ModernaTX, Inc.

Protocol mRNA-1273-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 Less Than 12 Years of Age

Statistical Analysis Plan
(Part 1 Open-Label Phase and Part 2 Blinded Phase)

SAP Version 5.0
Version Date of SAP: 28 July 2023

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Summary of Major Changes in SAP Version

SAP Version	Date	Section # and Name	Description of Change
V2.0 Based on Protocol Amendment 3	22Sep2021	3.1 Primary Endpoints 6.3 Safety Analysis	AESIs of myocarditis and/or pericarditis were added (in addition to MIS-C).
		3.1 Primary Endpoints	Seroresponse definition updated to as a change from below the LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline is equal to or above the LLOQ.
		4.1 Overall Study Design	1.The overall sample size for Part 2 was updated to approximately 12,000 participants. 2.The sample size for Study Arms 8, 10, and 12 were each updated to up to 3,000 participants. 3. The sample size for Study Arms 9, 11, and 13 were each updated to up to 1,000 participants.
		4.2 Sample size and Power 4.3 Randomization	The overall sample size for each age group was updated to up to 4,000 participants.
		6.6.1 Assay Specific Definition of Seroresponse	Definition of assay specific seroesponse is included and updated based on a more conservative approach
		6.8 Data Safety Monitoring Board	Included language for the addition of an independent Cardiac Event Adjudication Committee that will adjudicate any suspected cases of myocarditis, pericarditis, or myopericarditis and enable the DSMB to make recommendations to the Sponsor.
		5.4 Immunogenicity Subset 8.5 Appendix E: Schedule of Events	Day 30 (+3 days) blood draw was added to indicate that participants in Cohort D (remainder of the age group) will provide a blood sample at Day 1 and at Day 30 (+3 days)
V3.0 Based on Protocol Amendment 5	16Dec2021	4.1.2 Part 2, the Blinded Phase	Made updates in figure 2 footnotes to explain that blood sample collection for participants in Cohort D will be prior to randomization and the first dose at Day

			1 and within 4 days of receiving Dose 2 at Day 30 (+ 3 days).
		6.1 General Considerations	Analysis Period for blinded phase for safety and efficacy analysis
		8.5 Appendix E: Schedule of Events	Updated footnote #2 in appendix E
V4.0 Based on Protocol Amendment 8	06June2022	1 Introduction 2 Study Objectives 3 Study Endpoints 4 Study Design	1. Added Part 3 (Study Arm 14) which is the 25 µg dose to be evaluated as an alternative (lower dosing) dosing regimen with a primary series (2 doses) followed by a third dose. 2. An optional booster dose for all participants in Part 1(all age groups) and 6 to < 12 year old in Part 2 of the study (10 or 25 µg, depending on age at time of booster) was added.
		5 Analysis Population	Updated to clarify the definitions are defined for Part 1 open-label phase and Part 2 blinded phase
		6.6 Long-term Analysis 6.7 Booster Dose Analysis	Added to reflect Part 3 and optional booster dose in Protocol Amendment 7. Details will be included in a separate SAP
		8.5.Appendix E: Schedule of Assessments (Parts 1 and 2, Study Arms 1 Through 13)	Updated Appendix header to clarify the schedule of assessments for Part 1 and 2 Arm 1 through 13
V5.0 Based on Protocol Amendment 9	28July2023	2.1 Primary Objective	Updated to evaluate the safety of mRNA-1273.214.
		4.1.3 Optional Booster Doses	1. Specified all participants who have not yet received a booster dose will be offered a booster dose with mRNA-1273.214 (instead of mRNA-1273). 2. Updated Table 4 to include mRNA-1273.214 in the column titled booster dose.
		6.5.1.3 Derivation of CDC Case Definition of COVID-19	Stated that Covid-19 surveillance (illness visits and convalescent visits) would only be performed while there is still a blinded Part 2 for any age group, after unblinding of trial, this would be discontinued.

		6.9 Interim Analyses	Added details for the interim analysis of safety for Part 3 and mRNA-1273.214 booster
		8.5 Appendix E	Updated to describe changes made to SoA tables
		6.1 General Consideration	Added details that immunogenicity data at Day 57 are analyzed regardless of participant unblinding status.
		3.1 Primary Endpoints 4.2 Sample size and Power	The P301 comparator in SAP for Part 3 immunogenicity analysis is young adults ≥18 to 25 years of age instead of protocol P301 comparator ≥18 years of age, because the originally planned hypothesis testing in protocol for part 3 will not be performed due to the small number of participants enrolled in Part 3, which is insufficient to power the hypothesis testing.
		6.9 Interim Analyses	Added details that additional interim analysis of immunogenicity and safety may be performed after all or subset of participants who receive booster dose have completed BD-Day 29 after the booster dose in an age group for Part 1 and Part 2.

List of Abbreviations

Abbreviation	Definition
AB	antibody
AE	adverse event
AR	adverse reaction
AESI	AEs of special interest
BMI	body mass index
bAb	binding antibody
BD	booster dose
BLA	Biologics License Application
CI	confidence interval
CDC	US Centers for Disease Control and Prevention
CEAC	Cardiac Event Adjudication Committee
CMI	Cell-Mediated Immunity
CRO	contract research organization
CSP	clinical study protocol
CSR	clinical study report
DHHS	Department of Health and Human Services
DSMB	Data Safety Monitoring Board
eCRF	electronic case report form
eDiary	electronic diary
EUA	Emergency Use Authorization
ELISA	enzyme-linked immunosorbent assay
FAS	full analysis set
GLSM	geometric least squares mean
GM	geometric mean
GMFR	geometric mean fold rise
GMT	geometric mean titer
GMR	geometric mean ratio
HAART	highly active anti-retroviral therapy
IgG	immunoglobulin G
IP	investigational product
IRT	interactive response technology
IST	internal safety team
LAR	legally authorized representative
LLOQ	lower limit of quantification
MAAEs	medically-attended adverse events
MedDRA	Medical Dictionary for Regulatory Activities
MIS-C	multisystem inflammatory syndrome in children
mITT	modified Intent-to-Treat
mITT1	modified Intent-to-Treat-1
mRNA	messenger ribonucleic acid
nAb	neutralizing antibody
PP	per-protocol

Abbreviation	Definition
PT	preferred term
PsVNA	Pseudovirus neutralizing antibody
RT-PCR	reverse transcriptase polymersa chain reaction
SAE	serious adverse event
SAP	statistical analysis plan
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SAS	Statistical Analysis System
SD	standard deviation
SoA	schedule of assessments
SOC	system organ class
SRR	seroresponse rate
Study P301	Study mRNA-1273-P301; NCT04470427
TEAE	treatment-emergent adverse event
ULOQ	upper limit of quantification
WHO	World Health Organization
WHODD	World Health Organization drug dictionary

1. Introduction

This statistical analysis plan (SAP), which describes the planned analyses for Study mRNA-1273-P204, is based on the most recent approved clinical study protocol (CSP), Version Amendment 9, dated 04-Aug-2022. The most recent approved electronic case report form (eCRF) Version 20.006 dated 31-Jan-2023.

In addition to the information presented in the statistical analysis plan section of the protocol (Section 8) which provides the principal features of analyses for this study, this SAP provides statistical analysis details/data derivations. It also documents modifications or additions to the analysis plan that are not "principal" in nature and result from information that was not available at the time of protocol finalization.

Study mRNA-1273-P204 is 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.

The study will be conducted in 3 parts. Part 1 of the study will be open-label and consist of dose-escalation and age de-escalation in approximately 1,275 participants to select the dose for each age group with the highest number enrolled in the oldest age group. Part 2 of the study will be a placebo-controlled observer-blind evaluation of the selected dose in up to 12,000 participants (up to 4,000 participants each in the 6 years to < 12 years, 2 years to < 6 years, and the 6 months to < 2 years of age groups). Part 3 will be an open-label alternative dosing assessment in approximately 300 participants in the 6 year to < 12 year old age group to assess reactogenicity and immunogenicity of a lower dose regimen.

Per Amendment 7, Part 1 (all ages) and 6 years to < 12 years Part 2 participants will be offered an optional booster dose lower than the chosen primary series for each age group at least 6 months after Dose 2 of mRNA-1273 (Part 1 participants and Part 2 participants in Study Arm 8; Part 2 placebo recipients from Study Arms 9, who crossed over to mRNA-1273 after unblinding). In Amendment 9, all participants in all age groups in Part 1 and Part 2 who have not yet received a booster dose will be offered a booster dose with mRNA-1273.214 (instead of mRNA-1273).

PPD Biostatistics and programming team, designee of Moderna Biostatistics and Programming department, will perform the statistical analysis of the safety, tolerability, reactogenicity, and effectiveness data; Statistical Analysis System (SAS) Version 9.4 or higher will be used to generate all statistical outputs (tables, figures, listings, and datasets).

The SAP will be finalized and approved prior to the primary analysis clinical database lock and treatment unblinding for the study. If the methods in this SAP differ from the methods described in the protocol, the SAP will prevail.

In this document, subject and participant are used interchangeably; injection of IP, injection, and dose are used interchangeably; vaccination group and treatment group are used interchangeably.

A separate SAP will provide more details for part 2 open-label phase, booster doses for part 1 and part 2, and part 3 open-label phase.

2. Study Objectives

2.1. Primary Objective

The primary objectives are the following:

- To evaluate the safety and reactogenicity of up to 3 dose levels (25, 50, and 100 µg) of mRNA-1273 vaccine administered as 2 doses 28 days apart in 3 age groups
- To infer the efficacy of mRNA-1273 (25, 50, and 100 µg, administered as 2 doses 28 days apart) based on immunogenicity in 3 age groups
- To evaluate the safety of mRNA-1273 booster or third dose
- To evaluate the safety of mRNA-1273.214 booster dose
- To infer effectiveness of the mRNA-1273 booster or third dose by establishing noninferiority of Ab response after the booster dose or third 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)

2.2. Secondary Objectives

The secondary objectives are the following:

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

- To evaluate the incidence of COVID-19 after vaccination with mRNA-1273 or placebo. COVID-19 is defined as clinical symptoms consistent with COVID-19 AND positive RT-PCR for SARS-CoV-2

2.3. Exploratory Objectives

The exploratory objectives are the following:

- To evaluate the genetic and/or phenotypic relationships of isolated SARS-CoV-2 strains to the vaccine sequence
- To describe the ratio or profile of specific S protein bAb relative to nAb in serum
- To characterize the clinical profile and immune responses of participants with COVID-19 or with SARS-CoV-2 infection
- To assess, in a subset of participants, the SARS-CoV-2 S protein-specific T-cell responses
- To explore asymptomatic SARS-CoV-2 infection after vaccination with mRNA-1273 or placebo in participants with serologic evidence of infection at baseline
- To evaluate immune response elicited by the primary series or mRNA-1273 booster dose or third dose of mRNA-1273 against variant(s) of interest

3. Study Endpoints

3.1. Primary Endpoints

The primary safety objective for Part 1 open-label phase or Part 2 blinded phase and open-label phase will be evaluated by the following safety endpoints:

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

The primary safety objective of mRNA-1273 booster or third dose will be evaluated by the following safety endpoints:

For mRNA-1273 Booster/Third Dose:

- Solicited local and systemic ARs through 7 days after booster or third dose
- Unsolicited AEs through 28 days after booster or third dose
- MAAEs through the entire study period after booster or third dose
- SAEs through the entire study period after booster or third dose
- AESIs through the entire study period after booster or third dose
- AEs leading to discontinuation from study participation after booster or third dose through the last day of study participation

For mRNA-1273.214 Booster Dose:

- MAAEs through the entire study period after booster dose
- SAEs through the entire study period after booster dose
- AESIs through the entire study period after booster dose
- AEs leading to discontinuation from study participation after booster dose through the last day of study participation

The primary immunogenicity objective for Part 1 open-label phase or Part 2 blinded phase and open-label phase will be evaluated by either:

- The proportion of participants with a serum antibody level at Day 57 ≥ antibody threshold of protection. If an accepted serum antibody threshold of vaccine protection against COVID-19 is available, this analysis will form the basis to infer efficacy.
- The GM value of serum antibody level and seroresponse rate 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). If a threshold of protection is not available, efficacy will be inferred based on establishing noninferiority for each age group (6 years to < 12 years, 2 years to < 6 years, and 6 months to < 2 years in Study P204) compared with 18- to

25-year old participants (Study P301) by both GM value of serum antibody levels and seroresponse rate.

For Part 1 and Part 2, among the two Pseudovirus tests, Pseudovirus Neutralizing Antibody (PsVNA) ID50 and PsVNA ID80 (if applicable), PsVNA ID50 is considered the most appropriate measure of subject response because it falls in the middle of the dynamic range of the dilution response curve while PsVNA ID80 is close to the plateau and thus subject to restriction. The GM and seroresponse rate comparisons between children in P204 and young adults (≥18 to 25 years of age) in P301 will be compared for the bAb and nAb measures, with PsVNA (ID50) considered as the primary assay test for the immunobridging.

As a descriptive analysis for Part 3 primary immunogenicity objective with the first two doses of primary series, the GM value of serum antibody level and SRR from Study P204 vaccine recipients at Day 57 will be compared with those for adult (≥18 to 25 years of age) vaccine recipients at Day 57 in the clinical endpoint efficacy trial (Study P301). The P301 comparator in SAP for Part 3 immunogenicity analysis is young adults ≥≥18 to 25 years of age instead of protocol P301 comparator ≥18 years of age, because the originally planned hypothesis testing in protocol for part 3 will not be performed due to the small number of participants enrolled in Part 3, which is insufficient to power the hypothesis testing. As a result, all part 3 immunogenicity analysis will be descriptive using P301 comparator (≥18 to 25 years), to be consistent with the comparator group in immunogenicity analyses in part 1 and part 2 of the study.

The primary immunogenicity objective to infer effectiveness of the mRNA-1273 booster or third dose will be evaluated by:

- Co-primary endpoints for mRNA-1273 booster in part 1 and 2,
  - GM value of post-booster Ab in Study P204 compared with post-primary series (post-Dose 2) in adults (≥18 to 25 years) in Study P301
  - Seroresponse rate of post-booster from baseline (pre-Dose 1) compared with post-primary series (post-Dose 2) from baseline (pre-Dose 1) in the adults (≥18 to 25 years) in Study P301, using 4-fold rise definition
- For Part 3, the GM value and SRR of post-third dose Ab in Study P204 compared with post-primary series (post-Dose 2) from young adults (≥18 to 25 years of age) in Study P301

Seroresponse due to vaccination at a subject level is defined as a value change from baseline (pre-Dose 1) below the LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline is equal to or above the LLOQ.

There is no primary immunogenicity objective associated with the mRNA-1273.214 booster.

3.2. Secondary Endpoints

The secondary objective will be evaluated by the following endpoints:

- The GM values of SARS-CoV-2 S protein-specific bAb on Day 1, Day 57 (1 month after Dose 2), Day 209 (6 months after Dose 2), Day 394 (1 year after Dose 2), BD-Day 1 (at least 3 months or 6 months after Dose 2), BD-Day 29 (1 month after mRNA-1273 booster dose or third dose), BD-Day 181 (6 months after mRNA-1273 booster dose or third dose), and BD-Day 366 (1 year after mRNA-1273 booster dose or third dose).
- The GM values of SARS-CoV-2-specific nAb on Day 1, Day 57 (1 month after Dose 2), Day 209 (6 months after Dose 2), Day 394 (1 year after Dose 2), BD-Day 1 (at least 3 months or 6 months after Dose 2), BD-Day 29 (1 month after mRNA-1273 booster dose or third dose), BD-Day 181 (6 months after mRNA-1273 booster dose or third dose), and BD-Day 366 (1 year after mRNA-1273 booster dose or third dose).
- The incidence of SARS-CoV-2 infection including symptomatic and asymptomatic infection (by serology and/or RT-PCR), starting 14 days after the second dose of IP, and starting 14 days after the first dose of IP. SARS-CoV-2 infection will be defined in participants with negative SARS-CoV-2 at baseline:
    - 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.
- 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 COVID19 symptoms, starting 14 days after the second dose of IP, and starting 14 days after the first dose of IP

- The incidence of the first occurrence of CDC Case Definition of COVID-19 post baseline, starting 14 days after the second dose of IP, and starting 14 days after the first dose of IP. COVID-19 is defined as symptomatic disease based on the following criteria according to CDC case definition:
    - The participant must have a positive test for SARS-CoV-2 by RT-PCR; AND
    - Either
        - The participant must have experienced 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
        - The participant must have experienced 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)
- The incidence of the first occurrence of the P301 primary definition of COVID-19 case post baseline, starting 14 days after the second dose of IP, and starting 14 days after the first dose of IP.

  The alternative case definition of COVID-19 is defined by the following criteria:
    - The participant must have experienced at least TWO of the following systemic symptoms: Fever (≥ 38° C/≥ 100.4° F), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s), OR
    - The participant must have experienced at least ONE of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, OR clinical or radiographical evidence of pneumonia; AND
    - At least one positive RT-PCR test for SARS-CoV-2

3.3. Exploratory Endpoints

The exploratory endpoints are the following:

- Alignment of genetic sequence of viral isolates with that of the vaccine sequence
- Relative amounts or profiles of S protein-specific bAb and specific nAb values in serum
- Description of clinical severity and immune responses of participants who are identified as infected by SARS-CoV-2 (COVID-19)
- Magnitude, phenotype, and percentage of cytokine-producing S protein-specific T cells, as measured by flow cytometry at different time points after vaccination relative to baseline
- GM and GMFR of bAb levels against SARS-CoV-2 nucleocapsid protein (quantitative IgG)
- GM, SRR, and GMFR of Ab against variant(s) of concern or interest

4. Study Design

4.1. Overall Study Design

This is 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 children aged 6 months to < 12 years. The study population will be divided into 3 age groups (6 years to < 12 years, 2 years to < 6 years, and 6 months to < 2 years) and up to 3 dose levels (25, 50, and 100 μg) of mRNA-1273 will be evaluated (and a third dose or an optional booster of 10 or 25 μg).

