRNATY or placebo, 51.4% or 50.3% were male and
through 64 years of age, 20.9% or 20.8% were 65 years
9.6% were Black or African American, 1.0% or 0.9%
were Asian, 0.3% or 0.2% Native Hawaiian or other
73.9% or 74.1% were non-Hispanic/Latino, 0.5% or
rbidities [participants who have 1 or more
disease: defined as subjects who had at least one of the
x (BMI) ≥30 kg/m^2], respectively. The mean age at
51.0 or 51.0 in participants who received

fied primary efficacy endpoint included
the COMIRNATY group and 18,379 in the placebo
n SARS-CoV-2 through 7 days after the second dose.
icacy analysis included all participants 12 years of age
d followed for the development of COVID-19 through
age and 56 years of age and older began enrollment
rollment from September 16, 2020, and 12 through
0.

tion prior to 7 days after Dose 2, vaccine efficacy
fter Dose 2 was 95.0% (95% credible interval: 90.3,
case split was 8 COVID-19 cases in the
s in the placebo group.

included participants 16 years of age and older who
the development of COVID-19 during blinded
epresenting up to 6 months of follow-up after Dose 2.
IATY group and 12,449 (58.7%) in the placebo group
ebo-controlled follow-up period.

	833 5.857 (19,741)	91.1 (88.8, 93.1)
	709 4.654 (15,515)	90.5 (87.9, 92.7)
	124 1.202 (4226)	94.5 (88.3, 97.8)

2 in participants with or without* evidence of prior -2 infection

n2[d])	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
	854 6.110 (20,595)	90.9 (88.5, 92.8)
	726 4.879 (16,269)	90.2 (87.5, 92.4)
	128 1.232 (4326)	94.7 (88.7, 97.9)

Polymerase Chain Reaction (RT-PCR) and at least 1 symptom
eased cough; new or increased shortness of breath; chills; new or
hea; vomiting).
n (i.e., N-binding antibody [serum] negative at Visit 1 and
d 2), and had negative NAAT (nasal swab) at any unscheduled visit

oint across all participants within each group at risk for the endpoint.
se 2 to the end of the surveillance period.

ed based on the Clopper and Pearson method adjusted to the

	Placebo Cases n1[a] Surveillance Time[b] (n2[c])	Vaccine Efficacy % (95% CI[d])
n2[c])		
	21 6.237 (20,629)	95.3 (70.9, 99.9)
-19 Occurrence Based on CDC Definition		
	Placebo Cases n1[a] Surveillance Time[b] (n2[c])	**Vaccine Efficacy % (95% CI[d])**
n2[c])		
	31 6.225 (20,593)	100 (87.6, 100.0)

Polymerase Chain Reaction (RT-PCR) and at least 1 symptom
eased cough; new or increased shortness of breath; chills; new or
hea; vomiting).
n (i.e., N-binding antibody [serum] negative at Visit 1 and
d 2), and had negative NAAT (nasal swab) at any unscheduled visit

med COVID-19 and presence of at least 1 of the following:
respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per
l, or ratio of arterial oxygen partial pressure to fractional inspired

noninvasive ventilation, mechanical ventilation or extracorporeal

astolic blood pressure <60 mm Hg, or requiring vasopressors);

OVID-19 and presence of at least 1 of the following:

oint across all participants within each group at risk for the endpoint.

thermal containers with dry ice. Once received, remove
and preferably store in an ultra-low temperature freezer
y date printed on the label. Alternatively, vials may be
s. Vials must be kept frozen and protected from light, in
5°C to -15°C (-13°F to 5°F) for up to 2 weeks may be
f -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative
) should be tracked and should not exceed 2 weeks.

hermal container in which COMIRNATY arrives may
to the top of the container with dry ice. Refer to the
ner for instructions regarding the use of the thermal
maintains a temperature range of -90ºC to -60ºC (-130ºF
141°F to -76°F) is not considered an excursion from

ng vials cannot be transported at -90°C to -60°C
15°C (-13°F to 5°F). Any hours used for transport
k limit for storage at -25°C to -15°C (-13°F to 5°F).
) may be returned 1 time to the recommended storage

9

ed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

77°F) and use within 6 hours from the time of dilution.
void exposure to direct sunlight and ultraviolet light.
6 hours. Do not refreeze.

ks of vaccination with COMIRNATY.

g the two dose vaccination series.

Y. Encourage individuals exposed to COMIRNATY
gister by visiting https://mothertobaby.org/ongoing-

their healthcare provider or to the Vaccine Adverse
aers.hhs.gov.

0

1

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: YYYY

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

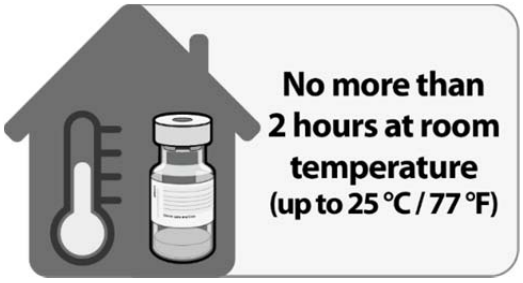
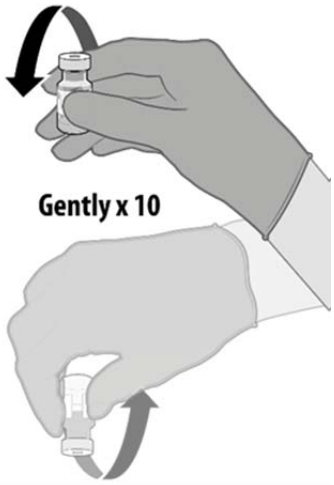
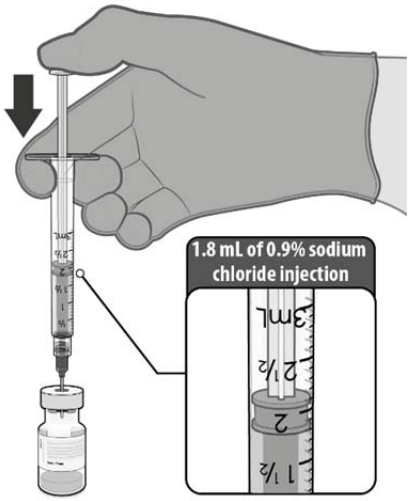
2.1 Preparation for Administration

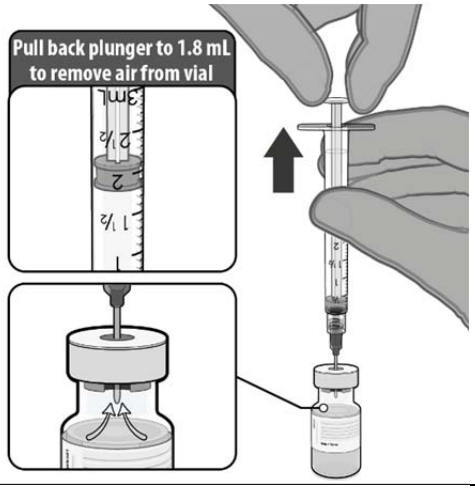
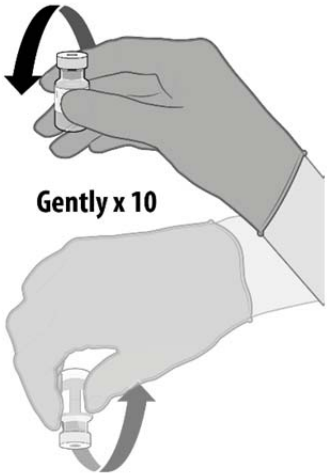
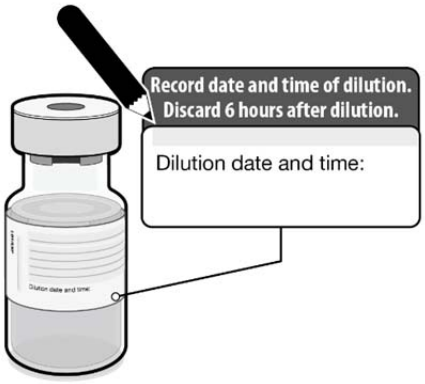
Prior to Dilution

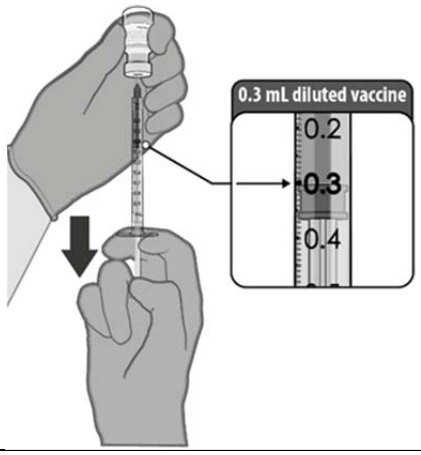
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

In clinical studies, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

Unsolicited adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded

follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4,396 (33.8%) participants who received COMIRNATY and 2,136 (16.4%) participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), all events, which include nonserious adverse events were reported by 2,551 (28.6%) participants who received COMIRNATY and 1,432 (16.1%) participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 29 (29%) participants who received COMIRNATY and 15 (15%) participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were

immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of the primary efficacy endpoint (although some subgroups had limited numbers of participants) showed similar efficacy point estimates across genders, ethnic groups, geographies, and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior

SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium

Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/ or www.comirnatyglobal.com.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.5

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE ----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

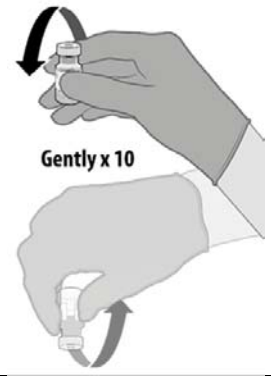
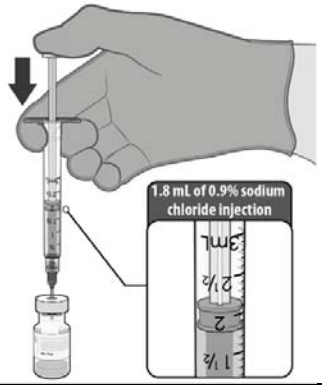
2.1 Preparation for Administration

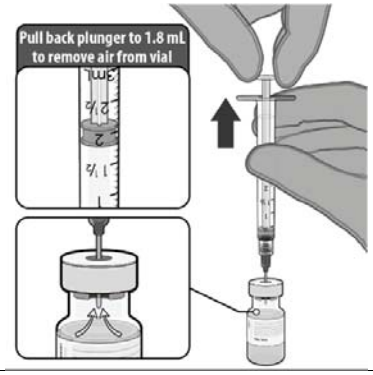
Prior to Dilution

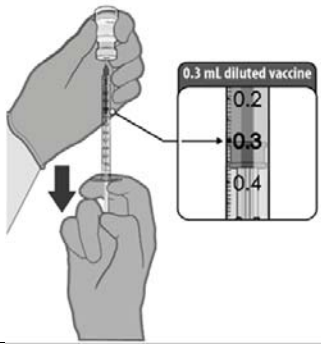
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • <u>Do not shake</u>. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

~~In clinical studies, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).~~

~~In clinical studies, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).~~

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

Unsolicited adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded

Comment [A1]: FDA comment:

Pfizer, The events not contained in the Tables 1-4 above were not solicited, thus they should be categorized correctly and moved into the discussion of Non-Serious Unsolicited Adverse Events, below, using a format consistent with presentation of those events, by treatment arm and follow-up time period.
Events discussed elsewhere should not be included (lymphadenopathy, injection site redness).

Comment [A2]:
Pfizer-BioNTech response:
The Sponsor accepts and has provided the follow-up period and treatment arm data in the Non Serious Adverse Event section below.

Source:

Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Tables 14.86 and 14.87

follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Among the total participants who received COMIRNATY or placebo 1 month after Dose 2, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were nausea (1.4% or 0.5%), malaise (0.7% or 0.1%), asthenia (0.4% or 0.1%), decreased appetite (0.2% or 0.0%), hyperhidrosis (0.1% or 0.0%), lethargy (0.1% or 0.0%), and night sweats (0.1% or 0.0%).

Among the total participants who received COMIRNATY or placebo 1 month after Dose 2, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0% or 0.3%), malaise (0.5% or 0.1%), asthenia (0.3% or 0.1%), lethargy (0.2% or 0.0%), decreased appetite (0.1% or 0.0%), hyperhidrosis (0.1% or 0.0%), and night sweats (0.1% or 0.0%).

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4,396 (33.8%) participants who received COMIRNATY and 2,136 (16.4%) participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), all events, which include nonserious adverse events were reported by 2,551 (28.6%) participants who received COMIRNATY and 1,432 (16.1%) participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 29 (29%) participants who received COMIRNATY and 15 (15%) participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including

Comment [A3]: FDA comment:

Pfizer, The events not contained in the Tables 1-4 above were not solicited, thus they should be categorized correctly and moved into the discussion of Non-Serious Unsolicited Adverse Events, below, using a format consistent with presentation of those events, by treatment arm and follow-up time period.
Events discussed elsewhere should not be included (lymphadenopathy, injection site redness).

Pfizer-BioNTech response:
The Sponsor accepts and has provided the follow-up period and treatment arm data.

Source:

Interim Clinical Study Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals: Tables 14.86 and 14.87

under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, and participants with obesity and medical comorbidities associated with high risk of severe COVID-19.

Comment [A4]: FDA comment:

Pfizer,
Please see our revised statement regarding subgroup analyses off vaccine efficacy.

Comment [A5]: Pfizer-BioNTech response:
The Sponsor accepts the FDA's revision to this paragraph.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint.

Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

c. n2 = Number of participants at risk for the endpoint.

d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.6~~5~~

US Govt. License No. x

Comment [A6]: FDA comment:

Pfizer,
We continue to request to only provide a link to DailyMed as this is sufficient. Furthermore, the other site may contain elements that are promotional and have not been reviewed by FDA.

Comment [A7]: Pfizer-BioNtech response:
The Sponsor will comply but we reiterate our concern that there is a delay with labels being posted to DailyMed and we believe that including both websites will allow providers to obtain information about our product as quickly as possible. This is consistent with Pfizer's other approved labels and no objections have been raised. The Sponsor plans to revisit this discussion with the next labeling supplement post-approval.

ctions or subsections omitted from the full prescribing information are
isted.

thawed and diluted prior to administration.
ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC
g (16)].
.

9% Sodium Chloride Injection, USP to form
diluent.
on, USP as the diluent. Do not use bacteriostatic 0.9%

USP are provided but shipped separately. Use the
Chloride Injection, USP as the diluent.
; discard after 1.8 mL is withdrawn.
njection, USP is used as the diluent, discard after

NATY using the same diluent vial.
6 doses of 0.3 mL each.
as in the panels below.

