RESPONSE TO FDA COMMENTS ON CLINICAL RECEIVED ON 17 SEPTEMBER 2021

The Sponsor acknowledges FDA comments on CLINICAL topics (in **Bold)**

Our review of your August 24, 2021 submission (STN 125752/0) is ongoing. We have the following requests for additional information:

Please respond to the following request by October 4, 2021:

ITEM 1:

For the PTs in which there is an observed imbalance (mRNA-1273 or placebo mRNA-1273 > placebo), please provide in Excel sheet format a summary of demographics and relation to last vaccination for the subjects who contributed to the PT.

Treatment	Subject	Age / Sex / Race	Adverse event	Relative Day to Last Vaccination and Dose #
mRNA-1273	123456	56 / F / WHITE	Tachycardia	2 (dose 2)
mRNA-1273	78910	77/M/Asian	Tachyarrhythmia	14 (dose 1)

Sponsor Response

At the final analysis of the blinded phase data, in the summary of TEAE by SOC and PT (source: Table 14.3.1.8.1.1 included in Study P301 CSR), the rate ratio and its 95% CI were provided as a helpful descriptive measure in review, not a formal method for assessing the statistical significance of the between-group differences in adverse experiences, for the PTs with at least 7 participants in any group reported the event. The rate ratio was calculated as the ratio of percentage of participants reporting the event in mRNA-1273 divided by that in placebo. The 95% CI for rate ratio was provided using the Miettinen and Nurminen method (1985). The threshold of at least 7 participants was chosen because the 95% CI for rate ratio always included one when groups of equal size each had < 7 participants reporting the event, and thus would have added little for review purpose. (Section 4.2.3.2 of Study P301 CSR).

For the PTs in which the lower bound of the 95% CI is >1, an EXCLE(XML) file of listings of these AE events with demographics, baseline characteristics, dosing, and following up time after each dose is provided in this response.