The study will be conducted in 3 parts. Part 1 of the study will be open label and consist of dose-escalation, age de-escalation in 1,275 participants (see Table1 below for the number of participants in each age group) to select the dose for each age group. Part 2 of the study will be placebo-controlled, observer-blind evaluation of the selected dose in up to 12,000 participants (up to 4,000 participants each in the 6 years to < 12 years, 2 years to < 6 years, and the 6 months to < 2 years of age groups). Part 3 will be an open-label alternative dosing assessment in approximately 300 participants in the 6 years to < 12 years old age group to assess reactogenicity and immunogenicity of a lower dose regimen. No participants in Part 1 will participate in Part 2 or Part 3 of the study, and no participant in Part 2 will participate in Part 3 of the study.

Table 1: Planned Age Groups and mRNA-1273 Dose Levels in Part 1 and Part 2, and Part 3 of the Study

	Part 1			Part 2		Part 3
Age Group	**mRNA-1273 25 µg**	**mRNA-1273 50 µg**	**mRNA-1273 100 µg**	**Selected Dose Level of mRNA-1273 From Part 1**	**Placebo**	**mRNA-1273 25 µg 2 doses of primary series +a third dose (Month 0, 1, 5[1])**
6 years to < 12 years		Study Arm 1 (n=375)	Study Arm 2 (n=375)	Study Arm 8 (n=3,000)	Study Arm 9 (n=1,000)	Study Arm 14 (n= approximately 300)
2 years to < 6 years	Study Arm 7 (Optional) (n=75)	Study Arm 3 (n=75)	Study Arm 4 (n=75)	Study Arm 10 (n=up to 3,000)	Study Arm 11 (n=up to 1,000)	
6 months to < 2 years	Study Arm 5 (n=150)	Study Arm 6 (n=150)		Study Arm 12 (n=up to 3,000)	Study Arm 13 (n=up to 1,000)	

Note: mRNA = messenger RNA.
1. Four months post-Dose 2 ± 28 days (at least 3 months and up to 5 months after Dose 2)

The study will begin with the oldest age group (6 years to < 12 years) and age de-escalate. Each age group will begin with Part 1 and may advance to Part 2 and Part 3 independently. The mRNA-1273 investigational vaccine or placebo will be administered as 2 intramuscular (IM) injections, approximately 28 days apart for Part 1 and Part 2. For Part 3, the mRNA-1273 investigational vaccine will be administered as 3 IM injections approximately 28 days apart for the 2 doses of primary series followed by a third dose at least 3 months and up to 5 months after receipt of the second dose of the primary series. The mRNA-1273 dose levels that will be evaluated in each age group in Part 1, Part 2 and Part 3 of the study are given in Table 1.

4.1.1. Part 1, the Open-Label Phase

Part 1 of the study will be open label, dose-escalation and age de-escalation. The study schematic is presented in Figure 1.

The study will include 3 age groups: Group 1 with 750 participants (≥ 6 years to < 12 years old) and Group 2 with approximately 225 participants (≥ 2 years to < 6 years old) and Group 3 with 300 participants (≥ 6 months to < 2 years old). Up to three dose levels (25 µg , 50 µg and 100µg) will be evaluated in each age group in Part 1. Each age group will begin dosing

with the lowest dose planned for that group. Dose escalation and age de-escalation will progress only after confirming the safety of a dose level in each group after each IP injection.

The study will be initiated with enrollment of 375 participants in the 6 years to < 12 years age group (Study Arm 1), and dosing with 50 µg of mRNA-1273.

After at least 75 participants in Study Arm 1 have completed Day 8 (1 week after Dose 1 of mRNA-1273 50 µg), an internal safety team (IST) will review the available safety data and provide a recommendation whether to escalate the dose to 100 µg in the 6 years to < 12 years age group (Study Arm 2; n = 375) and independently whether to begin dosing at the 50 µg dose level in the 2 years to < 6 years age group (Study Arm 3; n = 75). After at least 75 participants in Study Arm 1 reach Day 36 (1 week after Dose 2 of mRNA-1273 50 µg), the IST will again review the available safety data and provide a recommendation whether to administer Dose 2 of mRNA-1273 100 µg in Study Arm 2 and whether to administer Dose 2 of mRNA-1273 50 µg in Study Arm 3. Simultaneously, the enrollment of the remaining 300 planned participants for both Arms 1 and 2 will be ongoing. A preliminary safety and immunogenicity data review of Arm 1, and Arm 2 as applicable, will aid in the selection of a dose level for Part 2. Once all or a subset of participants from each of Study Arms 1 and 2 reach Day 57 (1 month after Dose 2 of mRNA-1273), an interim analysis may be conducted to review the safety and immunogenicity data. Cumulative safety data for approximately 300 participants at the selected dose level will be reviewed by the Data Safety Monitoring Board (DSMB) before enrollment in Part 2, and the DSMB safety review recommendation will enable the expansion of the 6 years to < 12 years age group (Part 2) to receive either mRNA-1273 at the selected dose level (Study Arm 8; n = 3,000) or placebo (Study Arm 9; n = 1,000).

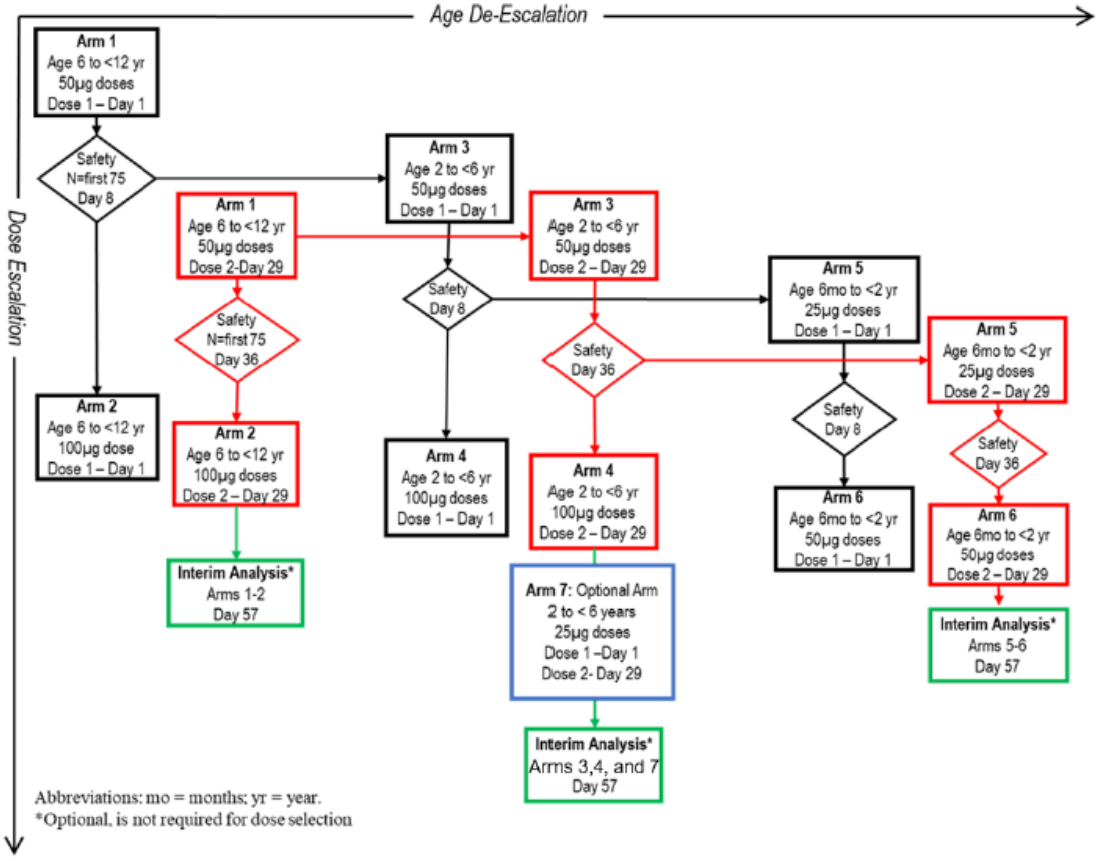
Similar analysis as above will apply to other age groups in part 1, details can be found in protocol section 3.1. An optional Arm 7 may be enrolled in middle age group (2 years to < 6 years, approximately 75 participants) at the 25 µg dose if the 100 µg dose is eliminated at any point during dose escalation process, to maintain dose ranging for this age group. A preliminary safety and immunogenicity data review of all applicable Arms will aid in the selection of a dose level for Part 2. Once all or a subset of participants in all applicable Arms reach Day 57 (1 month after Dose 2 of mRNA-1273), an interim analysis may be conducted to review safety and immunogenicity data. A preliminary safety and immunogenicity data review of all applicable Arms will aid in the selection of a dose level for Part 2 and for expansion of the 2 years to < 6 years age group (Part 2) to receive either mRNA-1273 at the

selected dose level (Study Arm 10; n = up to 3,000) or placebo (Study Arm 11; n = up to 1,000).

Once all participants in Study Arms 5 and 6 reach Day 57 (1 month after Dose 2 of mRNA-1273), an interim analysis may be conducted to review the tolerability and immunogenicity data at each dose level. A preliminary safety and immunogenicity data review of Arm 5 and Arm 6, as applicable, will aid in the selection of a dose level for Part 2 and allow for expansion of the 6 months to < 2 years age group (Part 2) to receive either mRNA-1273 at the selected dose level (Study Arm 12; n = up to 3,000) or placebo (Study Arm 13; n = up to 1,000). Detailed schematic of study arms and process can be found in Section 3.1 from protocol and Figure 1 below.

In general, if a decision is made not to proceed with administration of the higher dose and/or the second injection at a given dose level (eg, due to safety concerns), the participants scheduled to receive the higher dose may receive a lower dose, and the participants who had received the higher dose level as their first injection will likely be given the next lower dose level that was tolerated for their second injection. The dose level not tolerated in the older age group will not be administered in any of the younger age groups. Within an age group, if one of the dose levels is found to have an unacceptable tolerability profile, the age group may progress to Part 2 at a lower dose level.

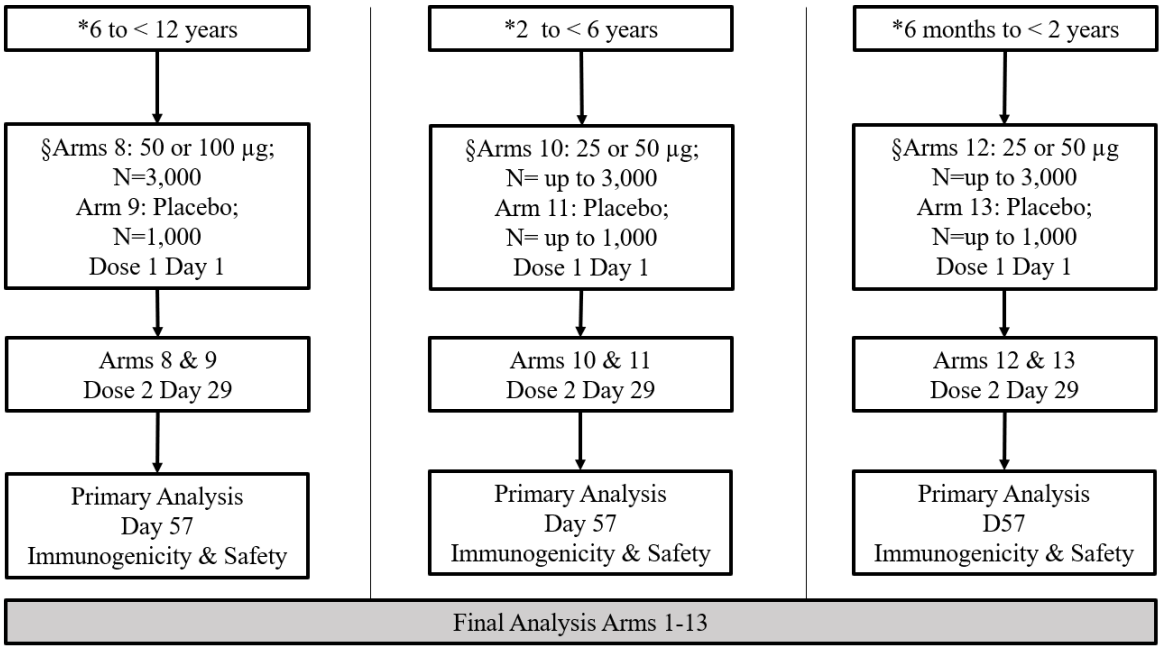
Figure 1 Study Design Schematic, Part 1: Dose-escalation, age de-escalation



4.1.2. Part 2, the Blinded Phase

The blinded phase of the study will be a placebo-controlled observer-blind evaluation of the selected dose in up to 12,000 participants (up to 4,000 participants each in the 6 years to < 12 years, 2 years to < 6 years, and the 6 months to < 2 years of age groups). No participants in Part 1 will participate in Part 2 of the study. Each age group will begin with Part 1 and advance to Part 2 independently. For each age group, the primary analysis immunogenicity in part 2 will be conducted after the pre-specified Immunogenicity Subset of participants reaches Day 57, and safety analysis will be conducted after a subset or all participants reach Day 57.

Figure 2 Study Design Schematic, Part 2: Expansion



Abbreviations: CMI = cell-mediated immunity; D = Day; S = spike; VTEU = Vaccine and Treatment Evaluation Units.
*Expansion and primary analysis for each age group may occur at different times.
§Participants in each age group will be assigned to one of 5 phlebotomy cohorts. Participants in 3 of these 5 cohorts will provide blood specimens for immunogenicity on D1 (prior to randomization and first dose), D57, and one of D29 (prior to the second dose), D209, or D394 (such that each participant provides a total of 3 blood samples only). Participants in the Cohort D (remainder of the age group) will provide a blood sample on D1 (prior to randomization and before the first dose) and within 4 days of receiving Dose 2 at D30 (+3 days) for storage and potential future biomarker testing. A fifth cohort of participants (selected VTEU sites only) will provide blood samples for assessment of exploratory serology and CMI (S protein-specific T-cell responses) on D1 (prior to randomization and before the first dose), D43, D209, and D394.

4.1.3. Optional Booster Doses

Per Amendment 7, Part 1 (all ages) and 6 years to < 12 years Part 2 participants will be offered an optional booster dose lower than the chosen primary series for each age group at least 6 months after Dose 2 of mRNA-1273 (Part 1 participants and Part 2 participants in Study Arm 8; Part 2 placebo recipients from Study Arms 9, who crossed over to mRNA-1273 after unblinding).

In Amendment 9, all participants in all age groups in Part 1 and Part 2 who have not yet received a booster dose will be offered a booster dose with mRNA-1273.214 (instead of mRNA-1273).

Optional Booster Doses for Part 1 and Part 2 Participants

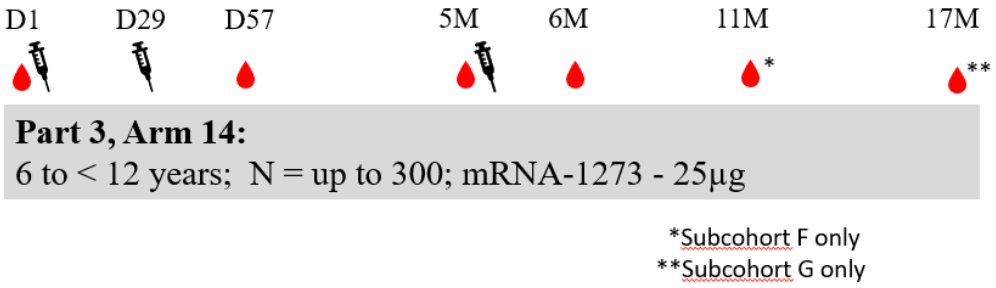
Age at Time of Booster	Booster dose (mRNA-1273 or mRNA-1273.214)

6 years to < 12 years	25 µg
2 years to < 6 years	10 µg
6 months to < 2 years	10 µg

4.1.4. Part 3, the Open-Label Phase (Alternative Dosing Assessment)

Part 3 of the study will be open-label. A total of approximately 300 participants in the 6 years to < 12 years old age group will be enrolled to receive 3 total doses of mRNA-1273 at 25 µg given as the primary series doses at Day 1 and Day 29 followed by a third dose at Day 149/booster dose (BD)-Day 1 (at least 3 months and up to 5 months after the second dose in the primary series). The primary analysis of immunogenicity and safety in Part 3 for Study Arm 14 will be conducted after all treated participants reach Day 57 (for primary series). The primary analysis of immunogenicity and safety for the third dose will be conducted after all participants who received a third dose reach Day 177/BD-Day 29.

Figure 3 Study Design Schematic, Part 3



4.2. Sample Size and Power

The initial age groups in Part 1 are for estimation purposes. With approximately 750 participants (approximately 375 participants at each dose level of mRNA-1273) in the initial 6 years to < 12 years age group, there is at least a 90% probability to observe at least 1 participant with an AE at a true AE rate of 1% for a given dose level. In each of the younger age groups (2 years to < 6 years and 6 months to < 2 years), the safety assessment will occur during the conduct of Part 2 after approximately 375 participants have been exposed to mRNA-1273 at the dose level selected for Part 2. For further details, please refer to protocol section 7.5.2.

The sample size in the expansion (Part 2) is considered to be sufficient to support a safety database in the pediatric participants 6 months to < 12 years of age. With up to 3,000

participants each in the 6 years to < 12 years, 2 years to < 6 years, and 6 months to < 2 years of age groups exposed to mRNA-1273 at a given dose level in Part 2, the study has at least a 95% probability to observe at least 1 participant with an AE at a true 0.1% AE rate for a given dose level.

The planned sample size in the lower dosing assessment (Part 3) is approximately 300 children 6 years to < 12 years of age receiving mRNA-1273 25 μg. There is at least a 90% probability to observe at least 1 participant with an AE at a true AE rate of 1% in this group.

A subset of Full Analysis Set (FAS) participants (Immunogenicity Subset) in each age group will be selected for measuring immunogenicity data. The immunogenicity samples of the Immunogenicity Subset will be processed, and the analysis of primary immunogenicity endpoint will be based on the PP Immunogenicity Subset.

If a threshold of protection is available, for the primary immunogenicity endpoint, with approximately 289 participants on mRNA-1273 in the PP Immunogenicity Subset of an age group, there will be at least 90% power to rule out 70% with a 2-sided 95% CI (lower bound of the 95% CI > 70%) for the percentage of mRNA-1273 participants exceeding the accepted threshold if the true rate of participants exceeding the threshold is 80%.