2

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e liquid in the vaccine vial prior to
The liquid is a white to off-white
n and may contain white to off-white
morphous particles.
e if liquid is discolored or if other particles
ved.

se sterile 0.9% Sodium Chloride Injection,
e diluent.
1.8 mL of diluent into a transfer syringe
e or narrower needle).
mL of sterile 0.9% Sodium Chloride
USP into the vaccine vial.

vert the vial containing COMIRNATY
to mix.
ake.
e vaccine in the vial.
ine will be an off-white suspension. Do not
cine is discolored or contains particulate

e date and time of dilution on the
NATY vial label.
ween 2°C to 25°C (35°F to 77°F).
ny unused vaccine 6 hours after dilution.

4

. If standard syringes and needles are used, there may
ngle vial. Irrespective of the type of syringe and needle,

mnot provide a full dose of 0.3 mL, discard the vial and

r particulate matter and discoloration prior to
The vaccine will be an off-white suspension. Do not
e matter.

muscularly.

es of 2 doses (0.3 mL each) 3 weeks apart.

OMIRNATY with other COVID-19 vaccines to complete
ose of COMIRNATY should receive a second dose of

ration, a single dose is 0.3 mL.

own history of a severe allergic reaction (e.g.,
ee Description (11)].

5

istration of injectable vaccines, including
njury from fainting.

eiving immunosuppressant therapy, may have a

adverse reactions in participants 16 through 55 years of
8.6%), fatigue (70.1%), headache (64.9%), muscle pain
%), and injection site swelling (10.6%).

adverse reactions in participants 56 years of age and
78.2%), fatigue (56.9%), headache, (45.9%), muscle
n site swelling (11.8%), fever (11.5%), and injection

ng conditions, adverse reaction rates observed in the
o rates in the clinical trials of another vaccine and may

5

12,620 placebo) 16 years of age and older followed for

set were monitored for solicited local and systemic
ccination in an electronic diary. Participants are being
ous adverse events, throughout the study [from Dose 1
nths (serious adverse events) after the last vaccination].

imilar with regard to age, gender, race, and ethnicity
se who received placebo. Overall, among the total
bo, 50.9% were male, 49.1% were female, 79.3% were
and older, 82.0% were White, 9.6% were Black or
ere Asian, and 1.0% were American Indian or Alaska

Study 2

f reported solicited local and systemic reactions,
IRNATY and placebo in the subset of participants
tion who were monitored for reactogenicity with an

f reported solicited local and systemic reactions,
Y and placebo for participants 56 years of age and

g Dose 2, the mean duration of pain at the injection site
range 1 to 9 days), and for swelling 2.1 days (range 1 to
participants 56 years of age and older after receiving
as 2.4 days (range 1 to 36 days), for redness 3.0 days
to 34 days) for participants in the COMIRNATY group.

14 (14.2)	2101 (78.3)	312 (11.6)
91 (13.4)	1274 (47.5)	284 (10.6)
20 (0.7)	788 (29.4)	28 (1.0)
3 (0.1)	39 (1.5)	0

m Day 1 to Day 7 after vaccination.
6 through 55 years of age.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
n the column header.

.0 cm.
activity; Severe: prevents daily activity.

articipants with Solicited Systemic Reactions, by Each Dose – Participants 16 Through 55 Years of Population*

lacebo Dose 1 N^a=2908 n^b (%)	**COMIRNATY Dose 2 N^a=2682 n^b (%)**	**Placebo Dose 2 N^a=2684 n^b (%)**
5 (0.9)	440 (16.4)	11 (0.4)
6 (0.6)	254 (9.5)	5 (0.2)
5 (0.2)	146 (5.4)	4 (0.1)
4 (0.1)	39 (1.5)	2 (0.1)
0	1 (0.0)	0
0 (33.0)	1649 (61.5)	614 (22.9)
0 (19.6)	558 (20.8)	317 (11.8)
2 (12.8)	949 (35.4)	283 (10.5)
8 (0.6)	142 (5.3)	14 (0.5)

5 (0.2)	12 (0.4)	10 (0.4)
1 (0.0)	4 (0.1)	0
3 (11.1)	269 (10.0)	205 (7.6)
64 (9.1)	219 (8.2)	169 (6.3)
8 (2.0)	44 (1.6)	35 (1.3)
1 (0.0)	6 (0.2)	1 (0.0)
9 (11.3)	1055 (39.3)	237 (8.8)
81 (7.9)	441 (16.4)	150 (5.6)
6 (3.3)	552 (20.6)	84 (3.1)
2 (0.1)	62 (2.3)	3 (0.1)
68 (5.8)	638 (23.8)	147 (5.5)
12 (3.9)	291 (10.9)	82 (3.1)
5 (1.9)	320 (11.9)	61 (2.3)
1 (0.0)	27 (1.0)	4 (0.1)
8 (13.7)	1213 (45.2)	320 (11.9)

lected in the electronic diary (e-diary) from Day 1 to Day 7 after

ts 16 through 55 years of age.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
herefore, this information was included in the column header.

ce with activity; Severe: prevents daily activity.
Severe: requires intravenous hydration.
ls in 24 hours; Severe: 6 or more loose stools in 24 hours.
on.

185 (9.3)	1230 (66.1)	143 (7.8)
177 (8.9)	873 (46.9)	138 (7.5)
8 (0.4)	347 (18.7)	5 (0.3)
0	10 (0.5)	0

m Day 1 to Day 7 after vaccination.
6 years of age and older.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
n the column header.

.0 cm.
activity; Severe: prevents daily activity.

articipants with Solicited Systemic Reactions, by Each Dose – Participants 56 Years of Age and y Population*

Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
8 (0.4)	219 (11.8)	4 (0.2)
3 (0.2)	158 (8.5)	2 (0.1)
3 (0.2)	54 (2.9)	1 (0.1)
2 (0.1)	7 (0.4)	1 (0.1)
0	0	0

0

49 (2.5)	229 (12.3)	45 (2.5)
19 (1.0)	185 (9.9)	12 (0.7)
1 (0.1)	21 (1.1)	0
9 (0.5)	13 (0.7)	5 (0.3)
9 (0.5)	10 (0.5)	5 (0.3)
0	1 (0.1)	0
0	2 (0.1)	0
130 (6.5)	152 (8.2)	102 (5.6)
109 (5.5)	125 (6.7)	76 (4.1)
20 (1.0)	25 (1.3)	22 (1.2)
1 (0.1)	2 (0.1)	4 (0.2)
165 (8.3)	537 (28.9)	99 (5.4)
111 (5.6)	229 (12.3)	65 (3.5)
51 (2.6)	288 (15.5)	33 (1.8)
3 (0.2)	20 (1.1)	1 (0.1)
124 (6.2)	353 (19.0)	72 (3.9)
78 (3.9)	183 (9.8)	44 (2.4)
45 (2.3)	161 (8.7)	27 (1.5)
1 (0.1)	9 (0.5)	1 (0.1)
224 (11.3)	688 (37.0)	170 (9.3)

lected in the electronic diary (e-diary) from Day 1 to Day 7 after

s 56 years of age and older was fatigue.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. N for each
herefore was included in the column header.

1 group and 11,516 (51.4%) participants in the
<6 months after Dose 2 in the blinded
,778 (8.1%) and 1,304 (5.9%) with ≥6 months of
o groups, respectively.

ts 16 years of age and older are for the
rticipants' unblinding dates.

ized to COMIRNATY had ≥6 months total (blinded

ge who had received at least 1 dose of vaccine or
rious adverse events from Dose 1 up to the participant
103 (0.8%) COMIRNATY recipients and 117 (0.9%)
56 years of age and older (COMIRNATY = 8,931,
y 165 (1.8%) COMIRNATY recipients and 151 (1.7%)
RNATY or placebo, respectively. In these analyses,
ow-up after Dose 2. Among participants with confirmed
up to the participant unblinding date in ongoing
ients and 2 (2%) placebo recipients.

there were no notable patterns between treatment
including neurologic, neuro-inflammatory, and
hip to COMIRNATY. In the analysis of unblinded
egories of serious adverse events that would suggest a

Y or placebo 1 month after Dose 2, the adverse
55 years of age following any dose were nausea (1.4%

NATY and 15 (15%) participants in the placebo group,

st 4 months of follow-up after Dose 2. The higher
vents among COMIRNATY recipients (inclusive of
s primarily attributed to local and systemic adverse
se of vaccine that are consistent with adverse reactions
and presented in Table 3 and Table 4.

ts of lymphadenopathy were imbalanced with notably
placebo group (8).

od to date, Bell's palsy (facial paralysis) was reported
cipants in the placebo group. Onset of facial paralysis
se 2) and Days 3, 9, and 48 after Dose 2. In the placebo
102. Currently available information is insufficient to
analysis of blinded, placebo-controlled follow-up, there
between treatment groups for specific categories of
r neuro-inflammatory, and thrombotic events) that
the analysis of unblinded follow-up, there were no
verse events that would suggest a causal relationship to

ring postmarketing use of COMIRNATY, including
ctions are reported voluntarily from a population of
ate their frequency or establish a causal relationship to

scarriage in clinically recognized pregnancies is 2% to
OMIRNATY administered to pregnant women are
ncy.

emale rats administered the equivalent of a single
or to mating and twice during gestation. These studies
cine *(see Animal Data)*.

formulation containing the same quantity of
A) (30 mcg) and other ingredients included in a single
le rats by the intramuscular route on 4 occasions: 21
20. No vaccine-related adverse effects on female
ere reported in the study.

man milk. Data are not available to assess the effects of
tion/excretion. The developmental and health benefits
other's clinical need for COMIRNATY and any
MIRNATY or from the underlying maternal condition.
on is susceptibility to disease prevented by the vaccine.

e suspension for injection for intramuscular use.
ltiple dose vials; each vial must be diluted with 1.8 mL
use to form the vaccine. Each dose of COMIRNATY
NA (mRNA) encoding the viral spike (S) glycoprotein

e following ingredients: lipids (0.43 mg
exyldecanoate), 0.05 mg 2-(polyethylene
stearoyl-sn-glycero-3-phosphocholine, and 0.2 mg
basic potassium phosphate, 0.36 mg sodium chloride,
sucrose. The diluent (0.9% Sodium Chloride Injection,
per dose.

rmulated in lipid particles, which enable delivery of the
CoV-2 S antigen. The vaccine elicits an immune
D-19.

rtility

o cause carcinogenicity, genotoxicity, or impairment of
with COMIRNATY there were no vaccine-related
ns (8.1)].

5

IRNATY or placebo, 51.4% or 50.3% were male and
through 64 years of age, 20.9% or 20.8% were 65 years
9.6% were Black or African American, 1.0% or 0.9%
were Asian, 0.3% or 0.2% Native Hawaiian or other
73.9% or 74.1% were non-Hispanic/Latino, 0.5% or
rbidities [participants who have 1 or more
disease: defined as subjects who had at least one of the
x (BMI) ≥30 kg/m^2], respectively. The mean age at
51.0 or 51.0 in participants who received

fied primary efficacy endpoint included
the COMIRNATY group and 18,379 in the placebo
n SARS-CoV-2 through 7 days after the second dose.
icacy analysis included all participants 12 years of age
d followed for the development of COVID-19 through
age and 56 years of age and older began enrollment
rollment from September 16, 2020, and 12 through
0.

tion prior to 7 days after Dose 2, vaccine efficacy
fter Dose 2 was 95.0% (95% credible interval: 90.3,
case split was 8 COVID-19 cases in the
s in the placebo group.

included participants 16 years of age and older who
the development of COVID-19 during blinded
epresenting up to 6 months of follow-up after Dose 2.
IATY group and 12,449 (58.7%) in the placebo group
ebo-controlled follow-up period.

	833 5.857 (19,741)	91.1 (88.8, 93.1)
	709 4.654 (15,515)	90.5 (87.9, 92.7)
	124 1.202 (4226)	94.5 (88.3, 97.8)

2 in participants with or without* evidence of prior -2 infection

n2[d])	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
	854 6.110 (20,595)	90.9 (88.5, 92.8)
	726 4.879 (16,269)	90.2 (87.5, 92.4)
	128 1.232 (4326)	94.7 (88.7, 97.9)

Polymerase Chain Reaction (RT-PCR) and at least 1 symptom
eased cough; new or increased shortness of breath; chills; new or
hea; vomiting).
n (i.e., N-binding antibody [serum] negative at Visit 1 and
d 2), and had negative NAAT (nasal swab) at any unscheduled visit

oint across all participants within each group at risk for the endpoint.
se 2 to the end of the surveillance period.

ed based on the Clopper and Pearson method adjusted to the

	Placebo Cases n1[a] Surveillance Time[b] (n2[c])	Vaccine Efficacy % (95% CI[d])
n2[c])		
	21 6.237 (20,629)	95.3 (70.9, 99.9)
-19 Occurrence Based on CDC Definition		
	Placebo Cases n1[a] Surveillance Time[b] (n2[c])	**Vaccine Efficacy % (95% CI[d])**
n2[c])		
	31 6.225 (20,593)	100 (87.6, 100.0)

Polymerase Chain Reaction (RT-PCR) and at least 1 symptom
eased cough; new or increased shortness of breath; chills; new or
hea; vomiting).
n (i.e., N-binding antibody [serum] negative at Visit 1 and
d 2), and had negative NAAT (nasal swab) at any unscheduled visit

med COVID-19 and presence of at least 1 of the following:
respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per
l, or ratio of arterial oxygen partial pressure to fractional inspired

noninvasive ventilation, mechanical ventilation or extracorporeal

astolic blood pressure <60 mm Hg, or requiring vasopressors);

OVID-19 and presence of at least 1 of the following:

oint across all participants within each group at risk for the endpoint.

thermal containers with dry ice. Once received, remove
and preferably store in an ultra-low temperature freezer
y date printed on the label. Alternatively, vials may be
s. Vials must be kept frozen and protected from light, in
5°C to -15°C (-13°F to 5°F) for up to 2 weeks may be
f -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative
) should be tracked and should not exceed 2 weeks.

hermal container in which COMIRNATY arrives may
to the top of the container with dry ice. Refer to the
ner for instructions regarding the use of the thermal
maintains a temperature range of -90ºC to -60ºC (-130ºF
141°F to -76°F) is not considered an excursion from

ng vials cannot be transported at -90°C to -60°C
15°C (-13°F to 5°F). Any hours used for transport
k limit for storage at -25°C to -15°C (-13°F to 5°F).
) may be returned 1 time to the recommended storage

9

ed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

77°F) and use within 6 hours from the time of dilution.
void exposure to direct sunlight and ultraviolet light.
6 hours. Do not refreeze.

ks of vaccination with COMIRNATY.

g the two dose vaccination series.

