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Application Type	BLA Supplement
STN	125752/276
CBER Received Date	1/7/2025
PDUFA Goal Date	7/9/2025
(b) (6)	(b) (6)
(b) (6)	(b) (6)(b) (6)
	(b) (6)
Priority Review	Yes
Reviewer Name	(b) (6)
Review Completion Date/Stamped Date	
Concurrence	(b) (6) (b) (6)
Supervisory Concurrence	(b) (6)
Applicant	ModernaTx, Inc
Established Name	COVID-19 Vaccine, mRNA
(Proposed) Trade Name	SPIKEVAX
Pharmacologic Class	Vaccine
Dosage Form(s) and Route(s) of Administration	Suspension for intramuscular injection (IM)
Dosing Regimen	• A single 25 µg dose in individuals 2 years through 11 years of age irrespective of COVID-19 vaccination status • Two 25 µg doses 1 month apart in individuals 6 months through 23 months of age with no history of COVID-19 vaccination • A single 25 µg dose in individuals 6 months through 23 months of age who have been previously vaccinated with a Moderna COVID-19 vaccine
Indication(s) and Intended Population(s)	Active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 6 months of age and older

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Glossary

AE	adverse event
AESI	adverse event of special interest
ANCOVA	analysis of covariance
AR	adverse reaction
bAb	binding antibody
BD	booster dose
BMI	body mass index
CDC	Centers for Disease Control and Prevention
CI	confidence interval
COVID-19	coronavirus disease 2019
CSR	clinical study report
EUA	Emergency Use Authorization
FAS	Full Analysis Set
GLSM	geometric least squares mean
GMC	geometric mean concentration
GMFR	geometric mean fold rise
GMR	geometric mean ratio
GMT	geometric mean titer
HIV	human immunodeficiency virus
ID50	50% inhibitory dose
IgG	immunoglobulin G
IS	Immunogenicity Set
LLOQ	lower limit of quantification
MAAE	medically attended adverse event
mITT	modified Intent-to-Treat
mRNA	messenger ribonucleic acid
nAb	neutralizing antibody
PP	per-protocol
PPIS	Per-Protocol Immunogenicity Set
PsVNA	Pseudovirus neutralizing antibody
RT-PCR	reverse transcription polymerase chain reaction
SAE	serious adverse event
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SD	standard deviation
SRR	seroresponse rate
ULOQ	upper limit of quantification
VE	vaccine efficacy
VOC	variant(s) of concern

1. Executive Summary

SPIKEVAX (mRNA-1273) is licensed for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 12 years of age and older. Use in individuals 6 months to 11 years of age is currently authorized under Emergency Use Authorization (EUA). ModernaTX, Inc. submitted an efficacy supplement to Biologics License Application (BLA) 125752 on January 7, 2025, to extend licensure of mRNA-1273 to individuals 6 months to 11 years of age, and to fulfill the deferred pediatric study under the Pediatric Research Equity Act (Study mRNA-1273-P204).

The basis for licensure includes clinical data from Studies mRNA-1273-P204 (hereafter referred to as "P204") and mRNA-1273-P306 (hereafter referred to as "P306") covering individuals 6 months to 11 years of age.

P204 was a Phase 2/3, dose-escalation, age de-escalation (Part 1, open-label) and randomized, observer-blind, placebo-controlled expansion study (Part 2) to evaluate the safety, reactogenicity, and effectiveness of mRNA-1273 (primary series and booster dose [BD]) and safety of mRNA-1273.214 (BD encoding Omicron BA.1 and the ancestral SARS-CoV-2 strain [D614G]) in children 6 months to 11 years of age.

P306 is an ongoing, open-label, Phase 3 study evaluating the safety and immunogenicity of mRNA-1273 variant-containing formulations (mRNA-1273.214 and mRNA-1273.815 encoding Omicron XBB.1.5) in participants 6 months through 5 years of age. P306 has 4 parts, of which Parts 1, 2, and 4 are completed and Part 3 is ongoing.

This review memo focuses on the immunogenicity, efficacy, and safety data obtained from the following studies to support licensure of this vaccine:

1. mRNA-1273-P301 (hereafter referred to as "P301"): A Phase 3, randomized, stratified, observer-blind, placebo-controlled study to evaluate the efficacy, safety, and immunogenicity of mRNA-1273 administered in two doses 28 days apart in adults 18 years and older. P301 was the pivotal efficacy study for SPIKEVAX primary series. Participants were randomized 1:1 to receive either 100 micrograms (μg) mRNA-1273 or placebo at Day 1 and Day 29, stratified by age category (18 to 64 years, ≥65 years) and health risk. Immunogenicity data from a random subset of young adults 18 to 25 years randomized to mRNA-1273 were provided to support immunobridging for P204.

2. P204 Part 2 Blinded Phase: In Part 2 Blinded Phase, participants (stratified into 6 to 11 years of age, 2 to 5 years of age, and 6 to 23 months of age) were randomized 3:1 to receive two doses of mRNA-1273 or placebo on Day 1 and Day 29. The selected primary series doses were 50 μg, 25 μg, and 25 μg for the three age groups, respectively.

Vaccine effectiveness was inferred from bridging the immune responses of children in P204 Blinded Phase to those of young adults 18 to 25 years of age from P301. For each age group, the coprimary endpoints were the geometric mean titer/concentration (GMT/GMC) of serum neutralizing antibody (nAb) levels and the seroresponse rate (SRR) at Day 57, where seroresponse was defined as change in nAb titer from either below the lower limit of quantitation (LLOQ) at baseline (i.e., Day 1) to ≥4 * LLOQ, or at least a 4-fold rise from baseline when the baseline titer is ≥ LLOQ. The success criteria were a lower bound of the 95% confidence interval (CI) of the geometric mean ratio (GMR) of >0.667 and a GMR point estimate of ≥0.8, and a lower bound of the 95% confidence interval (CI) of the SRR difference of >-10% and a SRR rate difference point estimate of ≥-5%. The success criteria were met for each age group.

In addition, a secondary efficacy objective was to evaluate the incidence of COVID-19 between vaccine groups after vaccination as measured by reverse transcriptase polymerase chain reaction (RT-PCR)-confirmed COVID-19 based on the Centers for Disease Control and Prevention (CDC) and P301 protocol case definitions starting at 14 days after Doses 1 and 2 in each age group. The observed COVID-19 incidence rates were lower among mRNA-1273 recipients compared to placebo recipients within each age group.

3. P204 BD Phase (6 to 11 years): The primary objectives of the BD Phase were to evaluate the safety (including reactogenicity) and to infer the effectiveness of mRNA-1273 25 μg BD given to P204 Parts 1 and 2 participants aged 6 to 11 years who had received a two-dose primary series of mRNA-1273 50 μg (i.e., Part 1 mRNA-1273 50 μg, Part 2 mRNA-1273 50 μg, and Part 2 Placebo-mRNA-1273 50 μg crossover participants) at least 6 months prior. Effectiveness of the mRNA-1273 25 μg BD was inferred based on establishing noninferiority in terms of both GMR and SRR difference of serum nAb against D614G in P204 participants 6 to 11 years of age at BD-Day 29 (28 days after the BD) compared with post-primary series (Day 57; 28 days after Dose 2) responses in P301 young adult participants (18 to 25 years of age). SSR was defined based on titers at pre-Dose 1 of the primary series. The success criteria were a lower bound of the 95% CI of the GMR of >0.667 and a lower bound of the 95% CI of the SRR difference of > -10%. The success criteria were met.

4. P306 Part 2: Part 2 enrolled participants 6 months to 5 years of age from P204 who previously received mRNA-1273 25 μg as a two-dose primary series. Participants received a single BD of mRNA-1273.214 10 μg at least 4 months after completion of the mRNA-1273 primary series. The primary immunogenicity objective was to infer the effectiveness of the mRNA-1273.214 10 μg BD by bridging the immune responses of P306 Part 2 participants 6 months to 5 years of age at BD-Day 29 (28 days after the BD) to post-primary series responses (Day 57; 28 days after Dose 2) in P204 participants 6 months to 5 years of age in terms of nAb levels and SRR against Omicron BA.1 and D614G. Superiority of the immune responses against Omicron BA.1 was considered met if the lower bound

of the CI for GMR (BD-Day 29 in Study P306 versus Day 57 in Study P204) was >1.0. Noninferiority of the immune responses against D614G was considered met if the lower bound of the CI for GMR (BD-Day 29 in Study P306 versus Day 57 in Study P204) was >0.667. Noninferiority based on SRR difference was considered met if the lower bound of the CI was >-5% for Omicron BA.1 and >-10% for D614G. The success criteria were met for all four endpoints.

5. P306 Part 4: Part 4 evaluated mRNA-1273.815 administered as a single 25 µg dose in participants 2 through 4 years of age with evidence of prior SARS-CoV-2 infection and had not been previously vaccinated against SARS-CoV-2 (Cohort 4A) in comparison to mRNA-1273.815 25 µg administered as two doses, 28 days apart in participants 6 months through 23 months of age with no evidence of prior SARS-CoV-2 infection and had not been previously vaccinated against SARS-CoV-2 (Cohort 4B). The effectiveness of a single 25 µg dose of mRNA-1273.815 was inferred based on bridging the Day 29 immune responses in participants 2 through 4 years of age to Day 57 immune responses in participants 6 to 23 months of age. Noninferiority criteria for the primary and secondary immunogenicity endpoints were a lower bound of the 95% CI for the GMR of >0.667 and a lower bound of the 95% CI for the SRR difference of >-10% for nAb against Omicron XBB.1.5. Success criteria were met for both GMR and SSR difference.

All participants in P204 (Part 2 Blinded and BD Phases) and P306 (Parts 2 and 4) recorded local and systemic reactions (ARs) from Day 1 through Day 7 after each dose. Unsolicited adverse events (AEs) were monitored up to 28 days after any dose. Serious adverse events (SAEs) and medically attended adverse events (MAAEs) were recorded for the entire study duration up to the respective data cutoffs. No notable patterns for safety profile were identified. No cases of myocarditis, pericarditis, or deaths were reported in these studies as of the cutoffs.

In summary, no major statistical issues have been identified. Both the immunogenicity and safety data support the licensure of SPIKEVAX in individuals 6 months to 11 years of age.

2. Clinical and Regulatory Background

SPIKEVAX is licensed for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 12 years of age and older. Use in individuals 6 months to 11 years of age is currently authorized under EUA. ModernaTX, Inc. submitted an efficacy supplement to BLA 125752 on January 7, 2025 to extend licensure of mRNA-1273 to individuals 6 months to 11 years of age, and to fulfill the deferred pediatric study under the Pediatric Research Equity Act (Study P204).

3. Submission Quality and Good Clinical Practices

3.1 Submission Quality and Completeness

The submission was adequately organized for conducting a complete statistical review without unreasonable difficulty.

3.2 Compliance With Good Clinical Practice and Data Integrity

No data integrity issues were identified during the review.

4. Significant Efficacy/Safety Issues Related to Other Review Disciplines

Please refer to reviews of other review disciplines.

5. Sources of Clinical Data and Other Information Considered

5.1 Review Strategy

This review memo focuses on the pivotal Phase 2/3 clinical study P204 and the pivotal Phase 3 clinical study P306. Specifically, this memo investigates mRNA-1273 (administered as a primary series and BD in Study P204 in participants 6 months through 11 years of age and 6 through 11 years of age, respectively), mRNA-1273.214 (Omicron BA.1-containing formulation; administered as a BD in Study P204 and as a BD in Study P306 Part 2 in participants 6 months through 5 years of age), and mRNA-1273.815 (monovalent Omicron XBB.1.5-containing formulation; administered as a single dose in participants 2 to 4 years of age who had not been previously vaccinated against SARS-CoV-2, compared to a two-dose series in participants 6 to 23 months of age who had not been previously vaccinated against SARS-CoV-2).

The Phase 2/3 clinical study P301 is not reviewed in this memo as it only served as the immunobridging comparator for P204.

5.2 BLA/IND Documents That Serve as the Basis for the Statistical Review

The following documents submitted to the BLA are reviewed:

STN 125752/276.0 (submitted on 01/07/2025)

1. Module 2. Clinical Summaries
   - Summary of Clinical Efficacy
   - Summary of Clinical Safety

2. Module 5. Clinical Study Reports
   - P204 Clinical Study Report for Primary Series (6 to 11 years)
   - P204 Clinical Study Report for Primary Series (2 to 5 years)
   - P204 Clinical Study Report for Primary Series (6 to 23 months)
   - P204 Clinical Study Report for Booster Dose (6 to 11 years)
   - P204 Statistical Analysis Plan (Version 5)
   - P306 Clinical Study Report for Part 1 and Part 2

STN 125752/276.6 (submitted on 03/14/2025)

1. Module 5. Clinical Study Reports
   - P306 Clinical Study Report for Part 4A
   - P306 Statistical Analysis Plan (Version 4)

5.3 Table of Studies/Clinical Trials

Table 1 provides an overview of the clinical trials considered in this review.

Table 1. Clinical Studies Considered

Study	Description	Age	N
P301 (young adult subset)	Phase 3, randomized, placebo-controlled study to evaluate safety and efficacy of mRNA-1273 administered as a two-dose, 100 µg mRNA-1273 primary series	18 to 25 years	878[a]
P204	A Phase 2/3, three-part, open-label, dose-escalation, age de-escalation, and randomized, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of mRNA-1273 SARS-CoV-2 vaccine in healthy children 6 months to 11 years of age.	Part 2 Blinded Phase: 6 months through 11 years BD Phase: 6 through 11 years	Part 2 Blinded Phase[a]: 6-23 months: 2664 2-5 years: 4048 6-11 years: 4015 BD Phase: 6-11 years: 2519[b]
P306	An open-label, Phase 3 study to evaluate the safety and immunogenicity of mRNA vaccines for SARS-CoV-2 variants in participants aged 6 months to 5 years	6 months to 5 years	Part 4[c]: Cohort 4A: 199 Cohort 4B: 399

[a] N is the number of enrolled participants.
[b] A total of 2519 participants aged 6 to 11 years received the mRNA-1273 BD.
[c] A total of 199 participants received a single dose of mRNA-1273.815 injection in Cohort 4A. In Cohort 4B, 399 participants received at least one mRNA-1273.815 injection.
Source: Adapted from P204 CSR for primary series (6 to 11 years, 2 to 5 years, and 6 months to 23 months), P204 CSR for BD (6 through 11 years), P306 CSR for Part 1 and Part 2, and P306 CSR for Part 4.

6. Discussion of Individual Studies/Clinical Trials

6.1 Clinical Study P301

Title of Study: A Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older

As data from P301 were only submitted to support immunobridging for participants 6 months to 11 years of age from P204 - Part 2 and BD Phase, a full review of P301 is not provided in this review memo. Instead, a summary of the design of P301 is provided.

P301 was a randomized, stratified, observer-blind, placebo-controlled study to evaluate the efficacy, safety, and immunogenicity of mRNA-1273 administered in two doses 28 days apart in adults 18 years of age and older. Participants were randomized 1:1 to receive either 100 μg mRNA-1273 vaccine or placebo at Day 1 and Day 29, stratified by age category (18 to 64 years, ≥65 years) and health risk. Baseline and Day 57 immunogenicity data from a random subset of young adults 18 to 25 years of age randomized to mRNA-1273 were provided to support immunobridging for P204 - Part 2 and BD Phase.

6.2 Study P204 (Part 2 Blinded Phase; BD Phase)

Title of Study: A Phase 2/3, Three-Part, Open-Label, Dose-Escalation, Age De-escalation and Randomized, Observer-Blind, Placebo-Controlled Expansion Study to Evaluate the Safety, Tolerability, Reactogenicity, and Effectiveness of mRNA- 1273 SARS-CoV-2 Vaccine in Healthy Children 6 Months to Less Than 12 Years of Age – mRNA-1273 Primary Series and mRNA-1273 BD Phases

6.2.1 Objectives

Primary Safety Objective:

1. To evaluate the safety and reactogenicity of up to three dose levels (25, 50, and 100 μg) of mRNA-1273 vaccine administered as two doses 28 days apart in three age groups.
2. To evaluate the safety of mRNA-1273 booster dose.
3. To evaluate the safety of mRNA-1273.214 booster dose.

Primary Immunogenicity Objective:

1. To infer the effectiveness of mRNA-1273 (25, 50, and 100 μg, administered as two doses 28 days apart) based on immunogenicity in three age groups.
2. To infer effectiveness of the mRNA-1273 booster dose by establishing noninferiority of Ab response after the booster dose in children in Study P204 compared with post-primary series in adult recipients of mRNA-1273 in the clinical endpoint efficacy trial (Study P301).

Secondary Efficacy Objective:

1. To evaluate the persistence of the immune response to mRNA-1273 vaccine (25, 50, and 100 μg).
2. To evaluate the incidence of SARS-CoV-2 infection after vaccination with mRNA-1273 or placebo.
3. To evaluate the incidence of asymptomatic SARS-CoV-2 infection after vaccination with mRNA-1273 or placebo.
4. To evaluate the incidence of COVID-19 after vaccination with mRNA-1273 or placebo.

6.2.2 Design Overview

Study P204 was a Phase 2/3, three-part, open-label, dose-escalation, age de-escalation and randomized, observer-blind, placebo-controlled, expansion study intended to infer the effectiveness of mRNA-1273 in participants aged 6 months to 11 years. The study population was divided into three discrete age groups (6 to 11 years, 2 to 5 years, and 6 to 23 months) and conducted in three parts.

Each age group started with Part 1 to select a dose and advanced to Part 2 independently. Part 1 of the study was open-label and consisted of dose-escalation, age de-escalation in 1275 participants to select the dose for each age group. Part 2 was a placebo-controlled, observer-blind evaluation of the selected dose in up to 12000 participants (4000 for each age group and within each age group, participants in the Blinded Phase were randomized 3:1 to receive either mRNA-1273 or placebo on Day 1 and Day 29).

In each age group, the availability of any COVID-19 vaccine authorized under EUA triggered eligibility for unblinding and optional crossover vaccination for placebo recipients. For participants 6 to 11 years of age, Part 2 entered the open-label phase on November 1, 2021, with the Blinded Phase ending on November 30, 2021. For participants 2 to 5 years and 6 to 23 months of age, the open-label phase began on June 17, 2022, and the Blinded Phase concluded on June 30, 2022. The effective data cutoff date for all three age groups was the end-of-study database lock date of May 17, 2024. Part 3 was an open-label alternative dosing assessment in approximately 300 participants 6 to 11 years of age to assess reactogenicity and immunogenicity of a lower dose regimen (two doses of mRNA-1273 25 μg on Days 1 and 29 followed by Dose 3 of mRNA-1273 25 μg at least 3 months and up to 5 months after Dose 2). No participants in Part 1 participated in Part 2 or Part 3 of the study, and no participant in Part 2 participated in Part 3 of the study. Discussion of Part 3 study is beyond the scope of this review memo.

