EXECUTIVE SUMMARY OF CLINICAL SAFETY

The mRNA-1273 Phase 3 safety and efficacy study was analyzed at 2 different timepoints:

- The initial interim analysis for efficacy ("Interim Dataset"), based on 95 adjudicated cases (data snapshot on November 11, 2020 with a cutoff date for efficacy of November 7, 2020). Interim analyses were prespecified as early stopping criteria for efficacy. The efficacy and safety data from this analysis were summarized in a clinical overview submitted as Module 2.5.

- The Primary Dataset based on the prespecified primary efficacy analysis from 196 adjudicated cases (data snapshot on November 25, 2020 with a cutoff date for efficacy of November 21, 2020) 1. This dataset provides a 2-month median exposure following the second injection of mRNA-1273 for both safety and efficacy analyses.

This summary reflects the review of the statistical analysis output for clinical safety from Study mRNA-1273-P301 (data snapshot date: 25 Nov 2020).

There were slightly more participants who discontinued study participation in the placebo vs vaccine group of the study (Table 2). Withdrawal of consent was the most common reason for discontinuation of participants in the placebo (146 participants) vs the vaccine groups (85 participants) in the Randomized Set (Table 2). Adverse events (AEs) led to vaccine discontinuation in 80 participants in the placebo group vs 50 participants in the vaccine group (Table 10). There was a slightly higher percentage of seropositive participants in both treatment groups who had an AE leading to withdrawal (1.7% of seropositive participants vs 0.3% of seronegative participants in the vaccine group; 1.5% of seropositive participants vs 0.5% of seronegative participants in the placebo group) (Table 10).

There were more solicited local adverse reactions (AR) in the vaccine group vs the placebo group (Table 11). Local ARs were more common than systemic ARs in the vaccine group, and grade 3 reactions were more common in the vaccine group vs the placebo group. Injection site pain was the most common local solicited AR (92.0% of participants in the vaccine group vs 26.6% of participants in the placebo group after any dose) (Table 11). Grade 3 pain was reported in 6.1% of participants in the vaccine group vs 0.6% of participants in the placebo group. Lymphadenopathy was the next most common local solicited AR (19.8% on active arm vs 7.2% of placebo). Induration (14.7% of participants in the vaccine group vs 0.6% of participants in the placebo group) and erythema (10.0% of participants in the vaccine group vs 0.8% of participants in the placebo group) were also common and grade 3 ARs were also more common in the vaccine group. Solicited local ARs were more common after the second dose compared with the first dose in the vaccine group (Table 11).

Solicited systemic ARs were also more common in the vaccine group vs the placebo group and were more common after the second dose compared to the first dose in the vaccine group (Table 12). After any dose, fatigue was the most common solicited systemic AR (70.0% of participants in the vaccine group vs 36.6% of participants in the placebo group), followed by headache (64.7% of participants in the vaccine group vs 37.0% of participants in the placebo group) and myalgia (61.5% of participants in the vaccine group vs 20.5% of participants in the placebo group). Grade 3 fatigue was the most common solicited systemic AR after any dose with 10.1% of participants in the vaccine group vs 1.3% of participants in the placebo group, followed by myalgia (9.1% of participants in the vaccine group vs 0.6% of participants in the placebo group) and headache (5.7% of participants in the vaccine group vs 2.2% of participants in the placebo group).

Unsolicited treatment emergent AEs (TEAE) up to 28 days after any injection were more common in the vaccine group (23.9%) vs the placebo group (21.6%) (Table 10). Related unsolicited AEs were more common in the vaccine group (8.2%) vs the placebo group (4.5%). However, medically-attended AEs (MAAEs) were less common in the vaccine group vs the placebo group; in fact, there were more MAAEs in the placebo group, largely due to an imbalance in COVID-19 cases (105 vs 19). Being SARS-CoV-2 seropositive did not seem to increase the risk of unsolicited TEAEs, medically-attended AEs, SAEs or related TEAEs when compared with seronegative participants. Grade 3 non-serious unsolicited TEAEs were slightly more common in the vaccine group (1.3%) vs the placebo group (1.1%) arms (Table 10). The most common unsolicited AEs (reported in <1% of participants) were similar to the most common solicited AEs (fatigue, headache, myalgia, arthralgia, erythema, injection site pain and similar terms accounted for most of the imbalance).

When examining the System Organ Class (SOC) of the unsolicited TEAEs, the number of participants experiencing skin, musculoskeletal and general disorders was more common in the vaccine group vs the placebo group (Table 13). Most of the imbalance can be accounted for with solicited event terms reported as TEAEs, for example fatigue was more common in the vaccine group under the general disorders and administration site SOC.

The number of participants who experienced an unsolicited SAE up to 28 days after any injection was roughly balanced between the treatment groups (Table 10 and Table 15). The number of SAEs with a fatal outcome was balanced between treatment groups as well and none were considered related to study treatment. At the time of the data cutoff date, 10 deaths were reported (4 in the vaccine group and 6 in the placebo group) (Table 10). However, based on the pharmacovigilance database which includes data from study start through 03 Dec 2020, there have been 13 deaths during the study. Six participants who died received mRNA-1273 and 7 received placebo. The most common preferred term was myocardial infarction, reported by 3

participants, 2 who received placebo and 1 who received mRNA-1273. The participant who received mRNA-1273 was a 50s-year old male with a history of hypercholesterolemia and died 45 days from administration of the study product. Another death, due to cardiopulmonary arrest, occurred 21 days after mRNA-1273 dose 1 in a 70s-year-old with a history of cerebrovascular accident. The other deaths which were reported in participants who received mRNA-1273 included suicide, head trauma due to fall, multisystem organ failure, and death due to unknown causes. None of the deaths were assessed by Investigator or Sponsor as related to study product.

There is no apparent cluster of SAEs that suggest an imbalance between vaccine and placebo groups in any specific SOC. At the level of subject incidence of SAE a few numerical imbalances were noted. The first was a small imbalance in the gastrointestinal disorders SOC, with more upper abdominal pain and nausea reported in the vaccine group. The imbalance in the hepatobiliary SOC is primarily due to cholecystitis and bile stones reported in the vaccine group. In the reproductive and breast disorders SOC there was an ovarian cyst, uterine hemorrhage, and 2 benign prostatic hypertrophy serious events reported in the vaccine group. The imbalance in the nervous system disorder SOC is partially due to more cerebrovascular accident, embolic stroke, and seizures reported in the vaccine group, while syncope was slightly more common in the placebo group. All participants who had strokes had 1 or more cardiovascular risk factors. The subjects with seizures are discussed in the next paragraph.

There were more events of “hypersensitivity” under the corresponding SMQ in the vaccine group (1.5%) vs the placebo group (1.1%) (Table 17). The majority of the mismatch occurred due to injection site rash and urticaria. Of note the event of anaphylaxis in the vaccine group was in 1 participant on a cephalosporin antibiotic and thought not related to treatment by the Investigator. The angioedema SMQ showed a similar incidence between the groups, with slightly more urticaria associated with the vaccine group (Table 19). Table 22 shows 3 subjects with seizure in the active cohort. On review of these cases, 2 were considered serious, none were considered related and all participants in the vaccine group had previous seizure histories. The participant in the placebo group did not report a previous seizure history.

There have been 13 pregnancies reported during Study mRNA-1273-P301 through 03 Dec 2020 (reported in the pharmacovigilance database; details available upon request). Six pregnancies were reported by participants who had received mRNA-1273 and 7 pregnancies were reported by participants who received placebo. Amongst the recipients of mNRA-1273, all pregnancies are continuing to term without any complications reported to date.