

**RESPONSE TO CBER COMMUNICATION REGARDING CLINICAL TOPICS (IR#8)  
RECEIVED ON DECEMBER 06, 2020**

The Sponsor acknowledges CBER's communication regarding Clinical topics (IR#8).

This document provides the Sponsor's responses to CBER's requests (in **Bold**).

**Item 3:**

**As a follow up to your response to Item D from IR EUA #0001, please provide the following additional information on subject US3772037:**

- A. Please indicate any interventions received by the subject during hospitalization (eg ICU admission, mechanical ventilation, treatment specifically for COVID-19)**
- B. Please comment if this case will be eligible to be counted as a severe COVID-19 case and sent to the adjudication committee in future efficacy analyses**

**Sponsor Response:**

Participant US3772037 was hospitalized from 7 to 12 November with a diagnosis of acute hypoxemic respiratory failure due to COVID-19 infection and mild acute asthma exacerbation. According to the discharge summary, after an initial O2 sat reading of 88% on admission, she received supplemental oxygen and dexamethasone but had an otherwise uneventful hospitalization and was discharged home. She was not admitted to the ICU and did not require mechanical ventilation. This case will be sent to the adjudication committee for their determination as a COVID-19 case and severe COVID-19 case for future efficacy analysis.

**Item 4:**

**Please provide a table similar to the one you provided for response to Item A in IR EUA #0001 for severe COVID-19 cases (i.e., Vaccine efficacy of mRNA-1273 to prevent severe COVID-19 in subjects who only received one dose—mITT set).**

**Sponsor Response:**

At IA1 (DS1, 11-Nov-2020), in the mITT population, 2075/28682 (7.2%) of subjects only received one dose: 996/14312 (7.0%) subjects in mRNA-1273 group and 1079/14370 (7.5%) subjects in Placebo group. There are 6 severe COVID-19 cases (4 on Placebo and 2 on mRNA-1273) starting from randomization in the mITT subjects who only received one dose. Below is a summary by group and a list of these 6 subjects based on data snapshot 1 occurred on 11-Nov-2020.

- Subject US3162078 (49 year old white Hispanic male, does not have health risk for developing severe COVID-19) randomized to and received mRNA-1273 on 07-Aug,

discontinued study vaccination due to SARS-CoV-2 or positive COVID-19, started to report symptoms on 19-Aug, positive RT-PCR on 19-Aug, had O<sub>2</sub> saturation of 93% on 29-Aug. The AE was considered recovered/resolved on 3 Sept.

- Subject US3532279 (66 years old white not-Hispanic female, does not have health risk for developing severe COVID-19) randomized to and received mRNA-1273 on 10-Sep, started to report symptoms on 04-Aug, had positive RT-PCR on 08-Aug, and O<sub>2</sub> saturation of 80% on 10-Oct. The AE was considered recovered/resolved on 21 Oct.
- Subject US3252638 (41 years old white Hispanic female, with severe obesity) randomized to and received Placebo on 07-Oct, started to report symptoms on 24-Oct, had positive RT-PCR on 28-Oct, O<sub>2</sub> Saturation of 92% on 07-Nov. The AE was considered recovered/resolved on 24 Nov.
- Subject US3322006 (50 years old black not-Hispanic female, with severe obesity) randomized to and received Placebo on 17-Aug, discontinued study vaccination due to SARS-CoV-2 or positive COVID-19, started to report symptoms on 14-Sep, had positive RT-PCR on 14-Sep, had O<sub>2</sub> saturation of 92% on 17-Sep. The AE was considered recovered/resolved on 6 Oct.
- Subject US3942079 (42 years old white not-Hispanic male, with severe obesity, hypertension) randomized to and received Placebo on 08-Sep, discontinued study vaccination due to SARS-CoV-2 or positive COVID-19, started to report symptoms on 24-Sep, positive RT-PCR on 24-Sep, had lowest O<sub>2</sub> saturation of 85% on 29-Sep. The AE was considered recovered/resolved on 16 Oct.
- Subject US3952033 (52 years old white not-Hispanic female, with severe obesity) randomized to and received Placebo on 02-Sep, discontinued study vaccination due to SARS-CoV-2 or positive COVID-19, started to report symptoms on 03-Oct, had positive RT-PCR on 08-Oct, had lowest O<sub>2</sub> saturation of 89% on 09-Oct. Temperature was 103.7F on 10 Oct. The AE was considered recovered/resolved on 25 Oct. The participant was subsequently hospitalized from 31 Oct to 5 Nov with pericarditis reported as an SAE.

	<b>Vaccine Group</b>	<b>Placebo Group</b>
	<b>(N=996)</b>	<b>(N=1079)</b>
	<b>Case n (%)</b>	<b>Case n (%)</b>
Number of subjects with COVID-19 starting after randomization, n (%)	2 (0.2)	4 (0.4)

Number of subjects with  
COVID-19 starting 14 days  
after the 1<sup>st</sup> dose, n (%)

2 (0.2)

**Item 5:**

**Please provide for the safety set**

<b>Baseline SARS-CoV-2 status****</b>	<b>mRNA vaccine</b>	<b>Placebo</b>	<b>overall</b>
<b>Negative</b>			
<b>Positive</b>			
<b>Missing</b>			

**Sponsor Response:** Please see below for the requested table based on the Safety Set using data snapshot 1 (11-Nov-2020) data

<b>Baseline SARS-CoV-2 status****</b>	<b>mRNA vaccine N=15184</b>	<b>Placebo N=15165</b>	<b>Overall N=30350</b>
<b>Negative</b>	<b>14316 (94.3%)</b>	<b>14366 (94.7%)</b>	<b>28682 (94.5%)</b>
<b>Positive</b>	<b>341 (2.2%)</b>	<b>334 (2.2%)</b>	<b>675 (2.2%)</b>
<b>Missing</b>	<b>527 (3.5%)</b>	<b>465 (3.1%)</b>	<b>993 (3.3%)</b>

Subjects in Safety Set are analyzed in the group of treatment they actually received.

Source: Table 14.1.3.2.2, submitted in EUA SN 0004