All participants enrolled in Part 1 or Part 2 who met the eligibility criteria for BD were offered an optional BD of mRNA-1273 (BD Phase). Of note, participants enrolled later in the study were offered mRNA-1273.214 instead. This review focuses on safety and immunogenicity data from only those who received the mRNA-1273 BD.

Section 6.2 focuses on the P204 Part 2 Blinded Phase (all three age groups) evaluating a two-dose primary series of mRNA-1273 and BD Phase (6 to 11 years of age) evaluating a

BD of mRNA-1273 25 µg given to P204 Parts 1 and 2 participants 6 through 11 years of age who had completed a two-dose primary series of mRNA-1273 50 µg at least 6 months prior.

6.2.3 Population

P204 Part 2 enrolled healthy, COVID-19 vaccine-naïve participants aged 6 months through 11 years. P204 BD Phase enrolled healthy participants aged 6 months to 11 years who received a two-dose primary series with mRNA-1273 in Part 1 or Part 2 of P204.

6.2.4 Study Treatments or Agents Mandated by the Protocol

For Part 2, the volume of study intervention injected was 0.5 mL consisting of either mRNA-1273 (25 µg for 6 months to 5 years of age or 50 µg for 6 to 11 years of age) or placebo (0.9% sodium chloride; normal saline). Each participant received two doses of the study intervention by intramuscular (IM) injection approximately 28 days apart (Day 1 and Day 29). For the BD Phase, participants 6 to 11 years of age received a single dose of 25 µg of mRNA-1273 by IM injection on BD-Day 1.

6.2.6 Sites and Centers

Study P204 was conducted in 88 study sites in the U.S. and Canada.

6.2.7 Surveillance/Monitoring

Please refer to the clinical review.

6.2.8 Endpoints and Study Success Criteria

P204 Part 2 Blinded Phase

The following endpoints apply to each of the three age groups:

Primary Safety Endpoints:

1. Solicited local and systemic adverse reactions (ARs) through 7 days after each injection.
2. Unsolicited adverse events (AEs) through 28 days after each injection.
3. Medically-attended AEs (MAAEs) through the entire study period.
4. Serious AEs (SAEs) through the entire study period.
5. AEs of special interest (AESIs), including multisystem inflammatory syndrome in children (MIS-C) and myocarditis and/or pericarditis, through the entire study period.

Co-Primary Immunogenicity Endpoints:

1. The GMT/GMC of serum neutralizing antibody level and seroresponse rate (SRR) from Study P204 vaccine recipients at Day 57 compared with those from young

adult (18 to 25 years of age) vaccine recipients (Day 57) in the clinical endpoint efficacy trial (Study P301).

- Seroresponse is defined as a value change from baseline (pre-Dose 1 of primary series) below the LLOQ to ≥ 4 × LLOQ, or at least a 4-fold rise if baseline is ≥ LLOQ.

Success criteria for noninferiority based on GMR and SSR against D614G: the lower bound of the 95% CI of the GMR >0.667 and a GMR point estimate ≥0.8; AND the lower bound of the 95% CI of the SRR difference >-10% and the SRR difference point estimate ≥-5%.

Secondary Efficacy Endpoints:

1. The incidence of SARS-CoV-2 infection including symptomatic and asymptomatic infection (by serology and/or RT-PCR) post-baseline.
   - SARS-CoV-2 infection in participants with negative SARS-CoV-2 at baseline: binding antibody (bAb) level against SARS-CoV-2 nucleocapsid protein negative at Day 1, that becomes positive (as measured by Roche Elecsys) post-baseline, OR positive RT-PCR post-baseline.
2. The incidence of SARS-CoV-2 infection measured by RT-PCR and/or bAb levels against SARS-CoV-2 nucleocapsid protein (by Roche Elecsys) post-baseline in participants with negative SARS-CoV-2 at baseline, in the absence of any COVID-19 symptoms.
3. The incidence of the first occurrence of COVID-19 post-baseline, where COVID-19 is defined as symptomatic disease based on CDC case definition (see Table 3).

P204 BD Phase (6 to 11 Years of Age)

Primary Safety Endpoints:

1. Solicited local and systemic ARs through 7 days after booster dose.
2. Unsolicited AEs through 28 days after booster dose.
3. MAAEs through the entire study period after booster dose.
4. SAEs through the entire study period after booster dose.
5. AESIs through the entire study period after booster dose.
6. AEs leading to discontinuation from study participation after booster dose through the last day of study participation.

Co-Primary Immunogenicity Endpoints:

1. The GMT of Day 29 post-booster nAb in Study P204 compared with that post-primary series (Day 57) in adults (≥18 to 25 years) in Study P301.
2. SRR at Day 29 post-booster from baseline (pre-Dose 1 of primary series) compared with post-primary series (Day 57) from baseline (pre-Dose 1 of primary series) in the adults (≥18 to 25 years) in Study P301.

Success criteria for noninferiority against D614G: 95% CI lower bound of GMR >0.667 AND 95% CI lower bound of SRR difference >-10.0%.

6.2.9 Statistical Considerations & Statistical Analysis Plan

For P204 Part 2 Blinded Phase (all three age groups), the primary analysis population for the immunogenicity analyses (unless otherwise specified) was the Per-Protocol Immunogenicity Subset (PPIS). The Protocol Set for Efficacy (PPE) was the primary analysis set used in the efficacy analyses. Solicited ARs and unsolicited AEs were summarized in the Solicited Safety Set (SSS) and Safety Set (SS), respectively. Participants were analyzed according to the randomized vaccine for PPIS, modified intent-to-treat 1 (mITT1) set, and PPE, and according to the vaccine actually received for SSS and SS.

For P204 BD Phase (6 to 11 years of age), the primary analysis population for immunogenicity analyses was PPIS – Pre-BD SARS-CoV-2 Negative (PPIS-NEG). Solicited ARs and unsolicited AEs were summarized in the SSS and SS, respectively. Participants were analyzed according to the randomized vaccine for PPIS-NEG and according to the vaccine actually received for SSS and SS.

Table 2 defines the analysis populations for P204 Part 2 Blinded Phase and P204 BD Phase.

Table 2. Analysis Populations for Study P204 (Part 2 Blinded Phase and BD Phase)

Analysis Population	Description
P204 Part 2 Blinded Phase (All three Age Groups)	-
Immunogenicity Subset	A subset of participants in the Full Analysis Set (FAS)[a] selected for immunogenicity testing, who had baseline SARS-CoV-2 status available and had baseline and at least 1 post-dose antibody assessment for the analysis endpoint.

Analysis Population	Description
Per-protocol Immunogenicity Subset (PPIS)	All participants in the Immunogenicity Subset who also received planned doses of the study vaccine per schedule, complied with immunogenicity testing schedule, had no major protocol deviations that impacted key or critical data, were not receiving HAART if diagnosed with HIV, had baseline and Day 57 antibody assessments for the analysis endpoint, and had a negative SARS-CoV-2 status at baseline (pre-Dose 1), defined as no immunologic or virologic evidence of prior SARS-CoV-2 infection (both negative RT-PCR test for SARS-CoV-2 and negative serology test based on bAb specific to SARS-CoV-2 nucleocapsid) at baseline. The PPIS was used for analyses of immunogenicity unless specified otherwise.
Per-protocol (PP) Set for Efficacy (PPE)	All participants in the FAS[a] who received planned doses of the study vaccine, complied with Dose 2 timing, had a negative SARS-CoV-2 status at baseline (pre-Dose 1), and had no major protocol deviations that impacted key or critical efficacy data.
Modified Intent-to-treat 1 (mITT1) Set	All participants in the FAS[a] who had a negative SARS-CoV-2 status at baseline (pre-Dose 1). Additionally, the set excluded participants who received the wrong treatment (i.e., at least 1 dose received was not as randomized or planned).
Solicited Safety Set	All participants in the Safety Set who contributed any solicited AR data. In addition, this set was defined for each dose separately – First Injection Solicited Safety Set (all participants in the Solicited Safety Set who received the first dose) and Second Injection Solicited Safety Set (all participants in the Solicited Safety Set who received the second dose).
Safety Set	All randomized participants who received at least 1 dose. This set was used for analyses of safety data other than solicited ARs.
P204 BD Phase (6 to 11 Years of Age)	-

Analysis Population	Description
Immunogenicity Subset	Participants in the FAS (BD Analysis)[b] who received the mRNA-1273 BD, had baseline (pre-Dose 1) SARS-CoV-2 status available, and had at least 1 post-BD antibody assessment for the analysis endpoint.
PPIS	Participants in the Immunogenicity Subset who received two planned doses of the study vaccine in Study P204 Part 1 Open-label Phase or Part 2 Blinded Phase per schedule and received a BD, had a negative SARS-CoV-2 status at baseline (pre-Dose 1), had BD-Day 29 antibody assessments for the analysis endpoint, had no major protocol deviations that impacted key or critical data, had not received off-study COVID-19 vaccination prior to BD-Day 29 Visit, and were not receiving HAART if diagnosed with HIV.
PPIS – Pre-BD SARS-CoV-2 Negative (PPIS-NEG)	All participants in the PPIS who were pre-BD SARS-CoV-2 negative, defined as no virologic or serologic evidence of SARS-CoV-2 infection on or before BD-Day 1.
mITT1 Set	All participants in the FAS (BD Analysis)[b] who were pre-BD SARS-CoV-2 negative, and received the correct BD.
Solicited Safety Set	All participants who received the BD and contributed any solicited AR data.
Safety Set	All participants who received the BD.

Abbreviations: BD = booster dose; COVID-19 = coronavirus disease 2019; FAS = Full Analysis Set; HAART = highly active antiretroviral therapy; HIV = human immunodeficiency virus; mITT1 = modified intent-to-treat 1; mRNA = messenger ribonucleic acid; PP = per-protocol; PPIS = Per-protocol Immunogenicity Subset; RT-PCR = reverse transcription polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

[a] Included all participants randomized in Study P204 Part 2 who received at least 1 dose of the study vaccine.

[b] Included all Study P204 Part 1 and Part 2 participants who received the BD.

Source: Adapted from Tables 2 and 4 in the summary of clinical safety and summary of clinical efficacy, respectively.

P204 Part 2 Blinded Phase (All Three Age Groups)

Analysis of Immunogenicity:

The log10-transformed antibody levels at Day 57 for each age group (6 to 11 years, 2 to 5 years, 6 to 23 months) in P204 were analyzed using an analysis of covariance (ANCOVA) model with the group variable (the age group in Study P204 and young adults in Study P301) as a fixed effect. The resulting least squares (LS) means, difference of LS means, and 95% CI were back transformed to the original scale for presentation. The corresponding two-sided 95% CI was provided to assess the difference in immune response between the pediatric age group (Study P204) compared to young adults (≥18 to 25 years of age) in Study P301 at Day 57. Values below LLOQ were set to LLOQ/2.

The number and percentage of participants with seroresponse due to vaccination were provided with two-sided 95% CI using the Clopper-Pearson method at each post baseline time point with Day 57 being of primary interest. The SRR difference with 95% CI using the Miettinen-Nurminen (score) confidence limits at Day 57 was provided between children receiving mRNA-1273 in Study P204 and young adults receiving mRNA-1273 from Study P301.

Analysis of Efficacy:
For each age group in the Part 2 Blinded Phase, the incidence rates of COVID-19, SARS-CoV-2 infection regardless of symptoms, and asymptomatic SARS-CoV-2 infection (see Table 3 for case definitions) between mRNA-1273 and placebo groups were assessed. Incidence rates were calculated as the number of cases divided by the total person-time of follow-up. Person-time was defined as the total time from randomization date to the date of event, last date of study participation, censoring time, or efficacy data cutoff date, whichever was earlier. Vaccine efficacy (VE) was defined as 1 – ratio of incidence rate (mRNA-1273 versus placebo). The 95% CI of the ratio was calculated using the exact method, conditional upon the total number of cases adjusted by the total person-years of follow-up. Cases were counted starting at 14 days post Dose 2 (PPE) and 14 days post Dose 1 (mITT1).

November 30, 2021 (6 to 11 years of age) and June 30, 2022 (2 to 5 years of age and 6 to 23 months of age) were cutoffs for VE analyses in Part 2 Blinded Phase as significant loss of placebo participants after this date precluded meaningful analyses of VE.

Table 3. Case Definitions

Endpoint	Definition
CDC	At least ONE of the following systemic symptoms: fever (temperature > 38°C/≥ 100.4°F) or chills (of any duration, including ≤ 48 hours), fatigue, headache, myalgia, nasal congestion or rhinorrhea, new loss of taste or smell, sore throat, abdominal pain, diarrhea, nausea/vomiting, poor appetite/poor feeding, **OR** at least ONE of the following respiratory signs/symptoms: cough (of any duration, including ≤ 48 hours), shortness of breath or difficulty breathing (of any duration, including ≤ 48 hours), **AND** post-baseline positive PCR result.

Endpoint	Definition
P301	At least one positive RT-PCR test for SARS CoV-2 **AND** At least 2 systemic symptoms: fever (≥ 38°C/≥ 100.4°F), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s), **OR** At least 1 of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, OR clinical or radiographical evidence of pneumonia.
Asymptomatic SARS-CoV-2 infection	Absence of COVID-19 symptoms, **AND** at least 1 from below: bAb level against SARS-CoV-2 nucleocapsid protein negative (as measured by Roche Elecsys) at Day 1 that becomes positive (as measured by Roche Elecsys) post-baseline, **OR** Positive RT-PCR test post-baseline at scheduled or unscheduled/illness visits.
SARS-CoV-2 infection (regardless of symptoms)	A combination of COVID-19 and asymptomatic SARS-CoV-2 infection for participants with negative SARS-CoV-2 status at baseline: bAb levels against SARS-CoV-2 nucleocapsid protein negative (as measured by Roche Elecsys) at Day 1 that becomes positive (as measured by Roche Elecsys) post-baseline, **OR** Positive RT-PCR test post-baseline.

Source: Table 4 in P204 Statistical Analysis Plan (Version 5).

Analysis of Safety:
All safety data were summarized descriptively using frequencies and percentages.

Multiplicity Adjustment:
Hierarchical sequential hypothesis testing was used to preserve the family-wise Type I error rate at a two-sided alpha = 0.05, starting with the oldest age group, followed by the middle age group, and then by the youngest age group. Success criteria for all coprimary endpoints must be met in each age group.

Sample Size Determination:
In Part 2 Blinded Phase, the sample size was driven by safety and immunogenicity considerations. For safety, up to 4000 participants were randomized 3:1 to receive either mRNA-1273 or placebo in each age group. With up to 3000 participants exposed to mRNA-1273 in each age group, the study had at least 95% probability to observe at least 1 participant with an AE at a true 0.1% rate.

For immunogenicity analysis, with approximately 289 participants who received mRNA-1273 in the PPIS in each age group, there was 90% power to demonstrate noninferiority

in terms of GMR at a two-sided alpha of 0.05, assuming an underlying GMR value of 1, a noninferiority margin of 1.5, a point estimate minimum threshold of 0.8, and a standard deviation of the natural log-transformed levels of 1.5. Additionally, with the same number of participants, there was at least 90% power to demonstrate noninferiority as measured by SRR at a two-sided alpha of 0.05, assuming a true SRR of 85% in young adults aged 18 to 25 years from P301 and a true SRR of 85% in each of the three age groups (i.e., true SRR difference was 0 for each age group compared with young adults from P301), a noninferiority margin of -10%, and a point estimate minimum threshold of -5%.

P204 BD Phase (6 to 11 Years Age Group)

Analysis of Immunogenicity:
Immunogenicity analyses were based on participants 6 to 11 years of age in Part 1 and Part 2 of P204 who received a two-dose primary series of mRNA-1273 50 µg and received a BD of mRNA-1273 25 µg in the BD Phase. ANCOVA model was performed with immune response (log titers at BD-Day 29 for P204 and at Day 57 for P301) as a dependent variable and group (children in Study P204 and young adults in Study P301) as the fixed effect. The GMR was estimated by the back-transformed difference in GLSM from the model. The estimated 95% CIs were provided based on the t-distribution of the log-transformed values.

The number and percentage of participants with seroresponse due to vaccination were provided with two-sided 95% CI using the Clopper-Pearson method. The SRR difference with 95% CI using the Miettinen-Nurminen (score) method were provided.

Analysis of Safety:
Safety analyses in this memo were based on participants 6 to 11 years of age in Part 2 of P204 who received a two-dose primary series of mRNA-1273 50 µg and received a BD of mRNA-1273 25 µg in the BD Phase. Participants originally enrolled in Part 1 are not included for safety analyses. All safety data were summarized descriptively using frequencies and percentages.

Multiplicity Adjustment:
No additional multiplicity adjustment was necessary as success criteria for both coprimary endpoints must be met.

6.2.10 Study Population and Disposition

P204 Part 2 Blinded Phase (All 3 Age Groups)

Dispositions of the randomized populations in P204 Part 2 Blinded Phase for each age group are presented in Table 4 and Table 5. A total of 4015 participants (1004 in the placebo group and 3011 in the mRNA-1273 group), 4048 participants (1008 in the placebo group and 3040 in the mRNA-1273 group), and 2664 participants (669 in the placebo group and 1995 in the mRNA-1273 group) were randomized in age groups 6 to

11 years, 2 to 5 years, and 6 to 23 months, respectively. For each age group, positive baseline SARS-CoV-2 status and lack of immunogenicity data at Day 57 were the two main reasons for exclusion from the PPIS.

Table 4. Disposition of Participants in Study P204 Part 2 Blinded Phase (6 to 11 Years)

-	**Placebo n (%)**	**mRNA-1273 50 µg n (%)**
Randomization set	1004	3011
Full analysis set[a]	997 (99.3)	3005 (99.8)
Per-protocol set for efficacy set[a]	849 (84.6)	2606 (86.5)
Modified Intent-to-Treat set[a]	886 (88.2)	2708 (89.9)
Modified Intent-to-Treat-1 set[a]	884 (88.0)	2694 (89.5)
Immunogenicity subset	87	379
Per-protocol immunogenicity subset[b]	76 (87.4)	311 (82.1)
Excluded from per-protocol immunogenicity subset[b]	-	68 (17.9)
Reasons for exclusion[b]	-	-
Positive Baseline SARS-CoV-2 status	-	38 (10.0)
Did not receive Dose 2 per schedule	-	0
Received incorrect vaccination	-	0
Received Dose 2 out of window	-	1 (0.3)
Had no immunogenicity data at Day 57	-	17 (4.5)
Had other major protocol deviations	-	12 (3.2)
Participants with HIV infection	-	0
Age outside of randomized age group	-	0
Received off-study COVID-19 vaccine at or before Day 57	-	0
Safety set	995	3007
Solicited safety set[c]	994 (99.9)	3005 (>99.9)
First injection solicited safety set[c]	993 (99.8)	3003 (99.9)
Second injection solicited safety set[c]	970 (97.5)	2993 (99.5)

[a] Numbers were based on planned study group and percentages were based on the number of randomized participants.
[b] Numbers were based on planned study group and percentages were based on the number of participants in the immunogenicity subset.
[c] Numbers were based on actual study group and percentages were based on the number of safety participants.
Source: Adapted from Tables 13 and 14 in P204 CSR for primary series (6 through 11 years).