Y. Encourage individuals exposed to COMIRNATY
gister by visiting https://mothertobaby.org/ongoing-

their healthcare provider or to the Vaccine Adverse
aers.hhs.gov.

0

1

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

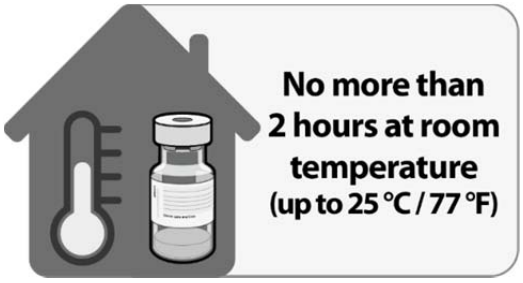
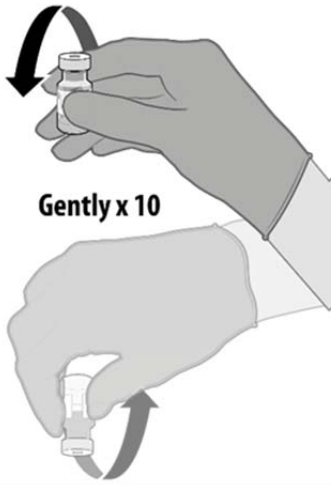
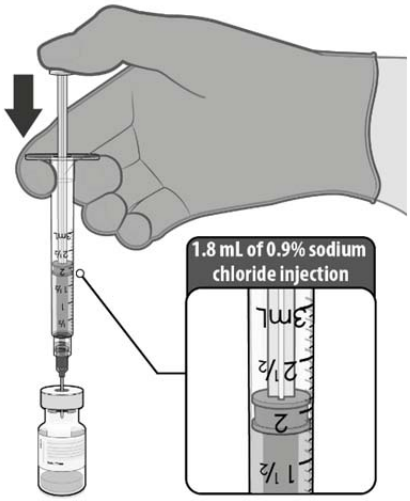
2.1 Preparation for Administration

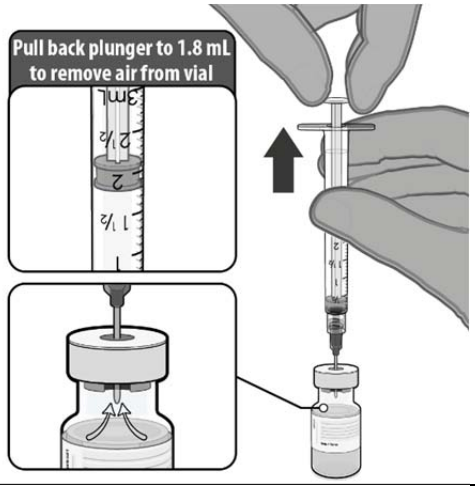
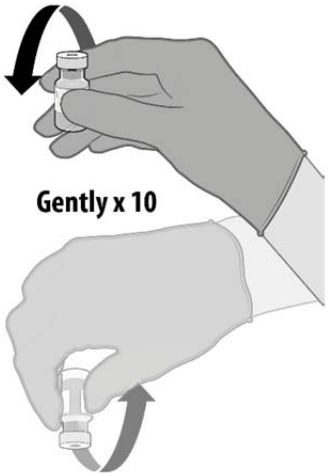
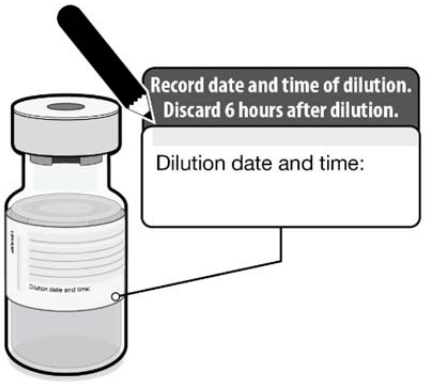
Prior to Dilution

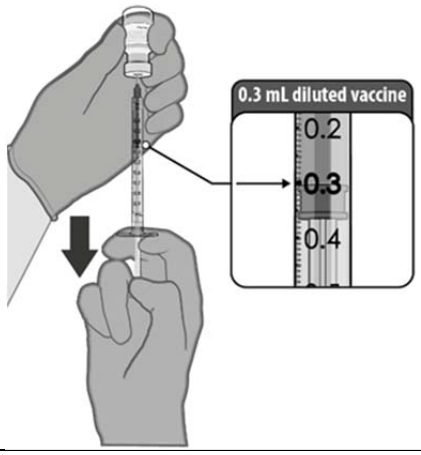
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

~~In clinical studies, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).~~

~~In clinical studies, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).~~

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

Unsolicited adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded

follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

Non-Serious Adverse Events

Among the total participants who received COMIRNATY or placebo 1 month after Dose 2, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were nausea (1.4% or 0.5%), malaise (0.7% or 0.1%), asthenia (0.4% or 0.1%), decreased appetite (0.2% or 0.0%), hyperhidrosis (0.1% or 0.0%), lethargy (0.1% or 0.0%), and night sweats (0.1% or 0.0%).

Among the total participants who received COMIRNATY or placebo 1 month after Dose 2, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0% or 0.3%), malaise (0.5% or 0.1%), asthenia (0.3% or 0.1%), lethargy (0.2% or 0.0%), decreased appetite (0.1% or 0.0%), hyperhidrosis (0.1% or 0.0%), and night sweats (0.1% or 0.0%).

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4,396 (33.8%) participants who received COMIRNATY and 2,136 (16.4%) participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931, placebo = 8,895), all events, which include nonserious adverse events were reported by 2,551 (28.6%) participants who received COMIRNATY and 1,432 (16.1%) participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 29 (29%) participants who received COMIRNATY and 15 (15%) participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including

under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, and participants with obesity and medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.

b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint.

Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

c. n2 = Number of participants at risk for the endpoint.

d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.6~~5~~

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE ----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

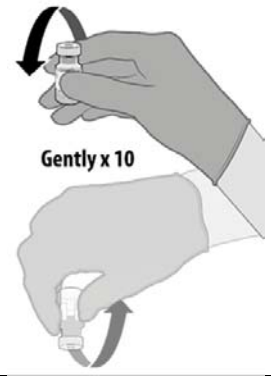
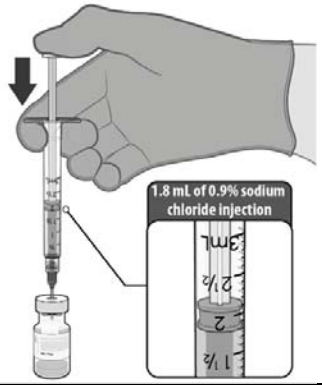
2.1 Preparation for Administration

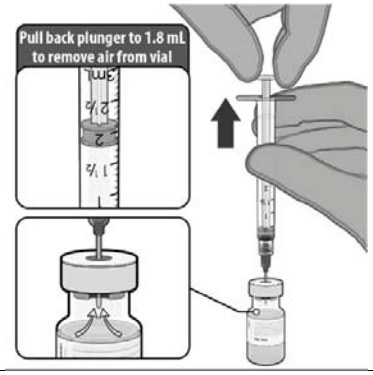
Prior to Dilution

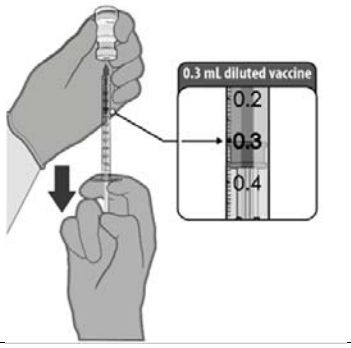
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • <u>Do not shake</u>. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of ~~serious and~~ all adverse events (including serious and non-serious unsolicited adverse events) reported through 1 month after Dose 2 in participants 16 through 55 years of age following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.4% vs. 0.5%), malaise (0.7% vs. 0.1%), asthenia (0.4% vs. 0.1%), decreased appetite (0.2% vs. <0.0~~1~~%), hyperhidrosis (0.1% vs. <0.0~~1~~%), lethargy (0.1% vs. <0.0~~1~~%), and night sweats (0.1% ~~-~~vs. <0.0~~1~~%).

In an analysis of all adverse events (including serious and non-serious unsolicited adverse events) reported through 1 month after Dose 2 in participants 56 years of age and older following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.0% vs. 0.3%), malaise (0.5% vs. 0.1%), asthenia (0.3% vs. 0.1%), lethargy (0.2% vs. <0.0~~1~~%), decreased appetite (0.1% vs. <0.0~~1~~%), hyperhidrosis (0.1% vs. <0.0~~1~~%), and night sweats (0.1% vs. <0.0~~1~~%).

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931~~,~~; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed

Comment [A1]: Pfizer-BioNTech response:

The Sponsor accepts this deletion.

Comment [A2]: Pfizer-BioNTech response:

The Sponsor proposes leaving the frequencies as originally proposed as we do not have a source table for non-serious AEs only, but rather any AEs including non-serious.

stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

~~*Non-Serious*~~ *Adverse Events*

In analyses of all events (including serious and non-serious unsolicited adverse events) in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, non-serious unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, non-serious unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection, non-serious unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87, one of which was serious) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Comment [A3]: FDA comment:

Pfizer,
Please ensure that the numbers in this paragraph only include the non-serious adverse events.

Comment [A4]: Pfizer-BioNTech response:

The Sponsor proposes retaining all events in this section as it is consistent with the data provided in the clinical study reports.

Comment [A5]: Pfizer-BioNTech comment:

The sponsor accepts the insertion of this text.

Comment [A6]: Pfizer-BioNTech comment:

The sponsor accepts this deletion.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Comment [A7]: Pfizer-BioNTech response:

The Sponsor accepts the revisions to this paragraph.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.

b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint.

Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

c. n2 = Number of participants at risk for the endpoint.

d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.~~76~~

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ctions or subsections omitted from the full prescribing information are
isted.

thawed and diluted prior to administration.
ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC
g (16)].
.

9% Sodium Chloride Injection, USP to form
diluent.
on, USP as the diluent. Do not use bacteriostatic 0.9%

USP are provided but shipped separately. Use the
Chloride Injection, USP as the diluent.
; discard after 1.8 mL is withdrawn.
njection, USP is used as the diluent, discard after

NATY using the same diluent vial.
6 doses of 0.3 mL each.
as in the panels below.

2

ake.
e liquid in the vaccine vial prior to
The liquid is a white to off-white
n and may contain white to off-white
morphous particles.
e if liquid is discolored or if other particles
ved.

se sterile 0.9% Sodium Chloride Injection,
e diluent.
1.8 mL of diluent into a transfer syringe
e or narrower needle).
mL of sterile 0.9% Sodium Chloride
USP into the vaccine vial.

vert the vial containing COMIRNATY
to mix.
ake.
e vaccine in the vial.
ine will be an off-white suspension. Do not
cine is discolored or contains particulate

e date and time of dilution on the
NATY vial label.
ween 2°C to 25°C (35°F to 77°F).
ny unused vaccine 6 hours after dilution.

4

. If standard syringes and needles are used, there may
ngle vial. Irrespective of the type of syringe and needle,

mnot provide a full dose of 0.3 mL, discard the vial and

r particulate matter and discoloration prior to
The vaccine will be an off-white suspension. Do not
e matter.

muscularly.

es of 2 doses (0.3 mL each) 3 weeks apart.

OMIRNATY with other COVID-19 vaccines to complete
ose of COMIRNATY should receive a second dose of

ration, a single dose is 0.3 mL.

own history of a severe allergic reaction (e.g.,
ee Description (11)].

5

istration of injectable vaccines, including
njury from fainting.

eiving immunosuppressant therapy, may have a

adverse reactions in participants 16 through 55 years of
8.6%), fatigue (70.1%), headache (64.9%), muscle pain
%), and injection site swelling (10.6%).

adverse reactions in participants 56 years of age and
78.2%), fatigue (56.9%), headache, (45.9%), muscle
n site swelling (11.8%), fever (11.5%), and injection

ng conditions, adverse reaction rates observed in the
o rates in the clinical trials of another vaccine and may

5

12,620 placebo) 16 years of age and older followed for

set were monitored for solicited local and systemic
ccination in an electronic diary. Participants are being
ous adverse events, throughout the study [from Dose 1
nths (serious adverse events) after the last vaccination].

imilar with regard to age, gender, race, and ethnicity
se who received placebo. Overall, among the total
bo, 50.9% were male, 49.1% were female, 79.3% were
and older, 82.0% were White, 9.6% were Black or
ere Asian, and 1.0% were American Indian or Alaska

Study 2

f reported solicited local and systemic reactions,
IRNATY and placebo in the subset of participants
tion who were monitored for reactogenicity with an

f reported solicited local and systemic reactions,
Y and placebo for participants 56 years of age and

g Dose 2, the mean duration of pain at the injection site
range 1 to 9 days), and for swelling 2.1 days (range 1 to
participants 56 years of age and older after receiving
as 2.4 days (range 1 to 36 days), for redness 3.0 days
to 34 days) for participants in the COMIRNATY group.

14 (14.2)	2101 (78.3)	312 (11.6)
91 (13.4)	1274 (47.5)	284 (10.6)
20 (0.7)	788 (29.4)	28 (1.0)
3 (0.1)	39 (1.5)	0

m Day 1 to Day 7 after vaccination.
6 through 55 years of age.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
n the column header.