If an acceptable antibody threshold of protection against COVID-19 is not available at the time of analysis for the primary immunogenicity endpoint, noninferiority tests of the 2 null hypotheses based on the 2 coprimary endpoints will be performed, respectively. The sample size calculation for each of the 2 noninferiority tests was performed, and the larger sample size was chosen for the study.

- With approximately 289 participants receiving mRNA-1273 in the PP Immunogenicity Subset of each age group in Study P204 and young adults (≥18 to 25 years of age) in Study P301, there will be a 90% power to demonstrate noninferiority of the immune response, as measured by the antibody GM value, in pediatric population at a 2-sided alpha of 0.05, compared with that in young adults (≥18 to 25 years of age) in Study P301 receiving mRNA-1273, assuming an underlying GMR value of 1, a noninferiority margin of 1.5 (lower bound > 0.667), and a point estimate minimum threshold of 0.8. The standard deviation of the natural log-transformed levels is assumed to be 1.5.
- With approximately 289 participants receiving mRNA-1273 in the PP Immunogenicity Subset of each age group in Study P204 and young adults (≥18 to 25 years of age) in Study P301, there will be an at least 90% power to demonstrate

noninferiority of the immune response as measured by SRR in children at a 2-sided alpha of 0.05, compared with that in young adults ≥18 to 25 years of age in Study P301 receiving mRNA-1273, assuming SRR of 85% in young adults of ≥18 to 25 years of age from Study P301, true SRR of 85% in children (or true rate difference is 0 compared with young adults from Study P301), a noninferiority margin of 10% and a point estimate minimum threshold of -5% in SRR difference.

- In the 1273-P203 interim analysis (data snapshot on 08 May 2021), the observed seroresponse rates at Day 57 were high in both ≥18 to 25 years of age group from Study P301 (98.6% with 95% CI: 96.6, 99.6) and 12 to17 years of age group (98.8% with 95% CI: 97.0, 99.7), based on pseudovirus nAb ID50 values. For this Study P204, if the true seroresponse rates were assumed to be 95% or higher in both ≥18 to 25 years of age group from Study P301 and an age group in children, with between-group true difference within 4%, there will be a >90% power to demonstrate noninferiority by seroresponse rate in children compared with ≥18 to 25 years of age in Study P301, at a 2-sided alpha of 0.05 and a noninferiority margin of 10%.
- Assuming approximately 25% of participants in the Immunogenicity Subset in Part 2 will not meet the criteria to be included in the PP Immunogenicity Subset, approximately 528 participants in Part 2 (~396 receiving mRNA-1273 and ~132 receiving placebo) will be selected for the Immunogenicity Subset from which approximately 289 participants on mRNA-1273 will be suitable for the PP Immunogenicity Subset in Part 2.
- In Part 1 or Part 2 for the booster dose primary immunogenicity analysis in an age group, with approximately 289 participants receiving mRNA-1273 booster dose in the PP Immunogenicity Subset with pre-booster negative SARS-CoV-2 in Study P204 and 289 young adults (≥18 to 25 years of age) receiving mRNA-1273 100 µg primary series in Study P301, there will be a 90% power to demonstrate noninferiority of the immune response, as measured by the antibody GM value, in children receiving a booster dose compared with that in adults (≥18 to 25 years of age) receiving mRNA-1273 primary series in Study P301, at a 2-sided alpha of 0.05, assuming an underlying true GMR value of 1.0 and a noninferiority margin of 1.5. The standard deviation of the natural log-transformed GMT levels is assumed to be 1.5. Also, if the true SRRs were assumed to be 95% or higher in children receiving mRNA-1273 booster dose in Study P204 and adults receiving mRNA-

1273 primary series in Study P301, with between-group true difference within 4%, there will be a > 90% power to demonstrate noninferiority by SRR in children receiving a booster dose compared with adults receiving primary series in Study P301, at a 2-sided alpha of 0.05.

- In Part 3 for the primary series primary immunogenicity analysis, with approximately 289 participants receiving mRNA-1273 25 µg primary series in the PP Immunogenicity Subset in Study P204 and 289 adults (≥ 18 years of age) receiving mRNA-1273 100 µg primary series in Study P301, there will be a 84% power to demonstrate noninferiority of the immune response, as measured by the antibody GM value, in children compared with that in adults (≥ 18 years of age) receiving mRNA-1273 in Study P301, at a 2-sided alpha of 0.025, assuming a true GMR value of 1.0 and a noninferiority margin of 1.5. The standard deviation of the natural log-transformed GMT levels is assumed to be 1.5. Also, if the true SRRs were assumed to be 95% or higher in children in Study P204 and adults from Study P301, with between-group true difference within 4%, there will be a > 90% power to demonstrate noninferiority by SRR in children compared with adults in Study P301, at a 2-sided alpha of 0.025.
- In Part 3 for the third dose primary immunogenicity analysis, with approximately 289 participants receiving a third dose of mRNA-1273 dose in the PP Immunogenicity Subset with pre-third dose negative SARS-CoV-2 in Study P204 and 289 adults (≥ 18 years of age) receiving mRNA-1273 100 µg primary series in Study P301, there will be a 84% power to demonstrate noninferiority of the immune response, as measured by the antibody GM value, in children receiving a third dose compared with that in adults (≥ 18 years of age) receiving mRNA-1273 primary series in Study P301, at a 2-sided alpha of 0.025, assuming an underlying true GMR value of 1.0 and a noninferiority margin of 1.5. The standard deviation of the natural log-transformed GMT levels is assumed to be 1.5. Also, if the true SRRs were assumed to be 95% or higher in children receiving a third dose of mRNA-1273 dose in Study P204 and adults receiving mRNA-1273 primary series in Study P301, with between-group true difference within 4%, there will be a > 90% power to demonstrate noninferiority by SRR in children receiving a third dose compared with adults receiving primary series in Study P301, at a 2-sided alpha of 0.025.

Part 3 (Arm 14) was originally planned to enroll ~300 children aged 6 to <12 years to receive mRNA-1273 25 µg (2 doses of primary series and a third dose). However, arm 14 was closed to enrollment at an enrollment number of N = 91. All participants enrolled in Arm 14 will continue to be followed as per protocol, including receipt of third doses if not received yet, as well as immunogenicity samples.

Given that the number of participants enrolled in Part 3 (n=91) is substantially smaller than the planned sample size of ~300 required for the immunogenicity hypothesis testing after dose 2 of mRNA-1273 25 µg primary series and after a third dose of mRNA-1273 25 µg, the hypothesis testing will not be performed. Instead, all the analyses of immunogenicity endpoints will be descriptive.

Thus, the study objective of Part 3 was updated to evaluate descriptively safety and immune responses to 2 doses of mRNA-1273 25 µg primary series and a third dose of mRNA-1273 25 µg in 6 to <12 years of age. For the descriptive analysis purpose, the comparator will be young adults ≥18 to 25 years of age from P301, instead of ≥18 years of age, to be consistent with the comparator group in immunogenicity analyses in part 1 and part 2 of the study.

4.3. Randomization

Random assignment of participants in Part 2 of the study will use a centralized interactive response technology, in accordance with pregenerated randomization schedules. Up to 4,000 participants each in the 6 years to < 12 years, 2 years to < 6 years, and 6 months to < 2 years age groups will be randomized in a 3:1 ratio to the mRNA-1273 arm (n = up to 3,000 participants in each group) or placebo arm (n = up to 1,000 participants in each group).

4.4. Blinding and Unblinding

This study is conducted in three parts, Part 1 of this study will be open label, blinding procedures will not be applicable.

Part 2 of this study will be conducted in an observer-blind manner. The investigator, study staff, study participants, study site monitors, and Sponsor personnel (or its designees) will be blinded to the IP administered until study end, with certain exceptions, please refer to Section 8.1 of the protocol for details.

Part 3 is open label; however, if blinded administration is ongoing at the site, blinded procedure for Part 2 still applies.

The final analysis of all endpoints will be performed after all participants have completed all planned study procedures.

At the time of interim analysis, only pre-identified Sponsor and unblinded Contract Research Organization (CRO) team members as specified in the study Data Blinding Plan will be unblinded to review treatment level results and individual listings. Please also refer to Section 6.9. Study sites will remain blinded to individual treatment assignments until the end of the study.

If a COVID-19 vaccine is authorized or licensed for a specific age group before the end of the study, please refer to protocol section 3.3 for unblinding and/or cross-over plans.

Participants under 6 years of age in Part 2 who have reached at least 6 months follow up after Dose 2 will be eligible for unblinding via a telephone call to learn which treatment they received. Participants who received placebo will be offered the option of cross-over vaccination with mRNA-1273 at that point as described above.

5. Analysis Populations

The following analysis sets are defined for Part 1 open-label phase and Part 2 blinded phase: Randomization Set, Full Analysis Set (FAS), Per-Protocol (PP) Set for Efficacy, Immunogenicity Subset, Per-Protocol (PP) Immunogenicity Subset, Safety Set, Solicited Safety Set, Modified Intent-to-Treat (mITT) Set, Modified Intent-to-Treat-1 (mITT1) Set.

5.1. Randomization Set

The Randomization Set consists of all participants who are randomized in the Part 2 of study, regardless of the participant's treatment status in the study. Participants will be analyzed according to the treatment group to which they were randomized.

5.2. Full Analysis Set

The Full Analysis Set (FAS) for Part 1 consists of all enrolled participants who receive at least 1 injection of IP, and the FAS for Part 2 consists of all randomly assigned participants who receive at least 1 injection of IP. Participants will be analyzed according to the treatment group for the treatment they actually received in Part 1 and will be analyzed according to the treatment group to which they were randomized in Part 2.

5.3. Per-Protocol (PP) Set for Efficacy

The Per-protocol (PP) Set for Efficacy consists of all participants in the FAS who meet all the following criteria:

a) Received planned doses of IP per schedule

b) Complied with the 2nd dose injection timing

c) Had no major protocol deviations that impact key or critical efficacy data

d) Had a negative RT-PCR test for SARS-CoV-2 and negative serology test based on bAb specific to SARS-CoV-2 nucleocapsid protein at baseline

The PP Set for Efficacy in both parts will be used as the primary analysis population in the efficacy analyses unless otherwise specified. Participants will be analyzed according to the treatment group for the treatment they actually received in Part 1 and to which they were randomized in Part 2.

5.4. Immunogenicity Subset

A subset of participants in the FAS will be selected for immunogenicity sampling and testing. Participants in Part 1 and 2 of the study and in different age groups who receive the same mRNA-1273 dose level may be combined for analysis.

Immunogenicity Subset consists of

a) a subset of participants in the FAS, and

b) have baseline (Day 1) SARS-CoV-2 status available, and

c) have baseline and at least one post-injection antibody assessment for the analysis endpoint.

Immunogenicity Subset will be used for sensitivity analyses or supportive analysis. Participants will be analyzed according to the treatment group to which they were randomized.

Table 2: Phlebotomy Schedule for Serology, Biomarker Sample, and CMI for Part 2 (Expansion) of the Study

For participants that chose to receive a booster dose under protocol Amendment 7, please see separate SAP for part 2 open-label phase and booster doses's section 8.7 appendix G for the booster dose phlebotomy schedule.

If Day 209/Day 394 blood draw is within 30 days of planned BD-Day 1, BD-Day 1 blood draw can be used for Day 209/Day 394.

Cohort	Number of Subjects	Study Visit Day						
		D1[1,2]	D29[1]	D30 (+3)[3]	D43	D57	D209 (+30 days)[4]	D394 (+30 days)[4]
Phlebotomy Schedule for Serology: To be Executed Within Age Group								
A	First 176 (132 mRNA-1273: 44 placebo)	X	X			X		
B	Next 176 (132 mRNA-1273: 44 placebo)	X				X	X	
C	Next 176 (132 mRNA-1273: 44 placebo)	X				X		X
D	Remainder of the age group	X		X[3]				
Phlebotomy Schedule for Cell-Mediated Immunity: To be Executed Within Each Age Group at Selected VTEU Sites only								
E (CMI with exploratory serology)	24 (18 mRNA-1273: 6 placebo)	X			X		X	X

Abbreviations: CMI = cell-mediated immunity; D = day; VTEU = Vaccine and Treatment Evaluation Units.
1. On Day 1, sample must be collected prior to randomization and dosing. On Day 29, sample must be collected prior to dosing.
2. If a Day 1 (baseline) blood sample cannot be obtained in either Part 1 or Part 2, the participant will be considered either a screen failure due to inability to satisfy inclusion criterion 3 or could be scheduled for rescreening. Participants may be rescreened 1 time, either within same screening period for Part 1 or Part 2 or in a new screening period for Part 2 if the initial screening was in Part 1. If the participant is rescreened and a blood sample still cannot be obtained, then he/she will be considered a screen failure due to inability to satisfy inclusion criterion 3.
3. Serum sample from ~4 ml of blood only, to be stored for potential future use for biomarker assessment
4. If the participant decides to receive a booster dose, the BD1 blood draw (Protocol Table 15) can be used for Day 209 or Day 394 (Protocol Table 14).

5.5. Per-Protocol (PP) Immunogenicity Subset

Per-Protocol (PP) Immunogenicity Subset consists of all participants in Immunogenicity Subset who meet all the following criteria:

a) Received planned doses of IP per schedule

b) Complied with the immunogenicity window based on 2nd dose injection timing

c) Had a negative RT-PCR test for SARS-CoV-2 and a negative serology test based on bAb specific to SARS-CoV-2 nucleocapsid protein at baseline

d) If participants have a diagnosis of HIV, they are not receiving highly active anti-retroviral therapy (HAART)

e) Had baseline (Day 1) and Day 57 Ab assessment for the analysis endpoint

f) Had no major protocol deviations that impact key or critical data

The PP Immunogenicity Subset will serve as the primary population for the analysis of immunogenicity data in this study unless specified otherwise. Participants will be analyzed according to the treatment group for the treatment which they actually received in Part 1 and to which they were randomized in Part 2.

5.6. Safety Set

The Safety Set of Part 1 consists of all enrolled participants and of Part 2 consists of all randomized participants who received any study injection. The Safety Set will be used for analysis of safety except for the solicited ARs. In addition, the following Safety Set is defined for each injection separately. The First (Second) Injection Safety Set consists of all subjects in the Safety Set who have received the first (second) study injection. Participants will be included in the vaccination group corresponding to the vaccination they actually received. For a participant who was randomized to placebo in Part 2 but received any dose of mRNA-1273 at any injection, the participant will be included in the mRNA-1273 group in the Safety Set.

5.7. Solicited Safety Set

The Solicited Safety Set consists of all participants in the safety set who contribute any solicited AR data, i.e., have at least one post-baseline solicited safety assessment. The Solicited Safety Set will be used for the analyses of solicited ARs and participants will be included in the vaccination group corresponding to the study injection they actually received. In addition, the following Solicited Safety Set is defined for each injection separately.

The First (Second) Injection Solicited Safety Set consists of all subjects in the Solicited Safety Set who have received the first (second) study injection and have contributed any

solicited AR data from the time of first (second) study injection through the following 6 days.

Participants will be analyzed according to the vaccination group a participant received, rather than the vaccination group to which the subject was randomized. A participant who was randomized to placebo but received any dose of mRNA-1273 at any injection will be included in the mRNA-1273 group in the Solicited Safety Set.

5.8. Modified Intent-to-Treat (mITT) Set

The Modified Intent-to-Treat (mITT) Set consists of all participants in the FAS who had no serologic 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, i.e., all FAS participants excluding those with positive or missing RT-PCR test or serology test at baseline.

Participants will be analyzed according to the treatment group to which they were randomized.

5.9. Modified Intent-to-Treat-1 (mITT1) Set

The Modified Intent-to-Treat-1 (mITT1) Set consists of all participants in the mITT Set excluding those who received wrong treatment (i.e., at least one dose received that is not as randomized or planned).

Participants will be analyzed according to the treatment group to which they were randomized.

6. Statistical Analysis

6.1. General Considerations

The Schedule of Assessments is provided in Appendix E for Part 1 and 2 study arms 1 through 13.

Continuous variables will be summarized using the following descriptive summary statistics: the number of subjects (n), mean, standard deviation (SD), median, minimum (min), and maximum (max).

Categorical variables will be summarized using counts and percentages.

Baseline value, unless specified otherwise, is defined as the most recent non-missing measurement (scheduled or unscheduled) collected before the first dose of IP. For

immunogenicity tests and nasal swab tests, the baseline is defined as the most recent non-missing measurement (scheduled or unscheduled) collected before or on the date of first dose of IP (Day 1).

For the summary statistics of all numerical variables unless otherwise specified, the display precision will follow programming standards. Please see Appendix A for variable display standards.

When count data are presented, the percentage will be suppressed when the count is zero in order to draw attention to the non-zero counts. A row denoted "Missing" will be included in count tabulations where specified on the shells to account for dropouts and missing values. The denominator for all percentages will be the number of subjects in that age group and vaccination group within the analysis set of interest, unless otherwise specified.

Baseline SARS-CoV-2 status is determined by using virologic and serologic evidence of SARS-CoV-2 infection on or before Day 1.

Negative status at Baseline is defined as the most recent RT-PCR for SARS-CoV-2 result is negative and the most recent serology test based on bAb specific to SARS-CoV-2 nucleocapsid result is negative on or before Day 1.

Positive SARS-CoV-2 status at Baseline is defined as the most recent RT-PCR for SARS-CoV-2 result is positive and/or the most recent serology test based on bAb specific to SARS-CoV-2 nucleocapsid result is positive on or before Day 1.

Study day relative to the first injection will be calculated as below:

a) study day prior to the first injection will be calculated as: date of assessment/event – date of the first injection;

b) study day on or after the date of the first injection will be calculated as: date of assessment/event – date of the first injection + 1

Study day relative to the most recent injection will be calculated as below:

a) study day prior to the first injection will be calculated as: date of assessment/event – date of the first injection;

b) study day on or after the date of the first injection but before the second injection (if applicable) will be calculated as: date of assessment/event – date of the first injection + 1;

c) study day on or after the date of the second injection will be calculated as: date of assessment/event – date of the second injection + 1; if study day is on the same day as the second injection, date and time will be compared with the second injection date and time.