Table 5. Disposition of Participants in Study P204 Part 2 Blinded Phase (6 Months to 5 Years)

-	**Placebo; 6-23 months n (%)**	**mRNA-1273 25 µg; 6-23 months n (%)**	**Placebo; 2-5 years n (%)**	**mRNA-1273 25 µg; 2-5 years n (%)**
Randomization set	669	1995	1008	3040
Full analysis set[a]	667 (99.7)	1993 (99.9)	1007 (>99.9)	3031 (99.7)
Per-protocol set for efficacy set[a]	563 (84.2)	1686 (84.5)	854 (84.7)	2592 (85.3)
Modified Intent-to-Treat set set[a]	594 (88.8)	1768 (88.6)	899 (89.2)	2697 (88.7)
Modified Intent-to-Treat-1 set[a]	593 (88.6)	1766 (88.5)	899 (89.2)	2695 (88.7)
Immunogenicity subset	74	340	73	351
Per-protocol immunogenicity subset[b]	65 (87.8)	286 (84.1)	62 (84.9)	304 (86.6)
Excluded from per-protocol immunogenicity subset[b]	-	54 (15.9)	-	47 (13.4)
Reasons for exclusion[b]	-	-	-	-
Positive Baseline SARS-CoV-2 status	-	19 (5.6)	-	28 (8.0)
Did not receive Dose 2 per schedule	-	0	-	1 (0.3)
Received incorrect vaccination	-	0	-	0
Received Dose 2 out of window	-	5 (1.5)	-	2 (0.6)
Had no immunogenicity data at Day 57	-	29 (8.5)	-	15 (4.3)
Had other major protocol deviations	-	0	-	0
Participants with HIV infection	-	0	-	0
Age is outside of the randomized age group	-	1 (0.3)	-	1 (0.3)
Received off-study COVID-19 vaccine at or before Day 57	-	0	-	0
Safety set	666	1994	1007	3031
Solicited safety set[c]	664 (99.7)	1991 (99.8)	998 (99.1)	3014 (99.4)

-	**Placebo; 6-23 months n (%)**	**mRNA-1273 25 µg; 6-23 months n (%)**	**Placebo; 2-5 years n (%)**	**mRNA-1273 25 µg; 2-5 years n (%)**
First injection solicited safety set[c]	661 (99.2)	1982 (99.4)	971 (96.4)	2955 (97.5)
Second injection solicited safety set[c]	646 (97.0)	1975 (99.0)	974 (96.7)	2977 (98.2)

[a] Numbers were based on planned study group and percentages were based on the number of randomized participants.
[b] Numbers were based on planned study group and percentages were based on the number of participants in the immunogenicity subset.
[c] Numbers were based on actual study group and percentages were based on the number of safety participants.
Source: Adapted from Tables 3 and 4 in P204 CSR for primary series (6 through 23 months) and Tables 4 and 5 in P204 CSR for primary series (2 through 5 years).

For P204 Part 2 Blinded Phase, the distributions of demographic characteristics were generally similar between the placebo and mRNA-1273 groups in the Safety Set for each age group (Table 6, Table 7, and Table 8). Of note, for participants 2 to 5 years of age and 6 to 23 months of age, some participants were enrolled in error. Among participants 2 to 5 years of age, the median age was 3.0 years (ranging from 1 to 5 years); 11 and 18 participants aged <2 years were erroneously enrolled in the placebo and mRNA-1273 groups, respectively. Among participants 6 to 23 months of age, six participants aged ≥2 years were enrolled in the mRNA-1273 group in error.

Table 6. Demographic and Baseline Characteristics in Study P204 Part 2 Blinded Phase (Safety Set; 6 to 11 Years)

-	**Placebo (N=995)**	**mRNA-1273 50 µg (N=3007)**
Age (years)	-	-
n	995	3007
Mean (SD)	8.5 (1.64)	8.5 (1.65)
Median	9	8
Q1, Q3	7.0, 10.0	7.0, 10.0
Min, Max	6, 11	6, 11
Age group (years), n (%)	-	-
≥6 and <9	486 (48.8)	1515 (50.4)
≥9 and <12	509 (51.2)	1492 (49.6)
Sex, n (%)	-	-
Male	481 (48.3)	1554 (51.7)

-	**Placebo (N=995)**	**mRNA-1273 50 µg (N=3007)**
Female	514 (51.7)	1453 (48.3)
Race, n (%)	-	-
White	668 (67.1)	1958 (65.1)
Black	93 (9.3)	310 (10.3)
Asian	100 (10.1)	296 (9.8)
American Indian or Alaska Native	3 (0.3)	14 (0.5)
Native Hawaiian or Other Pacific Islander	0	4 (0.1)
Multiracial	98 (9.8)	330 (11.0)
Other	22 (2.2)	62 (2.1)
Not reported	10 (1.0)	23 (0.8)
Unknown	1 (0.1)	10 (0.3)
Ethnicity, n (%)	-	-
Hispanic or Latino	181 (18.2)	560 (18.6)
Not Hispanic or Latino	804 (80.8)	2419 (80.4)
Not reported	5 (0.5)	21 (0.7)
Unknown	5 (0.5)	7 (0.2)
Race and ethnicity group, n (%)[a]	-	-
White non-Hispanic	536 (53.9)	1542 (51.3)
Communities of color	456 (45.8)	1459 (48.5)
Missing	3 (0.3)	6 (0.2)
Country, n (%)	-	-
U.S.	985 (99.0)	2977 (99.0)
Canada	10 (1.0)	30 (1.0)
Weight (kg)	-	-
n	995	3007
Mean (SD)	33.52 (11.434)	33.28 (11.111)
Median	30.91	30.6
Q1, Q3	25.75, 38.55	25.45, 38.50
Min, Max	14.2, 99.8	15.4, 103.7
Height (cm)	-	-
n	995	3007
Mean (SD)	135.58 (11.936)	135.35 (11.837)
Median	135.4	134.9

-	**Placebo (N=995)**	**mRNA-1273 50 µg (N=3007)**
Q1, Q3	126.70, 144.78	126.40, 143.51
Min, Max	102.8, 167.6	86.4, 178.0
BMI (kg/m²)	-	-
n	995	3007
Mean (SD)	17.83 (3.859)	17.78 (3.751)
Median	16.8	16.69
Q1, Q3	15.37, 19.17	15.26, 19.26
Min, Max	10.7, 42.9	9.9, 43.6
BMI subgroup (obesity vs. non-obesity), n (%)	-	-
Obesity	195 (19.6)	606 (20.2)
Non-obesity	800 (80.4)	2401 (79.8)
Baseline RT-PCR results, n (%)	-	-
Negative	968 (97.3)	2950 (98.1)
Positive	9 (0.9)	26 (0.9)
Missing	18 (1.8)	31 (1.0)
Baseline Elecsys Anti-SARS-CoV-2 results, n (%)	-	-
Negative	909 (91.4)	2759 (91.8)
Positive	79 (7.9)	236 (7.8)
Missing	7 (0.7)	12 (0.4)
Baseline SARS-CoV-2 status, n (%)[b]	-	-
Negative	884 (88.8)	2710 (90.1)
Positive	87 (8.7)	257 (8.5)
Missing	24 (2.4)	40 (1.3)

[a] White non-Hispanic was defined as White and non-Hispanic, and Communities of color included all the others whose race or ethnicity was not unknown, unreported, or missing.
[b] Positive was defined as a positive RT-PCR test for SARS-CoV-2, and/or a positive serology test based on binding antibody (bAb) specific to SARS-CoV-2 nucleocapsid on or before Day 1. Negative was defined as a negative RT-PCR test for SARS-CoV-2, and a negative serology test based on bAb specific to SARS-CoV-2 nucleocapsid on or before Day 1.
Source: Table 16 in P204 CSR for primary series (6 through 11 years).

Table 7. Demographic and Baseline Characteristics in Study P204 Part 2 Blinded Phase (Safety Set; 2 to 5 Years)

-	**Placebo (N=1007)**	**mRNA-1273 25 µg (N=3031)**
Age (years)	-	-
n	1007	3031
Mean (SD)	3.0 (0.89)	3.0 (0.87)
Median	3	3
Q1, Q3	2.0, 4.0	2.0, 4.0
Min, Max	1, 5	1, 5
Age group, n (%)	-	-
<2 years	11 (1.1)	18 (0.6)
≥2 years and <4 years	657 (65.2)	2069 (68.3)
≥4 years and <6 years	339 (33.7)	944 (31.1)
Sex, n (%)	-	-
Male	510 (50.6)	1543 (50.9)
Female	497 (49.4)	1488 (49.1)
Race, n (%)	-	-
White	792 (78.6)	2299 (75.8)
Black	38 (3.8)	142 (4.7)
Asian	51 (5.1)	191 (6.3)
American Indian or Alaska Native	3 (0.3)	11 (0.4)
Native Hawaiian or Other Pacific Islander	3 (0.3)	5 (0.2)
Multiracial	100 (9.9)	323 (10.7)
Other	16 (1.6)	43 (1.4)
Not reported	4 (0.4)	13 (0.4)
Unknown	0	4 (0.1)
Ethnicity, n (%)	-	-
Hispanic or Latino	142 (14.1)	429 (14.2)
Not Hispanic or Latino	856 (85.0)	2584 (85.3)
Not reported	8 (0.8)	13 (0.4)
Unknown	1 (<0.1)	5 (0.2)
Race and ethnicity group, n (%)	-	-
White non-Hispanic	678 (67.3)	1980 (65.3)
Communities of color	327 (32.5)	1049 (34.6)
Missing	2 (0.2)	2 (<0.1)
Country, n (%)	-	-
U.S.	952 (94.5)	2866 (94.6)

-	**Placebo (N=1007)**	**mRNA-1273 25 µg (N=3031)**
Canada	55 (5.5)	165 (5.4)
Weight (kg)	-	-
n	1006	3029
Mean (SD)	15.99 (2.838)	16.11 (3.136)
Median	15.64	15.73
Q1, Q3	14.09, 17.60	14.05, 17.70
Min, Max	9.6, 35.4	7.0, 56.9
Height (cm)	-	-
n	1006	3029
Mean (SD)	99.60 (8.703)	99.81 (8.615)
Median	99.08	99.9
Q1, Q3	93.90, 105.41	93.98, 105.50
Min, Max	64.3, 143.0	64.0, 129.5
BMI (kg/m²)	-	-
n	1006	3029
Mean (SD)	16.10 (1.919)	16.12 (2.002)
Median	15.87	15.9
Q1, Q3	14.99, 16.92	15.00, 16.83
Min, Max	10.1, 35.2	10.2, 39.9
BMI subgroup (obesity vs. non-obesity), n (%)	-	-
Obesity	107 (10.6)	326 (10.8)
Non-obesity	899 (89.3)	2703 (89.2)
Missing	1 (<0.1)	2 (<0.1)
Baseline RT-PCR results, n (%)	-	-
Negative	986 (97.9)	2973 (98.1)
Positive	7 (0.7)	21 (0.7)
Missing	14 (1.4)	37 (1.2)
Baseline Elecsys Anti-SARS-CoV-2 results, n (%)	-	-
Negative	916 (91.0)	2746 (90.6)
Positive	78 (7.7)	251 (8.3)
Missing	13 (1.3)	34 (1.1)
Baseline SARS-CoV-2 status, n (%)	-	-
Negative	899 (89.3)	2697 (89.0)

-	**Placebo (N=1007)**	**mRNA-1273 25 µg (N=3031)**
Positive	82 (8.1)	267 (8.8)
Missing	26 (2.6)	67 (2.2)

Source: Adapted from Table 7 in P204 CSR for primary series (2 through 5 years).

Table 8. Demographic and Baseline Characteristics in Study P204 Part 2 Blinded Phase (Safety Set; 6 to 23 Months)

-	**Placebo (N=666)**	**mRNA-1273 25 µg (N=1994)**
Age (months)	-	-
n	666	1994
Mean (SD)	15.9 (4.88)	15.7 (5.05)
Median	17	16
Q1, Q3	13.0, 20.0	12.0, 20.0
Min, Max	6, 23	6, 51
Age group, n (%)	-	-
6 months and <1 year	142 (21.3)	454 (22.8)
≥1 year and <2 years	524 (78.7)	1534 (76.9)
≥2 years	0	6 (0.3)
Sex, n (%)	-	-
Male	326 (48.9)	1013 (50.8)
Female	340 (51.1)	981 (49.2)
Race, n (%)	-	-
White	524 (78.7)	1568 (78.6)
Black	18 (2.7)	62 (3.1)
Asian	38 (5.7)	94 (4.7)
American Indian or Alaska Native	0	7 (0.4)
Native Hawaiian or Other Pacific Islander	0	0
Multiracial	76 (11.4)	215 (10.8)
Other	7 (1.1)	33 (1.7)
Not reported	2 (0.3)	10 (0.5)
Unknown	1 (0.2)	5 (0.3)
Ethnicity, n (%)	-	-
Hispanic or Latino	94 (14.1)	256 (12.8)
Not Hispanic or Latino	565 (84.8)	1719 (86.2)

-	**Placebo (N=666)**	**mRNA-1273 25 µg (N=1994)**
Not reported	6 (0.9)	17 (0.9)
Unknown	1 (0.2)	2 (0.1)
Race and ethnicity group, n (%)	-	-
White non-Hispanic	445 (66.8)	1379 (69.2)
Communities of color	219 (32.9)	613 (30.7)
Missing	2 (0.3)	2 (0.1)
Country, n (%)	-	-
US	628 (94.3)	1880 (94.3)
Canada	38 (5.7)	114 (5.7)
Weight (kg)	-	-
n	665	1992
Mean (SD)	10.83 (1.929)	10.83 (1.983)
Median	10.7	10.8
Q1, Q3	9.50, 12.09	9.50, 12.00
Min, Max	4.6, 17.7	5.0, 29.3
Height (cm)	-	-
n	665	1992
Mean (SD)	79.29 (6.566)	78.92 (6.887)
Median	79.5	79.4
Q1, Q3	75.00, 83.82	74.35, 83.82
Min, Max	55.9, 109.2	47.0, 108.0
BMI (kg/m^2)	-	-
n	665	1992
Mean (SD)	17.18 (1.999)	17.39 (2.519)
Median	17.1	17.16
Q1, Q3	15.87, 18.24	16.04, 18.33
Min, Max	8.3, 28.4	7.3, 48.4
BMI subgroup (obesity vs. non-obesity), n (%)	-	-
Obesity	135 (20.3)	416 (20.9)
Non-obesity	530 (79.6)	1576 (79.0)
Missing	1 (0.2)	2 (0.1)
Baseline RT-PCR results, n (%)	-	-
Negative	654 (98.2)	1954 (98.0)
Positive	6 (0.9)	18 (0.9)

-	**Placebo (N=666)**	**mRNA-1273 25 µg (N=1994)**
Missing	6 (0.9)	22 (1.1)
Baseline Elecsys Anti-SARS-CoV-2 results, n (%)	-	-
Negative	603 (90.5)	1800 (90.3)
Positive	42 (6.3)	118 (5.9)
Missing	21 (3.2)	76 (3.8)
Baseline SARS-CoV-2 status, n (%)	-	-
Negative	593 (89.0)	1769 (88.7)
Positive	47 (7.1)	133 (6.7)
Missing	26 (3.9)	92 (4.6)

Source: Table 6 in P204 CSR for primary series (6 through 23 months).

Table 9 displays the demographic and baseline characteristics in Study P204 Part 2 Blinded Phase (PPIS; 6 months to 11 years) and Study 301 (PPIS; 18 to 25 years) for the mRNA-1273 group. For P204 Part 2 Blinded Phase, the demographics and baseline characteristics for each age group from the PPIS were generally similar to the Safety Set for the mRNA-1273 group. Specifically, compared to the young adult population in P301 PPIS, all three age groups included a higher proportion of white non-Hispanic participants (55.3%, 57.2%, and 63.6% vs 49.3%, respectively). The 6 to 11 years age group had a slightly higher percentage of Black participants (11.6% vs 9.8%), while the 2 to 5 years and 6 to 23 months age groups had slightly lower percentages (7.9% and 4.5% vs 9.8%, respectively). All pediatric groups had a lower percentage of Asian participants (6.8%, 5.9%, and 5.2% vs 10.1%) and lower percentages of obesity (19.3%, 7.9%, and 16.8% vs 23.0%) compared to the young adult population.