.0 cm.
activity; Severe: prevents daily activity.

articipants with Solicited Systemic Reactions, by Each Dose – Participants 16 Through 55 Years of Population*

lacebo Dose 1 N^a=2908 n^b (%)	**COMIRNATY Dose 2 N^a=2682 n^b (%)**	**Placebo Dose 2 N^a=2684 n^b (%)**
5 (0.9)	440 (16.4)	11 (0.4)
6 (0.6)	254 (9.5)	5 (0.2)
5 (0.2)	146 (5.4)	4 (0.1)
4 (0.1)	39 (1.5)	2 (0.1)
0	1 (0.0)	0
0 (33.0)	1649 (61.5)	614 (22.9)
0 (19.6)	558 (20.8)	317 (11.8)
2 (12.8)	949 (35.4)	283 (10.5)
8 (0.6)	142 (5.3)	14 (0.5)

5 (0.2)	12 (0.4)	10 (0.4)
1 (0.0)	4 (0.1)	0
3 (11.1)	269 (10.0)	205 (7.6)
64 (9.1)	219 (8.2)	169 (6.3)
8 (2.0)	44 (1.6)	35 (1.3)
1 (0.0)	6 (0.2)	1 (0.0)
9 (11.3)	1055 (39.3)	237 (8.8)
81 (7.9)	441 (16.4)	150 (5.6)
6 (3.3)	552 (20.6)	84 (3.1)
2 (0.1)	62 (2.3)	3 (0.1)
68 (5.8)	638 (23.8)	147 (5.5)
12 (3.9)	291 (10.9)	82 (3.1)
5 (1.9)	320 (11.9)	61 (2.3)
1 (0.0)	27 (1.0)	4 (0.1)
8 (13.7)	1213 (45.2)	320 (11.9)

lected in the electronic diary (e-diary) from Day 1 to Day 7 after

ts 16 through 55 years of age.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
herefore, this information was included in the column header.

ce with activity; Severe: prevents daily activity.
Severe: requires intravenous hydration.
ls in 24 hours; Severe: 6 or more loose stools in 24 hours.
on.

185 (9.3)	1230 (66.1)	143 (7.8)
177 (8.9)	873 (46.9)	138 (7.5)
8 (0.4)	347 (18.7)	5 (0.3)
0	10 (0.5)	0

m Day 1 to Day 7 after vaccination.
6 years of age and older.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
n the column header.

.0 cm.
activity; Severe: prevents daily activity.

articipants with Solicited Systemic Reactions, by Each Dose – Participants 56 Years of Age and y Population*

Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
8 (0.4)	219 (11.8)	4 (0.2)
3 (0.2)	158 (8.5)	2 (0.1)
3 (0.2)	54 (2.9)	1 (0.1)
2 (0.1)	7 (0.4)	1 (0.1)
0	0	0

0

49 (2.5)	229 (12.3)	45 (2.5)
19 (1.0)	185 (9.9)	12 (0.7)
1 (0.1)	21 (1.1)	0
9 (0.5)	13 (0.7)	5 (0.3)
9 (0.5)	10 (0.5)	5 (0.3)
0	1 (0.1)	0
0	2 (0.1)	0
130 (6.5)	152 (8.2)	102 (5.6)
109 (5.5)	125 (6.7)	76 (4.1)
20 (1.0)	25 (1.3)	22 (1.2)
1 (0.1)	2 (0.1)	4 (0.2)
165 (8.3)	537 (28.9)	99 (5.4)
111 (5.6)	229 (12.3)	65 (3.5)
51 (2.6)	288 (15.5)	33 (1.8)
3 (0.2)	20 (1.1)	1 (0.1)
124 (6.2)	353 (19.0)	72 (3.9)
78 (3.9)	183 (9.8)	44 (2.4)
45 (2.3)	161 (8.7)	27 (1.5)
1 (0.1)	9 (0.5)	1 (0.1)
224 (11.3)	688 (37.0)	170 (9.3)

lected in the electronic diary (e-diary) from Day 1 to Day 7 after

s 56 years of age and older was fatigue.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. N for each
herefore was included in the column header.

2

age and older following any dose (COMIRNATY
tions not already captured by solicited local and
e (0.5% vs. 0.1%), asthenia (0.3% vs. 0.1%), lethargy
hyperhidrosis (0.1% vs. <0.0%), and night sweats

ge who had received at least 1 dose of vaccine or
rious adverse events from Dose 1 up to the participant
103 (0.8%) COMIRNATY recipients and 117 (0.9%)
56 years of age and older (COMIRNATY = 8,931;
by 165 (1.8%) COMIRNATY recipients and 151 (1.7%)
RNATY or placebo, respectively. In these analyses,
ow-up after Dose 2. Among participants with confirmed
up to the participant unblinding date in ongoing
ients and 2 (2%) placebo recipients.

there were no notable patterns between treatment
including neurologic, neuro-inflammatory, and
hip to COMIRNATY. In the analysis of unblinded
egories of serious adverse events that would suggest a

ous unsolicited adverse events) in Study 2 from Dose 1
rticipants had at least 4 months of follow-up after
who received at least one dose of study vaccine,
whom received placebo, non-serious unsolicited
nts in the COMIRNATY group and 2,136 (16.4%)
participants 56 years of age and older that included
ients, non-serious unsolicited adverse events were

n the analysis of unblinded follow-up, there were no
verse events that would suggest a causal relationship to

ring postmarketing use of COMIRNATY, including
ctions are reported voluntarily from a population of
ate their frequency or establish a causal relationship to

luding anaphylaxis, and other hypersensitivity reactions

in extremity (arm)

gnancy outcomes in women exposed to COMIRNATY
MIRNATY during pregnancy are encouraged to enroll
ing-study/covid19-vaccines/.

adverse outcomes. In the US general population, the
scarriage in clinically recognized pregnancies is 2% to
OMIRNATY administered to pregnant women are
ncy.

man milk. Data are not available to assess the effects of
tion/excretion. The developmental and health benefits
other's clinical need for COMIRNATY and any
MIRNATY or from the underlying maternal condition.
on is susceptibility to disease prevented by the vaccine.

s 16 through 17 years of age is based on safety and
dverse Reactions (6) and Clinical Studies (14.1)].

duals younger than 16 years of age have not been

y 2 as of March 13, 2021 (N = 22,026),
2% (n = 925) were 75 years of age and older *[see*
or effectiveness were observed between these

e suspension for injection for intramuscular use.
ltiple dose vials; each vial must be diluted with 1.8 mL
use to form the vaccine. Each dose of COMIRNATY
NA (mRNA) encoding the viral spike (S) glycoprotein

e following ingredients: lipids (0.43 mg
exyldecanoate), 0.05 mg 2-(polyethylene
stearoyl-sn-glycero-3-phosphocholine, and 0.2 mg

rtility

o cause carcinogenicity, genotoxicity, or impairment of
ith COMIRNATY there were no vaccine-related
s (8.1)].

mized, placebo-controlled, observer-blind, dose-finding,
ipants 12 years of age and older. Randomization was
55 years of age, or 56 years of age and older, with a
. The study excluded participants who were
al or microbiological diagnosis of COVID-19.
isease not requiring significant change in therapy or
before enrollment, were included as were participants
(HCV), or hepatitis B virus (HBV).

21, approximately 44,000 participants 16 years of age
of COMIRNATY or placebo. Participants are planned
afety and efficacy against COVID-19.

IIRNATY or placebo, 51.4% or 50.3% were male and
through 64 years of age, 20.9% or 20.8% were 65 years
9.6% were Black or African American, 1.0% or 0.9%
were Asian, 0.3% or 0.2% Native Hawaiian or other
73.9% or 74.1% were non-Hispanic/Latino, 0.5% or
rbidities [participants who have 1 or more
disease: defined as subjects who had at least one of the
x (BMI) ≥30 kg/m^2], respectively. The mean age at

6

s in the placebo group.

included participants 16 years of age and older who
the development of COVID-19 during blinded
epresenting up to 6 months of follow-up after Dose 2.
JATY group and 12,449 (58.7%) in the placebo group
ebo-controlled follow-up period.

D-19 cases in this study include B.1.1.7 (Alpha) and
ong cases in vaccine versus placebo recipients did not
riants.

Table 5.

rence From 7 Days After Dose 2, by Age Subgroup – Without Evidence of Infection and Participants With 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Follow-up Period

Dose 2 in participants without evidence of prior -2 infection*		
	Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])	**Vaccine Efficacy % (95% CI[e])**
n2[d])		
	833 5.857 (19,741)	91.1 (88.8, 93.1)
	709 4.654 (15,515)	90.5 (87.9, 92.7)
	124 1.202 (4226)	94.5 (88.3, 97.8)

oint across all participants within each group at risk for the endpoint.
se 2 to the end of the surveillance period.

ed based on the Clopper and Pearson method adjusted to the

by small numbers of cases in some subgroups) did not
rs, ethnic groups, geographies, or for participants with
sk of severe COVID-19.

rted benefit of COMIRNATY in preventing severe
is presented only for participants with or without prior
counts in participants without prior SARS-CoV-2
without prior SARS-CoV-2 infection in both the

Occurrence in Participants 16 Years of Age and -2 Infection Based on Protocol[†] or Centers for efinition From 7 Days After Dose 2 – Evaluable lacebo-Controlled Follow-up

vere COVID-19 Occurrence		
n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
	21 6.237 (20,629)	95.3 (70.9, 99.9)

astolic blood pressure <60 mm Hg, or requiring vasopressors);

OVID-19 and presence of at least 1 of the following:

oint across all participants within each group at risk for the endpoint.
se 2 to the end of the surveillance period.

l based on the Clopper and Pearson method adjusted to the

Multiple Dose Vials are supplied in a carton containing
tiple dose vials (NDC 0069-1000-02). A 0.9% Sodium
separately, and should be stored at controlled room
trolled Room Temperature]. The provided 0.9% Sodium
s cartons of 10 mL single-use vials manufactured by
ials manufactured by Fresenius Kabi USA, LLC

void exposure to direct sunlight and ultraviolet light.

ng vials cannot be transported at -90°C to -60°C
15°C (-13°F to 5°F). Any hours used for transport
k limit for storage at -25°C to -15°C (-13°F to 5°F).
) may be returned 1 time to the recommended storage

ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of
tively, to thaw in the refrigerator, whereas a fewer

ature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials

o more than 2 hours.

ed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

0

aers.hhs.gov.

most recent prescribing information, please visit

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

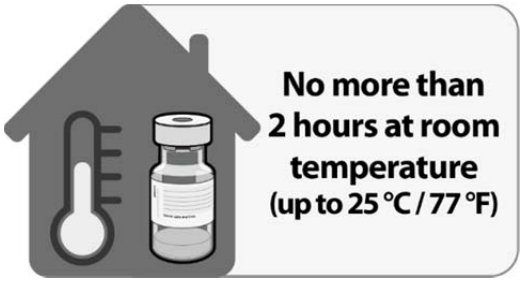
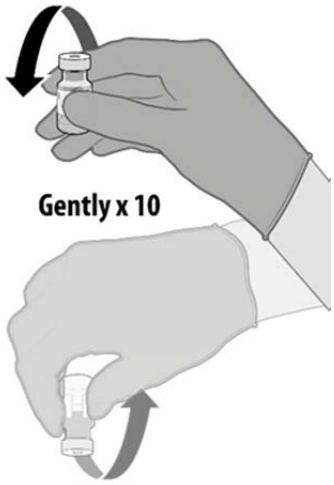
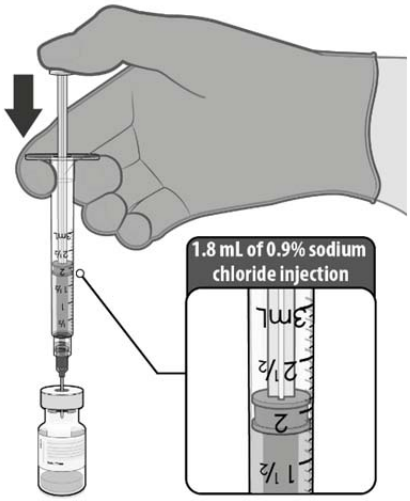
2.1 Preparation for Administration

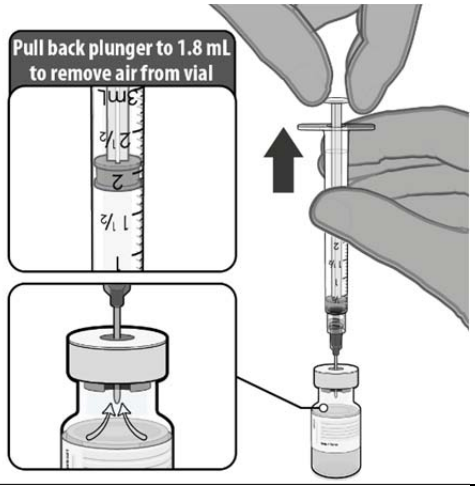
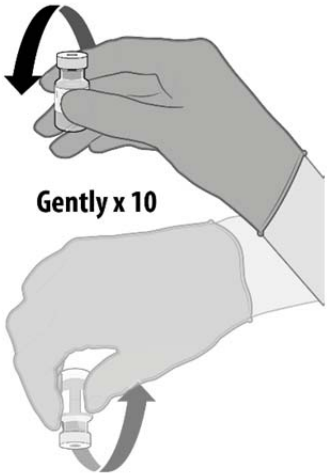
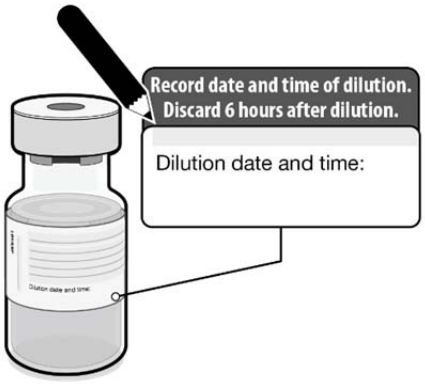
Prior to Dilution

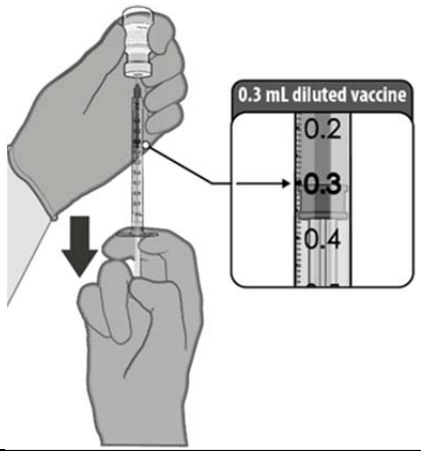
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of ~~serious and~~ all adverse events (including serious and non-serious unsolicited adverse events) reported through 1 month after Dose 2 in participants 16 through 55 years of age following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.4% vs. 0.5%), malaise (0.7% vs. 0.1%), asthenia (0.4% vs. 0.1%), decreased appetite (0.2% vs. <0.0~~1~~%), hyperhidrosis (0.1% vs. <0.0~~1~~%), lethargy (0.1% vs. <0.0~~1~~%), and night sweats (0.1% ~~-~~vs. <0.0~~1~~%).

In an analysis of all adverse events (including serious and non-serious unsolicited adverse events) reported through 1 month after Dose 2 in participants 56 years of age and older following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.0% vs. 0.3%), malaise (0.5% vs. 0.1%), asthenia (0.3% vs. 0.1%), lethargy (0.2% vs. <0.0~~1~~%), decreased appetite (0.1% vs. <0.0~~1~~%), hyperhidrosis (0.1% vs. <0.0~~1~~%), and night sweats (0.1% vs. <0.0~~1~~%).