For calculation regarding antibody value, antibody values reported as LLOQ will be replaced by 0.5 × LLOQ. Values that are greater than the upper limit of quantification (ULOQ) will be converted to the ULOQ if actual values are not available, and actual values will be used if available. Missing results will not be imputed.

The following **analysis periods or stages for safety analyses** will be used in this study:

- Up to 28 days after any vaccination: this stage starts at the day of each vaccination and continue through the earliest date of (the day of each vaccination and 27 subsequent days, next vaccination [if applicable]). This analysis period will be used as the primary analysis period for safety analyses including unsolicited AE, except for solicited AR, unless specified otherwise.

- Follow-up analysis period:

  For unsolicited AE or assessments that will be collected throughout the study, this analysis period starts from 28 days after the last injection date (i.e. the day of last injection + 28 days, regardless of number of injections received) and continues until the earliest date of (study completion, discontinuation from the study, or death).

  For assessments that will be collected at study visits, if a subject receives two injections, this stage starts from the day after Day 57 visit and continues until the earliest date of (study completion, discontinuation from the study, or death); if a subject receives first injection only, this stage starts from the day after Day 29 visit and continues until the earliest date of (study completion, discontinuation from the study, or death).

- Overall period (throughout the study): this analysis period starts at the first injection on Day 1 and continues through the earliest date of (study completion, discontinuation from the study, or death).

Unscheduled visits: Unscheduled visit measurements will be included in analysis as follows:

- In scheduled visit windows per specified visit windowing rules.
- In the derivation of baseline/last on-treatment measurements.
- In the derivation of maximum/minimum on-treatment values and maximum/minimum change from baseline values for safety analyses.
- In individual subject data listings as appropriate.

Visit windowing rules: The analysis visit windows for protocol-defined visits are provided in Appendix B.

Incomplete/missing data:

- Imputation rules for missing prior/concomitant medications, non-study vaccinations and procedures are provided in Appendix C.
- Imputation rules for missing AE dates are provided in Appendix D.
- For laboratory assessments, if majority of results are indefinite, imputation of these values will be considered. If the laboratory results are reported as below the LLOQ (e.g., <0.1), the numeric values will be imputed by 0.5 × LLOQ in the summary. If the laboratory results are reported as greater than the ULOQ (e.g., >3000), the numeric values will be imputed by ULOQ in the summary.
- Other incomplete/missing data will not be imputed, unless specified otherwise.

Treatment groups:

The following vaccination groups will be used for summary purposes:

- Part 1, Open-Label Phase:
    - mRNA-1273 vaccine 25 µg
    - mRNA-1273 vaccine 50 µg
    - mRNA-1273 vaccine 100 µg

- mRNA-1273 vaccine Total

- Part 2, Blinded Phase:

  Treatment in Part 2 will be the selected dose level in each of the age groups from Part 1 or Placebo

  - mRNA-1273 vaccine 25 μg, or
  - mRNA-1273 vaccine 50 μg, or
  - mRNA-1273 vaccine 100 μg

    And

  - Placebo

Subjects in an age group who received at least one dose of mRNA-1273 in Part 2 will be included in the mRNA-1273 selected dose level group (as actual treatment) for that age group in Part 2 in the safety analyses.

Summary by age group:

All analyses and data summaries/displays will be provided by vaccination group for each age cohort (6 months to < 2 years, 2 years to < 6 years, and 6 years to < 12 years), unless otherwise specified. Participants in Part 1 and 2 of the study and in different age groups who receive the same mRNA-1273 dose level may be combined for safety analysis.

Summary by study part:

Separate shells will be provided for Part 1 and Part 2 of the study. In Part 1, all analyses and data summaries/displays will be provided by age and vaccination group. In Part 2, all analyses and data summaries/ displays will be provided by age and vaccination group.

Analysis Periods

The following analysis periods and treatment groups will be used for efficacy analyses for Part 2, the blinded phase, unless specified otherwise:

Part 2 Group	**Description**	**Part 2 Blinded Phase Analysis Period for Efficacy**
mRNA-1273	Participants randomized to mRNA-1273 in the Blinded Phase	From randomization to the earliest date of unblinding (date on Participant Decision Visit / Crossover Day 1 or unblinding day) inclusive,
Placebo	Participants randomized to Placebo in the Blinded Phase	

		study discontinuation, study completion, death, and data cutoff date

Immunogenicity data at Day 57 are analyzed regardless of participant unblinding status at Day 57. The analysis period for efficacy specified above will not be applied to immunogenicity analysis. Since immunogenicity samples are handled and tested in a blinded manner and lab testing results are objective which are not impacted by unblinding status in individual participants. Therefore, the immunogenicity data at Day 57 after participant unblinding can still be included for the Day 57 immunogenicity analysis.

The following analysis period and treatment groups will be used for safety analysis for Part 2, the blinded phase, unless specified otherwise:

Part 2 Group	**Description**	**Part 2 Blinded Phase Analysis Period for Safety**
mRNA-1273	Participants received at least one dose of mRNA-1273 in the Blinded Phase	From the date of 1st injection to the earliest date of unblinding (date on Participant Decision Visit / Crossover Day 1 or unblinding day) exclusive, study discontinuation, study completion, death, and data cutoff date
Placebo	Participants only received Placebo in the Blinded Phase	

Subgroup Analysis

Safety, efficacy and immunogenicity endpoints may be analyzed in select subgroups specified below as applicable:

- Baseline SARS-CoV-2 Status (Positive, Negative)
- Age (6 Months to < 2 Years, 2 Years to < 6 Years, and 6 Years to < 12 Years)
- Sex (Female, Male)
- Race
- Ethnicity

- Obesity status (Obesity is defined as BMI >= 95th percentile based on WHO growth reference data)

All analyses will be conducted using SAS Version 9.4 or higher.

6.2. Background Characteristics

6.2.1. Subject Disposition

The number and percentage of subjects in the following categories will be summarized by age and vaccination group as defined in Section 6.1 based on the Full analysis for Part 1 and Randomization Set for Part 2:

- Randomization Set (Part 2)
- Full Analysis Set (Part 1 and Part 2)
- Per-Protocol (PP) Set for Efficacy (Part 1 and Part 2)
- Immunogenicity Subset (Part 1 and Part 2)
- Per-Protocol (PP) Immunogenicity Subset (Part 1 and Part 2)
- Safety Set (Part 1 and Part 2)
- Solicited Safety Set (Part 1 and Part 2)
- mITT Set (Part 1 and Part 2)
- mITT1 Set (Part 1 and Part 2)

The percentage will be based on subjects in that age and vaccination group within the Full Analysis Set for Part 1 and in that age and vaccination group within the Randomization Set (as randomized) for Part 2, except the Solicited Safety Set and Safety Set for which the percentages will be based on the age and vaccination group in the Safety Set (as treated).

The number of subjects in the following categories will be summarized based on subjects screened:

- Number of subjects screened
- Number and percentage of screen failure subjects and the reason for screen failure

The percentage of subjects who screen failed will be based on the number of subjects screened. The reason for screen failure will be based on the number of subjects who screen failed.

The number and percentage of subjects in each of the following disposition categories will be summarized by age and vaccination group based on Full Analysis Set for Part 1 and summarized by age and vaccination group based on the Randomization Set for Part 2:

- Received each dose of IP
- Prematurely discontinued before receiving the second dose of IP and the reason for discontinuation
- Completed study
- Prematurely discontinued the study and the reason for discontinuation

A subject disposition listing will be provided, including informed consent date, subjects who completed the study injection schedule, subjects who completed study, subjects who discontinued from study vaccine or who discontinued from participation in the study, with reasons for discontinuation. A separate listing will be provided for screen failure subjects with reasons for screen failure.

A subject who completed 12 months of follow up after the last injection received is considered to have completed the study.

6.2.2. Demographics

Descriptive statistics will be calculated for the following continuous demographic and baseline characteristics: age (months or years), weight (kg, z-score), height (cm, z-score), and body mass index (BMI) (kg/m^2, z-score). Number and percentage of subjects will be provided for categorical variables such as gender, race, ethnicity. The summaries will be presented separately by age and vaccination group as defined in Section 6.1, based on the FAS, Randomization Set (Part 2), Per-Protocol (PP) Set for Efficacy, Immunogenicity Subset, Per-Protocol (PP) Immunogenicity Subset, Safety Set, mITT Set and mITT1 Set.

Participants in Part 1 and Part 2 of the study and in different age groups who receive the same mRNA-1273 dose level may be combined. If the Safety Set differs from the Randomization Set in Part 2 (e.g., subjects randomized but not received any study injection; subjects received study vaccination other than the vaccination group they were randomized to), the analysis will also be conducted using the Randomization Set.

For screened failure subjects, age (months or years), as well as gender, race, ethnicity will be presented in a listing.

In addition, subjects with any inclusion and exclusion criteria violation will also be provided in a listing.

6.2.3. Medical History

Medical history data will be coded by system organ class (SOC) and preferred term (PT) using the Medical Dictionary for Regulatory Activities (MedDRA).

The number and percentage of participants with any medical history will be summarized by SOC and PT based on Safety Set. A participant will be counted only once for multiple events within each SOC and PT. SOC will be displayed in internationally agreed order. PT will be displayed in descending order of frequency and then alphabetically within SOC.

Medical history data will be presented in a listing.

6.2.4. Prior and Concomitant Medications

Prior and concomitant medications and non-study vaccination will be coded using the World Health Organization (WHO) drug dictionary (WHODD). The summary of concomitant medications will be based on the Safety Set. Categorization of prior, concomitant, and post medications is summarized in Appendix C Table 6.

The number and percentage of subjects using concomitant medications and non-study vaccination during the 7-day follow-up period (i.e., on the day of injection and the 6 subsequent days) and during the 28-day follow-up period after each injection (i.e., on the day of injection and the 27 subsequent days) will be summarized by vaccination groups as defined in Section 6.1 as follows:

- Any concomitant medications and non-study vaccination within 7 Days Post Injection
- Any concomitant medications and non-study vaccination within 28 Days Post Injection
- Seasonal influenza vaccine within 28 Days Post Injection
- Antipyretic or analgesic medication within 28 Days Post Injection

A summary table of non-study vaccination that continued or newly received at or after the first injection through 14 days after the last injection will be provided by PT in descending frequency in the mRNA-1273 group with all dose level combined.

A summary table of concomitant medications that continued or newly received at or after the first injection through 28 days after the last injection will be provided by PT in descending frequency of the total mRNA-1273 group.

Prior, concomitant and post medications and non-study vaccination will be presented in a listing.

Concomitant Procedures will be presented in a listing.

6.2.5. Study Exposure

Study IP administration data will be presented in a listing.

Study duration will be summarized since randomization, since the first injection, and since the second injection.

6.2.6. Major Protocol Deviations

Major protocol deviations are a subset of protocol deviations that may significantly impact the completeness, accuracy, or reliability of the study data or that may significantly affect a subject's rights, safety, or well-being. Major protocol deviations rules will be developed and finalized before database lock.

The number and percentage of the subjects with each major protocol deviation type will be provided by age and vaccination group as defined in Section 6.1 based on the Full Analysis Set for Part 1 and will be provided by age and vaccination group based on the Randomization Set for Part 2.

Major protocol deviations will be presented in a listing.

6.2.7. COVID-19 Impact

A listing will be provided for COVID-19 impact.

6.3. Safety Analysis

Safety and reactogenicity will be assessed by clinical review of all relevant parameters including solicited ARs (local and systemic), unsolicited AEs, SAEs, MAAEs, AESIs, AEs leading to withdrawal from study vaccine and/or study participation, and physical

examination findings. Solicited ARs and unsolicited AEs will be coded by SOC and PT according to the MedDRA. Two modified versions of The Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventative Vaccine Clinical Trials (DHHS 2007) are used in this study for solicited ARs as presented in protocol section 7.4.3's Table 8 and 9; Table 8 is the pediatric toxicity scale used for children older than 36 months, and Table 9 is the infant/toddler toxicity scale used for children 6 to 36 months of age, inclusive

All safety analyses will be based on the Safety Set, except summaries of solicited ARs which will be based on the Solicited Safety Set. All safety analyses will be provided by age and vaccination group unless otherwise specified.

6.3.1. Adverse Events

A treatment-emergent AE (TEAE) is defined as any event occurring during the study not before exposure to study vaccine or any event already present that worsens after exposure to study vaccine. [Note: worsening of a pre-existing condition after vaccination will be reported as a new AE.]

Adverse events will also be evaluated by the investigator for the coexistence of MAAE which is defined as an AE that leads to an unscheduled visit to a healthcare practitioner.

Unsolicited AEs will be coded by PT and SOC using MedDRA and summarized by age and vaccination group, and stage (up to 28 days after any vaccination for Part 1 and Part 2 separately, follow-up analysis period and overall stage (throughout the study); see Section 6.1 for definitions of vaccination group and stage).

All summary tables (except for the overall summary of AEs) for unsolicited AEs will be presented by SOC and PT for TEAEs with counts of subjects included. SOC will be displayed in internationally agreed order. PT will be displayed in descending order of frequency of total mRNA-1273 group with all dose level combined in Part 1 and in Part 2 correspondingly and then alphabetically within SOC. When summarizing the number and percentage of subjects with an event, subjects with multiple occurrences of the same AE or a continuing AE will be counted once. Subjects will be presented according to the highest severity (the strongest relationship) in the summaries by severity (of related AEs), if subjects reported multiple events under the same SOC and/or PT.

Percentages will be based upon the number of subjects in the Safety Set within each age and vaccination group for Part 1 and Part 2 separately.

6.3.1.1. Incidence of Adverse Events

An overall summary of unsolicited TEAEs including the number and percentage of subjects who experience the following will be presented:

- Any unsolicited TEAEs
- Any serious TEAEs
- Any fatal TEAEs
- Any unsolicited medically-attended TEAEs
- Any unsolicited TEAEs leading to discontinuation from study vaccine
- Any unsolicited TEAEs leading to discontinuation from participation in the study
- Any unsolicited Grade 3/Severe TEAEs
- Any unsolicited Grade 3 or higher TEAEs
- Any unsolicitd Non-serious TEAEs
- Any unsolicited Non-serious and Grade 3/Severe TEAEs
- Any unsolicited Non-serious and Grade 3 or higher TEAEs
- Any AESI of MIS-C
- Any AESI of myocarditis and/or pericarditis
- Any AESI other than MIS-C and myocarditis and/or pericarditis

The table will also include number and percentage of subjects with unsolicited TEAEs that are treatment-related in each of the above categories.

In addition, separate listings containing individual subject adverse event data for unsolicited AEs, unsolicited TEAEs leading to discontinuation from study vaccine, unsolicited TEAEs leading to discontinuation from participation in the study, serious AEs, unsolicited medically-attended AEs, AESI other than MIS-C and myocarditis and/or pericarditis, AESI of MIS-C and AESI of myocarditis and/or pericarditis will be provided separately.

6.3.1.2. TEAEs by System Organ Class and Preferred Term

The following summary tables of TEAEs will be provided by SOC and PT using frequency counts and percentages (i.e., number and percentage of subjects with an event):

- All unsolicited TEAEs
- All unsolicited TEAEs that are treatment-related
- All serious TEAEs
- All serious TEAEs that are treatment-related
- All unsolicited TEAEs leading to discontinuation from study vaccine
- All unsolicited TEAEs leading to discontinuation from participation in the study
- All unsolicited Severe TEAEs
- All unsolicited Severe TEAEs that are treatment-related
- All unsolicited medically-attended TEAEs
- All unsolicited medically-attended TEAEs that are treatment-related
- All AESI of MIS-C
- All AESI of myocarditis and/or pericarditis
- All AESI other than MIS-C and myocarditis and/or pericarditis

6.3.1.3.TEAEs by System Organ Class, Preferred Term and Severity

The following summary tables of TEAEs will be provided by SOC, PT, and maximum severity (mild < moderate < severe) using frequency counts and percentages:

- All unsolicited TEAEs
- All unsolicited TEAEs that are treatment-related
- Summary tables of TEAEs by SOC, PT, and severity (Any vs. Grade >=3) will be provided as well.

6.3.2. Solicited Adverse Reactions

An AR is any AE for which there is a reasonable possibility that the test product caused the AE. The term “Solicited Adverse Reactions” refers to selected signs and symptoms occurring after injection administration during a specified post-injection follow-up period

(day of injection and 6 subsequent days). The solicited ARs are recorded by the subject in eDiary. The occurrence and intensity of selected signs and symptoms is actively solicited from the participant during a specified post-injection follow-up period (day of injection and 6 subsequent days), using a pre-defined checklist (i.e., solicited ARs).

The following local ARs will be solicited by the eDiary: pain at injection site, erythema (redness) at injection site, swelling (hardness) at injection site, localized axillary swelling or tenderness ipsilateral to the injection arm, and groin or underarm swelling or tenderness ipsilateral to the side of injection.

The following systemic ARs will be solicited by the eDiary: headache, fatigue, myalgia (muscle aches all over the body), arthralgia (aching in several joints), nausea/vomiting, fever, chills, irritability/crying, sleepiness, and loss of appetite.

The AR categories are different for younger population between Age 37 months to <12 years and Age 6 months to ≤ 36 months. Details presented in Table 8 and 9 in the protocol.

The solicited ARs will be graded based on the grading scales presented in Table 8 and 9 in the protocol, modified from the Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventative Vaccine Clinical Trials (DHHS 2007). Investigator will assess Grade 4 events (with exception of fever).

If a solicited local or systemic AR continues beyond 7 days post injection, the participant's parent(s)/ LAR(s) will be prompted to capture details of the solicited local or systemic AR in the eDiary until it resolves or the next IP injection occurs, whichever occurs first.

All solicited ARs (local and systemic) will be considered causally related to injection.

After booster doses with mRNA-1273.214, local or systemic ARs will only be reported on the eCRF if they are medically attended, considered serious or lead to discontinuation from the study. No eDiaries will be used after booster doses with mRNA-1273.214.

Analyses of solicited ARs will be provided by age and treatment group for each injection (first or second) based on the associated subset of Solicited Safety Set, i.e. First (Second) Injection Solicited Safety Set; and for any injection based on the Solicited Safety Set, unless otherwise specified.