Table 9. Demographic and Baseline Characteristics in Study P204 Part 2 Blinded Phase (PPIS; 6 Months to 11 Years) and Study 301 (PPIS; 18 to 25 Years) for the mRNA-1273 Group

-	**P204 mRNA-1273 25 µg; 6-23 months (N=286)**	**P204 mRNA-1273 25 µg; 2-5 years (N=304)**	**P204 mRNA-1273 50 µg; 6-11 years (N=311)**	**P301 mRNA-1273 100 µg; 18-25 years (N=296)**
Age*	-	-	-	-
n	286	304	311	296
Mean (SD)	16.3 (4.39)	3.3 (0.94)	8.5 (1.73)	22.4 (2.19)
Median	16.5	3	9	23
Q1, Q3	13.0, 20.0	3.0, 4.0	7.0, 10.0	21.0, 24.0
Min, Max	6, 23	2, 5	6, 11	18, 25
Sex, n (%)	-	-	-	-

-	**P204 mRNA-1273 25 µg; 6-23 months (N=286)**	**P204 mRNA-1273 25 µg; 2-5 years (N=304)**	**P204 mRNA-1273 50 µg; 6-11 years (N=311)**	**P301 mRNA-1273 100 µg; 18-25 years (N=296)**
Male	141 (49.3)	160 (52.6)	165 (53.1)	143 (48.3)
Female	145 (50.7)	144 (47.4)	146 (46.9)	153 (51.7)
Race, n (%)	-	-	-	-
White	218 (76.2)	216 (71.1)	214 (68.8)	207 (69.9)
Black	13 (4.5)	24 (7.9)	36 (11.6)	29 (9.8)
Asian	15 (5.2)	18 (5.9)	21 (6.8)	30 (10.1)
American Indian or Alaska native	1 (0.3)	1 (0.3)	1 (0.3)	3 (1.0)
Native Hawaiian or other Pacific Islander	0	0	0	2 (0.7)
Multiracial	27 (9.4)	38 (12.5)	29 (9.3)	14 (4.7)
Other	11 (3.8)	3 (1.0)	6 (1.9)	8 (2.7)
Not reported	1 (0.3)	3 (1.0)	4 (1.3)	3 (1.0)
Unknown	0	1 (0.3)	0	0
Ethnicity, n (%)	-	-	-	-
Hispanic or Latino	48 (16.8)	56 (18.4)	50 (16.1)	78 (26.4)
Not Hispanic or Latino	235 (82.2)	248 (81.6)	258 (83.0)	216 (73.0)
Not reported	3 (1.0)	0	3 (1.0)	0
Unknown	0	0	0	2 (0.7)
Race and ethnicity group, n (%)	-	-	-	-
White non-Hispanic	182 (63.6)	174 (57.2)	172 (55.3)	146 (49.3)
Communities of color	104 (36.4)	130 (42.8)	138 (44.4)	150 (50.7)
Missing	0	0	1 (0.3)	0
Country, n (%)	-	-	-	-
US	286 (100)	304 (100)	311 (100)	296 (100)
Canada	0	0	0	0
Weight (kg)	-	-	-	-
n	286	304	311	295
Mean (SD)	11.09 (2.260)	16.43 (2.941)	33.58 (11.657)	77.57 (19.283)

-	**P204 mRNA-1273 25 µg; 6-23 months (N=286)**	**P204 mRNA-1273 25 µg; 2-5 years (N=304)**	**P204 mRNA-1273 50 µg; 6-11 years (N=311)**	**P301 mRNA-1273 100 µg; 18-25 years (N=296)**
Median	11	16.09	31.27	73.6
Q1, Q3	9.80, 11.91	14.38, 18.18	24.82, 39.55	63.64, 88.18
Min, Max	7.0, 29.3	9.2, 34.8	16.8, 102.1	44.0, 158.2
Height (cm)	-	-	-	-
n	286	304	311	295
Mean (SD)	80.10 (6.877)	101.99 (9.230)	135.50 (12.208)	171.19 (9.310)
Median	80.72	101.95	135.2	170.6
Q1, Q3	76.20, 84.00	95.35, 107.88	126.50, 144.78	165.10, 177.80
Min, Max	48.5, 108.0	68.1, 129.5	111.0, 166.9	147.3, 201.9
BMI (kg/m²)	-	-	-	-
n	286	304	311	295
Mean (SD)	17.34 (2.458)	15.77 (1.640)	17.85 (3.854)	26.39 (5.936)
Median	16.82	15.68	16.75	24.91
Q1, Q3	15.79, 18.03	14.68, 16.63	15.13, 19.37	21.99, 29.56
Min, Max	12.7, 46.8	10.2, 24.3	13.1, 43.6	16.7, 48.7
BMI subgroup (obesity vs non-obesity), n (%)	-	-	-	-
Obesity	48 (16.8)	24 (7.9)	60 (19.3)	68 (23.0)
Non-obesity	238 (83.2)	280 (92.1)	251 (80.7)	227 (76.7)
Missing	0	0	0	1 (0.3)
Baseline RT-PCR results, n (%)	-	-	-	-
Negative	286 (100)	304 (100)	311 (100)	296 (100)
Positive	0	0	0	0
Baseline Elecsys Anti-SARS-CoV-2 results, n (%)	-	-	-	-
Negative	286 (100)	304 (100)	311 (100)	296 (100)
Positive	0	0	0	0
Baseline SARS-CoV-2 status, n (%)[b]	-	-	-	-
Negative	286 (100)	304 (100)	311 (100)	296 (100)
Positive	0	0	0	0

*The units of age for the 6-23 months, 2-5 years, and 6-11 years age groups were months, years, and years, respectively.
Source: Adapted from Table 7 in P204 CSR for primary series (6 through 23 months), Table 8 in P204 CSR for primary series (2 through 5 years), and Table 17 in P204 CSR for primary series (6 through 11 years).

Study P204 BD Phase (6 to 11 Years Age Group)

Table 10 presents the disposition of participants in P204 BD Phase for the age group of 6 to 11 years. A total of 2519 participants 6 to 11 years of age who received a two-dose primary series with mRNA-1273 in Part 1 or Part 2 of P204 received a 25 µg dose of mRNA-1273 as a booster vaccination, where 2290 participants were from Part 2. Positive baseline SARS-CoV-2 status and lack of immunogenicity data at Day 57 were the two main reasons for exclusion from the PPIS.

Table 10. Disposition of Participants in P204 BD Phase (6 to 11 Years)

-	**Part 1 + Part 2 mRNA-1273 50 µg Primary Series - Booster 25 µg (N=2519) n (%)**	**Part 2 mRNA-1273 50 µg Primary Series - Booster 25 µg (N=2290) n (%)**
Full analysis set	2519	-
Modified Intent-to-Treat-1 set	1231 (48.9)	-
Immunogenicity subset	676	-
Per-protocol immunogenicity subset, n (%)	189 (28.0)	-
Excluded from Per-Protocol Immunogenicity Subset, n (%)	486 (72.0)	-
Reasons for exclusion, n(%)	-	-
Positive Baseline SARS-CoV-2 status	54 (8.0)	-
Did not receive Dose 2 per schedule	0	-
Received incorrect vaccination in Primary Series	3 (0.4)	-
Received incorrect vaccination in BD	0	-
Received Dose 2 out of window	7 (1.0)	-
Had no immunogenicity data at BD+Day 29 P204/Day 57 P301	409 (60.6)	-

-	**Part 1 + Part 2 mRNA-1273 50 µg Primary Series - Booster 25 µg (N=2519) n (%)**	**Part 2 mRNA-1273 50 µg Primary Series - Booster 25 µg (N=2290) n (%)**
Off-study intervention received before BD	0	-
Had other major protocol deviations	13 (1.9)	-
Participants with HIV infection	0	-
Per-protocol immunogenicity subset – pre-booster SARS-CoV-2 negative, n (%)	137 (20.3)	-
Safety set	-	2290
Solicited safety set, n (%)	-	2259 (98.6)

Source: Adapted from Table 14.1.1.3.4.2 (6y12y) and Table 14.1.2.3.4 (6y12y) in P204 CSR for BD Phase (6 through 11 years).

Table 11 displays the demographic and baseline characteristics in P204 BD Phase (SS and PPIS; 6 to 11 years) and P301 (PPIS; 18-25 years). For the 6 to 11 years age group in P204 BD Phase, the distributions between the SS and the PPIS were similar. Aside from age differences, there was a higher percentage of white non-Hispanic participants in the PPIS for P204 BD Phase (63.5%) than in the PPIS for P301 young adults (49.3%).

Table 11. Demographic and Baseline Characteristics in P204 BD Phase (SS and PPIS; 6 to 11 Years) and P301 (PPIS; 18-25 Years)

-	**Part 1 + Part 2 mRNA-1273 50 µg Primary Series - Booster 25 µg (N=2519) n (%) SS**	**Part 1 + Part 2 P204 mRNA-1273 50 µg Booster 25 µg (N=189) n (%) PPIS**	**P301 mRNA-1273 100 µg (N=296) n (%) PPIS**
Age (years)	-	-	-
n	2519	189	296
Mean (SD)	8.5 (1.61)	8.4 (1.56)	22.4 (2.19)
Median	8	8	23
Min, Max	6, 11	6, 11	18, 25
Age group (years), n (%)	-	-	-
≥6 and <9	1272 (50.5)	95 (50.3)	-

-	**Part 1 + Part 2 mRNA-1273 50 µg Primary Series - Booster 25 µg (N=2519) n (%) SS**	**Part 1 + Part 2 P204 mRNA-1273 50 µg Booster 25 µg (N=189) n (%) PPIS**	**P301 mRNA-1273 100 µg (N=296) n (%) PPIS**
≥9 and <12	1247 (49.5)	94 (49.7)	-
Sex, n (%)	-	-	-
Male	1330 (52.8)	93 (49.2)	143 (48.3)
Female	1189 (47.2)	96 (50.8)	153 (51.7)
Race, n (%)	-	-	-
White	1657 (65.8)	139 (73.5)	207 (69.9)
Black	279 (11.1)	11 (5.8)	29 (9.8)
Asian	203 (8.1)	13 (6.9)	30 (10.1)
American Indian or Alaska Native	11 (0.4)	3 (1.6)	3 (1.0)
Native Hawaiian or other Pacific Islander	4 (0.2)	1 (0.5)	2 (0.7)
Multiracial	291 (11.6)	14 (7.4)	14 (4.7)
Other	49 (1.9)	5 (2.6)	8 (2.7)
Not reported	21 (0.8)	2 (1.1)	3 (1.0)
Unknown	4 (0.2)	1 (0.5)	0
Ethnicity, n (%)	-	-	-
Hispanic or Latino	425 (16.9)	28 (14.8)	78 (26.4)
Not Hispanic or Latino	2072 (82.3)	159 (84.1)	216 (73.0)
Not reported	15 (0.6)	1 (0.5)	0
Unknown	7 (0.3)	1 (0.5)	2 (0.7)
Race and ethnicity group, n (%)	-	-	-
White non-Hispanic	1349 (53.6)	120 (63.5)	146 (49.3)
Communities of color	1166 (46.3)	68 (36.0)	150 (50.7)
Missing	4 (0.2)	1 (0.5)	0
Country, n (%)	-	-	-
U.S.	2513 (99.8)	189 (100)	296 (100)
Canada	6 (0.2)	0	0

-	**Part 1 + Part 2 mRNA-1273 50 µg Primary Series - Booster 25 µg (N=2519) n (%) SS**	**Part 1 + Part 2 P204 mRNA-1273 50 µg Booster 25 µg (N=189) n (%) PPIS**	**P301 mRNA-1273 100 µg (N=296) n (%) PPIS**
Weight (kg)	-	-	-
n	2519	189	295
Mean (SD)	33.45 (11.191)	32.51 (10.292)	77.57 (19.283)
Median	30.8	29.4	73.6
Min, Max	15.4, 103.7	16.8, 76.4	44.0, 158.2
Height (cm)	-	-	-
n	2519	189	295
Mean (SD)	135.49 (11.821)	135.58 (11.708)	171.19 (9.310)
Median	135	134.87	170.6
Min, Max	86.4, 178.0	110.5, 177.8	147.3, 201.9
Body mass index (kg/m^2)	-	-	-
n	2519	189	295
Mean (SD)	17.84 (3.796)	17.32 (3.189)	26.39 (5.936)
Median	16.72	16.32	24.91
Min, Max	9.9, 43.6	11.8, 29.0	16.7, 48.7
BMI subgroup (obesity vs. non-obesity), n (%)	-	-	-
Obesity	514 (20.4)	33 (17.5)	68 (23.0)
Non-obesity	2005 (79.6)	156 (82.5)	227 (76.7)
Missing	0	0	1 (0.3)
Baseline RT-PCR result, n (%)	-	-	-
Negative	2473 (98.2)	189 (100)	296 (100)
Positive	21 (0.8)	0	0
Missing	25 (1.0)	0	0
Baseline Elecsys anti-SARS-CoV-2 result, n (%)	-	-	-
Negative	2329 (92.5)	189 (100)	296 (100)
Positive	181 (7.2)	0	0
Missing	9 (0.4)	0	0

-	**Part 1 + Part 2 mRNA-1273 50 µg Primary Series - Booster 25 µg (N=2519) n (%) SS**	**Part 1 + Part 2 P204 mRNA-1273 50 µg Booster 25 µg (N=189) n (%) PPIS**	**P301 mRNA-1273 100 µg (N=296) n (%) PPIS**
Baseline SARS-CoV-2 status, n (%)	-	-	-
Negative	2288 (90.8)	189 (100)	296 (100)
Positive	199 (7.9)	0	0
Missing	32 (1.3)	0	0
Pre-booster RT-PCR result, n (%)	-	-	-
Negative	2446 (97.1)	183 (96.8)	-
Positive	38 (1.5)	1 (0.5)	-
Missing	35 (1.4)	5 (2.6)	-
Pre-booster Elecsys anti-SARS-CoV-2 result, n (%)	-	-	-
Negative	1309 (52.0)	142 (75.1)	-
Positive	1036 (41.1)	43 (22.8)	-
Missing	174 (6.9)	4 (2.1)	-
Pre-booster SARS-CoV-2 status, n (%)	-	-	-
Negative	1248 (49.5)	137 (72.5)	-
Positive	1060 (42.1)	43 (22.8)	-
Missing	191 (7.6)	9 (4.8)	-

Source: Adapted from Tables 8 and 9 in P204 CSR for BD (6 through 11 years).

6.2.11 Efficacy Analyses

P204 Part 2 Blinded Phase

Coprimary Endpoints – Immunogenicity Objective to Infer Effectiveness

Noninferiority were met for both GMR and SRR in each age group. Results are summarized in Table 12.

Across the subgroups of sex, race, ethnicity, race and ethnicity, and obesity status, no meaningful differences in GMRs or SRR differences were observed within each age group.

Table 12. Immunobridging Analysis - Comparison of Day 57 nAb Levels and SRRs Against SARS-CoV-2 (D614G) in Study P204 Part 2 Participants (by Age Group) and Study P301 Young Adult Participants 18 To 25 Years of Age (PPIS)

-	**Study P204 Part 2 6 to 11 Years Age Group mRNA-1273 50 µg (N=311)**	**Study P301 18 to 25 Years Age Group mRNA-1273 100 µg (N=296)**	**Study P204 Part 2 2 to 5 Years Age Group mRNA-1273 25 µg (N=304)**	**Study P301 18 to 25 Years Age Group mRNA-1273 100 µg (N=296)**	**Study P204 Part 2 6 to 23 Months Age Group mRNA-1273 25 µg (N=286)**	**Study P301 18 to 25 Years Age Group mRNA-1273 100 µg (N=296)**
Day 57	-	-	-	-	-	-
n	309	294	289	294	268	294
GMT/GMC (model based)	1618.3	1321.9	1394.1	1400.4	1759.8	1400.4
95% CI	1464.3, 1788.6	1193.1, 1464.6	1267.0, 1533.9	1273.8, 1539.6	1599.2, 1936.5	1278.1, 1534.4
GMR (P204 versus P301)[a]	1.224	-	0.995	-	1.257	-
95% CI [a]	1.061, 1.413	-	0.870, 1.139	-	1.101, 1.434	-
N1	307	294	284	294	264	294
SRR, n (%)[b]	304 (99.0)	292 (99.3)	281 (98.9)	292 (99.3)	264 (100)	292 (99.3)
95% CI [c]	97.2, 99.8	97.6, >99.9	96.9, 99.8	97.6, >99.9	98.6, 100.0	97.6, >99.9
Difference (P204 versus P301) %	-0.3	-	-0.4	-	0.7	-
95% CI [d]	-2.2, 1.6	-	-2.5, 1.5	-	-0.8, 2.4	-

Abbreviations: ANCOVA = analysis of covariance; CI = confidence interval; GMR = geometric mean ratio; LLOQ = lower limit of quantification; LS = least squares; mRNA = messenger ribonucleic acid; N1 = number of participants with nonmissing data at baseline and the corresponding timepoint; nAb = neutralizing antibody; PPIS = Per-Protocol Immunogenicity Subset; SRR = seroresponse rate.

[a] The log-transformed antibody levels were analyzed using an ANCOVA model with the group variable (participants in Study P204 and young adult participants in Study P301) as

fixed effect. The resulted LS means, difference of LS means, and 95% CI were back-transformed to the original scale for presentation.
[b] Seroresponse at a participant level was defined as a change from baseline below the LLOQ to ≥4×LLOQ, or at least a 4-fold rise if baseline was ≥LLOQ. Percentages were based on N1.
[c] 95% CI was calculated using the Clopper-Pearson method.
[d] 95% CI was calculated using the Miettinen-Nurminen (score) confidence limits.
Source: Adapted from Tables 5, 6, and 7 in the summary of clinical efficacy.

Reviewer's Comments:

1. *In Table 12, the nAb levels against D614G used the pseudovirus neutralization assay (PsVNA; ID_{50}) at Duke University, PsVNA (VAC62) at PPD Laboratories, and PsVNA (VAC62) at PPD Laboratories for participants 6 to 11 years, 2 to 5 years, and 6 to 23 months of age, respectively. PsVNA (ID_{50}) assay reported nAb levels in titers and PsVNA (VAC62) assay reported nAb levels in concentrations.*
2. *All immunogenicity results reported by the applicant were verified by my independent analyses based on datasets submitted in the Standard Data Tabulation Model (SDTM) format.*

Secondary Endpoint – Vaccine Efficacy

Vaccine efficacy (VE) was descriptively analyzed as a secondary endpoint of the study for all three age groups. The efficacy analysis results (based on the PPE and the mITT1 Set) for participants 6 to 11 years of age are presented in Table 13 for each COVID-19 definition. The median duration of follow-up was 48 days post Dose 2 in the PP Set for Efficacy. Overall, a lower incidence of COVID-19 was observed after vaccination with mRNA-1273.

Table 13. Summary of Secondary Efficacy Endpoint Analysis Up to Unblinding for Study P204 Part 2 Participants 6 to 11 Years of Age (mITT1 and PPE)

-	**PP Set for Efficacy[a]**	**PP Set for Efficacy[a]**	**mITT1 Set[b]**	**mITT1 Set[b]**
-	**mRNA-1273 50 µg (N=2606)**	**Placebo (N=849)**	**mRNA-1273 50 µg (N=2694)**	**Placebo (N=884)**
CDC case definition of COVID-19	-	-	-	-
Cases, n/N1 (%)[c]	3/2606 (0.1)	4/849 (0.5)	12/2687 (0.4)	19/881 (2.2)
Person-years	566.9	181.1	507.1	155
Incidence rate per 1000 person-years (95% CI)[d]	5.292 (1.091, 15.466)	22.088 (6.018, 56.554)	23.665 (12.228, 41.338)	122.584 (73.804, 191.431)

-	**PP Set for Efficacy[a]**	**PP Set for Efficacy[a]**	**mITT1 Set[b]**	**mITT1 Set[b]**
-	**mRNA-1273 50 µg (N=2606)**	**Placebo (N=849)**	**mRNA-1273 50 µg (N=2694)**	**Placebo (N=884)**
VE based on incidence rate (95% CI)[e]	0.760 (-0.416, 0.965)	-	0.807 (0.581, 0.915)	-
P301 case definition of COVID-19	-	-	-	-
Cases, n/N1 (%)[c]	3/2606 (0.1)	3/849 (0.4)	9/2688 (0.3)	16/881 (1.8)
Person-years	567.3	181.4	507.7	155.3
Incidence rate per 1000 person-years (95% CI)[d]	5.288 (1.091, 15.454)	16.542 (3.411, 48.342)	17.728 (8.106, 33.653)	103.052 (58.903, 167.351)
VE based on incidence rate (95% CI)[e]	0.680 (-1.387, 0.957)	-	0.828 (0.587, 0.933)	-

[a] The number of participants with an event in the PP Set for Efficacy was counted from 14 days or more after Dose 2 up to before or on the Blinded Phase cutoff date.
[b] The number of participants with an event in the mITT1 Set was counted from 14 days or more after Dose 1 up to before or on the unblinding date.
[c] Percentages were based on N1, where N1 = number of participants with no missing data at Baseline and the corresponding timepoint.
[d] The 95% CI was calculated using the exact method (Poisson distribution) and adjusted by person-years.
[e] VE was defined as 1 - ratio of incidence rate (mRNA-1273 versus placebo). The 95% CI of the ratio was calculated using the exact method conditional upon the total number of cases, adjusting for person-years.
Source: Adapted from Tables 25 and 26 in P204 CSR for primary series (6 through 11 years).