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931~~,~~; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed

stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

~~*Non-Serious*~~ *Adverse Events*

In analyses of all events (including serious and non-serious unsolicited adverse events) in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, non-serious unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, non-serious unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection, non-serious unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87, one of which was serious) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.

b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint.

Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

c. n2 = Number of participants at risk for the endpoint.

d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.7~~6~~

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

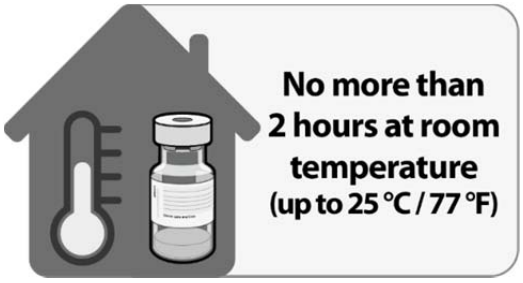
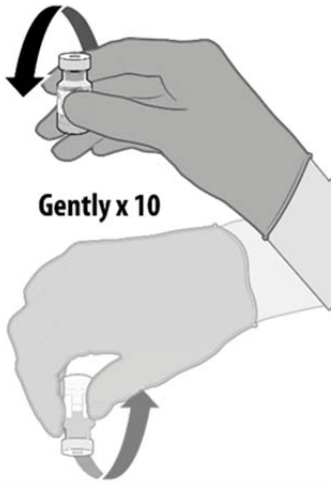
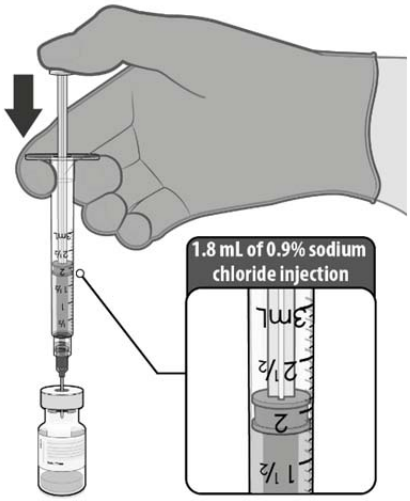
2.1 Preparation for Administration

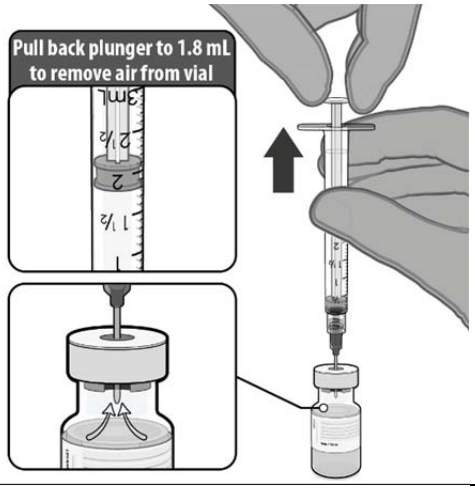
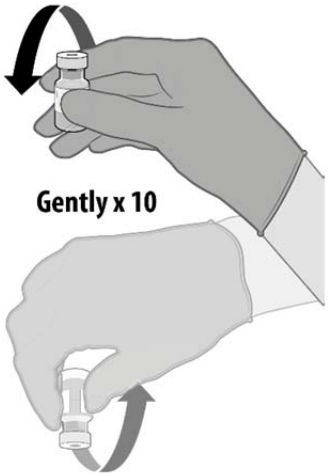
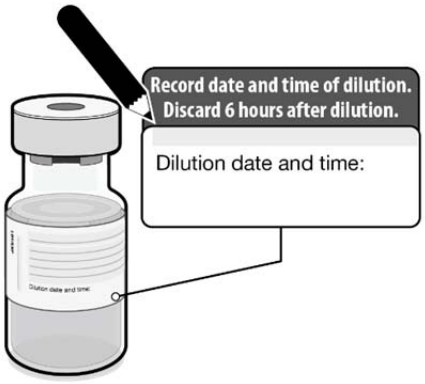
Prior to Dilution

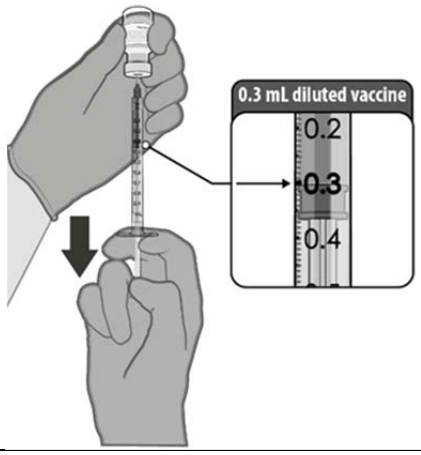
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of all unsolicited adverse events reported through 1 month after Dose 2 in 43,847 (21,926 COMIRNATY; 21,921 placebo) participants 16 years of age and older following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (274 vs. 87), malaise (130 vs. 22), lymphadenopathy (83 vs. 7), asthenia (76 vs. 25), decreased appetite (39 vs. 9), hyperhidrosis 31 vs. 9), lethargy (25 vs. 6), and night sweats (17 vs. 3).

In analyses of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, non-serious unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, non-serious unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection, non-serious unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to

determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to

4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more

comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by

Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.8

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE ----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

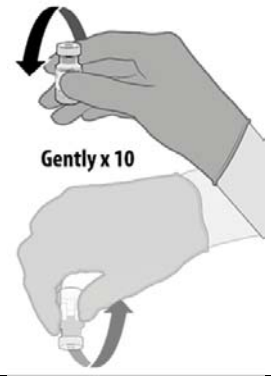
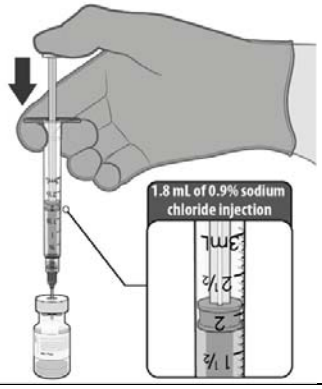
2.1 Preparation for Administration

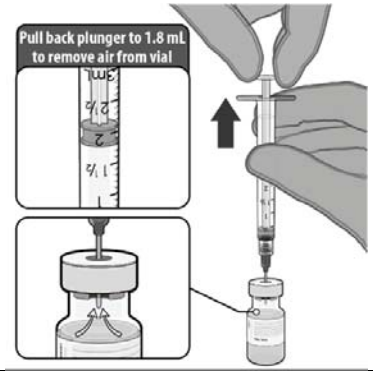
Prior to Dilution

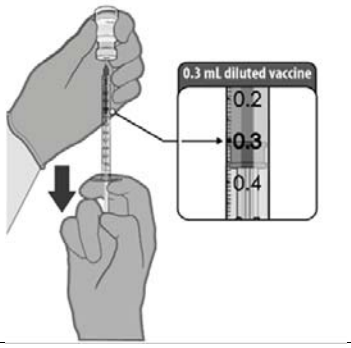
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • <u>Do not shake</u>. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

~~In an analysis of all adverse events (including serious and non-serious unsolicited adverse events) reported through 1 month after Dose 2 in participants 16 through 55 years of age following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.4% vs. 0.5%), malaise (0.7% vs. 0.1%), asthenia (0.4% vs. 0.1%), decreased appetite (0.2% vs. <0.01%), hyperhidrosis (0.1% vs. <0.01%), lethargy (0.1% vs. <0.01%), and night sweats (0.1% vs. <0.01%).~~

~~In an analysis of all adverse events (including serious and non-serious unsolicited adverse events) reported through 1 month after Dose 2 in participants 56 years of age and older following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (1.0% vs. 0.3%), malaise (0.5% vs. 0.1%), asthenia (0.3% vs. 0.1%), lethargy (0.2% vs. <0.01%), decreased appetite (0.1% vs. <0.01%), hyperhidrosis (0.1% vs. <0.01%), and night sweats (0.1% vs. <0.01%).~~

In an analysis of all unsolicited adverse events reported through 1 month after Dose 2 in 43,847 (21,926 COMIRNATY; 21,921 placebo) participants 16 years of age and older following any dose (COMIRNATY group vs. placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (274 vs. 87), malaise (130 vs. 22), lymphadenopathy (83 vs. 7), asthenia (76 vs. 25), decreased appetite (39 vs. 9), hyperhidrosis 31 vs. 9), lethargy (25 vs. 6), and night sweats (17 vs. 3).

In analyses of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, non-serious unsolicited adverse events were reported by 4,396 (33.8%)

Comment [A1]: FDA comment:

Pfizer,
Instead of presenting percentages for the two age groups separately, report the number of subjects (16 years of age and older) in the vaccine group and the placebo group reporting each event. Please also include lymphadenopathy and delete the sentence pertaining to lymphadenopathy below.

Comment [A2]: Pfizer-BioNTech response:

The Sponsor accepts and has added the paragraph below.

Source:

Interim Report – 6 Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals (April 2021), Table 30. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

Comment [A3]: Pfizer-BioNTech response:

The Sponsor accepts FDA's movement of the Serious Adverse Events paragraphs to end of section.

Comment [A4]: Pfizer-BioNTech response:

The Sponsor accepts this revision.

participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, non-serious unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection, non-serious unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Comment [A5]: Pfizer-BioNTech response:

The Sponsor accepts this deletion and has included lymphadenopathy above.

Comment [A6]: Pfizer-BioNTech response:

The Sponsor accepts the movement of this section from above.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.

b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint.

Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

c. n2 = Number of participants at risk for the endpoint.

d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.8~~7~~

US Govt. License No. x

ctions or subsections omitted from the full prescribing information are
isted.

thawed and diluted prior to administration.
ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC
g (16)].
.

9% Sodium Chloride Injection, USP to form
diluent.
on, USP as the diluent. Do not use bacteriostatic 0.9%

USP are provided but shipped separately. Use the
Chloride Injection, USP as the diluent.
; discard after 1.8 mL is withdrawn.
njection, USP is used as the diluent, discard after

NATY using the same diluent vial.
6 doses of 0.3 mL each.
as in the panels below.

2

ake.
e liquid in the vaccine vial prior to
The liquid is a white to off-white
n and may contain white to off-white
morphous particles.
e if liquid is discolored or if other particles
ved.

se sterile 0.9% Sodium Chloride Injection,
e diluent.
1.8 mL of diluent into a transfer syringe
e or narrower needle).
mL of sterile 0.9% Sodium Chloride
USP into the vaccine vial.

vert the vial containing COMIRNATY
to mix.
ake.
e vaccine in the vial.
ine will be an off-white suspension. Do not
cine is discolored or contains particulate

e date and time of dilution on the
NATY vial label.
ween 2°C to 25°C (35°F to 77°F).
ny unused vaccine 6 hours after dilution.

4

. If standard syringes and needles are used, there may
ngle vial. Irrespective of the type of syringe and needle,

mnot provide a full dose of 0.3 mL, discard the vial and

r particulate matter and discoloration prior to
The vaccine will be an off-white suspension. Do not
e matter.

muscularly.

es of 2 doses (0.3 mL each) 3 weeks apart.

OMIRNATY with other COVID-19 vaccines to complete
ose of COMIRNATY should receive a second dose of

ration, a single dose is 0.3 mL.

own history of a severe allergic reaction (e.g.,
ee Description (11)].

5

istration of injectable vaccines, including
njury from fainting.

eiving immunosuppressant therapy, may have a

adverse reactions in participants 16 through 55 years of
8.6%), fatigue (70.1%), headache (64.9%), muscle pain
%), and injection site swelling (10.6%).

adverse reactions in participants 56 years of age and
78.2%), fatigue (56.9%), headache, (45.9%), muscle
n site swelling (11.8%), fever (11.5%), and injection

ng conditions, adverse reaction rates observed in the
o rates in the clinical trials of another vaccine and may

5

12,620 placebo) 16 years of age and older followed for

set were monitored for solicited local and systemic
ccination in an electronic diary. Participants are being
ous adverse events, throughout the study [from Dose 1
nths (serious adverse events) after the last vaccination].

imilar with regard to age, gender, race, and ethnicity
se who received placebo. Overall, among the total
bo, 50.9% were male, 49.1% were female, 79.3% were
and older, 82.0% were White, 9.6% were Black or
ere Asian, and 1.0% were American Indian or Alaska

Study 2

f reported solicited local and systemic reactions,
IRNATY and placebo in the subset of participants
tion who were monitored for reactogenicity with an

f reported solicited local and systemic reactions,
Y and placebo for participants 56 years of age and

g Dose 2, the mean duration of pain at the injection site
range 1 to 9 days), and for swelling 2.1 days (range 1 to
participants 56 years of age and older after receiving
as 2.4 days (range 1 to 36 days), for redness 3.0 days
to 34 days) for participants in the COMIRNATY group.

14 (14.2)	2101 (78.3)	312 (11.6)
91 (13.4)	1274 (47.5)	284 (10.6)
20 (0.7)	788 (29.4)	28 (1.0)
3 (0.1)	39 (1.5)	0

m Day 1 to Day 7 after vaccination.
6 through 55 years of age.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
n the column header.

.0 cm.
activity; Severe: prevents daily activity.

articipants with Solicited Systemic Reactions, by Each Dose – Participants 16 Through 55 Years of Population*

lacebo Dose 1 N^a=2908 n^b (%)	**COMIRNATY Dose 2 N^a=2682 n^b (%)**	**Placebo Dose 2 N^a=2684 n^b (%)**
5 (0.9)	440 (16.4)	11 (0.4)
6 (0.6)	254 (9.5)	5 (0.2)
5 (0.2)	146 (5.4)	4 (0.1)
4 (0.1)	39 (1.5)	2 (0.1)
0	1 (0.0)	0
0 (33.0)	1649 (61.5)	614 (22.9)
0 (19.6)	558 (20.8)	317 (11.8)
2 (12.8)	949 (35.4)	283 (10.5)
8 (0.6)	142 (5.3)	14 (0.5)

5 (0.2)	12 (0.4)	10 (0.4)
1 (0.0)	4 (0.1)	0
3 (11.1)	269 (10.0)	205 (7.6)
64 (9.1)	219 (8.2)	169 (6.3)
8 (2.0)	44 (1.6)	35 (1.3)
1 (0.0)	6 (0.2)	1 (0.0)
9 (11.3)	1055 (39.3)	237 (8.8)
81 (7.9)	441 (16.4)	150 (5.6)
6 (3.3)	552 (20.6)	84 (3.1)
2 (0.1)	62 (2.3)	3 (0.1)
68 (5.8)	638 (23.8)	147 (5.5)
12 (3.9)	291 (10.9)	82 (3.1)
5 (1.9)	320 (11.9)	61 (2.3)
1 (0.0)	27 (1.0)	4 (0.1)
8 (13.7)	1213 (45.2)	320 (11.9)

lected in the electronic diary (e-diary) from Day 1 to Day 7 after

ts 16 through 55 years of age.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
herefore, this information was included in the column header.

ce with activity; Severe: prevents daily activity.
Severe: requires intravenous hydration.
ls in 24 hours; Severe: 6 or more loose stools in 24 hours.
on.