The number and percentage of subjects who reported each individual solicited local AR (has a toxicity grade of Grade 1 or greater) and solicited systemic AR (has a toxicity grade of Grade 1 or greater) during the 7-day follow-up period after each injection will be tabulated by age group, vaccination group, toxicity grade, and injection. The number and

percentage of subjects who reported each individual solicited AR will also be summarized by age group, vaccination group, toxicity grade, days of reporting and injection.

The number and percentage of subjects experiencing fever (a temperature greater than or equal to 38.0°C/100.4°F by the oral, axillary, or tympanic route) by toxicity grade will be provided.

A two-sided 95% exact confidence interval (CI) using the Clopper-Pearson method will be provided for the percentage of subjects who reported any solicited local AR, solicited systemic AR, or any solicited AR.

The onset of individual solicited AR is defined as the time point after each injection at which the respective solicited AR first occurred. The number and percentage of subjects with onset of individual solicited AR will be summarized by age group, vaccination group, study day relative to the corresponding injection (Day 1 through Day 7), and injection.

The duration will be calculated as the end date/day of the solicited AR event – start date/day of the solicited AR event + 1, regardless of whether it is intermittent or continued. If the solicited AR continues beyond 7 days, the days a solicited AR is reported after 7 days will be included (e.g., an event that lasted 5 days in the first 7 days post injection and 3 days beyond 7 days post injection, the duration will be reported as 8 (5+3) days.)

Solicited ARs collected on eDiary and those collected on reactogenicity aCRF will be provided in a listing, and the maximum grade from eDiary and aCRF will be presented. All solicited ARs that continue beyond 7 days post injection will be presented in separate data listings.

6.3.3. Pregnancy Tests

A point-of-care urine pregnancy test will be performed, if deemed appropriate by the investigator, at the Screening Visit and before each vaccine dose in female participants of childbearing potential. At any time during the study, a pregnancy test either via blood or point-of-care urine can be performed, at the discretion of the investigator. A by-subject listing will be provided for pregnancy tests.

6.3.4. Physical Examinations

A full physical examination, including body temperature (oral [for participants > 4 years of age] or tympanic [for participants ≤ 4 years of age]), length/height, weight and BMI will be presented in a listing.

6.4. Immunogenicity Analysis

The analyses of immunogenicity will be based on the PP Immunogenicity Subset for both parts and will be performed for each pediatric age group separately at the selected dose level in Part 1 and Part 2 based on the participants in the PP Immunogenicity Subset. The PP Immunogenicity Subset is the primary analysis population used in the immunogenicity analyses, unless otherwise specified. For each pediatric age group, participants from Part 1 and Part 2 in the PP Immunogenicity Subset who receive the same mRNA-1273 dose level selected for expansion may be combined for immunogenicity analyses. If the same dose level is selected for expansion for more than one age group, these age groups may be combined for immunogenicity analyses.

The GMT and geometric mean (GM) level will be calculated using the following formula:

$$10^{\left\{\frac{\sum_{i=1}^{n}\log_{10}(t_i)}{n}\right\}}$$

where $t_1, t_2, \ldots, t_n$ are n observed immunogenicity values.

The geometric mean fold-rise (GMFR) measures the changes in immunogenicity values within subjects. The GMFR will be calculated using the following formula:

$$10^{\left\{\frac{\sum_{i=1}^{n}\log_{10}\left(v_{ij}/v_{ik}\right)}{n}\right\}} = 10^{\left\{\frac{\sum_{i=1}^{n}\log_{10}(v_{ij})-\log_{10}(v_{ik})}{n}\right\}}$$

where, for n subjects, v_{ij} and v_{ik} are observed immunogenicity values for subject i at time points j and k, $j \neq k$,where j represent pre-injection baseline at Day 1.

6.4.1. Immunogenicity Assessments

Immunogenicity assessments for both Part 1 and Part 2:

- Serum nAb value against SARS-CoV-2 as measured by pseudovirus and/or live virus neutralization assays.
- Serum bAb specific to the SARS-CoV-2 S protein.

- For Part 1, testing for serologic markers for SARS-CoV-2 infection using a nonvaccine antigen-based blood test at Day 1 (prior to the first dose), Day 57, Day 209, and Day 394.

Immunogenicity assessment for SARS-CoV-2 infection and CMI in Part 2:

- For Part 2, participants in each age group will be assigned to one of 5 phlebotomy cohorts (Table 2). Blood sampling will be performed in 3 of these 5 cohorts for immunogenicity at 3 of the following time points: Day 1 (prior to randomization and the first dose), Day 57, and one of Day 29 (prior to the second dose), Day 209, and Day 394. Participants in the fourth cohort (remainder of the age group) will provide a blood sample at Day 1 only (prior to randomization and the first dose). A fifth cohort of participants at selected VTEU sites only, will provide blood samples for assessment of exploratory serology and CMI on Day 1 (prior to randomization and the first dose), Day 43, Day 209, and Day 394.

6.4.2. Primary Analysis of Antibody-Mediated Immunogenicity Endpoints

If an accepted serum Antibody (Ab) threshold of protection against COVID-19 is available based on data from other mRNA-1273 studies or external data, the number and percentage of participants with Ab greater than or equal to the threshold at Day 57 will be provided with a 2-sided 95% CI using the Clopper-Pearson method. If the lower bound of the 95% CI on the mRNA-1273 group is > 70%, the primary immunogenicity objective of this study will be considered to be met for that age group.

The number and percentage of participants with serum Ab greater than or equal to the threshold with 2-sided 95% CI will be provided by age and vaccination group as defined in Section 6.1 at each post baseline time point. The CI will be calculated using the Clopper-Pearson method.

If an accepted serum Ab threshold of protection against COVID-19 is not established, immune response as measured by GM value and seroresponse rate in each age group based on Day 57 Ab levels will be compared with that in young adults (≥18 to 25 years of age) using data from Study P301. An analysis of covariance model will be carried out with Ab at Day 57 as dependent variable and a group variable (a pediatric age group in Study P204 versus young adults [≥18 to 25 years of age] in Study P301) as the fixed variable for each pediatric age group. The GM values of the pediatric age group at Day 57 will be estimated by the geometric least square mean (GLSM) from the model. The GMR (ratio of GM values) will be estimated by the ratio of GLSM from the model. The corresponding 2-sided 95% CI

will be provided to assess the difference in immune response between the pediatric age group (Study P204) compared to the young adults (≥18 to 25 years of age) in Study P301 at Day 57. For each pediatric age group, the noninferiority of GM value will be considered demonstrated if the lower bound of the 95% CI of the GMR is > 0.667 based on the noninferiority margin of 1.5 and the GMR point estimate ≥ 0.8 (minimum threshold). In addition, GMR with 95% CI calculated using t-distribution will be provided to assess if the two methods are consistent in the analysis results.

The number and percentage of participants with seroresponse due to vaccination will be provided with 2-sided 95% CI using the Clopper-Pearson method at each post baseline time point with Day 57 being of the primary interest. The seroresponse rate difference with 95% CI using the Miettinen-Nurminen (score) confidence limits at Day 57 will be provided between children receiving mRNA-1273 in Study P204 and young adults of ≥18 to 25 years of age receiving mRNA-1273 from Study P301. For each pediatric age group, the noninferiority of seroresponse rate will be considered demonstrated if the lower bound of the 95% CI of the seroresponse rate difference is > -10% based on the noninferiority margin of 10% and the seroresponse rate difference point estimate ≥ -5% (minimum threshold).

Multiplicity adjustment between age groups:

A hierarchical sequential hypothesis testing (fixed-sequence method) will be used to adjust multiplicity to preserve the family-wise Type I error rate (alpha = 0.05), starting with the oldest age group, followed by the middle age group, and then followed by the youngest age group. The primary series immunogenicity coprimary endpoint hypotheses for the oldest age group (6 years to < 12 years of age) will be tested first at alpha level of 0.05 in Part 1 expansion or Part 2. If the testing in the oldest age group in Part 2 is statistically significant (meeting the noninferiority success criteria of the coprimary endpoints), the alpha level of 0.05 will be passed to the testing of the primary series coprimary endpoint hypotheses in the middle age group (2 years to < 6 years of age) in Part 2. If the testing in the middle age group is statistically significant at alpha level of 0.05, then the alpha 0.05 is preserved for testing the primary series coprimary endpoint hypotheses in the youngest age group (6 months to < 2 years of age) in Part 2.

6.4.3. Secondary Analysis of Antibody-Mediated Immunogenicity Endpoints

For each group, the following evaluations will be performed at each time point at which blood samples are collected for immunogenicity (unless otherwise specified).

- GM level of anti-SARS-CoV-2-specific bAb with corresponding 95% CI will be provided at each time point. The 95% CIs will be calculated based on the t-distribution of the log-transformed values then back transformed to the original scale for presentation. The following descriptive statistics will be also provided at each time point: the number of subjects (n), median, minimum and maximum.
- GM fold-rise (GMFR) of SARS-CoV-2-specific bAb levels with corresponding 95% CI will be provided at each post-baseline timepoint over pre-injection baseline at Day 1. The 95% CIs will be calculated based on the t-distribution of the log-transformed values then back transformed to the original scale for presentation. The following descriptive statistics will be also provided at each time point: the number of subjects (n), median, minimum and maximum.

  Proportion of subjects with fold-rise ≥ 2, and fold-rise ≥ 4 of serum SARS-CoV-2 specific bAb levels from Visit Day 1 (baseline) at each post injection time points will be tabulated with 2-sided 95% Clopper Pearson CIs
- GMT of SARS-CoV-2-specific nAb values with corresponding 95% CI will be provided at each time point using the same method mentioned above.
- GMFR of SARS-CoV-2-specific nAb values with corresponding 95% CI will be provided at each post-baseline timepoint over pre-injection baseline at Day 1 using the same method mentioned above.

  Proportion of subjects with fold-rise ≥ 2, and fold-rise ≥ 4 of serum nAb from Visit Day 1 (baseline) at each post-injection time points will be tabulated with 2-sided 95% Clopper-Pearson CIs.
- Proportion of subjects with seroresponse due to vaccination will be tabulated with 2-sided 95% Clopper-Pearson CIs at each post-baseline timepoint. The definition of seroresponse can be found in Section 3.1.
- Per the study protocol, if the visit for the second dose (Day 29) is disrupted and cannot be completed at Day 29 (+7 days) as a result of the COVID-19 pandemic (self-quarantine or disruption of clinical site activities following business continuity plans and/or local government mandates for “stay at home” or “shelter in place”), the window may be extended to Day 29 + 21 days. More rigid visit window will be used in the Per-Protocol Immunogenicity Subset, -7/+14 for Day 29 visit, as appropriate.

6.5. Efficacy Analysis

Efficacy analyses will be performed using the FAS, mITT, mITT1 and PP Set for Efficacy. The mITT1 Set will be the primary analysis set used for efficacy analysis of efficacy endpoints starting from 14 days after first dose, and PP Set for Efficacy will be the primary analysis set used in the efficacy analyses for efficacy endpoints starting 14 days after second dose, unless otherwise specified. Subjects will be included in the treatment group to which they were randomized.

Baseline SARS-CoV-2 status is described in Section 6.1. Baseline SARS-CoV-2 status, the serology test results at baseline, the RT-PCR test results at baseline will be summarized by age group and treatment group.

Participants with baseline positive or missing SARS-CoV-2 status will be excluded from the PP Set for Efficacy Analysis.

In this study, the serology test results and the RT-PCR test results will be summarized by visit.

6.5.1. Endpoint Definition/Derivation

6.5.1.1. Derivation of SARS-CoV-2 Infection

This is a secondary efficacy endpoint, which is a combination of COVID-19 and asymptomatic SARS-CoV-2 infection for participants with negative SARS-CoV-2 status at baseline: the incidence of SARS-CoV-2 infection counted starting 14 days after the second dose of IP will be summarized by treatment group. SARS-CoV-2 infection will be defined in participants with negative SARS-CoV-2 at baseline:

- 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 post-baseline.

Derivation of this secondary efficacy endpoint is summarized in Table 3 below.

Table 3. Derivation for SARS-CoV-2 Infection

	Post-baseline assessments		
Baseline SARS-CoV-2 Status	PCR test post baseline	bAb levels against SARS-CoV-2 Nucleocapsid	**Endpoint**: SARS-CoV-2 infection

Negative at Baseline	**Positive** (either at nasal swab test, or at symptom-prompt nasal swab test)		Case
Negative at Baseline		**Positive** (at Post baseline visit or later) as measured by *Roche Elecsys*	Case

The date of documented infection will be the earlier of:

- Date of positive post-baseline RT-PCR result, or
- Date of positive serology test result based on bAb specific to SARS-CoV-2 nucleocapsid

The time to the first SARS-CoV-2 infection will be calculated as:

Time to the 1st SARS-CoV-2 infection = Date of the 1st documented infection – Date of randomization + 1. (For Part 1, switch date of randomization to date of 1st injection)

Cases will be counted starting 14 days after the second injection, i.e. date of documented infection – Date of the 2nd injection ≥ 14.

SARS-CoV-2 infection cases will also be summarized based on tests performed at least 14 days after first dose.

6.5.1.2. Derivation of Asymptomatic SARS-CoV-2 Infection

This is a secondary efficacy endpoint: the incidence of asymptomatic SARS-CoV-2 infection measured by RT-PCR and/or serology tests obtained post-baseline visits counted starting 14 days after the second injection in participants with negative SARS-COV-2 status at baseline.

Asymptomatic SARS-CoV-2 infection is identified by absence of symptoms and infections as detected by RT-PCR or serology tests. Specifically:

- Absent of COVID-19 symptoms
- AND at least one 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)

The date of documented asymptomatic infection is the earlier date of positive serology test result based on bAb specific to SARS-CoV-2 nucleocapsid due to infection, or positive RT-PCR at scheduled visits, with absence of symptoms.

The time to the asymptomatic SARS-CoV-2 infection will be calculated as:

Time to the asymptomatic SARS-CoV-2 infection = Date of asymptomatic SARS-CoV-2 infection test – Date of randomization + 1. (For Part 1, switch date of randomization to date of first injection)

6.5.1.3 Derivation of CDC Case Definition of COVID-19

This is a secondary efficacy endpoint: the incidence of the first occurrence of cases (CDC Case Definition of COVID-19) starting 14 days after the first dose of IP, and cases starting 14 days after the second dose of IP. CDC Case Definition of COVID-19 is defined as symptomatic disease based on the criteria specified in the table listed below. Cases are defined as participants meeting clinical criteria based on both symptoms for COVID-19 and positive RT-PCR test results.

While Part 2 is still blinded for any age group, surveillance for COVID-19 symptoms will be conducted via biweekly telephone calls or eDiary. Subjects reporting CDC Case Definition of COVID-19 symptoms, as defined in Section 7.3.2 of the protocol, will be arranged an illness visit to collect a nasal swab for SARS-CoV-2.

For this efficacy endpoint, a CDC Case Definition of COVID-19 case will be identified as a positive post-baseline RT-PCR test result that is prompted by symptom(s), together with eligible symptoms, i.e. a positive PCR result of the eligible symptoms summarized below in Table 4.

Table 4. Derivation for CDC Case Definition of COVID-19

	COVID-19
Post-baseline PCR results	Positive, **AND**
Systemic Symptoms	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
Respiratory symptoms	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).

The date of documented CDC Case Definition of COVID-19 (case) will be the later date of ([1 systemic symptom reported, or respiratory symptom reported] and, [date of positive PCR test]). Specifically, the date of documented CDC Case Definition of COVID-19 will be the later date of the following two dates (date of positive PCR test, and the date of eligible symptom(s)), and the two dates should be within 14 days of each other.

- Date of positive PCR test,
- Date of eligible symptom(s), defined as earliest of
    - Respiratory symptom: earliest date of an eligible respiratory symptom is reported
    - Systemic symptoms: earliest date of the eligible systemic symptom is reported

The time to the first occurrence of CDC Case Definition of COVID-19 will be calculated as:

Time to the 1st occurrence of CDC Case Definition of COVID-19 = Date of documented CDC Case Definition of COVID-19 – Date of randomization + 1. (For Part 1, switch date of randomization to date of first injection).

Cases will be counted start 14 days after the 2nd injection, i.e. date of documented CDC Case Definition of COVID-19 - Date of the 2nd injection ≥ 14.

6.5.1.4 Derivation of COVID-19 (P301 Primary Definition)

This is a secondary efficacy endpoint: the incidence of the first occurrence of COVID-19 cases meeting the P301 primary definition, starting 14 days after the first dose of IP, and COVID-19 cases starting 14 days after the second dose of IP.

The P301 primary definition of COVID-19 is defined by the following criteria:

- At least TWO of the following systemic symptoms: Fever (≥ 38ºC/≥ 100.4ºF), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s), OR
- The participant must have experienced at least ONE of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, OR clinical or radiographical evidence of pneumonia; AND
- At least one positive RT-PCR test for SARS CoV-2

Date of the documented definition of COVID-19 (P301 Primary Definition) will be later date of:

- Date of the positive RT-PCR test (prompt by symptom)
- Date of eligible symptom(s), defined as earliest of
    - Respiratory symptom: earliest date of an eligible respiratory symptom is reported
    - Systemic symptoms: earliest date of the eligible systemic symptoms are reported.

and the two dates should be within 14 days of each other.

COVID-19 (P301 Primary Definition) cases will also be summarized based on tests performed after randomization (For Part 1, switch date of randomization to date of first injection).

6.5.2. Analysis Method

The number and percentage of subjects who had an event (i.e. the first asymptomatic SARS-CoV-2 infection) will be summarized in the PP set for Efficacy.

The incidence rate will be provided by age and vaccination group, calculated as the number of cases divided by the total person-time. The 95% CI of the incidence rate will be calculated using the exact method (Poisson distribution) and adjusted by person-time.

Person-time is defined in Part 2 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 is earlier. For Part 1, switch randomization date to date of first injection.

6.5.3 Sensitivity and Subgroup Analysis

Sensitivity analysis for these efficacy endpoints will be performed with the same methods described above based on the FAS, mITT Set and mITT1 Set, with cases counted starting from date of first injection in Part 1 and starting from randomization in Part 2. A sensitivity analysis will be performed to include subjects with positive SARS-CoV-2 status at baseline.