The efficacy analysis results for participants 2 to 5 years and 6 to 23 months of age are presented in Table 14. Using the CDC case definition, there were 207 cases among the 2592 mRNA-1273 recipients and 125 cases among the 854 placebo recipients with an estimated VE of 0.466 (95% CI: 0.328, 0.574) among 2 to 5 year-olds. There were 130 cases among 1686 mRNA-1273 recipients and 73 cases among 563 placebo recipients with an estimated VE of 0.432 (95% CI: 0.232, 0.576) among 6 to 23 month-olds.

Using the P301 case definition, there were 142 cases in the mRNA-1273 group and 83 cases in the placebo group with an estimated VE of 0.443 (95% CI: 0.261, 0.578) among 2 to 5 year-olds, and there were 88 cases in the mRNA-1273 group and 37 cases in the

placebo group with an estimated VE of 0.219 (95% CI: -0.180, 0.474) among 6 to 23 month-olds.

The median duration of follow-up for efficacy was 186 and 182 days post Dose 2 among participants 2 to 5 years and 6 to 23 months of age, respectively.

Table 14. Summary of Secondary Efficacy Endpoint Analysis Up to the Blinded Phase Cutoff Date for Study P204 Part 2 Participants in the 6 to 23 Months and 2 to 5 Years Age Groups (PPE)

-	**6 to 23 Months mRNA-1273 25 µg (N=1686)**	**6 to 23 Months Placebo (N=563)**	**2 to 5 Years mRNA-1273 25 µg (N=2592)**	**2 to 5 Years Placebo (N=854)**
CDC case definition of COVID-19	-	-	-	-
Cases, n (%)	130 (7.7)	73 (13.0)	207 (8.0)	125 (14.6)
Person-years	865.6	276.3	1359.9	438.6
Incidence rate per 1000 person-years (95% CI)	150.184 (125.478, 178.331)	264.181 (207.076, 332.168)	152.215 (132.185, 174.424)	285.018 (237.247, 339.587)
VE based on incidence rate (95% CI)	0.432 (0.232, 0.576)	-	0.466 (0.328, 0.574)	-
P301 case definition of COVID-19	-	-	-	-
Cases, n (%)	88 (5.2)	37 (6.6)	142 (5.5)	83 (9.7)
Person-years	874.6	287.2	1380.3	449.2
Incidence rate per 1000 person-years (95% CI)	100.617 (80.698, 123.963)	128.820 (90.701, 177.561)	102.874 (86.650, 121.254)	184.778 (147.174, 229.060)
VE based on incidence rate (95% CI)	0.219 (-0.180, 0.474)	-	0.443 (0.261, 0.578)	-

Source: Adapted from Table 12 in P204 CSR for primary series (6 through 23 months) and Table 14 in P204 CSR for primary series (2 through 5 years).

P204 BD Phase (6 to 11 Years Age Group)

Primary Endpoint – Immunogenicity Objective to Infer Effectiveness

Noninferiority criteria for GMR and SRR difference were both met for participants 6 to 11 years of age. Results are summarized in Table 15.

Across the subgroups of sex, race, ethnicity, and obesity status, no meaningful differences in GMRs or SRR differences were observed within each age group.

Table 15. Immunobridging Analysis – Comparison of BD-Day 29 nAb Levels and SRRs Against D614G Between Study P204 Participants 6 to 11 Years of Age who were Pre-BD SARS-CoV-2 Negative and Study P301 Young Adult Participants 18 to 25 Years of Age

-	**Study P204 6 Years Through 11 Years mRNA-1273 50 µg PS - mRNA-1273 25 µg BD (N=137)** **PPIS-Pre-BD SARS-CoV-2 Negative (PPIS-NEG)**	**Study P301 18 Years Through 25 Years mRNA-1273 100 µg PS (N=296)** **PPIS**
BD-Day 29 P204/Day 57 P301	-	-
n	137	294
GMC (model based) (95% CI)	5575.9 (4899.2, 6346.0)	1400.4 (1282.0, 1529.7)
GMR (P204 versus P301)[a] (95% CI)	3.982 (3.404, 4.657)	-
N1	129	294
SRR n (%)[b]	129 (100.0)	292 (99.3)
95% CI[c]	97.2, 100.0	97.6, >99.9
Difference (P204 versus P301) % (95% CI)[d]	0.7 (-2.2, 2.4)	-

N1 = number of participants with non-missing data at pre-vaccination baseline and the corresponding timepoint.
[a] The log-transformed antibody levels were analyzed using an ANCOVA model with the group variable (participants in Study P204 and young adult participants in Study P301) as fixed effect. The resulted LS means, difference of LS means, and 95% CI were back-transformed to the original scale for presentation.
[b] Seroresponse from pre-Dose 1 baseline at a participant level was defined as a change from below the LLOQ to ≥4×LLOQ, or at least a 4-fold rise if baseline was ≥LLOQ. Percentages were based on N1.
[c] 95% CI was calculated using the Clopper-Pearson method.
[d] 95% CI was calculated using the Miettinen-Nurminen (score) confidence limits.
Source: Table 12 in P204 CSR for BD (6 through 11 years).

6.2.12 Safety Analyses

P204 Part 2 Blinded Phase (All Three Age Groups) – Solicited ARs

Incidences of solicited adverse reactions (ARs), both local and systemic, reported after each dose within 7 days (i.e., day of vaccination and the next 6 days) in Study P204 Part

2 Blinded Phase are presented by toxicity grade and treatment group for participants 6 to 11 years (Table 16), 2 to 5 years (Table 17 and Table 18), and 6 to 23 months (Table 19) of age using the First Injection SSS and Second Injection SSS. For the 2 to 5 years age group, solicited ARs were reported in two subgroups – 24 to 36 months and 37 months to 5 years – because the toxicity grading scales and assessments of solicited ARs differed for these age ranges.

Solicited ARs were reported at higher rates in mRNA-1273 recipients than placebo recipients after each dose. Pain was the most frequently reported solicited local AR after any dose within each age group. The most frequently reported solicited systemic AR was fatigue in the 6 to 11 years and 37 months to 5 years age groups and irritability/crying in the 24 to 36 months and 6 to 23 months age groups. There were no Grade 4 solicited ARs in the 6 years to 11 years age group. Grading for Grade 4 events was based on investigator assessment (with exception of fever). Grade 4 solicited ARs in the 24 to 36 months, 37 months to 5 years, and 6 to 23 months age groups were all cases of fever.

Table 16. Number and Percentage of Participants with Solicited Local and Systemic Adverse Reactions Starting within 7 Days After Each Dose in Participants 6 to 11 Years - First Injection SSS and Second Injection SSS

-	**Grade**	**mRNA-1273 50 µg**	**mRNA-1273 50 µg**	**Placebo**	**Placebo**
-	-	**Dose 1 (N=3003) n (%)**	**Dose 2 (N=2993) n (%)**	**Dose 1 (N=993) n (%)**	**Dose 2 (N=970) n (%)**
Solicited Local ARs	-	-	-	-	-
Pain	Any	2794 (93.0)	2839 (94.9)	466 (46.9)	479 (49.4)
-	Grade 3	28 (0.9)	81 (2.7)	0	2 (0.2)
-	Grade 4	0	0	0	0
Axillary (or groin) swelling or tenderness	Any	464 (15.5)	539 (18.0)	84 (8.5)	65 (6.7)
-	Grade 3	3 (<0.1)	3 (0.1)	1 (0.1)	2 (0.2)
-	Grade 4	0	0	0	0
Swelling	Any	353 (11.8)	507 (16.9)	11 (1.1)	12 (1.2)
-	Grade 3	19 (0.6)	20 (0.7)	1 (0.1)	0
-	Grade 4	0	0	0	0
Erythema	Any	350 (11.7)	561 (18.7)	13 (1.3)	9 (0.9)
-	Grade 3	16 (0.5)	33 (1.1)	1 (0.1)	1 (0.1)

-	Grade	mRNA-1273 50 µg	mRNA-1273 50 µg	Placebo	Placebo
-	-	Dose 1 (N=3003) n (%)	Dose 2 (N=2993) n (%)	Dose 1 (N=993) n (%)	Dose 2 (N=970) n (%)
-	Grade 4	0	0	0	0
Solicited Systemic ARs	-	-	-	-	-
Fatigue	Any	1298 (43.2)	1927 (64.4)	335 (33.7)	335 (34.5)
-	Grade 3	32 (1.1)	191 (6.4)	8 (0.8)	8 (0.8)
-	Grade 4	0	0	0	0
Headache	Any	938 (31.2)	1636 (54.3)	307 (30.9)	275 (28.4)
-	Grade 3	18 (0.6)	119 (4.0)	4 (0.4)	8 (0.8)
-	Grade 4	0	0	0	0
Myalgia	Any	438 (14.6)	844 (28.2)	96 (9.7)	104 (10.7)
-	Grade 3	11 (0.4)	71 (2.4)	1 (0.1)	1 (0.1)
-	Grade 4	0	0	0	0
Arthralgia	Any	260 (8.7)	484 (16.2)	75 (7.6)	84 (8.7)
-	Grade 3	3 (<0.1)	25 (0.8)	1 (0.1)	0
-	Grade 4	0	0	0	0
Chills	Any	309 (10.3)	906 (30.3)	67 (6.7)	73 (7.5)
-	Grade 3	3 (<0.1)	19 (0.6)	0	0
-	Grade 4	0	0	0	0
Nausea/vomiting	Any	327 (10.9)	717 (24.0)	107 (10.8)	97 (10.0)
-	Grade 3	5 (0.2)	19 (0.6)	0	0
-	Grade 4	0	0	0	0
Fever	Any	98 (3.3)	717 (24.0)	15 (1.5)	18 (1.9)
-	Grade 3	17 (0.6)	114 (3.8)	2 (0.2)	2 (0.2)
-	Grade 4	0	0	0	0
Use of antipyretic or pain medication	-	730 (24.3)	1429 (47.7)	95 (9.6)	93 (9.6)

Note: Toxicity grade for injection pain and axillary (groin) swelling or tenderness was defined as: Grade 1 = No interference with activity; Grade 2 = Some interference with activity; Grade 3 = Prevents daily activity; Grade 4 = Requires emergency room visit or hospitalization. Toxicity grade for injection site erythema (redness) and injection site swelling/induration (hardness) was defined as: Grade 1 = 25 – 50 mm; Grade 2 = 51 – 100 mm; Grade 3 ≥100 mm; Grade 4 = Necrosis or exfoliative dermatitis. Toxicity grade for fever was defined as: Grade 1 = 38 – 38.4°C; Grade 2 = 38.5 – 38.9°C; Grade 3 = 39 – 40°C; Grade 4 >40°C. Toxicity grade for headache, fatigue, myalgia, and arthralgia was defined as: Grade 1 = No interference with activity; Grade 2 = Some interference with activity; Grade 3 = Significant, prevents daily activity; Grade 4 = Requires emergency room visit or hospitalization.
Source: Adapted from Table 13 in the summary of clinical safety and Tables 40 and 41 in P204 CSR for primary series (6 through 11 years).

Table 17. Number and Percentage of Participants with Solicited Local and Systemic Adverse Reactions Starting within 7 Days After Each Dose in Participants 37 Months to 5 Years - First Injection SSS and Second Injection SSS

-	**Grade**	**mRNA-1273 25 µg**	**mRNA-1273 25 µg**	**Placebo**	**Placebo**
-	-	**Dose 1 (N=2014) n (%)**	**Dose 2 (N= 2005) n (%)**	**Dose 1 (N=649) n (%)**	**Dose 2 (N= 636) n (%)**
Solicited Local ARs	-	-	-	-	-
Pain	Any	1313 (65.2)	1464 (73.0)	263 (40.5)	253 (39.8)
-	Grade 3	1 (<0.1)	6 (0.3)	0	0
-	Grade 4	0	0	0	0
Axillary (or groin) swelling/tenderness	Any	157 (7.8)	186 (9.3)	38 (5.9)	18 (2.8)
-	Grade 3	0	0	0	0
-	Grade 4	0	0	0	0
Erythema	Any	72 (3.6)	147 (7.3)	1 (0.2)	6 (0.9)
-	Grade 3	6 (0.3)	4 (0.2)	1 (0.2)	0
-	Grade 4	0	0	0	0
Swelling	Any	60 (3.0)	135 (6.7)	6 (0.9)	5 (0.8)
-	Grade 3	5 (0.2)	6 (0.3)	0	0
-	Grade 4	0	0	0	0
Solicited Systemic ARs	-	-	-	-	-

-	Grade	mRNA-1273 25 µg	mRNA-1273 25 µg	Placebo	Placebo
-	-	Dose 1 (N=2014) n (%)	Dose 2 (N= 2005) n (%)	Dose 1 (N=649) n (%)	Dose 2 (N= 636) n (%)
Fatigue	Any	807 (40.1)	962 (48.0)	236 (36.4)	187 (29.4)
-	Grade 3	21 (1.0)	45 (2.2)	11 (1.7)	9 (1.4)
-	Grade 4	0	0	0	0
Headache	Any	232 (11.5)	313 (15.6)	78 (12.0)	52 (8.2)
-	Grade 3	5 (0.2)	8 (0.4)	2 (0.3)	1 (0.2)
-	Grade 4	0	0	0	0
Fever	Any	154 (7.6)	316 (15.8)	33 (5.1)	28 (4.4)
-	Grade 3	23 (1.1)	58 (2.9)	4 (0.6)	2 (0.3)
-	Grade 4	0	2 (<0.1)	1 (0.2)	0
Myalgia	Any	200 (9.9)	312 (15.6)	59 (9.1)	48 (7.5)
-	Grade 3	5 (0.2)	9 (0.4)	2 (0.3)	3 (0.5)
-	Grade 4	0	0	0	0
Chills	Any	129 (6.4)	246 (12.3)	40 (6.2)	31 (4.9)
-	Grade 3	1 (<0.1)	4 (0.2)	0	2 (0.3)
-	Grade 4	0	0	0	0
Nausea/vomiting	Any	137 (6.8)	195 (9.7)	50 (7.7)	32 (5.0)
-	Grade 3	7 (0.3)	7 (0.3)	2 (0.3)	0
-	Grade 4	0	0	0	0
Arthralgia	Any	124 (6.2)	170 (8.5)	32 (4.9)	29 (4.6)
-	Grade 3	2 (<0.1)	3 (0.1)	1 (0.2)	0
-	Grade 4	0	0	0	0
Use of antipyretic or pain medication	-	305 (15.1)	517 (25.8)	62 (9.6)	43 (6.8)

Note: Toxicity grade for solicited ARs for 36 months to 5 years was the same as for 6 to 11 years age group.
Source: Adapted from Table 13 in the summary of clinical safety and Tables 29 and 30 in P204 CSR for primary series (2 through 5 years).

Table 18. Number and Percentage of Participants with Solicited Local and Systemic Adverse Reactions Starting within 7 Days After Each Dose in Participants 24 to 36 Months - First Injection SSS and Second Injection SSS

-	**Grade**	**mRNA-1273 25 µg**	**mRNA-1273 25 µg**	**Placebo**	**Placebo**
-	-	**Dose 1 (N=941) n (%)**	**Dose 2 (N=972) n (%)**	**Dose 1 (N=322) n (%)**	**Dose 2 (N=338) n (%)**
Solicited Local ARs	**-**	-	-	-	-
Pain	Any	500 (53.3)	663 (68.2)	119 (37.0)	149 (44.2)
-	Grade 3	3 (0.3)	5 (0.5)	0	0
-	Grade 4	0	0	0	0
Axillary (or groin) swelling/tenderness	Any	49 (5.2)	85 (8.7)	18 (5.6)	15 (4.5)
-	Grade 3	0	1 (0.1)	0	0
-	Grade 4	0	0	0	0
Erythema	Any	94 (10.0)	118 (12.1)	13 (4.0)	11 (3.3)
-	Grade 3	6 (0.6)	9 (0.9)	2 (0.6)	0
-	Grade 4	0	0	0	0
Swelling	Any	77 (8.2)	112 (11.5)	11 (3.4)	8 (2.4)
-	Grade 3	5 (0.5)	8 (0.8)	2 (0.6)	0
-	Grade 4	0	0	0	0
Solicited Systemic ARs	**-**	-	-	-	-
Irritability/crying	Any	511 (54.5)	532 (54.7)	163 (51.1)	153 (45.5)
-	Grade 3	12 (1.3)	10 (1.0)	5 (1.6)	3 (0.9)
-	Grade 4	0	0	0	0
Sleepiness	Any	284 (30.3)	352 (36.2)	92 (28.8)	90 (26.8)
-	Grade 3	2 (0.2)	1 (0.1)	0	0
-	Grade 4	0	0	0	0
Loss of appetite	Any	225 (24.0)	300 (30.9)	71 (22.3)	69 (20.5)
-	Grade 3	7 (0.7)	8 (0.8)	2 (0.6)	0

-	Grade	mRNA-1273 25 µg	mRNA-1273 25 µg	Placebo	Placebo
-	-	Dose 1 (N=941) n (%)	Dose 2 (N=972) n (%)	Dose 1 (N=322) n (%)	Dose 2 (N=338) n (%)
-	Grade 4	0	0	0	0
Fever	Any	108 (11.5)	187 (19.2)	26 (8.1)	37 (10.9)
-	Grade 3	4 (0.4)	15 (1.5)	4 (1.2)	0
-	Grade 4	4 (0.4)	3 (0.3)	1 (0.3)	0
Use of antipyretic or pain medication	-	193 (20.5)	294 (30.2)	60 (18.6)	63 (18.6)

Note: For participants aged 6 to ≤36 months, toxicity grades were defined as follows: Injection site pain/tenderness: Grade 1 = Mild discomfort, no interference; Grade 2 = Cries when limb moved/pain interferes; Grade 3 = Significant pain at rest/prevents activities; Grade 4 = Requires ER visit/hospitalization. Injection site erythema/swelling: Grade 1 = 5-20 mm; Grade 2 = >20-50 mm; Grade 3 = >50 mm; Grade 4 = Necrosis/exfoliative dermatitis. Groin/underarm swelling/tenderness: Grade 1 = Some swelling, no interference; Grade 2 = Interferes with activities; Grade 3 = Prevents activities; Grade 4 = ER visit/hospitalization. Fever: Grade 1 = 38-38.4°C; Grade 2 = 38.5-39.5°C; Grade 3 = 39.6-40°C; Grade 4 = >40°C. Irritability/crying: Grade 1 = <1h/easily consolable; Grade 2 = 1-3h/increased attention; Grade 3 = >3h/inconsolable; Grade 4 = ER visit/hospitalization. Sleepiness: Grade 1 = Sleepier than usual; Grade 2 = Not interested/sleeps through meals; Grade 3 = Sleeps most of time, hard to arouse; Grade 4 = Inability to arouse. Loss of appetite: Grade 1 = Less for 1-2 feeds/meals; Grade 2 = Missed 1-2 feeds/meals; Grade 3 = Missed >2 feeds/meals or refuses most; Grade 4 = ER visit/hospitalization.
Source: Adapted from Table 13 in the summary of clinical safety and Tables 29 and 30 in P204 CSR for primary series (2 through 5 years).