185 (9.3)	1230 (66.1)	143 (7.8)
177 (8.9)	873 (46.9)	138 (7.5)
8 (0.4)	347 (18.7)	5 (0.3)
0	10 (0.5)	0

m Day 1 to Day 7 after vaccination.
6 years of age and older.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
n the column header.

.0 cm.
activity; Severe: prevents daily activity.

articipants with Solicited Systemic Reactions, by Each Dose – Participants 56 Years of Age and y Population*

Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
8 (0.4)	219 (11.8)	4 (0.2)
3 (0.2)	158 (8.5)	2 (0.1)
3 (0.2)	54 (2.9)	1 (0.1)
2 (0.1)	7 (0.4)	1 (0.1)
0	0	0

0

49 (2.5)	229 (12.3)	45 (2.5)
19 (1.0)	185 (9.9)	12 (0.7)
1 (0.1)	21 (1.1)	0
9 (0.5)	13 (0.7)	5 (0.3)
9 (0.5)	10 (0.5)	5 (0.3)
0	1 (0.1)	0
0	2 (0.1)	0
130 (6.5)	152 (8.2)	102 (5.6)
109 (5.5)	125 (6.7)	76 (4.1)
20 (1.0)	25 (1.3)	22 (1.2)
1 (0.1)	2 (0.1)	4 (0.2)
165 (8.3)	537 (28.9)	99 (5.4)
111 (5.6)	229 (12.3)	65 (3.5)
51 (2.6)	288 (15.5)	33 (1.8)
3 (0.2)	20 (1.1)	1 (0.1)
124 (6.2)	353 (19.0)	72 (3.9)
78 (3.9)	183 (9.8)	44 (2.4)
45 (2.3)	161 (8.7)	27 (1.5)
1 (0.1)	9 (0.5)	1 (0.1)
224 (11.3)	688 (37.0)	170 (9.3)

lected in the electronic diary (e-diary) from Day 1 to Day 7 after

s 56 years of age and older was fatigue.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. N for each
herefore was included in the column header.

1 group and 11,516 (51.4%) participants in the
<6 months after Dose 2 in the blinded
,778 (8.1%) and 1,304 (5.9%) with ≥6 months of
o groups, respectively.

ized to COMIRNATY had ≥6 months total (blinded

~~d non-serious unsolicited adverse events) reported~~
~~55 years of age following any dose (COMIRNATY~~
~~tions not already captured by solicited local and~~
~~e (0.7% vs. 0.1%), asthenia (0.4% vs. 0.1%), decreased~~
~~01%), lethargy (0.1% vs. <0.01%), and night sweats~~

~~d non-serious unsolicited adverse events) reported~~
~~age and older following any dose (COMIRNATY~~
~~tions not already captured by solicited local and~~
~~e (0.5% vs. 0.1%), asthenia (0.3% vs. 0.1%), lethargy~~
~~%), hyperhidrosis (0.1% vs. <0.01%), and night sweats~~

through 1 month after Dose 2 in 43,847
years of age and older following any dose
d as adverse reactions not already captured by solicited
alaise (130 vs. 22), lymphadenopathy (83 vs. 7),
hidrosis 31 vs. 9), lethargy (25 vs. 6), and night sweats

rom Dose 1 up to the participant unblinding date,
ow-up after Dose- 2. Among participants 16 through
vaccine, 12,995- of whom received COMIRNATY and
ed adverse events were reported by 4,396 (33.8%)

n the analysis of unblinded follow-up, there were no
verse events that would suggest a causal relationship to

ge who had received at least 1 dose of vaccine or
rious adverse events from Dose 1 up to the participant
103 (0.8%) COMIRNATY recipients and 117 (0.9%)
56 years of age and older (COMIRNATY = 8,931;
by 165 (1.8%) COMIRNATY recipients and 151 (1.7%)
RNATY or placebo, respectively. In these analyses,
ow-up after Dose 2. Among participants with confirmed
up to the participant unblinding date in ongoing
ients and 2 (2%) placebo recipients.

there were no notable patterns between treatment
including neurologic, neuro-inflammatory, and
hip to COMIRNATY. In the analysis of unblinded
egories of serious adverse events that would suggest a

ring postmarketing use of COMIRNATY, including
ctions are reported voluntarily from a population of
ate their frequency or establish a causal relationship to

scarriage in clinically recognized pregnancies is 2% to
OMIRNATY administered to pregnant women are
ncy.

emale rats administered the equivalent of a single
or to mating and twice during gestation. These studies
cine *(see Animal Data)*.

formulation containing the same quantity of
A) (30 mcg) and other ingredients included in a single
le rats by the intramuscular route on 4 occasions: 21
20. No vaccine-related adverse effects on female
ere reported in the study.

man milk. Data are not available to assess the effects of
tion/excretion. The developmental and health benefits
other's clinical need for COMIRNATY and any
MIRNATY or from the underlying maternal condition.
on is susceptibility to disease prevented by the vaccine.

e suspension for injection for intramuscular use.
ltiple dose vials; each vial must be diluted with 1.8 mL
use to form the vaccine. Each dose of COMIRNATY
NA (mRNA) encoding the viral spike (S) glycoprotein

e following ingredients: lipids (0.43 mg
exyldecanoate), 0.05 mg 2-(polyethylene
stearoyl-sn-glycero-3-phosphocholine, and 0.2 mg
basic potassium phosphate, 0.36 mg sodium chloride,
sucrose. The diluent (0.9% Sodium Chloride Injection,
per dose.

rmulated in lipid particles, which enable delivery of the
CoV-2 S antigen. The vaccine elicits an immune
D-19.

rtility

o cause carcinogenicity, genotoxicity, or impairment of
with COMIRNATY there were no vaccine-related
ns (8.1)].

5

IRNATY or placebo, 51.4% or 50.3% were male and
through 64 years of age, 20.9% or 20.8% were 65 years
9.6% were Black or African American, 1.0% or 0.9%
were Asian, 0.3% or 0.2% Native Hawaiian or other
73.9% or 74.1% were non-Hispanic/Latino, 0.5% or
rbidities [participants who have 1 or more
disease: defined as subjects who had at least one of the
x (BMI) ≥30 kg/m^2], respectively. The mean age at
51.0 or 51.0 in participants who received

fied primary efficacy endpoint included
the COMIRNATY group and 18,379 in the placebo
n SARS-CoV-2 through 7 days after the second dose.
icacy analysis included all participants 12 years of age
d followed for the development of COVID-19 through
age and 56 years of age and older began enrollment
rollment from September 16, 2020, and 12 through
0.

tion prior to 7 days after Dose 2, vaccine efficacy
fter Dose 2 was 95.0% (95% credible interval: 90.3,
case split was 8 COVID-19 cases in the
s in the placebo group.

included participants 16 years of age and older who
the development of COVID-19 during blinded
epresenting up to 6 months of follow-up after Dose 2.
IATY group and 12,449 (58.7%) in the placebo group
ebo-controlled follow-up period.

	833 5.857 (19,741)	91.1 (88.8, 93.1)
	709 4.654 (15,515)	90.5 (87.9, 92.7)
	124 1.202 (4226)	94.5 (88.3, 97.8)

2 in participants with or without* evidence of prior -2 infection

n2[d])	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
	854 6.110 (20,595)	90.9 (88.5, 92.8)
	726 4.879 (16,269)	90.2 (87.5, 92.4)
	128 1.232 (4326)	94.7 (88.7, 97.9)

Polymerase Chain Reaction (RT-PCR) and at least 1 symptom
eased cough; new or increased shortness of breath; chills; new or
hea; vomiting).
n (i.e., N-binding antibody [serum] negative at Visit 1 and
d 2), and had negative NAAT (nasal swab) at any unscheduled visit

oint across all participants within each group at risk for the endpoint.
se 2 to the end of the surveillance period.

ed based on the Clopper and Pearson method adjusted to the

	Placebo Cases n1[a] Surveillance Time[b] (n2[c])	Vaccine Efficacy % (95% CI[d])
n2[c])		
	21 6.237 (20,629)	95.3 (70.9, 99.9)
-19 Occurrence Based on CDC Definition		
	Placebo Cases n1[a] Surveillance Time[b] (n2[c])	**Vaccine Efficacy % (95% CI[d])**
n2[c])		
	31 6.225 (20,593)	100 (87.6, 100.0)

Polymerase Chain Reaction (RT-PCR) and at least 1 symptom
eased cough; new or increased shortness of breath; chills; new or
hea; vomiting).
n (i.e., N-binding antibody [serum] negative at Visit 1 and
d 2), and had negative NAAT (nasal swab) at any unscheduled visit

med COVID-19 and presence of at least 1 of the following:
respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per
l, or ratio of arterial oxygen partial pressure to fractional inspired

noninvasive ventilation, mechanical ventilation or extracorporeal

astolic blood pressure <60 mm Hg, or requiring vasopressors);

OVID-19 and presence of at least 1 of the following:

oint across all participants within each group at risk for the endpoint.

thermal containers with dry ice. Once received, remove
and preferably store in an ultra-low temperature freezer
y date printed on the label. Alternatively, vials may be
s. Vials must be kept frozen and protected from light, in
5°C to -15°C (-13°F to 5°F) for up to 2 weeks may be
f -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative
) should be tracked and should not exceed 2 weeks.

hermal container in which COMIRNATY arrives may
to the top of the container with dry ice. Refer to the
ner for instructions regarding the use of the thermal
maintains a temperature range of -90ºC to -60ºC (-130ºF
141°F to -76°F) is not considered an excursion from

ng vials cannot be transported at -90°C to -60°C
15°C (-13°F to 5°F). Any hours used for transport
k limit for storage at -25°C to -15°C (-13°F to 5°F).
) may be returned 1 time to the recommended storage

9

ed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

77°F) and use within 6 hours from the time of dilution.
void exposure to direct sunlight and ultraviolet light.
6 hours. Do not refreeze.

ks of vaccination with COMIRNATY.

g the two dose vaccination series.

Y. Encourage individuals exposed to COMIRNATY
gister by visiting https://mothertobaby.org/ongoing-

their healthcare provider or to the Vaccine Adverse
aers.hhs.gov.

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HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

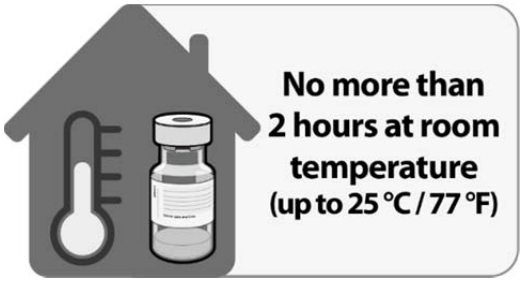
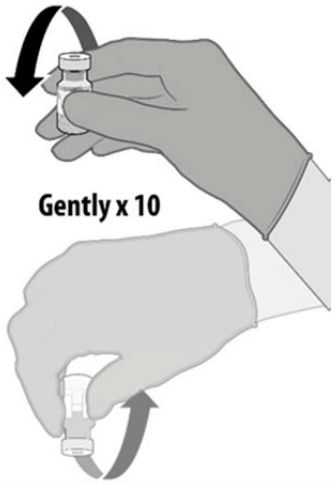
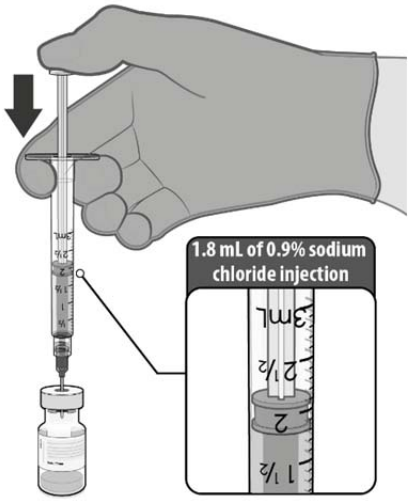
2.1 Preparation for Administration

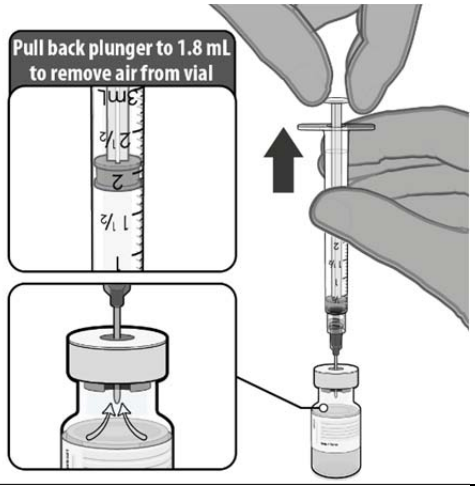
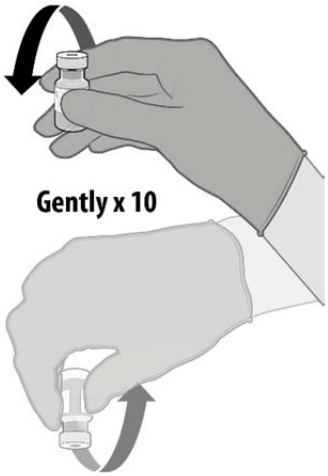
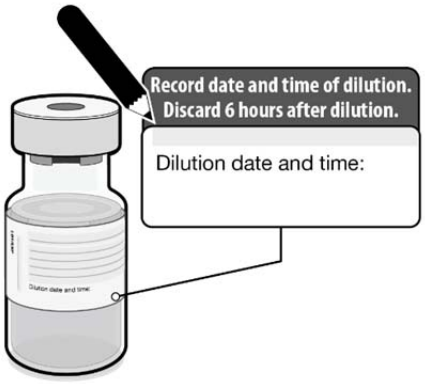
Prior to Dilution

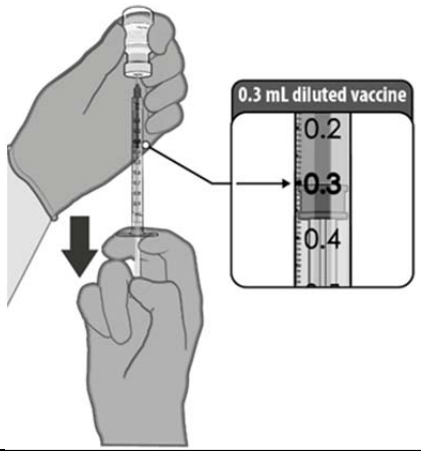
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of all unsolicited adverse events reported following any dose, through 1 month after Dose 2, in participants 16 years of age and older (N=43,847; 21,926 COMIRNATY group vs. 21,921 placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (274 vs. 87), malaise (130 vs. 22), lymphadenopathy (83 vs. 7), asthenia (76 vs. 25), decreased appetite (39 vs. 9), hyperhidrosis (31 vs. 9), lethargy (25 vs. 6), and night sweats (17 vs. 3).