In addition to the secondary efficacy endpoint COVID-19 (both CDC definition and P301 case definition) based on eligible symptoms and confirmed positive RT-PCR results (central lab or local diagnostic test) originally defined in section 6.5.1.3 and 6.5.1.4, a second set of COVID-19 (CDC definition and P301 case definition), considering both RT-PCR results and other non-RT-PCR test results including home antigen tests will also be derived, which may be considered as a sensitivity analysis of COVID-19 cases. For 6 to <12 years of age, the non-RT-PCR tests will be identified for associated sample collection dates on or after 01 Dec 2021 when home antigen tests started to become widely available, to be included in a sensitivity analysis of COVID-19 cases in the CSR. For 6 months to <2 years and 2 to <6 years of age groups, the non-RT-PCR tests will be identified in the entire study period for the sensitivity analysis for the EUA and CSR.

Subgroup analysis in Part 1 is not needed and it may be done for Part 2 (or Part 1 +Part 2).

6.6. Long-term Analysis (including Part 2 Open-Label Phase)

Long-term Analysis will be described in a separate SAP.

6.7. Booster Dose Analysis

Booster Phase Analysis will be described in a separate SAP.

6.8. Exploratory Analysis

6.8.1. Exploratory Analysis of Immunogenicity

The below exploratory analyses of immunogenicity may be performed:

- The genetic and/or phenotypic relationships of isolated SARS-CoV-2 strains to the vaccine sequence.
- Descriptive summaries of the ratio or profile of specific S protein bAb relative to nAb in serum during the study. The analysis may not be included in the Clinical Study Report (CSR).
- Descriptive summaries of clinical profile and immunologic endpoints to characterize participants with SARS-CoV-2 infection during the study.
- Assess the SARS-CoV-2 S protein-specific T-cell responses in a subset of participants.
- Descriptive summaries of GM and GMFR of bAb levels against SARS-CoV-2 nucleocapsid protein (quantitative IgG) and % of participants with 2x, 3x and 4x rise of bAb relative to baseline)
- The seroresponse rate comparisons between children in P204 and young adults (≥18 to 25 years of age) in P301 may be performed using the bAb and nAb measures based on assay-specific seroresponse definitions for select bAb or nAb.

6.8.2. SARS-CoV-2 Exposure and Symptoms

SARS-CoV-2 reported exposure history and symptoms assessment will be assessed during the study.

The number and percentage of subjects who had close contact with a person with SARS-CoV-2 infection or COVID-19, reasons for exposure, subjects with any symptoms of potential COVID-19, and subjects with each symptoms will be presented by visit, age and vaccination group as defined in Section 6.1. Descriptive statistics will be provided for length of exposure in days by vaccination group.

In addition, the following listings will be provided for subjects infected by SARS-CoV-2:

- Serum bAb level against SARS-CoV-2
- Serum nAb value against SARS-CoV-2
- Solicited ARs
- Unsolicited AEs

6.9. Interim Analyses

Part 1: Interim analyses may be performed after all or a subset of participants (with immunogenicity samples collected for D1 and D57) have completed Day 57 within an age group in Part 1 (one optional interim analysis for each age group, 3 interim analyses total for the 3 age groups in Part 1). Analyses of safety and immunogenicity may be conducted at each interim analysis. Additional interim analysis of immunogenicity and safety may be performed after all or subset of participants who receive booster dose have completed BD-Day 29 after the booster dose in an age group.

Part 2: An interim analysis of immunogenicity and safety will be performed after all or a subset of participants have completed Day 57 (1 month after the second dose) in Part 1 or Part 2 within an age group. This interim analysis will be considered the primary analysis of immunogenicity for a given age group. Another interim analysis on safety may be performed after a different subset or all participants have completed Day 57 in an age group. Additional interim analysis of immunogenicity and safety may be performed after all or subset of participants who receive booster dose have completed BD-Day 29 after the booster dose in an age group.

Part 3: An interim analysis of immunogenicity and safety will be performed after all or a subset of participants have completed Day 57 (1 month after the second dose) in Part 3 within an age group. This interim analysis will be considered the primary analysis of immunogenicity for the primary series in a given age group. A second interim analysis of immunogenicity and safety will be performed after all or a subset of participants have completed Day 177/BD-Day 29 (1 month after third dose).

An interim analysis of safety for mRNA-1273.214 booster may be performed after all or a subset of mRNA-1273.214 recipients have completed 6 months of follow-up after the booster dose.

The final analysis of all endpoints will be performed after all participants have completed all planned study procedures and after the database is cleaned and locked. Results of this analysis will be presented in an end of study CSR, including individual listings.

6.10. Data Safety Monitoring Board

Safety oversight will be under the direction of a DSMB composed of external independent consultants with relevant expertise. Members of the DSMB will be independent from study conduct and free of conflict of interest. The DSMB will meet at pre-specified timepoints during the study to assess safety throughout study conduct. For the 6 years to < 12 years age group, the DSMB will review cumulative safety data for approximately 300 participants enrolled at the selected dose level in Part 1 before enrollment begins in Part 2. For both the middle age group (2 years to < 6 years) and the youngest age group (6 months to < 2 years) the DSMB will review cumulative safety data in both younger age groups (2 years to < 6 years; 6 months to < 2 years) combined and at all dose levels administered in Part 1 before start of Part 2 (blinded phase) for each age group. The DSMB will operate under the rules of an approved charter that will be written and reviewed at the organizational meeting of the DSMB. Details regarding the DSMB composition, responsibilities, procedures, and frequency of data review will be defined in its charter.

If any of the study pause rules, described in protocol section 6.4, are met, the Sponsor will immediately suspend further enrollment and/or study dosing and the DSMB will convene on an ad hoc basis. The DSMB will review all available unblinded study data (as applicable) to help adjudicate any potential study pauses and make recommendations on further study conduct, including requesting additional information, recommending stopping the study, recommending changes to study conduct and/or the protocol, or recommending additional operational considerations due to safety issues that arise during the study.

The Cardiac Event Adjudication Committee (CEAC) consisting of pediatric and adult cardiologists will review suspected cases of myocarditis, pericarditis, or myopericarditis to determine if they meet CDC criteria of “probable” or “confirmed” event, and to assess severity and enable the DSMB to make recommendations to the Sponsor to continue vaccine dosing. The CEAC will operate under the rules of an approved charter that will be written and reviewed at the organizational meeting of the CEAC. Details regarding the CEAC composition, responsibilities, procedures, and frequency of data review will be defined in its charter.

7. References

Department of Health and Human Services (DHHS), Food and Drug Administration, Center for Biologics Evaluation and Research (US). Guidance for industry: Toxicity grading scale for healthy adult and adolescent volunteers enrolled in preventative vaccine clinical trials. September2007[cited2019 Apr 10][10 screens].

Available from:

https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/ucm091977.pdf.

8. List of Appendices

8.1. Appendix A Standards for Variable Display in TFLs

Continuous Variables: The precision for continuous variables will be based on the precision of the data itself. The mean and median will be presented to one decimal place more than the original results; the SD will be presented to two decimal places more than the original results; the minimum and maximum will be presented to the same precision as the original results.

Categorical Variables: Percentages will be presented to 1 decimal place.

8.2. Appendix B Analysis Visit Windows for Analysis

Safety and Immunogenicity Analysis will be summarized using the following analysis visit window for post injection assessments:

Step 1: If the safety and immunogenicity assessments are collected at scheduled visit, i.e. nominal scheduled visit, the data collected at scheduled visit will be used.

Step 2: If the safety and immunogenicity assessments are not collected at the scheduled visit, assessments collected at unscheduled visit will be used using the analysis visit windows described in Table 5 below.

If a subject has multiple assessments within the same analysis visit, the following rule will be used:

- If multiple assessments occur within a given analysis visit, the assessment closest to the target study day will be used.
- If there are 2 or more assessments equal distance to the target study day, the last assessment will be used.

Table 5 . Visit Window

Visit	Target Study Day	Visit Window in Study Day
Nasal Swabs for SARS-CoV-2		
Day 1	1 (Date of First Injection)	1, Pre-first-dose
Day 29 (Month 1)	29 (Date of Second Injection)	[2, 43]

Day 57 (Month 2)	57	[44,133]
Day 209 (Month 7)	209	[134, 301]
Day 394 (Month 13)	394	≥302
Immunogenicity		
Part 1		
Day 1	1 (Date of First Injection)	1, Pre-first-dose
Day 57 (Month 2)	57	[44,133]
Day 209 (Month 7)	209	[134, 301]
Day 394 (Month 13)	394	≥302
Part 2 where Day 29 is selected		
Day 1	1 (Date of First Injection)	1, Pre-first-dose and prior to the randomization
Day 29	29	[2,43], Pre-second-dose
Day 57	57	[44,133]
Part 2 where Day 209 is selected		
Day 1	1 (Date of First Injection)	1, Pre-first-dose and prior to the randomization
Day 57	57	[44,133]
Day 209	209	[134,301]
Part 2 where Day 394 is selected		
Day 1	1 (Date of First Injection)	1, Pre-first-dose and prior to the randomization
Day 57	57	[44,133]
Day 394	394	≥302

8.3. Appendix C Imputation Rules for Missing Prior/Concomitant Medications and Non-Study Vaccinations

Imputation rules for missing or partial medication start/stop dates are defined below:

1. Missing or partial medication start date:
   - If only Day is missing, use the first day of the month, unless:
     - The medication end date is after the date of first injection or is missing AND the start month and year of the medication coincide with the start month and year of the first injection. In this case, use the date of first injection
   - If Day and Month are both missing, use the first day of the year, unless:
     - The medication end date is after the date of first injection or is missing AND the start year of the medication coincide with the start year of the first injection. In this case, use the date of first injection
   - If Day, Month and Year are all missing, the date will not be imputed, but the medication will be treated as though it began prior to the first injection for purposes of determining if status as prior or concomitant.
2. Missing or partial medication stop date:
   - If only Day is missing, use the earliest date of (last day of the month, study completion, discontinuation from the study, or death).
   - If Day and Month are both missing, use the earliest date of (last day of the year, study completion, discontinuation from the study, or death).
   - If Day, Month and Year are all missing, the date will not be imputed, but the medication will be flagged as a continuing medication.

In summary, the prior, concomitant or post categorization of a medication is described in Table 6 below.

Table 6 . Prior, Concomitant, and Post Categorization of Medications and Non-study Vaccinations

	Medication Stop Date		
Medication Start Date	**< First Injection Date of IP**	**≥ First Injection Date and ≤ 28 Days After Last Injection**	**> 28 Days After Last Injection [2]**
< First injection date of IP [1]	P	P, C	P, C, A
≥ First injection date and ≤ 28 days after last injection	-	C	C, A
> 28 days after last injection [3]	-	-	A

A: Post; C: Concomitant; P: Prior
[1] includes medications with completely missing start date
[2] includes medications with completely missing end date
[3] on the day of last injection and the 27 subsequent days

8.4. Appendix A Imputation Rules for Missing AE dates

Imputation rules for missing or partial AE start dates and stop dates are defined below:

1. Missing or partial AE start date:

   - If only Day is missing, use the first day of the month, unless:
     - The AE end date is after the date of first injection or is missing AND the start month and year of the AE coincide with the start month and year of the first injection. In this case, use the date and time of first injection, even if time is collected.
   - If Day and Month are both missing, use the first day of the year, unless:
     - The AE end date is after the date of first injection or is missing AND the start year of the AE coincides with the start year of the first injection. In this case, use the date of first injection

- If Day, Month and Year are all missing, the date will not be imputed. However, if the AE end date is prior to the date of first injection, then the AE will be considered a pre-treatment AE. Otherwise, the AE will be considered treatment-emergent.

2. Missing or partial AE end dates will not be imputed.

8.5. Appendix E: Schedule of Assessments (Parts 1 and 2, Study Arms 1 Through 13)

For participants who received a booster dose with mRNA-1273 under Protocol Amendment 7, please see separate SAP for part 2 open-label phase and booster doses's section 8.6 Appendix F (Part 2 Open-Label Phase and Booster Phase and Part 3 SAP) for the mRNA-1273 booster dose SoA.

For participants who choose to receive a booster dose with mRNA-1273.214 under Protocol Amendment 9, please see separate SAP for part 2 open-label phase and booster doses's section 8.10 Appendix J (Part 2 Open-Label Phase and Booster Phase and Part 3 SAP) for the mRNA-1273.214 booster dose SoA.

Visit Number	0	1	2	3	3A	4	4S	5			6			7
Type of Visit	C	C	TMV	C	C	TMV	C	C	SFU		C	SFU		C
Month Time Point		M0		M1				M2	eDiary	SC	M7	eDiary	SC	M13
Study Visit Day	D-28 to D-1 (Screening)[1]	D1 (Baseline)	D8	D29[2]	D30	D36[2]	D43[2,3]	D57[2, 4]	Every 4 weeks D71 – D183[2, 5]	Every 4 weeks D85– D197[2, 6]	D209[2, 4]	Every 4 weeks D223– D363[2, 5]	Every 4 weeks D237– D377[2, 6]	D394[2, 4]
Window Allowance (Days)	-	-	+ 3	+ 7	+3	+ 3	± 2	+ 7	± 3	± 3	± 14	± 3	± 3	± 14
Days Since Most Recent Injection	-	0	7	28	1	7	14	28	-	-	180	-	-	365
Informed consent/assent form, demographics, concomitant medications, medical history	X													
Review of inclusion and exclusion criteria	X	X												

Visit Number	0	1	2	3	3A	4	4S	5			6			7
Type of Visit	C	C	TMV	C	C	TMV	C	C	SFU		C	SFU		C
Month Time Point		M0		M1				M2	eDiary	SC	M7	eDiary	SC	M13
Study Visit Day	D-28 to D-1 (Screening)[1]	D1 (Baseline)	D8	D29[2]	D30	D36[2]	D43[2,3]	D57[2, 4]	Every 4 weeks D71 – D183[2, 5]	Every 4 weeks D85– D197[2, 6]	D209[2, 4]	Every 4 weeks D223– D363[2, 5]	Every 4 weeks D237– D377[2, 6]	D394[2, 4]
Window Allowance (Days)	-	-	+ 3	+ 7	+3	+ 3	± 2	+ 7	± 3	± 3	± 14	± 3	± 3	± 14
Days Since Most Recent Injection	-	0	7	28	1	7	14	28	-	-	180	-	-	365
Physical examination including body temperature, length/height, weight, and BMI[7]	X	X		X			X	X			X			X
Pregnancy test[8]	X	X		X										
Randomization		X												
Study injection (including 30-minute postdose observation period)		X		X										
Blood sample for vaccine immunogenicity (Part 1)[9]		X						X[19]			X[19]			X[19]
Blood sample for vaccine immunogenicity (Part 2)[10]		X		X				X			X			X
Blood sample for exploratory serology and cell-mediated immunity (Part 2)[3,10]		X					X				X			X
Blood sample for potential biomarker analysis (Part 2)[10,11]					X[11]									
Nasal swab sample for SARS-CoV-2[12]		X		X			X	X			X			X
Unscheduled visit[13]			X	X		X	X	X	X	X	X	X	X	X
eDiary activation for recording solicited ARs (7 days)[15]		X		X										
Review of eDiary data			X			X								
Follow-up safety telephone calls[16]										X			X	

Visit Number	0	1	2	3	3A	4	4S	5			6			7
Type of Visit	C	C	TMV	C	C	TMV	C	C	SFU		C	SFU		C
Month Time Point		M0		M1				M2	eDiary	SC	M7	eDiary	SC	M13
Study Visit Day	D-28 to D-1 (Screening)[1]	D1 (Baseline)	D8	D29[2]	D30	D36[2]	D43[2,3]	D57[2, 4]	Every 4 weeks D71 – D183[2, 5]	Every 4 weeks D85– D197[2, 6]	D209[2, 4]	Every 4 weeks D223– D363[2, 5]	Every 4 weeks D237– D377[2, 6]	D394[2, 4]
Window Allowance (Days)	-	-	+ 3	+ 7	+3	+ 3	± 2	+ 7	± 3	± 3	± 14	± 3	± 3	± 14
Days Since Most Recent Injection	-	0	7	28	1	7	14	28	-	-	180	-	-	365
Recording of unsolicited AEs		X	X	X	X	X	X	X						
Recording of MAAEs and concomitant medications relevant to or for the treatment of the MAAE[17]		X	X	X	X	X	X	X	X		X	X		X
Recording of SAEs and concomitant medications relevant to or for the treatment of the SAE[17,18]		X	X	X	X	X	X	X	X		X	X		X
Recording of AESIs (eg, MIS-C, myocarditis/pericarditis)[18]		X	X	X	X	X	X	X	X		X	X		X
Recording of concomitant medications and nonstudy vaccinations[17]		X	X	X	X	X	X	X						
Study completion														X

Abbreviations: AE = adverse event; AESI = adverse event of special interest; AR = adverse reaction; BMI = body mass index; C = clinic visit; COVID-19 = coronavirus disease 2019; D = day; eCRF = electronic case report form; EDC = electronic data capture; eDiary = electronic diary; FDA = Food and Drug Administration; IP = investigational product; IRB = institutional review board; LAR = legally acceptable representative; M = month; MAAE = medically attended adverse event; MIS-C = multisystem inflammatory syndrome in children; RT-PCR = reverse transcriptase polymerase chain reaction; SAE = serious adverse event; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SC = safety (telephone) call; SFU = safety follow-up; TMV = telemedicine visit; VTEU = Vaccine and Treatment Evaluation Units.

Note: In accordance with FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency (FDA March 2020), investigators may convert study site visits to home visits or telemedicine visits (with the exception of Screening, Day 1, and Day 29) with the approval of the Sponsor.

1. Screening Visit and Day 1 may be combined on the same day. Additionally, the Screening Visit may be performed over multiple visits if performed within the 28-day screening window.