Table 19. Number and Percentage of Participants with Solicited Local and Systemic Adverse Reactions Starting within 7 Days After Each Dose in Participants 6 to 23 Months - First Injection SSS and Second Injection SSS

-	Grade	mRNA-1273 25 µg	mRNA-1273 25 µg	Placebo	Placebo
-	-	Dose 1 (N=1982) n (%)	Dose 2 (N=1975) n (%)	Dose 1 (N=661) n (%)	Dose 2 (N=646) n (%)
Solicited Local ARs	-	-	-	-	-
Pain	Any	722 (36.5)	893 (45.2)	196 (29.7)	169 (26.2)
-	Grade 3	0	1 (<0.1)	0	0

-	Grade	mRNA-1273 25 µg	mRNA-1273 25 µg	Placebo	Placebo
-	-	Dose 1 (N=1982) n (%)	Dose 2 (N=1975) n (%)	Dose 1 (N=661) n (%)	Dose 2 (N=646) n (%)
-	Grade 4	0	0	0	0
Axillary (or groin) swelling or tenderness	Any	116 (5.9)	173 (8.8)	31 (4.7)	31 (4.8)
-	Grade 3	0	0	0	0
-	Grade 4	0	0	0	0
Swelling	Any	166 (8.4)	293 (14.8)	20 (3.0)	16 (2.5)
-	Grade 3	6 (0.3)	17 (0.9)	0	0
-	Grade 4	0	0	0	0
Erythema	Any	171 (8.6)	270 (13.7)	25 (3.8)	25 (3.9)
-	Grade 3	6 (0.3)	17 (0.9)	2 (0.3)	0
-	Grade 4	0	0	0	0
Solicited Systemic ARs	-	-	-	-	-
Fever	Any	204 (10.3)	280 (14.2)	58 (8.8)	54 (8.4)
-	Grade 3	12 (0.6)	9 (0.5)	3 (0.5)	7 (1.1)
-	Grade 4	1 (<0.1)	5 (0.3)	1 (0.2)	0
Irritability/crying	Any	1325 (67.3)	1270 (64.5)	412 (62.5)	382 (59.2)
-	Grade 3	25 (1.3)	31 (1.6)	7 (1.1)	5 (0.8)
-	Grade 4	0	0	0	0
Sleepiness	Any	723 (36.7)	702 (35.7)	243 (36.9)	227 (35.2)
-	Grade 3	4 (0.2)	3 (0.2)	1 (0.2)	1 (0.2)
-	Grade 4	0	0	0	0
Loss of appetite	Any	579 (29.4)	625 (31.8)	177 (26.9)	171 (26.5)
-	Grade 3	13 (0.7)	18 (0.9)	1 (0.2)	2 (0.3)
-	Grade 4	0	0	0	0

-	Grade	mRNA-1273 25 µg	mRNA-1273 25 µg	Placebo	Placebo
-	-	**Dose 1 (N=1982) n (%)**	**Dose 2 (N=1975) n (%)**	**Dose 1 (N=661) n (%)**	**Dose 2 (N=646) n (%)**
Use of antipyretic or pain medication	-	527 (26.6)	648 (32.8)	161 (24.4)	134 (20.7)

Source: Adapted from Table 13 in the summary of clinical safety and Tables 27 and 28 in P204 CSR for primary series (6 through 23 months).

P204 Part 2 Blinded Phase (All Three Age Groups) – Unsolicited AEs

Table 20 displays unsolicited AEs up to 28 days after any injection in both the mRNA-1273 and placebo groups for the SS for all three age groups.

As of the blinded cutoff date of November 30, 2021, for P204 Part 2, among participants 6 to 11 years of age who had received at least 1 dose of mRNA-1273 or placebo (3007 vaccine recipients and 995 placebo recipients), unsolicited adverse events that occurred within 28 days following any vaccination were reported by 785 participants (26.1%) who received mRNA-1273 and 207 participants (20.8%) who received placebo. Serious adverse events (SAEs) within 28 days following any vaccination were reported by 5 participants (0.2%) who received mRNA-1273 and 1 participant (0.1%) who received placebo. None of the SAEs were considered related to study vaccination by the investigator.

As of the blinded cutoff date of June 30, 2022, for P204 Part 2, among participants 2 through 5 years of age who had received at least 1 dose of mRNA-1273 or placebo (3031 vaccine recipients and 1007 placebo recipients), unsolicited adverse events that occurred within 28 days following any vaccination were reported by 1087 participants (35.9%) who received mRNA-1273 and 325 participants (32.3%) who received placebo. SAEs within 28 days following any vaccination were reported by 4 participants (0.1%) who received mRNA-1273 and 1 participant (<0.1%) who received placebo. None of the SAEs were considered related to study vaccination by the investigator.

As of the blinded cutoff date of June 30, 2022, for P204 Part 2, among participants 6 to 23 months of age who had received at least 1 dose of mRNA-1273 or placebo (1994 vaccine recipients and 666 placebo recipients), unsolicited adverse events that occurred within 28 days following any vaccination were reported by 883 participants (44.3%) who received mRNA-1273 vaccine and 283 participants (42.5%) who received placebo. SAEs within 28 days following any vaccination were reported by 13 participants (0.7%) who received mRNA-1273 vaccine with none in the placebo group. One participant in the mRNA-1273 group reported two SAEs (pyrexia and febrile convulsion), both assessed as related to the study vaccine by the investigator.

During the entire P204 Part 2 Blinded Phase for each age group, SAEs were reported by 0.1% of placebo participants (n=1) and 0.3% of mRNA-1273 participants (n=8) in the 6 to 11 years group, 0.3% of placebo participants (n=3) and 0.6% of mRNA-1273 participants (n=19) in the 2 to 5 years group, and 0.9% of placebo participants (n=6) and 1.6% of mRNA-1273 participants (n=31) in the 6 to 23 months group. No cases of myocarditis, pericarditis, or deaths were reported.

Table 20. Summary of Unsolicited AEs During the 28 Days After Any Dose by Event Type, Treatment Group, and Age Group: Study P204 Part 2 Blinded Phase - SS

-	**6 Months Through 23 Months**	**6 Months Through 23 Months**	**2 Years Through 5 Years**	**2 Years Through 5 Years**	**6 Years Through 11 Years**	**6 Years Through 11 Years**
-	**Placebo (N=666)**	**mRNA-1273 25 µg (N=1994)**	**Placebo (N=1007)**	**mRNA-1273 25 µg (N=3031)**	**Placebo (N=995)**	**mRNA-1273 50 µg (N=3007)**
Unsolicited AEs regardless of relationship to study vaccine	-	-	-	-	-	-
All	283 (42.5)	883 (44.3)	325 (32.3)	1087 (35.9)	207 (20.8)	785 (26.1)
Serious	0	13 (0.7)	1 (<0.1)	4 (0.1)	1 (0.1)	5 (0.2)
Fatal	0	0	0	0	0	0
MAAE	182 (27.3)	567 (28.4)	195 (19.4)	628 (20.7)	123 (12.4)	401 (13.3)
Leading to study vaccine discontinuation	0	1 (<0.1)	0	2 (<0.1)	0	3 (<0.1)
Leading to study participation discontinuation	0	1 (<0.1)	0	1 (<0.1)	0	1 (<0.1)
Severe	1 (0.2)	15 (0.8)	2 (0.2)	5 (0.2)	1 (0.1)	5 (0.2)
AESI	0	5 (0.3)	1 (<0.1)	4 (0.1)	2 (0.2)	6 (0.2)
Unsolicited AEs related to study vaccine per investigator	-	-	-	-	-	-

-	6 Months Through 23 Months	6 Months Through 23 Months	2 Years Through 5 Years	2 Years Through 5 Years	6 Years Through 11 Years	6 Years Through 11 Years
-	Placebo (N=666)	mRNA-1273 25 µg (N=1994)	Placebo (N=1007)	mRNA-1273 25 µg (N=3031)	Placebo (N=995)	mRNA-1273 50 µg (N=3007)
All	17 (2.6)	90 (4.5)	34 (3.4)	135 (4.5)	11 (1.1)	188 (6.3)
Serious	0	1 (<0.1)	0	0	0	0
Fatal	0	0	0	0	0	0
MAAE	3 (0.5)	17 (0.9)	7 (0.7)	24 (0.8)	2 (0.2)	25 (0.8)
Leading to study vaccine discontinuation	0	1 (<0.1)	0	2 (<0.1)	0	1 (<0.1)
Leading to study participation discontinuation	0	1 (<0.1)	0	1 (<0.1)	0	0
Severe	0	2 (0.1)	1 (<0.1)	1 (<0.1)	0	1 (<0.1)
AESI	0	2 (0.1)	1 (<0.1)	2 (<0.1)	0	1 (<0.1)

Source: Table 16 in the summary of clinical safety.

Study P204 BD Phase (Part 2; 6 to 11 Years Age Group) – Solicited ARs

Incidences of solicited ARs, both local and systemic, reported within 7 days after mRNA-1273 25 µg BD for participants 6 to 11 years of age who received a two-dose primary series with mRNA-1273 50 µg in Part 2 of P204 are presented by toxicity grade in Table 21 using SSS. Pain was the most frequent solicited local AR, while fatigue was the most frequent solicited systemic AR. One case of fever was graded as Grade 4. The median duration of solicited local and systemic ARs was 2 days.

Table 21. Number and Percentage of Participants 6 Years Through 11 Years of Age with Solicited Local and Systemic Adverse Reactions Starting Within 7 Days After the mRNA-1273 BD (Part 2) - SSS

-	**Grade**	**Part 2 mRNA-1273 50 µg Primary Series - Booster 25 µg (N=2259) n (%)**
Solicited Local ARs	**-**	**-**
Pain	Any	2010 (89.1)
-	Grade 3	27 (1.2)
-	Grade 4	0
Axillary (or groin) swelling/tenderness	Any	570 (25.3)
-	Grade 3	6 (0.3)
-	Grade 4	0
Swelling	Any	218 (9.7)
-	Grade 3	7 (0.3)
-	Grade 4	0
Erythema	Any	213 (9.4)
-	Grade 3	7 (0.3)
-	Grade 4	0
Solicited Systemic ARs	**-**	**-**
Fatigue	Any	1018 (45.1)
-	Grade 3	56 (2.5)
-	Grade 4	0
Headache	Any	799 (35.4)
-	Grade 3	30 (1.3)
-	Grade 4	0
Myalgia	Any	434 (19.2)
-	Grade 3	23 (1.0)
-	Grade 4	0
Arthralgia	Any	253 (11.2)
-	Grade 3	14 (0.6)
-	Grade 4	0
Chills	Any	281 (12.5)
-	Grade 3	5 (0.2)

-	Grade	Part 2 mRNA-1273 50 µg Primary Series - Booster 25 µg (N=2259) n (%)
-	Grade 4	0
Nausea/vomiting	Any	272 (12.1)
-	Grade 3	11 (0.5)
-	Grade 4	0
Fever	Any	151 (6.7)
-	Grade 3	23 (1.0)
-	Grade 4	1 (<0.1)
Use of antipyretic or pain medication	-	738 (32.7)

Source: Adapted from Tables 14.3.1.3.7.1.2 (6y12y) and 14.1.8.3.2 (6y12y) in P204 CSR for BD (6 through 11 years).

Study P204 BD Phase (Part 2; 6 to 11 Years Age Group) – Unsolicited AEs

Table 22 displays unsolicited AEs up to 28 days after the BD in the SS. Among 2290 participants 6 to 11 years of age who received a two-dose primary series with mRNA-1273 in Part 2 of P204 and received a 25 µg BD of mRNA-1273, unsolicited AEs that occurred within 28 days following vaccination were reported by 10.0% of participants (n=229). SAEs within 28 days following the BD were reported by 1 participant (<0.1%) who received mRNA-1273 vaccine, which was not considered related to vaccination by the investigator.

During the entire P204 BD Phase, SAEs were reported by 10 participants who received a booster dose. None of the events were considered related to the vaccine per investigator. In addition, no cases of myocarditis, pericarditis, or deaths were reported.

Table 22. Summary of Unsolicited AEs During the 28 Days After mRNA-1273 BD by Event Type: Study P204 BD Phase (Part 2) - SS

-	Part 2 mRNA-1273 50 µg Primary Series - Booster 25 µg (N=2290) n (%)
Unsolicited TEAEs Regardless of Relationship to Study Vaccination	-
All	229 (10.0)

-	**Part 2 mRNA-1273 50 µg Primary Series - Booster 25 µg (N=2290) n (%)**
Serious	1 (<0.1)
Fatal	0
MAAE	156 (6.8)
Leading to Discontinuation from Study Vaccine	0
Leading to Discontinuation from Participation in the Study	0
Severe	1 (<0.1)
AESI	0
Unsolicited TEAEs Related to Study Vaccination	-
All	24 (1.0)
Serious	0
Fatal	0
MAAE	10 (0.4)
Leading to Discontinuation from Study Vaccine	0
Leading to Discontinuation from Participation in the Study	0
Severe	0
AESI	0

Source: Table 14.3.1.7.4.1.2 (6y12y) in P204 CSR for BD (6 through 11 years).

6.3 Study P306 Part 2

Title of Study P306: An Open-Label, Phase 3 Study to Evaluate the Safety and Immunogenicity of the mRNA Vaccines for SARS-CoV-2 Variants in Participants Aged 6 Months to <6 Years – mRNA-1273.214 BD Phase

6.3.1 Objectives

Primary Safety Objective:

1. To evaluate the safety and reactogenicity of 10 μg of the mRNA-1273.214 vaccine administered as a single BD at least 4 months post-Dose 2 in participants aged 6 months to 5 years, who have previously received mRNA-1273 as a primary series.

Primary Immunogenicity Objective:

1. To infer the effectiveness of mRNA-1273.214 BD (single dose, 10 μg), based on immune responses against ancestral SARS-CoV-2 and its VOC (Omicron BA. 1) obtained 28 days post BD (BD-D29) in participants aged 6 months to 5 years who previously received two doses of mRNA-1273 primary series and are pre-booster SARS-CoV-2 negative.

6.3.2 Design Overview

Study P306 Part 2 was an open-label, Phase 3 study that evaluated the safety and immunogenicity of the mRNA-1273.214 vaccine encoding for D614G and Omicron BA.1, which was administered as a single 10 μg BD for participants aged 6 months to 5 years who previously received two doses of the mRNA-1273 vaccine as a primary series from P204. Participants received the BD at least 4 months after completion of the primary series. Blood samples were collected on BD-D1, BD-D29, and BD-D181. Participants were followed for approximately 6 months after the BD.

6.3.3 Population

Part 2 enrolled participants 6 months to 5 years of age from P204 (Parts 1 and 2) who previously received mRNA-1273 25 μg as a two-dose primary series. Participants who had previously received a COVID-19 vaccine other than mRNA-1273 and/or experienced an SAE in Study P204 at the time of screening were excluded from P306 Part 2.

6.3.4 Study Treatments or Agents Mandated by the Protocol

Participants in Part 2 received a single injection of mRNA-1273.214 (10 μg) as a BD on BD-Day 1.

6.3.6 Sites and Centers

Part 2 of this study was conducted at 35 centers in the U.S.

6.3.7 Surveillance/Monitoring

Please refer to the clinical review.

6.3.8 Endpoints and Study Success Criteria

Primary Safety Endpoints:

1. Solicited local and systemic ARs through 7 days after booster dose.
2. Unsolicited AEs through 28 days after booster dose.

3. MAAEs through the entire study period.
4. SAEs through the entire study period.
5. AESIs through the entire study period.
6. AEs leading to discontinuation from study participation through the last day of study participation.

Co-Primary Immunogenicity Endpoints:

1. Co-primary Endpoint 1: Serum nAb levels against Omicron BA.1 28 days after mRNA-1273.214 single BD, compared with that after mRNA-1273 primary series in Study P204 of the same age group (superiority).
2. Co-primary Endpoint 2: SRR against Omicron BA.1 28 days after mRNA-1273.214 single BD, compared with that after mRNA-1273 primary series in Study P204 of the same age group (non-inferiority).
3. Co-primary Endpoint 3: Serum nAb levels against ancestral SARS-CoV-2 28 days after mRNA-1273.214 single BD, compared with that after mRNA-1273 primary series in Study P204 of the same age group (non-inferiority).
4. Co-primary Endpoint 4: SRR against ancestral SARS-CoV-2 28 days after mRNA-1273.214 single BD, compared with that after mRNA-1273 primary series in Study P204 of the same age group (non-inferiority).

Success criterion for Endpoint 1: the lower bound of the 95% CI for GMR (BD-Day 29 in Study P306 versus Day 57 in Study P204) was >1.0.

Success criterion for Endpoint 3: the lower bound of the 95% CI for GMR (BD-Day 29 in Study P306 versus Day 57 in Study P204) was >0.667.

Success criterion for Endpoints 2 and 4: the lower bound of the 95% CI was >-5% for Omicron BA.1 (Endpoint 2) and >-10% for ancestral SARS-CoV-2 (Endpoint 4).

Seroresponse was defined as an nAb value change from baseline (pre-Dose 1 of primary series) below the LLOQ to ≥ 4 × LLOQ, or at least a 4-fold rise if baseline was ≥ LLOQ.

6.3.9 Statistical Considerations & Statistical Analysis Plan

All safety analyses were based on the Safety Set (SS), except summaries of solicited ARs, which will be based on the Solicited Safety Set (SSS), where the SSS was a subset of the SS. Both analysis sets are defined below:

- SS: all enrolled participants who received at least 1 injection of the study intervention.
    - SSS: all participants in the Safety Set who contributed any solicited AR data, i.e., had at least 1 post vaccination solicited safety assessment.

