RESPONSE TO FDA COMMENTS ON POST-MARKETING STUDIES DATED NOVEMBER 19, 2021

The Sponsor acknowledges FDA Comments on post-marketing studies in **BOLD**

Product: COVID-19 Vaccine, mRNA (SPIKEVAX)

Subject: Postmarketing Studies

Our review of your August 24, 2021 submission (STN 125752/2) is ongoing. We have the following requests for additional information:

FDA is reviewing your response regarding postmarketing studies for SPIKEVAX.
You have stated that evaluation of the occurrence of myocarditis and pericarditis following administration of SPIKEVAX and quantification of the magnitude of risk by age, sex and dose will occur primarily in two large secondary database studies, mRNA-1273- P903 and mRNA-1273-P904. Please provide the following information on the sample size for these studies:

ITEM 1:

mRNA-1273- P903: It is stated that as per the most recent interim report, this study included >1.3 million vaccinated individuals 18 – 29 years of age. Please provide an estimated minimum number of Spikevax recipients <30 years of age that this data source will be able to identify.

Sponsor Response:
The number of SPIKEVAX recipients <30 years of age that will be identifiable in this data source will depend on uptake in the United States. All vaccine recipients meeting study entry criteria will be included. This includes individuals from the 50,000,000 person cohort used to establish background rates as well as additional vaccinees identified from other closed and open claims sources. With data available through 20 June 2021, a minimum of 1,464,242 vaccine recipients <30 years of age are expected to meet all study entry criteria for inclusion in the next interim report. Although this number is a minimum bound, it is expected that additional vaccine recipients will accrue depending on regulatory conditions and this number will increase.

ITEM 2:

mRNA-1273- P904: It is estimated that the participating databases together will be able to identify at least 431,216 recipients of Spikevax. Does 431,216 recipients refer to individuals <30 years? If not, then please provide an estimated minimum number of Spikevax recipients <30 years of age that this data source will be able to identify.

Sponsor Response:
In the mRNA-1273-P904 study protocol, the estimation of 431,216 recipients of SPIKEVAX was based on doses administered per the European Centers for Disease Control as of 01 June

2021 and represented all age groups. Considering data through 19 November 2021 on administration and the per protocol assumptions concerning population coverage in the participating countries (Denmark 100%; Italy 5%, Norway 100%; Spain 10%; UK 6%), the current estimated number of SPIKEVAX recipients expected to be included in the study is approximately 4,390,635. Of these, approximately 614,688 will be <30 years of age if the demographic distribution for SPIKEVAX is similar to the distribution published by the ECDC for all COVID-19 vaccines. Additional accrual over the course of the study will depend on uptake.