2. If the visit for the second dose (Day 29) is disrupted and cannot be completed at Day 29 (+7 days) as a result of the COVID-19 pandemic (self-quarantine or disruption of study site activities following business continuity plans and/or local government mandates for "stay at home" or "shelter in place"), the visit window may be extended to Day 29 + 21 days. When the extended visit window is used, the remaining study visits should be rescheduled to follow the intervisit interval from the actual date of the second dose. Refer to protocol section 6.1.1 for individual participant criteria for delay of study vaccination.
3. To be conducted during Part 2 of the study in a cohort of participants at selected VTEU sites only.
4. All scheduled study visits should be completed within the respective visit windows. If the participant is not able to attend a study site visit as a result of the COVID-19 pandemic (self-quarantine or disruption of study site activities following business continuity plans and/or local government mandates for "stay at home" or "shelter in place"), a telemedicine visit should be conducted in place of the study site visit. The telemedicine visit should encompass all scheduled visit assessments that can be completed remotely, such as assessment for AEs and concomitant medications (eg, as defined in scheduled safety telephone calls). Home visits will be permitted for all nondosing visits, with the exception of Screening, if a participant cannot visit the study site as a result of the COVID-19 pandemic. Home visits must be permitted by the study site IRB and the participant's parent(s)/LAR(s) via informed consent and have prior approval from the Sponsor (or its designee).
5. Safety follow-up via an eDiary questionnaire will be performed every 4 weeks from Day 71 to Day 183 and again from Day 223 to Day 363.
6. Safety follow-up via a safety telephone call will be performed every 4 weeks from Day 85 to Day 197 and again from Day 237 to Day 377.
7. A full physical examination, including body temperature (oral [for participants > 4 years of age] or tympanic [for participants ≤ 4 years of age]), length/height, and weight, will be performed at the Screening Visit or on Day 1. Symptom-directed physical examination will be performed on Day 1, Day 29, Day 43 (if the visit is applicable), Day 57, Day 209, and Day 394 and may be performed at other time points at the discretion of the investigator. Body mass index will be calculated only at Screening Visit. Body temperature (oral/tympanic) should be measured on each injection day prior to injection. On each injection day before injection and again 7 days after injection, the injection site should be examined. Any clinically significant finding identified during a study visit should be reported as an MAAE. Participants who are febrile (body temperature ≥ 38.0°C/≥ 100.4°F) before injection on Day 1 or Day 29 must have the visit rescheduled within the relevant visit window to receive the injection. Afebrile participants with minor illnesses may be injected at the discretion of the investigator.
8. Pregnancy test at Screening and Day 1 and before the second study injection will be a point-of-care urine test and will be performed if deemed appropriate by the investigator. At the discretion of the investigator, a pregnancy test either via blood or point-of-care urine test can be performed at any time during the study.
9. On Day 1, sample must be collected prior to randomization and dosing. If a Day 1 (baseline) blood sample cannot be obtained in Part 1, the participant will be considered either a screen failure due to inability to satisfy inclusion criterion 3 or could be scheduled for rescreening. Participants may be rescreened 1 time, either within the same screening period for Part 1 or for a new screening period for Part 2 later in the study. If the participant is rescreened and a blood sample still cannot be obtained, then he/she will be considered a screen failure due to inability to satisfy inclusion criterion 3.
10. On Day 1, sample must be collected prior to randomization and dosing. On Day 29, sample must be collected prior to dosing. In Part 2, participants in each age group will be assigned to 1 of 5 phlebotomy cohorts (Protocol Table 14). Participants in 3 of these 5 cohorts will provide blood specimens for immunogenicity at the following time points: Day 1, Day 57, and one of Day 29, Day 209, or Day 394 (such that each participant provides a total of 3 blood samples only). Participants in the Cohort D (remainder of the age group) will provide a blood sample at Day 1 (prior to randomization and the first dose) and within 4 days of receiving Dose 2 at Day 30 (+3 days) for storage and potential future biomarker testing. A fifth cohort of participants (selected VTEU sites only) will provide blood samples for assessment of exploratory serology and CMI (S protein-specific T-cell responses) on Day 1, Day 43, Day 209, and D394. Table 2 provides the blood sampling schedule in Part 2 of the study. If a Day 1 (baseline) blood sample cannot be obtained in either Part 1 or Part 2, the participant will be considered either a screen failure due to inability to satisfy inclusion criterion 3 or could be rescheduled for rescreening. Participants may be rescreened 1 time, either within the same screening period for Part 1 or Part 2 or in a new screening period of Part 2 if the initial screening was in Part 1. If the participant is rescreened and a blood sample still cannot be obtained, then he/she will be considered a screen failure due to inability to satisfy inclusion criterion 3.
11. Part 2, Cohort D participants only, one ~4 mL blood draw. For participants already enrolled in Cohort D prior to protocol amendment 4, this blood draw will be optional and confirmed at time of re-consenting; for all participants newly enrolled into Cohort D under amendment 4, it is mandatory.

12. The nasal swab sample (collected before dosing on injection day) will be used to ascertain the presence of SARS-CoV-2 via RT-PCR.
13. An unscheduled visit may be prompted by reactogenicity issues or new or ongoing AEs.
14. At each injection visit, participants' parent(s)/LAR(s) will record data into the eDiary starting approximately 30 minutes after injection under the supervision of the study site staff to ensure successful entry of assessment. Participants' parent(s)/LAR(s) will continue to record entries in the eDiary after they leave the study site, preferably in the evening and at the same time each day, on the day of injection and for 6 days following injection. If a solicited local or systemic AR continues beyond Day 7 after vaccination, the participant's parent(s)/LAR(s) will be prompted to capture details of the solicited local or systemic AR in the eDiary until the AR is resolved or the next IP injection occurs, whichever occurs first. Capturing details of ARs in the eDiary should not exceed 28 days after each vaccination. Adverse reactions recorded in eDiaries beyond Day 7 should be reviewed by the study site staff either during the next scheduled telephone call or at the next study site visit.
15. Trained study site personnel will call all participants to collect information relating to any MAAEs, SAEs, AEs leading to study withdrawal and information on concomitant medications associated with those events and any nonstudy vaccinations. In addition, study personnel will collect information on known participant exposure to someone with known COVID-19 or SARS-CoV-2 infection and on any COVID-19 symptoms the participant may experience.
16. All concomitant medications and nonstudy vaccinations will be recorded through 28 days after each injection; all concomitant medications relevant to or for the treatment of an SAE or MAAE will be recorded from Day 1 through the final visit (Day 394).
17. In addition to MIS-C and myocarditis and/or pericarditis, a list of AESIs pertinent to this study may be referenced in the list of AESIs that is maintained by the Sponsor and provided to each investigator. All SAEs and AESIs will be reported to the Sponsor or designee immediately and in all circumstances within 24 hours of becoming aware of the event via the EDC system. If a site receives a report of a new SAE or AESI from a study participant or receives updated data on a previously reported SAE or AESI and the eCRF has been taken offline, then the site can report this information on a paper SAE or AESI form using the SAE Mailbox, the SAE Hotline, or the SAE Fax line (Protocol Section 7.4.11).
18. For Part 1, only the first approximately 75 participants in Arm 1 and Arm 2 will have postbaseline scheduled blood draws;the 300 participants in each of the expansion part of Arm 1 and Arm 2 may have an optional blood draw on Day 57. All participants in Arm 3, 4, 5, 6 and 7 will have postbaseline blood draws on Day 57, Day 209 and Day 394.

ModernaTX, Inc.

Protocol mRNA-1273-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 Less Than 12 Years of Age

Statistical Analysis Plan
(Part 2 Open-Label Phase and Booster Dose and Part 3 Open-Label Phase)

SAP Version 5.0
Version Date of SAP: 28 July 2023

Prepared by:

PPD, part of Thermo Fisher Scientific
929 North Front Street
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TABLE OF CONTENTS

Summary of Major Changes in SAP Version

SAP Version	Date	Section # and Name	Description of Change
V1.0, V2.0, V3.0			Refer to the SAP document (Part 1 Open-Label Phase and Part 2 Blinded Phase)
V4.0	06June2022		Create based on protocol amendment 8
V5.0 Based on Protocol Amendment 9	28July2023	2.2.1 Primary Safety Objective 3.2.1 Primary Safety Endpoints	Updated to evaluate the safety of mRNA-1273.214.
		5. Analysis Populations 6. Statistical Analysis 6.4 Immunogenicity Analysis	To provide more information on the decripition of the statistical methods for participants in Part 3
		5.3 Per-protocol (PP) Immunogenicity Subset	Updated the criteira to exclude if subject received off-study COVID-19 vaccination prior to BD-Day 29 visit
		6.3.2 Solicited Adverse Reactions	Added text to indicate that no eDiaries will be used after booster doses with mRNA-1273.214.
		6.5.1.3 Derivation of CDC Case Definition of COVID-19	Stated that COVID-19 surveillance (illness visits and convalescent visits) would only be performed while there is still a blinded Part 2 for any age group, after unblinding of trial, this would be discontinued.
		8.6 Appendix F 8.7 Appendix G	Title updates and Surveillance removed from all SoA tables.
		8.8 Appendix H 8.9 Appendix I 8.10 Appendix J	Newly added
		5.3 Per-protocol (PP) Immunogenicity Subset	Updated that Per-Protocol (PP) Immunogenicity Subset need to meet the criterion that subjects have BD-Day 29 Ab assessment for the analysis endpoint, regardless of the availability of pre-booster (BD-Day 1) antibody values.

		2.3 Primary Series and Third Dose 6.4 Immunogenicity Analysis	Updated based on P204 clarification memo, discrepancy exisit with current Protocol Amendment 9
		2.3 Part 3, (First Two Doses of Primary Series), Open-label Phase 3.2 Part 3 (First Two Doses of Primary Series), Open-label Phase 4.2 Sample Size and Power 6.4.2 Primary Analysis of Antibody-Mediated Immunogenicity Endpoints	The P301 comparator in SAP for Part 3 immunogenicity analysis is young adults ≥18 to 25 years of age instead of protocol P301 comparator ≥18 years of age, because the originally planned hypothesis testing in protocol for part 3 will not be performed due to the small number of participants enrolled in Part 3, which is insufficient to power the hypothesis testing.
		2.2.4 Exploratory Objectives 3.3.4 Exploratory Endpoints 6.5 Efficacy Analysis	As protocol amendment 9 was implemented in October 2022, no surveillance was conducted thereafter, and, therefore, no incidence rates will be calculated after October 2022.
		5.3 Per-protocol (PP) Immunogenicity Subset	Updated Part 3 per-protocol immunogenicity set to remove the criteria: negative SARS-CoV-2 baseline for first two doses of primary series or negative SARS-CoV-2 pre-dose 1 of mRNA for third dose.
		8.2 Appendix B	Included Part 3 analysis visit window in Table 4.

List of Abbreviations

Abbreviation	Definition
AB	antibody
AE	adverse event
AR	adverse reaction
AESI	AEs of special interest
BMI	body mass index
bAb	binding antibody
BD	booster dose
BLA	Biologics License Application
CI	confidence interval
CDC	US Centers for Disease Control and Prevention
CEAC	Cardiac Event Adjudication Committee
CMI	Cell-Mediated Immunity
CRO	contract research organization
CSP	clinical study protocol
CSR	clinical study report
DHHS	Department of Health and Human Services
DSMB	Data Safety Monitoring Board
eCRF	electronic case report form
eDiary	electronic diary
EUA	Emergency Use Authorization
ELISA	enzyme-linked immunosorbent assay
FAS	full analysis set
GLSM	geometric least squares mean
GM	geometric mean
GMFR	geometric mean fold rise
GMT	geometric mean titer
GMR	geometric mean ratio
HAART	highly active anti-retroviral therapy
IgG	immunoglobulin G
IP	investigational product
IRT	interactive response technology
IST	internal safety team
LAR	legally authorized representative
LLOQ	lower limit of quantification
MAAEs	medically-attended adverse events
MedDRA	Medical Dictionary for Regulatory Activities
MIS-C	multisystem inflammatory syndrome in children
mITT	modified Intent-to-Treat
mITT1	modified Intent-to-Treat-1
mRNA	messenger ribonucleic acid
nAb	neutralizing antibody
PP	per-protocol

Abbreviation	Definition
PT	preferred term
RT-PCR	reverse transcriptase polymersa chain reaction
SAE	serious adverse event
SAP	statistical analysis plan
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SAS	Statistical Analysis System
SD	standard deviation
SoA	schedule of assessments
SOC	system organ class
SRR	seroresponse rate
Study P301	Study mRNA-1273-P301; NCT04470427
TEAE	treatment-emergent adverse event
ULOQ	upper limit of quantification
WHO	World Health Organization
WHODD	World Health Organization drug dictionary

1. Introduction

This statistical analysis plan (SAP), which describes the planned analyses for Part 2 open-label phase, booster dose for all participants in Part 1 and Part 2, and Part 3 of Study mRNA-1273-P204, is based on the approved clinical study protocol (CSP), Version Amendment 9, dated 04-Aug-2022. The most recent approved electronic case report form (eCRF) Version 20.006 dated 31-Jan-2023. Unless specified otherwise, the language in this SAP pertains to analysis for open-label phase in Part 2, booster dose in Part 1 and Part 2, and Part 3. SAP for Part 1 open-label phase and Part 2 blinded phase is in a separate document.

In addition to the information presented in the statistical analysis plan section of the protocol (Section 8), which provides the principal features of analyses for this study, this SAP provides statistical analysis details/data derivations. It also documents modifications or additions to the analysis plan that are not “principal” in nature and result from information that was not available at the time of protocol finalization.

Study mRNA-1273-P204 is 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.

PPD Biostatistics and programming team, designee of Moderna Biostatistics and Programming department, will perform the statistical analysis of the safety, reactogenicity, and effectiveness data; Statistical Analysis System (SAS) Version 9.4 or higher will be used to generate all statistical outputs (tables, figures, listings, and datasets). The SAP will be finalized and approved prior to the primary analysis clinical database lock and treatment unblinding for the study. If the methods in this SAP differ from the methods described in the protocol, the SAP will prevail.

In this document, subject and participant are used interchangeably; injection of IP, injection, and dose are used interchangeably; vaccination group and treatment group are used interchangeably.

2. Study Objectives

2.1. Part 2, Open-Label Phase

The study objectives in Part 2 open-label phase are to evaluate descriptively safety, persistence of the immune response to mRNA-1273 vaccine, and incidence rates of COVID-19, SAR-CoV-2 infection and asymptomatic SARS-CoV-2 infection in the long-term follow-up as exploratory analysis. Please also refer to section 2 in Part 1 open-label phase and Part 2 blinded phase SAP.

2.2. Part 1 and Part 2, Booster Dose Phase

2.2.1. Primary Safety Objective

The primary safety objective is to evaluate the safety of mRNA-1273/ mRNA-1273.214 booster dose.

2.2.2. Primary Immunogenicity Objective

The primary immunogenicity objective is to infer effectiveness of the mRNA-1273 booster dose by establishing noninferiority of antibody (Ab) response after the booster dose compared to primary series from adult recipients of mRNA-1273 in the clinical endpoint efficacy trial (Study P301).

There is no immunogenicity objective associated with the mRNA-1273.214 booster.

2.2.3. Secondary Objective

The secondary objective is to evaluate the persistence of the immune response to mRNA-1273 vaccine.

2.2.4. Exploratory Objectives

The exploratory objective is to evaluate immune response elicited by the primary series or booster dose of mRNA-1273 against variant(s) of interest and incidence rates of COVID-19, SAR-CoV-2 infection and asymptomatic SARS-CoV-2 infection as booster exploratory analysis for booster dose of mRNA-1273. As protocol amendment 9 was implemented in October 2022, no surveillance was conducted thereafter, and, therefore, no incidence rates will be calculated after October 2022.

2.3. Part 3, First Two Doses of Primary Series and Third Dose

Part 3 (Arm 14) was originally planned to enroll ~300 children aged 6 to <12 years to receive mRNA-1273 25 µg (2 doses of primary series and a third dose). However, arm 14 was closed to enrollment at an enrollment number of N = 91. All participants enrolled in Arm 14 will continue to be followed as per protocol, including receipt of third doses if not received yet, as well as immunogenicity samples.

Given that the number of participants enrolled in Part 3 (n=91) is substantially smaller than the planned sample size of ~300 required for the immunogenicity hypothesis testing after dose 2 of mRNA-1273 25 µg primary series and after a third dose of mRNA-1273 25 µg, the hypothesis testing will not be performed. Instead, all the analyses of immunogenicity endpoints will be descriptive.

Thus, the study objective of Part 3 was updated to evaluate descriptively safety and immune responses to 2 doses of mRNA-1273 25 µg primary series and a third dose of mRNA-1273 25 µg in 6 to <12 years of age. For the descriptive analysis purpose, the comparator will be young adults ≥18 to 25 years of age from P301, instead of ≥18 years of age, to be consistent with the comparator group in immunogenicity analyses in part 1 and part 2 of the study.

3. Study Endpoints

3.1. Part 2, Open-label Phase

The study endpoints in Part 2 open-label phase are same as Part 2 blinded phase. Please refer to section 3 in Part 1 open-label phase and Part 2 blinded phase SAP.

3.2. Part 3 (First Two Doses of Primary Series), Open-label Phase

The study endpoints in Part 3 first two doses open-label phase are the same as Part 1 open-label phase. For Part 3 endpoints related to immunogenicity objective, a comparator from P301 study (≥ 18 to 25 years of age) is used for descriptive analysis purpose. Please refer to section 3 in Part 1 open-label phase and Part 2 blinded phase SAP. For Part 3, all endpoints will be analyzed descriptively.

3.3. Booster (Part 1 and Part 2)/Third Dose (Part 3)

3.3.1. Primary Safety Endpoints

For mRNA-1273 Booster/Third Dose:

- Solicited local and systemic ARs through 7 days after booster or third dose
- Unsolicited AEs through 28 days after booster or third dose
- MAAEs through the entire study period after booster or third dose
- SAEs through the entire study period after booster or third dose
- AESIs through the entire study period after booster or third dose
- AEs leading to discontinuation from study participation after booster or third dose through the last day of study participation

For mRNA-1273.214 Booster Dose:

- MAAEs through the entire study period after booster dose
- SAEs through the entire study period after booster dose
- AESIs through the entire study period after booster dose
- AEs leading to discontinuation from study participation after booster dose through the last day of study participation

3.3.2. Primary Immunogenicity Endpoints

- Co-Primary endpoint(s) for mRNA-1273 booster in part 1 and part 2:
    - The GM value of post-booster Ab in Study P204 compared with post-primary series (post-Dose 2) in adults (≥18 to 25 years) in Study P301
    - The seroresponse rate of post-booster from baseline (pre-Dose 1 of primary series) compared with post-primary series (post-Dose 2) from baseline (pre-Dose 1 of primary series) in the adults (≥18 to 25 years) Study P301, using 4-fold rise definition
        - 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
- For Part 3, the GM value and seroresponse rate (SRR) of post-third dose Ab in Study P204 compared with post-primary series (post-Dose 2) from adults (>18 years of age) in Study P301
    - All part 3 immunogenicity analyses will be descriptive. The analysis will also be performed using alternative P301 compartor (≥18 to 25 years).