In analyses of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection that included 100 COMIRNATY recipients and 100 placebo recipients, unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there

were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to

4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Specific Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more

comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by

Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
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Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.9

US Govt. License No. x

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

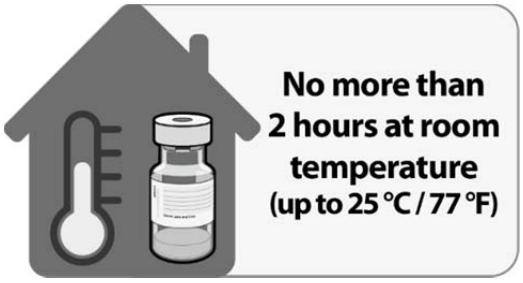
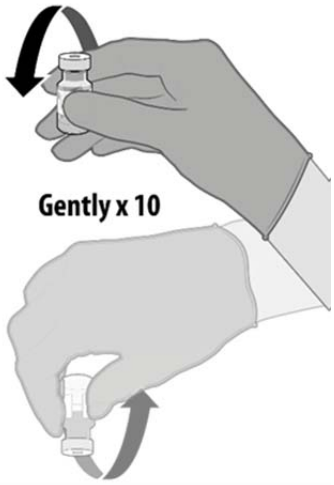
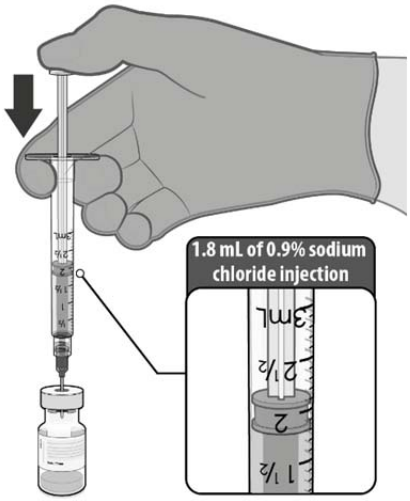
2.1 Preparation for Administration

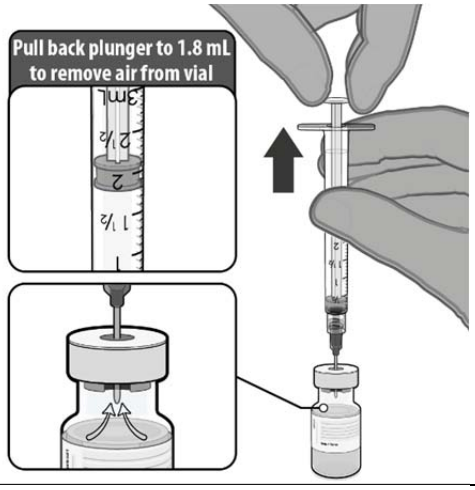
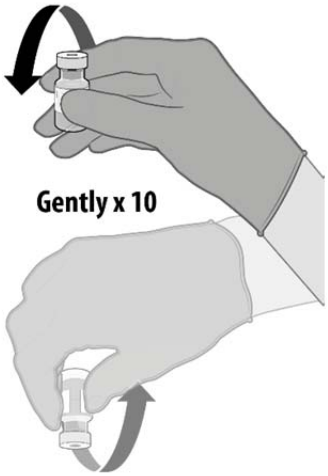
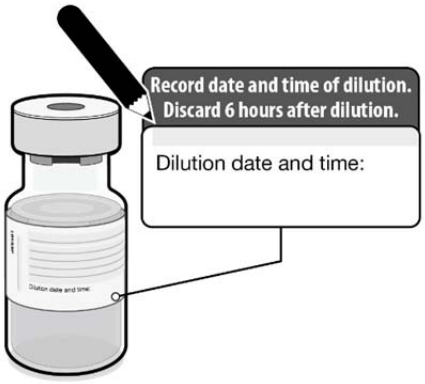
Prior to Dilution

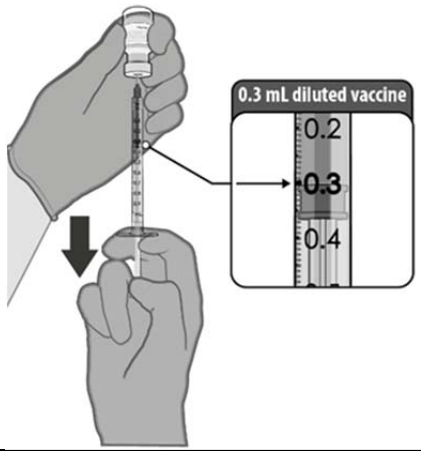
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of all unsolicited adverse events reported following any dose, through 1 month after Dose 2, in participants 16 years of age and older (N=43,847; 21,926 COMIRNATY group vs. 21,921 placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (274 vs. 87), malaise (130 vs. 22), lymphadenopathy (83 vs. 7), asthenia (76 vs. 25), decreased appetite (39 vs. 9), hyperhidrosis (31 vs. 9), lethargy (25 vs. 6), and night sweats (17 vs. 3).

In analyses of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection that included 100 COMIRNATY recipients and 100 placebo recipients, unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited ~~non-serious~~ adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there

were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to

4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Specific Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more

comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by

Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
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55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.9~~8~~

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HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE ----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

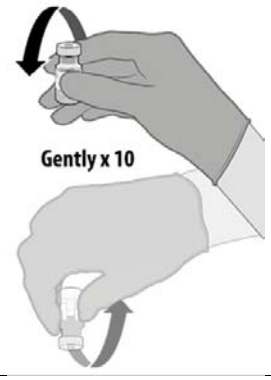
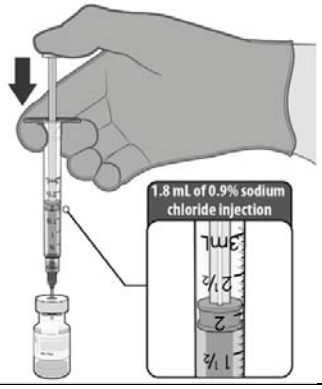
2.1 Preparation for Administration

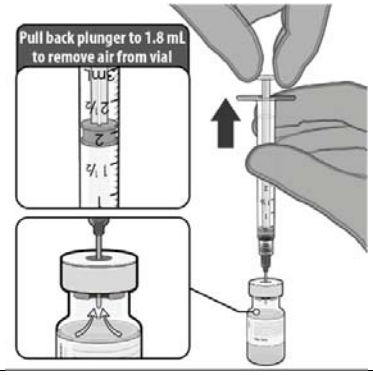
Prior to Dilution

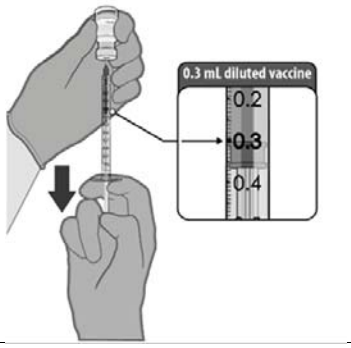
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • <u>Do not shake</u>. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of all unsolicited adverse events reported following any dose, through 1 month after Dose 2, in participants 16 years of age and older (N=43,847; 21,926 COMIRNATY group vs. 21,921 placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (274 vs. 87), malaise (130 vs. 22), lymphadenopathy (83 vs. 7), asthenia (76 vs. 25), decreased appetite (39 vs. 9), hyperhidrosis (31 vs. 9), lethargy (25 vs. 6), and night sweats (17 vs. 3).

In analyses of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection that included 100 COMIRNATY recipients and 100 placebo recipients, unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited ~~non-serious~~ adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there

Comment [A1]: Pfizer-BioNTech response: Sponsor accepts FDA's editorial revision to this sentence.

Comment [A2]: Pfizer-BioNTech response: Sponsor accepts FDA's editorial revision to this sentence.

Comment [A3]: Pfizer-BioNTech response: Sponsor accepts FDA's editorial revision to this sentence.

Comment [A4]: Pfizer-BioNTech response: Sponsor accepts FDA's editorial revision to this sentence.

Comment [A5]: Pfizer-BioNTech response: Sponsor accepts FDA's editorial revision to this sentence.
Table 14.84

Comment [A6]: Pfizer-BioNTech response: Sponsor proposes deletion of "non-serious" for consistency.

were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to

4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Specific Populations (8.1)]*.

Comment [A7]:
Pfizer-BioNTech response:
Sponsor accepts FDA's correction of section title.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more

comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by

Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

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thawed and diluted prior to administration.
ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC
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9% Sodium Chloride Injection, USP to form
diluent.
on, USP as the diluent. Do not use bacteriostatic 0.9%

USP are provided but shipped separately. Use the
Chloride Injection, USP as the diluent.
; discard after 1.8 mL is withdrawn.
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NATY using the same diluent vial.
6 doses of 0.3 mL each.
as in the panels below.

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n and may contain white to off-white
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e or narrower needle).
mL of sterile 0.9% Sodium Chloride
USP into the vaccine vial.

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ine will be an off-white suspension. Do not
cine is discolored or contains particulate

e date and time of dilution on the
NATY vial label.
ween 2°C to 25°C (35°F to 77°F).
ny unused vaccine 6 hours after dilution.

4

. If standard syringes and needles are used, there may
ngle vial. Irrespective of the type of syringe and needle,

mnot provide a full dose of 0.3 mL, discard the vial and

r particulate matter and discoloration prior to
The vaccine will be an off-white suspension. Do not
e matter.

muscularly.

es of 2 doses (0.3 mL each) 3 weeks apart.

OMIRNATY with other COVID-19 vaccines to complete
ose of COMIRNATY should receive a second dose of

ration, a single dose is 0.3 mL.

own history of a severe allergic reaction (e.g.,
ee Description (11)].

5

istration of injectable vaccines, including
njury from fainting.

eiving immunosuppressant therapy, may have a

adverse reactions in participants 16 through 55 years of
8.6%), fatigue (70.1%), headache (64.9%), muscle pain
%), and injection site swelling (10.6%).

adverse reactions in participants 56 years of age and
78.2%), fatigue (56.9%), headache, (45.9%), muscle
n site swelling (11.8%), fever (11.5%), and injection

ng conditions, adverse reaction rates observed in the
o rates in the clinical trials of another vaccine and may

5

12,620 placebo) 16 years of age and older followed for

set were monitored for solicited local and systemic
ccination in an electronic diary. Participants are being
ous adverse events, throughout the study [from Dose 1
nths (serious adverse events) after the last vaccination].

imilar with regard to age, gender, race, and ethnicity
se who received placebo. Overall, among the total
bo, 50.9% were male, 49.1% were female, 79.3% were
and older, 82.0% were White, 9.6% were Black or
ere Asian, and 1.0% were American Indian or Alaska

Study 2

f reported solicited local and systemic reactions,
IRNATY and placebo in the subset of participants
tion who were monitored for reactogenicity with an

f reported solicited local and systemic reactions,
Y and placebo for participants 56 years of age and

g Dose 2, the mean duration of pain at the injection site
range 1 to 9 days), and for swelling 2.1 days (range 1 to
participants 56 years of age and older after receiving
as 2.4 days (range 1 to 36 days), for redness 3.0 days
to 34 days) for participants in the COMIRNATY group.

14 (14.2)	2101 (78.3)	312 (11.6)
91 (13.4)	1274 (47.5)	284 (10.6)
20 (0.7)	788 (29.4)	28 (1.0)
3 (0.1)	39 (1.5)	0

m Day 1 to Day 7 after vaccination.
6 through 55 years of age.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
n the column header.

.0 cm.
activity; Severe: prevents daily activity.

articipants with Solicited Systemic Reactions, by Each Dose – Participants 16 Through 55 Years of Population*

lacebo Dose 1 N^a=2908 n^b (%)	**COMIRNATY Dose 2 N^a=2682 n^b (%)**	**Placebo Dose 2 N^a=2684 n^b (%)**
5 (0.9)	440 (16.4)	11 (0.4)
6 (0.6)	254 (9.5)	5 (0.2)
5 (0.2)	146 (5.4)	4 (0.1)
4 (0.1)	39 (1.5)	2 (0.1)
0	1 (0.0)	0
0 (33.0)	1649 (61.5)	614 (22.9)
0 (19.6)	558 (20.8)	317 (11.8)
2 (12.8)	949 (35.4)	283 (10.5)
8 (0.6)	142 (5.3)	14 (0.5)

5 (0.2)	12 (0.4)	10 (0.4)
1 (0.0)	4 (0.1)	0
3 (11.1)	269 (10.0)	205 (7.6)
64 (9.1)	219 (8.2)	169 (6.3)
8 (2.0)	44 (1.6)	35 (1.3)
1 (0.0)	6 (0.2)	1 (0.0)
9 (11.3)	1055 (39.3)	237 (8.8)
81 (7.9)	441 (16.4)	150 (5.6)
6 (3.3)	552 (20.6)	84 (3.1)
2 (0.1)	62 (2.3)	3 (0.1)
68 (5.8)	638 (23.8)	147 (5.5)
12 (3.9)	291 (10.9)	82 (3.1)
5 (1.9)	320 (11.9)	61 (2.3)
1 (0.0)	27 (1.0)	4 (0.1)
8 (13.7)	1213 (45.2)	320 (11.9)

lected in the electronic diary (e-diary) from Day 1 to Day 7 after

ts 16 through 55 years of age.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
herefore, this information was included in the column header.

ce with activity; Severe: prevents daily activity.
Severe: requires intravenous hydration.
ls in 24 hours; Severe: 6 or more loose stools in 24 hours.
on.

185 (9.3)	1230 (66.1)	143 (7.8)
177 (8.9)	873 (46.9)	138 (7.5)
8 (0.4)	347 (18.7)	5 (0.3)
0	10 (0.5)	0

m Day 1 to Day 7 after vaccination.
6 years of age and older.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. The N for each
n the column header.