The analyses of immunogenicity were based on the PPIS-Neg as the primary analysis population for Part 2. PPIS-Neg was a subset of the PPIS, which was a subset of the IS, which was a subset of the FAS. All four analysis sets are defined below:

- FAS: All enrolled participants who received at least 1 injection of study intervention.
  - Immunogenicity Set (IS): All participants in the FAS who provided immunogenicity samples and had at least 1 post-baseline immunogenicity assessment, regardless of baseline SARS-CoV-2 status.
    - PPIS: All participants in the IS who met all the following criteria: received planned doses of study intervention per schedule; complied with the immunogenicity sample collection window for specified timepoints; had baseline SARS-CoV-2 status available; had no major protocol deviations that impacted key or critical data; if participants had a diagnosis of HIV, they were not receiving HAART; and had immunogenicity assessment at BD-Day 29 for the analysis endpoint.
      - PPIS-Neg: Participants in the PPIS who were SARS-CoV-2 negative (no serologic or virologic evidence of prior SARS-CoV-2 infection) before they received the study injection.

Analysis of Safety:
All safety data were summarized descriptively using frequencies and percentages.

Analysis of Immunogenicity:
The analysis of primary immunogenicity endpoints involved the nAb GMC and seroresponse in Study P306 Part 2 and Study P204 and their comparison (GMR and SRR difference) against Omicron BA.1 and D614G.

The log10-transformed antibody levels on BD-D29 for mRNA-1273.214 in Study P306 and on Day 57 for mRNA-1273 primary series in Study P204 were analyzed using ANCOVA. The model included the group variable (mRNA-1273.214 vs. mRNA-1273) as a fixed effect, adjusted by age group (6 to 23 months and 2 to 5 years). The resulting LS means, difference of LS means, and 95% CI were back transformed to the original scale for presentation. The GMCs for each group were estimated by the GLSM from the model. The GMR (BD-D29 GMC of mRNA-1273.214 in Study P306 compared with Day 57 GMC of the mRNA-1273 primary series in Study P204) was estimated by the ratio of GLSMs from the model. The corresponding two-sided 95% CI was provided to assess the difference in immune response between the mRNA-1273.214 BD and mRNA-1273 primary series. Antibody levels below the LLOQ were replaced by LLOQ/2.

The number and percentage of participants with seroresponse on BD-D29 were provided with two-sided 95% CI using the Clopper-Pearson method. The SRR difference with its 95% CI (using the Miettinen-Nurminen score method) between participants receiving mRNA-1273.214 BD in Study P306 on BD-D29 and the same group of participants receiving mRNA-1273 primary series in Study P204 on Day 57 was provided. The stratified Miettinen-Nurminen method was used as a sensitivity analysis to adjust for the age group.

Multiplicity Adjustment:

No multiplicity adjustments were performed as success criteria for all four endpoints must be met.

Sample Size Determination:

For GMR, assuming a true GMR of 1.5, a superiority margin of 1.0, and a standard deviation of 1.5 for natural log-transformed levels, 289 participants in PPIS-Neg yielded approximately 90% power to demonstrate superiority in terms of GMR at the one-sided alpha = 0.025 level. For SRR difference, assuming a non-inferiority margin of -5% and a true SRR difference of 10% with SRRs of 80% in the mRNA-1273 primary series group (Study P204) and 90% in the mRNA-1273.214 BD group (Study P306), 289 participants in the PPIS-Neg yielded more than 90% power to demonstrate non-inferiority at the one-sided alpha = 0.025 level.

For safety, with 40% of participants excluded from the PPIS-Neg, the target enrollment of Part 2 in Study P306 was approximately 480 participants. There was > 90% probability to observe at least 1 participant with an AE at a true 0.5% AE rate.

6.3.10 Study Population and Disposition

Table 23 displays the dispositions of participants in Study P306 Part 2 by age subgroup for the FAS, where a total of 539 participants were included. The Modified Intent-to-Treat (mITT) set consisted of all participants in the FAS who had no serologic or virologic evidence of prior SARS-CoV-2 infection at baseline (prior to BD) and the Modified Intent-to-Treat-1 set consisted of all participants in the mITT set excluding those who received the wrong study intervention. Overall, the main reason for participants to be excluded from the P306 Part 2 PPIS-Neg was positive baseline SARS-CoV-2 Status (33.7%).

Table 23. Disposition of Participants in Study P306 Part 2 by Age Subgroup (FAS)

-	**6 to 23 Months**	**2 to 5 Years**	**Overall**
Full Analysis Set, n	114	425	539
Per-Protocol Set, n (%)[a]	78 (68.4)	274 (64.5)	352 (65.3)
Modified Intent-to-Treat Set, n (%)[a]	78 (68.4)	276 (64.9)	354 (65.7)
Modified Intent-to-Treat-1 Set, n (%)[a]	78 (68.4)	274 (64.5)	352 (65.3)
Immunogenicity Set, n	105	394	499
Per-Protocol Immunogenicity Set, n (%)[b]	99 (94.3)	369 (93.7)	468 (93.8)
Per-Protocol Immunogenicity Set – Negative, n (%)[b]	71 (67.6)	248 (62.9)	319 (63.9)

-	6 to 23 Months	2 to 5 Years	Overall
Excluded from Per-Protocol Immunogenicity Set - Negative, n (%)	34 (32.4)	146 (37.1)	180 (36.1)
Reasons for Exclusion, n (%)[b]	-	-	-
Positive/Missing Baseline SARS-CoV-2 Status	32 (30.5)	136 (34.5)	168 (33.7)
Had no Immunogenicity Data on BD-Day 29	2 (1.9)	10 (2.5)	12 (2.4)
Safety Set, n	114	425	539
Solicited Safety Set, n (%)[c]	114 (100)	425 (100)	539 (100)

[a] Numbers were based on planned study group and percentages were based on the number of vaccinated participants.
[b] Numbers were based on planned study group and percentages were based on the number of participants who provided immunogenicity results.
[c] Numbers were based on actual study group and percentages were based on the number of safety participants.
Source: Adapted from Tables 8 and 10 in P306 CSR for Part 1 and Part 2.

Table 24 displays the demographic and baseline characteristics in Study P306 Part 2 (SS and PPIS-Neg) and historical comparator Study P204 (PPIS-Neg). For P306 Part 2, the demographics and baseline characteristics from the PPIS-Neg were generally similar to the SS. For the PPIS-Neg, participants in P204 had a median age of 2 (range: 0.5, 5.0) years compared with a median age of 3 (range: 0.9, 5.0) years in P306 Part 2. The P204 PPIS-Neg had a slightly higher proportion of participants from Communities of Color compared with the P306 Part 2 PPIS-Neg (39.7% and 26.6%, respectively).

Table 24. Participant Demographics and Baseline Characteristics in Study P306 Part 2 (SS and PPIS-Neg) and Historical Comparator Study P204 (PPIS-Neg)

-	P306 mRNA-1273.214 BD 10 µg SS (N=539)	P306 mRNA-1273.214 BD 10 µg PPIS-Neg (N=319)	P204 mRNA-1273 Primary Series 25 µg PPIS-Neg (N=590)
Age (Years)	-	-	-
n	539	319	590
Mean (SD)	2.73 (1.277)	2.71 (1.281)	2.15 (1.339)
Median	3	3	2
Q1, Q3	2.00, 4.00	2.00, 4.00	1.00, 3.00
Min, Max	0.9, 5.0	0.9, 5.0	0.5, 5.0

-	**P306 mRNA-1273.214 BD 10 µg SS (N=539)**	**P306 mRNA-1273.214 BD 10 µg PPIS-Neg (N=319)**	**P204 mRNA-1273 Primary Series 25 µg PPIS-Neg (N=590)**
Sex, n (%)	-	-	-
Male	276 (51.2)	166 (52.0)	301 (51.0)
Female	263 (48.8)	153 (48.0)	289 (49.0)
Race, n (%)	-	-	-
White	437 (81.1)	259 (81.2)	434 (73.6)
Black	17 (3.2)	8 (2.5)	37 (6.3)
Asian	26 (4.8)	13 (4.1)	33 (5.6)
American Indian or Alaska Native	0	0	2 (0.3)
Native Hawaiian or Other Pacific Islander	1 (0.2)	1 (0.3)	0
Multiracial	53 (9.8)	35 (11.0)	65 (11.0)
Other	0	0	14 (2.4)
Unknown	1 (0.2)	0	1 (0.2)
Not Reported	4 (0.7)	3 (0.9)	4 (0.7)
Ethnicity, n (%)	-	-	-
Hispanic or Latino	59 (10.9)	33 (10.3)	104 (17.6)
Not Hispanic or Latino	476 (88.3)	286 (89.7)	483 (81.9)
Not Reported	2 (0.4)	0	3 (0.5)
Unknown	2 (0.4)	0	0
Race and Ethnicity Group, n (%)	-	-	-
White non-Hispanic	395 (73.3)	234 (73.4)	356 (60.3)
Communities of Color	143 (26.5)	85 (26.6)	234 (39.7)
Weight (kg)	-	-	-
n	539	319	590
Mean (SD)	15.39 (3.580)	15.42 (3.592)	13.84 (3.749)
Median	15.09	15.09	13.2
Q1, Q3	12.70, 17.64	12.80, 17.64	11.00, 16.30
Min, Max	8.4, 31.1	8.4, 31.1	7.0, 34.8
Height (cm)	-	-	-
n	539	319	590
Mean (SD)	96.79 (11.244)	96.78 (11.154)	91.38 (13.658)

-	**P306 mRNA-1273.214 BD 10 µg SS (N=539)**	**P306 mRNA-1273.214 BD 10 µg PPIS-Neg (N=319)**	**P204 mRNA-1273 Primary Series 25 µg PPIS-Neg (N=590)**
Median	96.52	96.52	89.6
Q1, Q3	87.63, 105.40	87.40, 105.70	81.00, 102.80
Min, Max	70.0, 124.5	71.1, 124.5	48.5, 129.5
Body Mass Index (kg/m²)	-	-	-
n	539	319	590
Mean (SD)	16.31 (1.758)	16.34 (1.796)	16.53 (2.790)
Median	16.18	16.31	16.2
Q1, Q3	15.13, 17.24	15.19, 17.22	15.18, 17.34
Min, Max	11.5, 26.2	11.5, 26.2	10.2, 46.8
Obesity Status, n (%)	-	-	-
Obesity	70 (13.0)	39 (12.2)	72 (12.2)
Non-obesity	469 (87.0)	280 (87.8)	518 (87.8)
Pre-BD/Pre-Dose 1 RT-PCR Results, n (%)	-	-	-
Negative	531 (98.5)	319 (100)	590 (100)
Positive	6 (1.1)	0	0
Missing	2 (0.4)	0	0
Pre-BD/Pre-Dose 1 Elecsys Anti-SARS-CoV-2 Results, n (%)	-	-	-
Negative	358 (66.4)	319 (100)	590 (100)
Positive	164 (30.4)	0	0
Missing	17 (3.2)	0	0
Pre-BD/Pre-Dose 1 SARS-CoV-2 Status, n (%)	-	-	-
Negative	354 (65.7)	319 (100)	590 (100)
Positive	170 (31.5)	0	0
Missing	15 (2.8)	0	0

Source: Adapted from Tables 13 and 14 in P306 CSR for Part 1 and Part 2.

6.3.11 Immunogenicity Analyses

Results of nAb GMC and seroresponse in Study P306 Part 2 and Study P204 PPIS-Neg and their comparison (GMR and SRR difference) for responses against Omicron BA.1 and against D614G are summarized in Table 25.

For Omicron BA.1, the GMR (P306 versus P204) was 12.085 (95% CI: 10.715, 13.631), meeting the prespecified superiority criterion (the lower bound of 95% CI of GMR >1.0), and the SRR difference was 14.2% (95% CI: 11.1%, 17.5%), meeting the prespecified noninferiority criterion (lower bound of 95% CI of SRR difference >-5%).

For D614G, the GMR (P306 versus P204) was 3.049 (95% CI: 2.725, 3.411), meeting the prespecified noninferiority criterion (the lower bound of 95% CI of GMR >0.667), and the SRR difference was 0.5% (95% CI: -0.7, 1.6), meeting the prespecified noninferiority criterion (lower bound of 95% CI of SRR difference >-10%).

Across the subgroups defined by age, sex, race, ethnicity, race and ethnicity, obesity, and intake of pain or fever medications within 72 hours after dosing, no meaningful differences were observed for nAb levels against both Omicron BA.1 and D614G.

Table 25. Analysis of Pseudovirus Neutralizing Antibody Values (GMR and SRR) Against Omicron BA.1 and D614G in Study P306 Part 2 and Historical Comparator Study P204 (PPIS-Neg)

-	**6 Months to 5 Years**	**6 Months to 5 Years**
-	**P306 mRNA-1273.214 BD 10 µg (N=319)**	**P204 mRNA-1273 Primary Series 25 µg (N=590)**
Omicron BA.1	-	-
n	316	567
GMC (model-based) (95% CI) (BD-Day 29 P306/Day 57 P204)	805.2 (731.2, 886.8)	66.6 (62.0, 71.6)
GMR (P306 vs P204; model-based) (95% CI)	12.085 (10.715, 13.631)	-
SRR (BD-Day 29 P306/Day 57 P204)	-	-
n1/N1 (%)	309/312 (99.0)	477/562 (84.9)
(95% CI)	(97.2, 99.8)	(81.6, 87.7)
SRR difference (P306 vs P204) (%) (95% CI)	14.2 (11.1, 17.5)	-
D614G	-	-
n	316	557
GMC (model-based) (95% CI) (BD-Day 29 P306/Day 57 P204)	4754.7 (4346.9, 5200.7)	1559.4 (1457.6, 1668.4)
GMR (P306 vs P204; model-based) (95% CI)	3.049 (2.725, 3.411)	-
SRR (BD-Day 29 P306/Day 57 P204)	-	-

-	6 Months to 5 Years	6 Months to 5 Years
-	**P306 mRNA-1273.214 BD 10 µg (N=319)**	**P204 mRNA-1273 Primary Series 25 µg (N=590)**
n1/N1 (%)	312/312 (100)	545/548 (99.5)
(95% CI)	(98.8, 100.0)	(98.4, 99.9)
SRR difference (P306 vs P204) (%) (95% CI)[f]	0.5 (-0.7, 1.6)	-

N = Number of participants in the PPIS-Neg.
N1 = number of participants with nonmissing data at baseline and the corresponding timepoint.
n = Number of participants with nonmissing data at the corresponding timepoint.
n1 = Number of participants with seroresponse.
Source: Adapted from Tables 18 in P306 CSR for Part 1 and Part 2.

Reviewer Comment:

1. *The SRR difference adjusted by age group was 14.2% (95% CI: 10.6, 17.8) for Omicron BA.1 and 0.6% (95% CI: -1.0, 2.2) for D614G, both of which met the prespecified noninferiority criterion. Thus, age adjustment did not change the conclusions for Omicron BA.1 and D614G.*
2. *Forty-three out of 319 participants for P306 Part 2 in the PPIS-Neg were also included in the historical comparator P204 in the PPIS-Neg. However, the analyses did not account for the potentially correlated data from these participants. Nonetheless, as the GMRs against both Omicron BA.1 and D614G did not differ notably between the two sets of participants and all were well above the respective margins, the conclusions remain the same.*

6.3.12 Safety Analyses

Incidences of solicited adverse reactions (ARs), both local and systemic, reported within 7 days of BD in Study P306 Part 2 are presented by toxicity grade and age group in the SSS (Table 26).

The most frequently reported solicited local AR was pain in both age groups. The most frequently reported solicited systemic AR was fatigue in the 36 months to 5 years age group (32.1%) and irritability/crying in the 6 to 36 months age group (53.1%). No Grade 4 solicited ARs were reported in either age group.

Table 26. Summary of Participants with Solicited Adverse Reactions Within 7 Days After Booster Injection by Age Group and Grade in P306 Part 2 - SSS

-	Grade	≥6 Months to ≤36 Months (N=258) n (%)	>36 Months to 5 Years (N=281) n (%)
Solicited Local ARs	-	-	-

-	Grade	≥6 Months to ≤36 Months (N=258) n (%)	>36 Months to 5 Years (N=281) n (%)
Pain	Any	89 (34.5)	154 (54.8)
-	Grade 3	1 (0.4)	2 (0.7)
-	Grade 4	0	0
Erythema (Redness)	Any	23 (8.9)	12 (4.3)
-	Grade 3	2 (0.8)	0
-	Grade 4	0	0
Swelling (Hardness)	Any	21 (8.1)	10 (3.6)
-	Grade 3	3 (1.2)	0
-	Grade 4	0	0
Axillary (or Groin) Swelling or Tenderness	Any	11 (4.3)	23 (8.2)
-	Grade 3	0	0
-	Grade 4	0	0
Solicited Systemic ARs	-	-	-
Fever	Any	22 (8.5)	17 (6.0)
-	Grade 3	0	3 (1.1)
-	Grade 4	0	0
Headache	Any	-	39 (14.2)
-	Grade 3	-	3 (1.1)
-	Grade 4	-	0
Fatigue	Any	-	88 (32.1)
-	Grade 3	-	5 (1.8)
-	Grade 4	-	0
Myalgia	Any	-	34 (12.4)
-	Grade 3	-	1 (0.4)
-	Grade 4	-	0
Arthralgia	Any	-	25 (9.1)
-	Grade 3	-	1 (0.4)
-	Grade 4	-	0
Nausea/Vomiting	Any	-	22 (8.0)
-	Grade 3	-	1 (0.4)
-	Grade 4	-	0
Chills	Any	-	16 (5.8)
-	Grade 3	-	0

-	Grade	≥6 Months to ≤36 Months (N=258) n (%)	>36 Months to 5 Years (N=281) n (%)
-	Grade 4	-	0
Irritability/Crying	Any	121 (53.1)	-
-	Grade 3	3 (1.3)	-
-	Grade 4	0	-
Sleepiness	Any	47 (20.6)	-
-	Grade 3	0	-
-	Grade 4	0	-
Loss of Appetite	Any	52 (22.8)	-
-	Grade 3	1 (0.4)	-
-	Grade 4	0	-

Source: Table 14.3.1.1.8.1.2 in P306 CSR for Part 1 and Part 2.

Table 27 displays the summary of unsolicited AEs up to 28 days after the BD in the SS for P306 Part 2. Among 539 participants in the SS, at least 1 unsolicited AE up to 28 days after BD injection was reported by 20.8% of participants (n=112). No SAEs were reported during the 28 days after BD injection. One participant experienced an AESI of erythema multiforme at Day 2 that was considered by the investigator to be related to the study vaccine.

Throughout Part 2, 9 (1.7%) participants reported SAEs and 4 (0.7%) participants reported AESIs. All SAEs were considered resolved and were assessed as not related to mRNA-1273.214 by the investigator. The four participants who experienced AESIs comprised the aforementioned participant with Day 2 erythema multiforme (considered by the investigator to be related to the study vaccine) and three participants who experienced AESIs beyond 28 days after BD, all of which were considered not related to the study vaccine by the investigator.

