RESPONSE TO BLA IR#1 RECEIVED ON 14 SEPTEMBER 2021

The Sponsor acknowledges FDA comments in **Bold**

Information Request #1

ITEM 1:

Please refer to Section 11, Table 5 of your Agreed Initial Pediatric Development Plan (iPSP). Please provide the estimated dates for protocol submission, study initiation, study completion and final study report submission for the following studies:

A Phase 2/3, randomized, observer-blind, placebo controlled, dose-finding, age de-escalation study to evaluate safety, reactogenicity, and effectiveness of the mRNA-1273 SARS-CoV-2 vaccine administered as two (or three) doses in healthy children 6 months to <12 years of age.

Safety and effectiveness study of mRNA-1273 SARS-CoV-2 vaccine administered in healthy infants birth to <6 months of age.

Sponsor Response:

The response for the 6 months to <12 years of age study was submitted to BLA125752 previously in SN0005 (21 Sep 2021).

The Sponsor recognizes the importance of providing protection from COVID-19 to children of all ages, including neonates and young infants. Infection has been reported early in the newborn period, and both vertical as well as well as postnatal routes of transmission have been described for newborn infections (Gale et al 2021). The Sponsor is of the opinion that COVID-19 occurring in the neonatal and early infancy period can only be prevented by maternal vaccination as there is insufficient time for newborns to develop protective immunity, even following immunization at birth. At present, numerous health agencies, including the United Kingdom (JCVI), Spain, Switzerland, Belgium, Denmark, Canada and the United States, have recommended use of mRNA COVID-19 vaccines in pregnancy (Please see the COVID-19 Maternal Immunization Tracker developed by Johns Hopkins University: https://www.comitglobal.org/). These recommendations are based on reports of increased severity of COVID-19 in pregnant women, including recently pregnant people (Please see the CDC website: Data about the Safety and Effectiveness of the COVID-19 Vaccination during Pregnancy: https://www.cdc.gov/coronavirus/2019ncov/vaccines/recommendations/pregnancy.html#anchor

1628692463325) and reports of the safety of such vaccines in pregnancy with no excess fetal loss (Zauche et al 2021).

mRNA vaccines have been shown to induce antibody responses in pregnant women that are comparable to responses induced in non-pregnant women (Gray et al 2021) and women receiving mRNA COVID-19 vaccines during pregnancy successfully transfer antibody to their newborn infants (Prabhu et al 2021). In one study, 66 of 67 umbilical cord blood samples obtained from newborns of women receiving mRNA vaccines in pregnancy had measurable Spike-specific IgG. Maternal specific IgG levels were linearly related to specific IgG levels in paired newborn cord blood (R=0.89) (Prabhu et al 2021). Maternally transferred antibody against SARS-CoV-2 would be expected to remain detectable in young infants for a duration similar to that observed for antibody against another viral pathogen: measles virus. Previous studies show that measles-specific, maternally-transferred IgG in infants remained close to protective levels to 6 month of life and remained detectable to 12 months of life (Fouda et al 2018).

Taken together, the demonstration of comparable immunogenicity in pregnant and non-pregnant, the linear maternal transfer of specific antibody and the recent recommendations for routine vaccination during pregnancy, predict that increasing numbers of newborns and infants under the age of 6 months will have passive immunity to SARS-COV-2. Based on this, the Sponsor plans to conduct a maternal immunization study to assess the antibody levels in neonates and infants , as well as in cord blood, after maternal immunization during the 3rd trimester. Based on this data, the Sponsor plans to request a partial pediatric waiver for the 0 to <6m age group. At this time, the Sponsor does not have further study milestone updates.