.0 cm.
activity; Severe: prevents daily activity.

articipants with Solicited Systemic Reactions, by Each Dose – Participants 56 Years of Age and y Population*

Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
8 (0.4)	219 (11.8)	4 (0.2)
3 (0.2)	158 (8.5)	2 (0.1)
3 (0.2)	54 (2.9)	1 (0.1)
2 (0.1)	7 (0.4)	1 (0.1)
0	0	0

0

49 (2.5)	229 (12.3)	45 (2.5)
19 (1.0)	185 (9.9)	12 (0.7)
1 (0.1)	21 (1.1)	0
9 (0.5)	13 (0.7)	5 (0.3)
9 (0.5)	10 (0.5)	5 (0.3)
0	1 (0.1)	0
0	2 (0.1)	0
130 (6.5)	152 (8.2)	102 (5.6)
109 (5.5)	125 (6.7)	76 (4.1)
20 (1.0)	25 (1.3)	22 (1.2)
1 (0.1)	2 (0.1)	4 (0.2)
165 (8.3)	537 (28.9)	99 (5.4)
111 (5.6)	229 (12.3)	65 (3.5)
51 (2.6)	288 (15.5)	33 (1.8)
3 (0.2)	20 (1.1)	1 (0.1)
124 (6.2)	353 (19.0)	72 (3.9)
78 (3.9)	183 (9.8)	44 (2.4)
45 (2.3)	161 (8.7)	27 (1.5)
1 (0.1)	9 (0.5)	1 (0.1)
224 (11.3)	688 (37.0)	170 (9.3)

lected in the electronic diary (e-diary) from Day 1 to Day 7 after

s 56 years of age and older was fatigue.
eceived at least 1 dose of the study intervention. Participants with

se for the specified reaction after the specified dose. N for each
herefore was included in the column header.

1 group and 11,516 (51.4%) participants in the
<6 months after Dose 2 in the blinded
,778 (8.1%) and 1,304 (5.9%) with ≥6 months of
o groups, respectively.

ized to COMIRNATY had ≥6 months total (blinded

following any dose, through 1 month after Dose 2, in
6 COMIRNATY group vs. 21,921 placebo group),
by solicited local and systemic reactions were nausea
vs. 7), asthenia (76 vs. 25), decreased appetite
nd night sweats (17 vs. 3).

rom Dose 1 up to the participant unblinding date,
ow-up after Dose 2. Among participants 16 through
vaccine, 12,995 of whom received COMIRNATY and
vents were reported by 4,396 (33.8%) participants in
s in the placebo group. In a similar analysis in
1 COMIRNATY recipients and 8,895
rted by 2,551 (28.6%) participants in the COMIRNATY
up. Among participants with confirmed stable HIV
d 100 placebo recipients, unsolicited adverse events
ATY group and 15 (15%) participants in the placebo
erse events among COMIRNATY recipients compared
hat are consistent with adverse reactions solicited
and Table 4).

od, Bell's palsy (facial paralysis) was reported by
ants in the placebo group. Onset of facial paralysis was
and Days 3, 9, and 48 after Dose 2. In the placebo
102. Currently available information is insufficient to
analysis of blinded, placebo-controlled follow-up, there

there were no notable patterns between treatment
including neurologic, neuro-inflammatory, and
hip to COMIRNATY. In the analysis of unblinded
egories of serious adverse events that would suggest a

ring postmarketing use of COMIRNATY, including
ctions are reported voluntarily from a population of
ate their frequency or establish a causal relationship to

uding anaphylaxis, and other hypersensitivity reactions

in extremity (arm)

gnancy outcomes in women exposed to COMIRNATY
MIRNATY during pregnancy are encouraged to enroll
ing-study/covid19-vaccines/.

adverse outcomes. In the US general population, the
scarriage in clinically recognized pregnancies is 2% to

man milk. Data are not available to assess the effects of
tion/excretion. The developmental and health benefits
other's clinical need for COMIRNATY and any
MIRNATY or from the underlying maternal condition.
on is susceptibility to disease prevented by the vaccine.

s 16 through 17 years of age is based on safety and
dverse Reactions (6) and Clinical Studies (14.1)].

duals younger than 16 years of age have not been

y 2 as of March 13, 2021 (N = 22,026),
2% (n = 925) were 75 years of age and older *[see*
or effectiveness were observed between these

e suspension for injection for intramuscular use.
tiple dose vials; each vial must be diluted with 1.8 mL
use to form the vaccine. Each dose of COMIRNATY
NA (mRNA) encoding the viral spike (S) glycoprotein

D-19.

rtility

o cause carcinogenicity, genotoxicity, or impairment of
ith COMIRNATY there were no vaccine-related
ns (8.1)].

mized, placebo-controlled, observer-blind, dose-finding,
ipants 12 years of age and older. Randomization was
55 years of age, or 56 years of age and older, with a
. The study excluded participants who were
al or microbiological diagnosis of COVID-19.
isease not requiring significant change in therapy or
before enrollment, were included as were participants
(HCV), or hepatitis B virus (HBV).

21, approximately 44,000 participants 16 years of age
of COMIRNATY or placebo. Participants are planned
afety and efficacy against COVID-19.

IRNATY or placebo, 51.4% or 50.3% were male and
through 64 years of age, 20.9% or 20.8% were 65 years
9.6% were Black or African American, 1.0% or 0.9%
were Asian, 0.3% or 0.2% Native Hawaiian or other
73.9% or 74.1% were non-Hispanic/Latino, 0.5% or
rbidities [participants who have 1 or more

ter Dose 2 was 95.0% (95% credible interval: 90.3,
case split was 8 COVID-19 cases in the
in the placebo group.

included participants 16 years of age and older who
he development of COVID-19 during blinded
epresenting up to 6 months of follow-up after Dose 2.
ATY group and 12,449 (58.7%) in the placebo group
bo-controlled follow-up period.

D-19 cases in this study include B.1.1.7 (Alpha) and
ong cases in vaccine versus placebo recipients did not
riants.

Table 5.

rence From 7 Days After Dose 2, by Age Subgroup – Without Evidence of Infection and Participants With 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Follow-up Period

Dose 2 in participants without evidence of prior -2 infection*		
	Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])	**Vaccine Efficacy % (95% CI[e])**
2[d])		
	833 5.857 (19,741)	91.1 (88.8, 93.1)
	709 4.654 (15,515)	90.5 (87.9, 92.7)
	124 1.202 (4226)	94.5 (88.3, 97.8)

oint across all participants within each group at risk for the endpoint.
se 2 to the end of the surveillance period.

ed based on the Clopper and Pearson method adjusted to the

by small numbers of cases in some subgroups) did not
rs, ethnic groups, geographies, or for participants with
sk of severe COVID-19.

rted benefit of COMIRNATY in preventing severe
is presented only for participants with or without prior
counts in participants without prior SARS-CoV-2
without prior SARS-CoV-2 infection in both the

	6.225 (20,593)	(87.6, 100.0)

Polymerase Chain Reaction (RT-PCR) and at least 1 symptom
eased cough; new or increased shortness of breath; chills; new or
ea; vomiting).
(i.e., N-binding antibody [serum] negative at Visit 1 and
d 2), and had negative NAAT (nasal swab) at any unscheduled visit

med COVID-19 and presence of at least 1 of the following:
respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per
l, or ratio of arterial oxygen partial pressure to fractional inspired

noninvasive ventilation, mechanical ventilation or extracorporeal

astolic blood pressure <60 mm Hg, or requiring vasopressors);

OVID-19 and presence of at least 1 of the following:

oint across all participants within each group at risk for the endpoint.
se 2 to the end of the surveillance period.

l based on the Clopper and Pearson method adjusted to the

Multiple Dose Vials are supplied in a carton containing
tiple dose vials (NDC 0069-1000-02). A 0.9% Sodium
separately, and should be stored at controlled room
trolled Room Temperature]. The provided 0.9% Sodium
s cartons of 10 mL single-use vials manufactured by

) should be tracked and should not exceed 2 weeks.

hermal container in which COMIRNATY arrives may
to the top of the container with dry ice. Refer to the
ner for instructions regarding the use of the thermal
maintains a temperature range of -90ºC to -60ºC (-130ºF
141°F to -76°F) is not considered an excursion from

ng vials cannot be transported at -90°C to -60°C
15°C (-13°F to 5°F). Any hours used for transport
k limit for storage at -25°C to -15°C (-13°F to 5°F).
) may be returned 1 time to the recommended storage

ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of
tively, to thaw in the refrigerator, whereas a fewer

ature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials

9

Y. Encourage individuals exposed to COMIRNATY
gister by visiting https://mothertobaby.org/ongoing-

their healthcare provider or to the Vaccine Adverse
aers.hhs.gov.

most recent prescribing information, please visit

0

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COMIRNATY safely and effectively. See full prescribing information for COMIRNATY.

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
Initial U.S. Approval: 2021

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular injection only. (2.2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. After preparation, a single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.4)

---------- ADVERSE REACTIONS ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). (6.1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

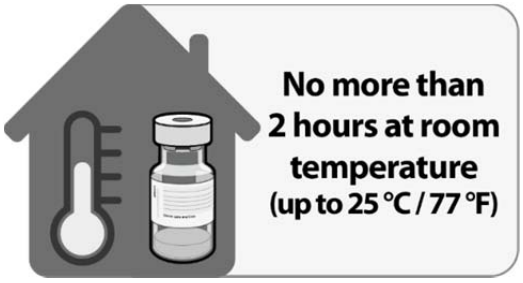
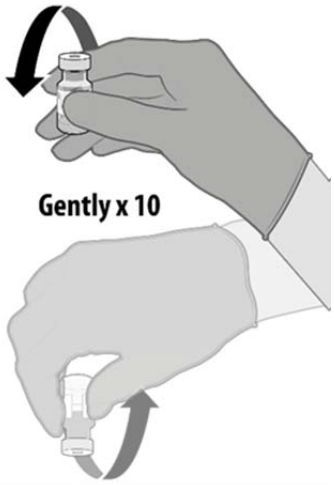
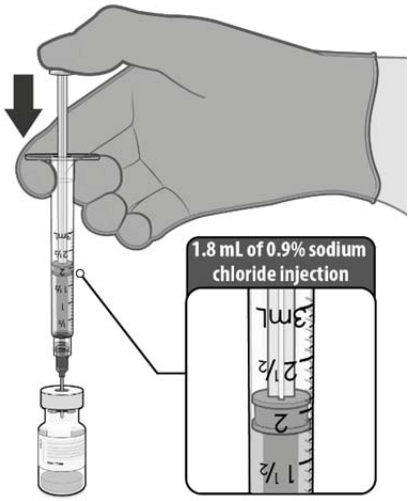
2.1 Preparation for Administration

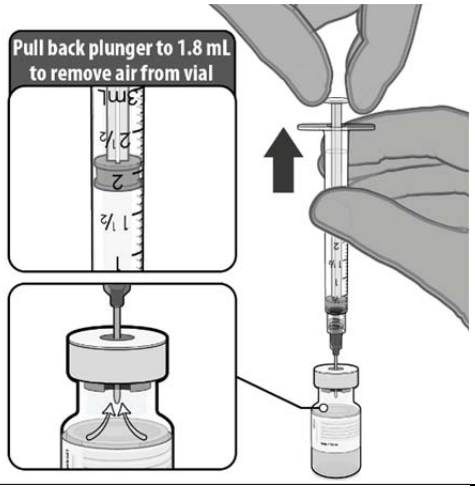
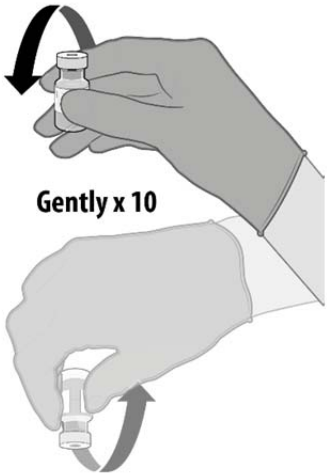
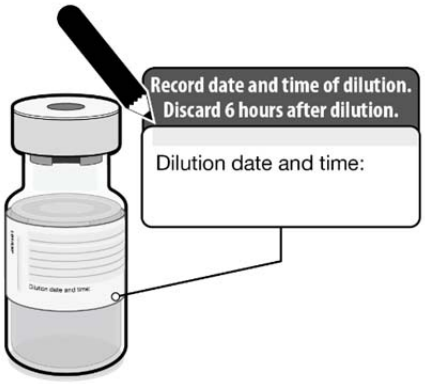
Prior to Dilution

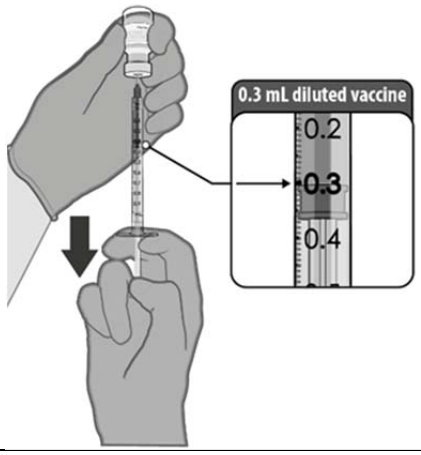
- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not dilute more than 1 vial of COMIRNATY using the same diluent vial.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study C4591001 (Study 2) is a Phase 1/2/3 multicenter, multinational, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Upon issuance of the Emergency Use Authorization (December 11, 2020) for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY. Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

At the time of the analysis of the ongoing Study 2 with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY and 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

f. Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.

	COMIRNATY Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of all unsolicited adverse events reported following any dose, through 1 month after Dose 2, in participants 16 years of age and older (N=43,847; 21,926 COMIRNATY group vs. 21,921 placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (274 vs. 87), malaise (130 vs. 22), lymphadenopathy (83 vs. 7), asthenia (76 vs. 25), decreased appetite (39 vs. 9), hyperhidrosis (31 vs. 9), lethargy (25 vs. 6), and night sweats (17 vs. 3).

In analyses of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least one dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection that included 100 COMIRNATY recipients and 100 placebo recipients, unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 3 and Table 4).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there

were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8,931; placebo = 8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COMIRNATY during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to

4% and 15% to 20%, respectively. Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY on 4 occasions; twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

8.2 Lactation

Risk Summary

It is not known whether COMIRNATY is excreted in human milk. Data are not available to assess the effects of COMIRNATY on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COMIRNATY and any potential adverse effects on the breastfed child from COMIRNATY or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 16 years of age have not been established.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY there were no vaccine-related effects on female fertility *[see Use in Specific Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 16 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more

comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 5.

Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants[f]	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 6) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

Table 6: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.
d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by

Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

Inform vaccine recipient of the potential benefits and risks of vaccination with COMIRNATY.

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

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