Table 27. Summary of Unsolicited AEs up to 28 Days After BD in P306 Part 2- SS

-	≥6 Months to 5 Years (N=539) n (%)
Unsolicited AEs regardless of relationship to study injection	-
All	112 (20.8)
Serious	0
Fatal	0
Medically-attended	75 (13.9)
Leading to discontinuation from study	0
Severe	0

-	**≥6 Months to 5 Years (N=539) n (%)**
AESI	1 (0.2)
Unsolicited AEs related to study injection	-
All	10 (1.9)
Serious	0
Fatal	0
Medically-attended	3 (0.6)
Leading to discontinuation from study	0
Severe	0
AESI	1 (0.2)

Source: Table 35 in P306 CSR for Part 1 and Part 2.

6.4 Study P306 Part 4

Title of Study P306: An Open-Label, Phase 3 Study to Evaluate the Safety and Immunogenicity of the mRNA Vaccines for SARS-CoV-2 Variants in Participants Aged 6 Months to <6 Years – mRNA-1273.815 Single Dose Phase

6.4.1 Objectives

Primary Safety Objective:

1. To evaluate the safety and reactogenicity of 25 µg of the mRNA-1273.815 vaccine administered as a single dose in participants aged 2 to 4 years (Cohort 4A) or as a two-dose primary series (28 days apart) in participants aged 6 months to 23 months (Cohort 4B). This review focuses on safety data from Cohort 4A only.

Primary Immunogenicity Objective:

1. To infer the effectiveness of mRNA-1273.815 (single dose, 25 µg) based on immune responses against SARS-CoV-2 Omicron XBB.1.5 obtained 28 days post dose (Day 29) in participants aged 2 to 4 years (Cohort 4A) who have evidence of prior SARS-CoV-2 infection.

6.4.2 Design Overview

Study P306 Part 4 was an open-label, Phase 3 study that evaluated the safety and immunogenicity of the mRNA-1273.815 vaccine (encoding Omicron XBB.1.5) when administered as a single 25 µg dose in COVID-19 vaccine-naïve participants aged 2 years through 4 years (Cohort 4A) with evidence of prior SARS-CoV-2 infection and as a 25 µg two-dose series in COVID-19 vaccine-naïve participants aged 6 months through 23 months (Cohort 4B).

Participants in Cohort 4A received a single 25 μg dose of the mRNA-1273.815 vaccine on Day 1, with blood samples collected on Day 1 and on Day 29 for immunogenicity. Participants in Cohort 4B received two doses of 25 μg of the mRNA-1273.815 vaccine 28 days apart, with blood samples collected on Day 1, Day 29, and Day 57. Participants in Cohort 4A were followed for safety for 3 months after dosing, while those in Cohort 4B were followed for 3 months after the second dose.

6.4.3 Population

P306 Part 4 enrolled participants in two cohorts: Cohort 4A consisting of participants aged 2 years to 4 years who had not previously received any COVID-19 vaccine and who had evidence of prior SARS-CoV-2 infection, and Cohort 4B consisting of participants aged 6 to 23 months who had not previously received any COVID-19 vaccine.

6.4.4 Study Treatments or Agents Mandated by the Protocol

Participants in Cohort 4A received a single 25 μg dose of the mRNA-1273.815 (monovalent Omicron XBB.1.5-containing formulation) vaccine on Day 1; participants in Cohort 4B received two doses of 25 μg of the mRNA-1273.815 vaccine 28 days apart.

6.4.6 Sites and Centers

A total of 34 centers enrolled participants in the U.S., Dominican Republic, and Panama.

6.4.7 Surveillance/Monitoring

Please refer to the clinical review.

6.4.8 Endpoints and Study Success Criteria

Primary Safety Endpoints:

1. Solicited local and systemic ARs through 7 days after injection.
2. Unsolicited AEs through 28 days after injection.
3. MAAEs through the entire study period.
4. SAEs through the entire study period.
5. AESIs through the entire study period.
6. AEs leading to discontinuation from study participation through the last day of study participation.

Primary Immunogenicity Endpoint:

1. nAb level against Omicron XBB.1.5 after mRNA- 1273.815 single dose (Day 29) in participants aged 2 years to 4 years (Cohort 4A) with evidence of prior SARS-CoV-2 infection compared with that after two doses of mRNA-1273.815 (Day 57) in participants aged 6 to 23 months (Cohort 4B) without evidence of prior SARS-CoV-2 infection (noninferiority).

Success criterion for noninferiority of the immune responses against XBB.1.5: the lower bound of the 95% CI for the GMR (mRNA-1273.815 single dose compared to the two-dose series) of >0.667.

6.4.9 Statistical Considerations & Statistical Analysis Plan

Analysis of Safety

All safety data were summarized descriptively based on the Safety Set, except summaries of solicited ARs, which were based on the Solicited Safety Set, both defined similarly to previous studies.

Analysis of Immunogenicity

The analyses of immunogenicity were based on the PPIS-Pos and PPIS-Neg as the primary analysis population for Cohort 4A and Cohort 4B, respectively. The PPIS-Pos included participants in the PPIS (defined similarly to previous studies) who were SARS-CoV-2 positive (serologic or virologic evidence of prior SARS-CoV-2 infection) before they received the study intervention.

The log10-transformed antibody levels at 28 days after the last dose (Cohort 4A on Day 29 and Cohort 4B on Day 57) were analyzed using ANCOVA which included the group variable (Cohort 4A and Cohort 4B) as a fixed effect, adjusted by baseline serum nAb value. The resulting GLSM means, difference of GLSM means, and 95% CI based on the t-distribution were back transformed to the original scale for presentation.

Sample Size Determination

Assuming a true GMR of 1.2, a noninferiority margin of 0.667, and a standard deviation of 1.5 for natural log-transformed levels, 138 participants in each cohort (PPIS-Pos for Cohort 4A and PPIS-Neg for Cohort 4B) yielded approximately 90% power to demonstrate noninferiority at a one-sided alpha = 0.025 level.

Considering the baseline seroprevalence in the age groups for each cohort (~80% for Cohort 4A and ~60% for Cohort 4B) and assuming ~15% of participants to be excluded from PPIS due to any reasons, a total sample size of approximately 600 participants was planned (~200 and ~400 participants in Cohorts 4A and 4B, respectively). With this sample size, there was >90% probability to observe at least one participant with an AE at a true rate of 1%.

6.4.10 Study Population and Disposition

Table 28 displays the dispositions of participants in Study P306 Part 4, where a total of 598 (199 in Cohort 4A and 399 in Cohort 4B) participants were dosed, of whom 143 (Cohort 4A) and 76 (Cohort 4B) participants were included in PPIS-Pos and PPIS-Neg, respectively.

Table 28. Disposition of Participants in Study P306 Part 4

-	**Cohort 4A mRNA-1273.815 25 µg**	**Cohort 4B mRNA-1273.815 25 µg**
Full Analysis Set	199	399
Immunogenicity Set	149	379
Per-Protocol Immunogenicity Set, n (%)[a]	148 (99.3)	352 (92.9)
Per-Protocol Immunogenicity Set – positive, n (%)[a]	143 (96.0)	276 (72.8)
Per-Protocol Immunogenicity Set – negative, n (%)[a]	5 (3.4)	76 (20.1)
Excluded from Per-Protocol Immunogenicity Set, n (%)[a]	1 (0.7)	27 (7.1)
Reasons for Exclusion, n (%)	-	-
Missing baseline SARS-CoV-2 status	1 (0.7)	0
Did not receive Dose 2 per schedule (Cohort 4B only)	-	4 (1.1)
Received Dose 2 out of window (Cohort 4B only)	-	18 (4.7)
Had no immunogenicity data at Day 29 Cohort 4A/Day 57 Cohort 4B	0	5 (1.3)
Safety Set	199	399
Solicited Safety Set, n (%)[b]	199 (100)	399 (100)
First injection solicited safety set	199 (100)	399 (100)
Second injection solicited safety set (Cohort 4B only)	-	386 (96.7)

[a] Numbers were based on planned study group and percentages were based on the number of participants in the immunogenicity set.
[b] Numbers were based on actual study group and percentages were based on the number of safety participants.
Source: Adapted from Tables 4 and 5 in P306 CSR for Part 4.

Table 29 presents the demographic and baseline characteristics in study P306 Part 4 (SS and PPIS-Pos for Cohort 4A; SS and PPIS-Neg for Cohort 4B). The demographic and baseline characteristics in the PPIS-Pos were similar to those of the SS for Cohort 4A, and the PPIS-Neg characteristics were similar to those of the SS for Cohort 4B.

Table 29. Demographic and Baseline Characteristics in Study P306 Part 4 (SS and PPIS-Pos for Cohort 4A; SS and PPIS-Neg for Cohort 4B)

-	**Cohort 4A mRNA-1273.815 25 µg SS (N=199)**	**Cohort 4B mRNA-1273.815 25 µg SS (N=399)**	**Cohort 4A mRNA-1273.815 25 µg PPIS-Pos (N=143)**	**Cohort 4B mRNA-1273.815 25 µg PPIS-Neg (N=76)**
Age (Years)	-	-	-	-
n	199	399	143	76
Mean (SD)	2.91 (0.860)	0.89 (0.158)	3.00 (0.856)	0.89 (0.141)
Median	3	1	3	1
Q1, Q3	2.00, 4.00	0.80, 1.00	2.00, 4.00	0.80, 1.00
Min, Max	2.0, 4.0	0.5, 1.0	2.0, 4.0	0.5, 1.0
Age (Months)	-	-	-	-
n	-	399	-	76
Mean (SD)	-	13.7 (5.08)	-	13.7 (5.08)
Median	-	13.0	-	13.0
Q1, Q3	-	9.0, 18.0	-	9.0, 17.5
Min, Max	-	6, 23	-	6, 23
Gender, n (%)	-	-	-	-
Male	100 (50.3)	208 (52.1)	73 (51.0)	33 (43.4)
Female	99 (49.7)	191 (47.9)	70 (49.0)	43 (56.6)
Race, n (%)	-	-	-	-
White	48 (24.1)	41 (10.3)	41 (28.7)	10 (13.2)
Black	66 (33.2)	100 (25.1)	53 (37.1)	21 (27.6)
American Indian or Alaska Native	1 (0.5)	1 (0.3)	1 (0.7)	0
Multiracial	11 (5.5)	29 (7.3)	8 (5.6)	6 (7.9)
Other	73 (36.7)	225 (56.4)	40 (28.0)	37 (48.7)
Unknown	0	1 (0.3)	0	1 (1.3)
Not Reported	0	2 (0.5)	0	1 (1.3)
Ethnicity, n (%)	-	-	-	-
Hispanic or Latino	138 (69.3)	338 (84.7)	91 (63.6)	61 (80.3)
Not Hispanic or Latino	58 (29.1)	57 (14.3)	51 (35.7)	15 (19.7)
Not Reported	1 (0.5)	1 (0.3)	1 (0.7)	0
Unknown	2 (1.0)	3 (0.8)	0	0
Race and Ethnicity Group, n (%)	-	-	-	-
White non-Hispanic	8 (4.0)	21 (5.3)	7 (4.9)	7 (9.2)

-	**Cohort 4A mRNA-1273.815 25 µg SS (N=199)**	**Cohort 4B mRNA-1273.815 25 µg SS (N=399)**	**Cohort 4A mRNA-1273.815 25 µg PPIS-Pos (N=143)**	**Cohort 4B mRNA-1273.815 25 µg PPIS-Neg (N=76)**
Communities of Color	191 (96.0)	377 (94.5)	136 (95.1)	69 (90.8)
Missing	0	1 (0.3)	0	0
Weight (kg)	-	-	-	-
n	199	399	143	76
Mean (SD)	15.59 (3.351)	9.98 (1.692)	16.00 (3.469)	9.81 (1.568)
Median	15	9.9	15.18	9.55
Q1, Q3	13.40, 17.15	8.75, 11.10	13.60, 17.50	8.66, 10.90
Min, Max	9.1, 29.2	5.6, 16.6	9.1, 29.2	6.9, 14.5
Height (cm)	-	-	-	-
n	199	399	143	76
Mean (SD)	96.95 (9.114)	76.17 (6.203)	97.70 (9.230)	75.38 (6.337)
Median	96	76	96.52	75.3
Q1, Q3	90.00, 104.14	71.12, 81.00	91.00, 105.00	71.00, 80.00
Min, Max	68.6, 118.0	61.0, 92.0	74.0, 118.0	62.0, 91.4
Body Mass Index (kg/m^2)	-	-	-	-
n	199	399	143	76
Mean (SD)	16.51 (2.179)	17.18 (2.030)	16.67 (2.171)	17.30 (2.204)
Median	16.28	17.06	16.42	17.26
Q1, Q3	14.92, 17.30	15.79, 18.22	15.14, 17.44	15.97, 18.62
Min, Max	11.8, 26.7	10.3, 27.5	11.8, 24.5	13.2, 27.5
Obesity Status, n (%)	-	-	-	-
Obesity	40 (20.1)	57 (14.3)	31 (21.7)	14 (18.4)
Nonobesity	159 (79.9)	342 (85.7)	112 (78.3)	62 (81.6)
Baseline RT-PCR Results, n (%), n (%)	-	-	-	-
Negative	192 (96.5)	383 (96.0)	138 (96.5)	76 (100)
Positive	5 (2.5)	15 (3.8)	3 (2.1)	0
Missing	2 (1.0)	1 (0.3)	2 (1.4)	0

-	Cohort 4A mRNA-1273.815 25 µg SS (N=199)	Cohort 4B mRNA-1273.815 25 µg SS (N=399)	Cohort 4A mRNA-1273.815 25 µg PPIS-Pos (N=143)	Cohort 4B mRNA-1273.815 25 µg PPIS-Neg (N=76)
Baseline Elecsys Anti-SARS-CoV-2 Results, n (%)	-	-	-	-
Negative	6 (3.0)	98 (24.6)	0	76 (100)
Positive	192 (96.5)	300 (75.2)	143 (100)	0
Missing	1 (0.5)	1 (0.3)	0	0
Baseline SARS-CoV-2 Status, n (%)	-	-	-	-
Negative	6 (3.0)	95 (23.3)	0	76 (100)
Positive	192 (96.5)	305 (76.4)	143 (100)	0
Missing	1 (0.5)	1 (0.3)	0	0

Source: Adapted from Tables 6 and 7 in P306 CSR for Part 4.

6.4.11 Immunogenicity Analyses

The GMR of nAb levels against Omicron XBB.1.5 (Cohort 4A Day 29 PPIS-Pos versus Cohort 4B Day 57 PPIS-Neg) was 1.195 (95% CI: 0.800, 1.784). The noninferiority criterion for GMR (lower bound of the 95% CI >0.667) was thus met (Table 30).

No meaningful differences were observed in subgroup analyses by sex, race, ethnicity, race/ethnicity, and obesity status.

Table 30. Analysis of Pseudovirus Neutralizing Antibody Values Against XBB.1.5 (VAC150) in P306 Part 4 (PPIS-Pos for Cohort 4A and PPIS-Neg for Cohort 4B)

-	Cohort 4A mRNA-1273.815 25 µg (N=143)	Cohort 4B mRNA-1273.815 25 µg (N=76)
Day 29 Cohort 4A/Day 57 Cohort 4B	-	-
n	143	76
GMC (model based)	2074.1	1736.3
95% CI	(1637.8, 2626.7)	(1255.8, 2400.6)
GMR (Cohort 4A vs. Cohort 4B) with 95% CI	1.195 (0.800, 1.784)	-

Source: Adapted from Table 9 in P306 CSR for Part 4.

6.4.12 Safety Analyses

Incidences of solicited ARs, both local and systemic, reported within 7 days of the single dose in Cohort 4A are presented by toxicity grade for the SSS (Table 31). The most frequently reported solicited local AR was pain (27.6%) and the most frequently reported solicited systemic ARs were sleepiness (12.6%) and irritability/crying (12.1%). There were no Grade 4 solicited ARs reported in this study population.

Table 31. Summary of Participants with Solicited Adverse Reactions Within 7 Days After Injection by Grade in Cohort 4A - SSS

-	**Grade**	**Cohort 4A - Single Dose: mRNA-1273.815 25 µg (N=199) n (%)**
Solicited Local ARs	**-**	**-**
Pain	Any	55 (27.6)
-	Grade 3	2 (1.0)
-	Grade 4	0
Erythema (Redness)	Any	7 (3.5)
-	Grade 3	0
-	Grade 4	0
Swelling (Hardness)	Any	7 (3.5)
-	Grade 3	0
-	Grade 4	0
Axillary (or groin) swelling or tenderness	Any	14 (7.0)
-	Grade 3	3 (1.5)
-	Grade 4	0
Solicited Systemic ARs	**-**	**-**
Sleepiness	Any	25 (12.6)
-	Grade 3	2 (1.0)
-	Grade 4	0
Loss of appetite	Any	17 (8.5)
-	Grade 3	1 (0.5)
-	Grade 4	0
Fever	Any	17 (8.5)
-	Grade 3	2 (1.0)
-	Grade 4	0
Irritability/crying	Any	24 (12.1)

-	Grade	Cohort 4A - Single Dose: mRNA-1273.815 25 µg (N=199) n (%)
-	Grade 3	2 (1.0)
-	Grade 4	0

Source: Table 11 in P306 CSR for Part 4.

Table 32 displays the summary of unsolicited AEs up to 28 days post injection in the SS for Cohort 4A. Among 199 participants in the SS for Cohort 4A, at least 1 unsolicited AE up to 28 days post injection was reported by 19.6% of participants (n=39). No SAEs or AESIs were reported during the 28 days. None of the events reported were assessed as related to study intervention by the investigator.

Throughout the study, no SAEs or AESIs were reported for Cohort 4A.

Table 32. Summary of Unsolicited AEs During 28 days Post Injection in Cohort 4A - SS

-	Cohort 4A mRNA-1273.815 25 µg (N=199) n (%)
Unsolicited AEs regardless of relationship to study vaccination	-
All	39 (19.6)
Serious	0
Fatal	0
Medically-attended	19 (9.5)
Leading to discontinuation from participation in the study	0
Severe	0
Special interest (AESI)	0
Unsolicited AEs related to study vaccination	-
All	0

Source: Table 13 in P306 CSR for Part 4.

7. Integrated Overview of Efficacy

An integrated summary of efficacy (ISE) was not submitted.

8. Integrated Overview of Safety

An integrated summary of safety (ISS) was not submitted.

9. Additional Statistical Issues

There are no additional statistical issues.

10. Conclusions

No major statistical issues have been identified. Success criteria for the immunogenicity objectives of P204 (Part 2 Blinded and BD Phases) and P306 (Parts 2 and 4) were all met and no notable patterns in safety results were identified. Overall, both the immunogenicity and safety data support the licensure of SPIKEVAX in individuals 6 months to 11 years of age.