3.3.3. Secondary Endpoints

For mRNA-1273 Booster/Third Dose:

- The GM values of SARS-CoV-2 S protein-specific bAb on Booster Dose (BD)-Day 1 (at least 3 months or 6 months after Dose 2), BD-Day 29 (1 month after booster dose or third dose), BD-Day 181 (6 months after booster dose or third dose), and BD-Day 366 (1 year after booster dose or third dose)
- The GM values of SARS-CoV-2-specific nAb on BD-Day 1 (at least 3 months or 6 months after Dose 2), BD-Day 29 (1 month after booster dose or third dose), BD-Day 181 (6 months after booster dose or third dose), and BD-Day 366 (1 year after booster dose or third dose)

3.3.4. Exploratory Endpoints

The exploratory endpoints are the following:

For mRNA-1273 Booster/Third Dose:

- GM, SRR, and GMFR of Ab against SARS-CoV-2 variant(s) of concern or interest

For mRNA-1273 Booster Dose:

- The incidence of COVID-19, SAR-CoV-2 infection and asymptomatic SARS-CoV-2 infection up to the implementation of protocol amendment 9 in October 2022.

4. Study Design

4.1. Overall Study Design

Overall study design is described in SAP for Part 1 open-label phase and Part 2 blinded phase.

4.2. Sample Size and Power

Please refer to section 4.2 in Part 1 open-label phase and Part 2 blinded phase SAP for sample size and power in Part 1 and Part 2.

All participants enrolled in Part 1 or Part 2 who meet the eligibility criteria for BD will be offered an optional BD 25 μg for 6 years to < 12 years, 10 μg for 2 to <6 years and 6 months to <2 years.

- In Part 1 or Part 2 for the booster dose primary immunogenicity analysis in an age group, with approximately 289 participants receiving mRNA-1273 booster dose in the PP Immunogenicity Subset with pre-booster negative SARS-CoV-2 in Study P204 and 289 young adults (≥18 to 25 years of age) receiving mRNA-1273 100 µg primary series in Study P301, there will be a 90% power to demonstrate noninferiority of the immune response, as measured by the antibody GM value, in children receiving a mRNA-1273 booster dose compared with that in adults (≥18 to 25 years of age) receiving mRNA-1273 primary series in Study P301, at a 2-sided alpha of 0.05, assuming an underlying true GMR value of 1.0 and a noninferiority margin of 1.5. The standard deviation of the natural log-transformed GMT levels is assumed to be 1.5. Also, if the true SRRs were assumed to be 95% or higher in children receiving mRNA-1273 booster dose in Study P204 and adults receiving mRNA-1273 primary series in Study P301, with between-group true difference within 4%, there will be a > 90% power to demonstrate noninferiority by SRR in children receiving a mRNA-1273 booster dose compared with adults receiving primary series in Study P301, at a 2-sided alpha of 0.05 and based on a noninferiority margin of 10%

The sample size in the lower dosing assessment (Part 3) was originally planned as approximately 300 children 6 years to < 12 years of age receiving mRNA-1273 25 µg (Please refer to protocol amendment 9 section 8.3). As described in Section 2.3, there are only 91 subjects enrolled in part 3, and this small number of participants enrolled in Part 3 is insufficient to power the hypothesis testing. As a result, the originally planned hypothesis testing in protocol for part 3 will not be performed and all the immunogenicity analyses for Part 3 will be descriptive.

4.3. Blinding and Unblinding

Part 2 open-label phase, booster dose analysis, and Part 3 open-label phase are all open-label.

5. Analysis Populations

The following analysis sets are defined: Full Analysis Set (FAS), Immunogenicity Subset, Per Protocol Immunogenicity Subset, Per-protocol (PP) Immunogenicity Subset – Pre-booster SARS-CoV-2 Negative Set, Modified Intent-to-Treat-1 (mITT1) Set, Solicited Safety Set and Safety Set.

5.1. Full Analysis Set

The Full Analysis Set (FAS) (Part 2, Cross-Over Subjects)

FAS (Part 2, Cross-Over Subjects) for Placebo-mRNA-1273 group consists of all participants from Part 2 placebo group who cross over and receive mRNA-1273 in open-label phase.

The Full Analysis Set (FAS) (Long-term Analysis)

The FAS (Long-term Analysis) consists of FAS (Part 2, Cross-Over Subjects) for Placebo-mRNA-1273 group and FAS for mRNA-1273 group. FAS for mRNA-1273 group is same as the FAS in Part 1 open-label phase and Part 2 blinded phase. Participants will be analyzed in the mRNA-1273 group or placebo-mRNA-1273 group if applicable.

The Full Analysis Set (FAS) (Part 3, First Two Doses of Primary Series)

The Full Analysis Set (FAS) for Part 3, first two doses of primary series consists of all enrolled participants who receive at least 1 injection of IP. Participants will be analyzed according to the treatment group for the treatment they planned to be received in Part 3.

The Full Analysis Set (FAS) (Booster/Third Dose Analysis)

The FAS for Booster/Third Dose Analysis consists of all participants who received at least one booster/third dose. Participants will be analyzed according to their treatment group (mRNA-1273-mRNA-1273 Booster/mRNA-1273.214 Booster or Placebo-mRNA-1273-mRNA-1273 Booster/mRNA-1273.214 Booster for booster dose analysis and mRNA-1273-Third Dose for third dose analysis) if applicable.

For mRNA-1273- mRNA-1273 Booster/Third Dose treatment group, participants from the Part 1 or Part 3 open-label phase or the Part 2 blinded phase mRNA-1273 group in primary series who received a booster/third dose of mRNA-1273 are included.

For Placebo-mRNA-1273-mRNA-1273 Booster treatment group, participants from the Part 2 blinded phase placebo group who crossed over to mRNA-1273 after unblinding and received a booster dose of mRNA-1273 are included.

For mRNA-1273- mRNA-1273.214 Booster treatment group, participants from the Part 1 open-label phase or the Part 2 blinded phase mRNA-1273 group in primary series who received a booster dose of mRNA-1273.214 are included.

For Placebo-mRNA-1273-mRNA-1273.214 Booster treatment group, participants from Part 2 blinded phase placebo group who crossed over to mRNA-1273 after unblinding and received a booster dose of mRNA-1273.214 are included.

5.2. Immunogenicity Subset

Immunogenicity Subset (Long-term Analysis)

Immunogenicity Subset for long-term analysis at Day 1, Day 57 and Day 209 consists of

a) a subset of participants in the FAS (Long-term Analysis) and

b) have baseline (pre-dose 1 of mRNA-1273) SARS-CoV-2 status available, and

c) have baseline (pre-dose 1 of mRNA-1273) and at least one post-injection antibody assessment for the analysis endpoint.

Immunogenicity Subset for long-term analysis only includes subjects who received mRNA-1273 in Part 1 open-label phase and Part 2 blinded and open-label phase.

Immunogenicity Subset (Part 3, First Two Doses of Primary Series)

a) a subset of participants in the FAS, and

b) have baseline (Day 1) SARS-CoV-2 status available, and

c) have baseline and at least one post-injection antibody assessment for the analysis endpoint.

Immunogenicity Subset (Booster/Third Dose Analysis)

Immunogenicity Subset for booster/third dose consists of

a) a subset of participants in the FAS (Booster/Third Dose Analysis) who took mRNA-1273 Booster/Third dose and

b) have baseline (pre-dose 1 of mRNA-1273) SARS-CoV-2 status available, and

c) have at least one post-booster/post-third antibody assessment for the analysis endpoint.

5.3. Per-protocol (PP) Immunogenicity Subset

Per-protocol (PP) Immunogenicity Subset (Long-term Analysis)

Per-Protocol (PP) Immunogenicity Subset (Long-term Analysis) at Day 1, Day 57 and Day 209 consists of all participants in Immunogenicity Subset (Long-term Analysis) who meet all the following criteria:

a) Received planned doses of study vaccination per schedule

b) Complied with the timing of second dose of injection

c) If participants have a diagnosis of HIV, they are not receiving highly active anti-retroviral therapy (HAART)

d) Had a negative SARS-CoV-2 status at baseline (pre-dose 1 of mRNA-1273)

e) Had no major protocol deviations that impact key or critical data

The PP Immunogenicity Subset (Long-term Analysis) will serve as the population for the long-term analysis of immunogenicity data.

Per-protocol (PP) Immunogenicity Subset (Part 3, First Two Doses of Primary Series)

Per-Protocol (PP) Immunogenicity Subset consists of all participants in Part 3 Immunogenicity Subset who meet all the following criteria:

a) Received planned doses of IP per schedule

b) Complied with the immunogenicity window based on 2nd dose injection timing

c) If participants have a diagnosis of HIV, they are not receiving highly active anti-retroviral therapy (HAART)

d) Had baseline (Day 1) and Day 57 Ab assessment for the analysis endpoint

e) Had no major protocol deviations that impact key or critical data

The PP Immunogenicity Subset will serve as the primary population for the analysis of immunogenicity data in this study unless specified otherwise. Participants will be analyzed according to the treatment group for the treatment which they actually received in Part 3.

Per-protocol (PP) Immunogenicity Subset (Booster/Third Dose Analysis)

Per-Protocol (PP) Immunogenicity Subset consists of all participants in Immunogenicity Subset for Booster/Third Dose Analysis who meet all the following criteria:

For mRNA-1273 Booster Dose:

a) Received 2 doses of planned doses of mRNA-1273 vaccination in Part 1 open-label phase or Part 2 blinded phase per schedule

b) Received booster dose in Booster Dose Analysis

c) If participants have a diagnosis of HIV, they are not receiving highly active anti-retroviral therapy (HAART)

d) Had a negative SAS-CoV-2 status at baseline (pre-dose 1 of mRNA-1273)

e) Had BD-Day 29 Ab assessment for the analysis endpoint

f) Had no major protocol deviations that impact key or critical data

g) Not receive off-study COVID-19 vaccination prior to BD-Day 29 visit

For mRNA-1273 Third Dose:

a) Received first 2 doses of planned doses of mRNA-1273 vaccination in Part 3 open-label phase per schedule

b) Received third dose in Third Dose Analysis

c) If participants have a diagnosis of HIV, they are not receiving highly active anti-retroviral therapy (HAART)

d) Had BD-Day 29 Ab assessment for the analysis endpoint

e) Had no major protocol deviations that impact key or critical data

f) Not receive off-study COVID-19 vaccination prior to BD-Day 29 visit

The PP Immunogenicity Subset for Booster/Third Dose analysis will serve as a population for the analysis of immunogenicity in booster/third dose by pre-booster SARS-CoV-2 status (negative vs. positive).

5.4. Per-protocol (PP) Immunogenicity Subset - Pre-booster SARS-CoV-2 Negative (Booster Dose Analysis)

PP Immunogenicity Subset - Pre-booster SARS-CoV-2 Negative (PP Immunogenicity Subset – Neg) for booster dose analysis consists of participants who are in PP Immunogenicity Subset (Booster Dose Analysis), and are pre-booster SARS-CoV-2 negative, defined as no virologic or serologic evidence of SARS-CoV-2 infection on or before BD-Day 1 (pre-booster), i.e. RT-PCR result is not positive if available at BD-Day 1 and a negative bAb specific to SARS-CoV-2 nucleocapsid on or before BD-Day 1.

PP Immunogenicity Subset - Pre-booster SARS-CoV-2 Negative for Booster Dose Analysis will serve as the population for the primary and secondary analysis of immunogenicity data in booster phase.

5.5. Modified Intent-to-Treat-1 (mITT1) Set

mITT1 Set (Part 2, Cross-Over Subjects)

mITT1 Set (Part 2 Cross-Over Subjects) for placebo-mRNA-1273 group consists of all cross-over participants who were previously included in the mITT1 set for the Part 2 blinded phase analysis and in the FAS (Part 2, Cross-Over Subjects) who had no serologic or virologic evidence of prior SARS-CoV-2 infection (no positive RT-PCR test and no positive serology test based on bAb specific to SARS-CoV-2 nucleocapsid) on or before the date of the first cross-over mRNA-1273 dose in open-label phase and received at least one dose of mRNA-1273 without wrong treatment, i.e., all FAS cross-over participants excluding those with positive or missing RT-PCR test or serology test prior to the first dose of mRNA-1273 and those who received the wrong treatment in open-label phase (i.e., at least one dose received in open-label phase is not as assigned).

mITT1 Set (Long-term Analysis)

The mITT1 Set (Long-term Analysis) consists of mITT1 Set (Part 2, Cross-Over Subjects) for Placebo-mRNA-1273 group and mITT1 Set for mRNA-1273 group. The mITT1 Set for mRNA-1273 group is same as the mITT1 Set in Part 1 open-label phase and Part 2 blinded phase.

mITT1 Set (Booster Dose Analysis)

The mITT1 Set for booster dose analysis consists of all participants in the FAS for booster dose who had no serologic 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) pre-booster dose and received one booster dose without wrong treatment, i.e., all FAS participants excluding those with pre-booster positive or missing RT-PCR test or serology test and those who received the wrong booster dose (i.e., dose received in booster dose is not as assigned).

Participants will be analyzed according to their treatment group (mRNA-1273-mRNA-1273 Booster or Placebo-mRNA-1273-mRNA-1273 Booster for booster dose analysis)

5.6. Solicited Safety Set

Solicited Safety Set (Part 3, First Two Doses of Primary Series)

The Solicited Safety Set consists of all participants in the safety set who contribute any solicited AR data, i.e., have at least one post-baseline solicited safety assessment. The

Solicited Safety Set will be used for the analyses of solicited ARs and participants will be included in the vaccination group corresponding to the study injection they actually received. In addition, the following Solicited Safety Set is defined for each injection separately.

The First (Second) Injection Solicited Safety Set consists of all subjects in the Solicited Safety Set who have received the first (second) study injection and have contributed any solicited AR data from the time of first (second) study injection through the following 6 days. Participants will be analyzed according to the vaccination group a participant actually received.

Solicited Safety Set (Booster/Third Dose Analysis)

The Solicited Safety Set for Booster/Third Dose Analysis consists of all participants who received booster/third dose, and contribute any solicited AR data, i.e., have at least one post-booster/post-third solicited safety assessment in booster/third dose phase. The Solicited Safety Set will be used for the analyses of solicited ARs in Booster/Third Dose analysis.

Participants will be analyzed according to their treatment groups (mRNA-1273-mRNA-1273 Booster or Placebo-mRNA-1273-mRNA-1273 Booster for booster dose analysis and mRNA-1273-Third Dose for third dose analysis).

5.7. Safety Set

Safety Set (Part 2, Cross-Over Subjects)

Safety Set (Part 2, Cross-Over Subjects) consists of all participants from Part 2 placebo group who cross over and receive mRNA-1273 in open-label phase.

Safety Set (Long-term Analysis)

The Safety Set (Long-term Analysis) consists of Safety Set (Part 2, Cross-Over Subjects) for Placebo-mRNA-1273 group and Safety Set for mRNA-1273 group. The Safety Set for Long-term Analysis for mRNA-1273 group is same as the Safety Set in Part 1 open-label phase and Part 2 blinded phase. The Safety Set will be used for analysis of safety except for the solicited ARs. Participants will be analyzed in the mRNA-1273 group or Placebo-mRNA-1273 group.

Safety Set (Part 3, First Two Doses of Primary Series)

The Safety Set of Part 3, first two doses of primary series consists of all enrolled participants who received any study injection. The Safety Set will be used for analysis of safety except for the solicited ARs. In addition, the following Safety Set is defined for each injection separately. The First (Second) Injection Safety Set consists of all subjects in the Safety Set who have received the first (second) study injection. Participants will be included in the vaccination group corresponding to the vaccination they actually received.

Safety Set (Booster/Third Dose Analysis)

The Safety Set in Booster/Third Dose Analysis consists of all participants who received a booster/third dose in booster/third dose analysis phase. The Safety Set will be used for analysis of safety except for the solicited ARs. Participants will be analyzed according to their treatment group (mRNA-1273-mRNA-1273 Booster/mRNA-1273.214 Booster or Placebo-mRNA-1273- mRNA-1273 Booster/mRNA-1273.214 Booster for booster dose analysis and mRNA-1273-Third Dose for third dose analysis).

For mRNA-1273- mRNA-1273 Booster/Third Dose treatment group, participants from the Part 1 or Part 3 open-label phase or the Part 2 blinded phase mRNA-1273 group in primary series who received booster/third dose of mRNA-1273 are included.

For Placebo-mRNA-1273-mRNA-1273 Booster treatment group, participants from the Part 2 blinded phase placebo group who crossed over to mRNA-1273 after unblinding and received a booster dose of mRNA-1273 are included.

For mRNA-1273- mRNA-1273.214 Booster treatment group, participants from the Part 1 open-label phase or the Part 2 blinded phase mRNA-1273 group in primary series who received a booster dose of mRNA-1273.214 are included.

For Placebo-mRNA-1273-mRNA-1273.214 Booster treatment group, participants from the Part 2 blinded phase placebo group who crossed over to mRNA-1273 after unblinding and received a booster dose of mRNA-1273.214 are included.

6. Statistical Analysis

Unless specified otherwise, the Part 3 statistical analysis for the first two doses open-label phase and third dose phase will be similar to the analysis for primary series (refer to the SAP for Part 1 Open-Label Phase and Part 2 Blinded Phase) and booster analysis in Part 1 and Part 2 respectively.

6.1. General Considerations

The Schedule of Assessments is provided in Appendix E for Part 2 open-label phase and Appendix F for Booster dose analysis, and Appendix H for Part 3 .

Continuous variables will be summarized using the following descriptive summary statistics: the number of subjects (n), mean, standard deviation (SD), median, minimum (min), and maximum (max).

Categorical variables will be summarized using counts and percentages.

Baseline Value for specific study phase

- **Part 2 pre-crossover**: unless specified otherwise, is defined as the most recent non-missing measurement (scheduled or unscheduled) collected before the first dose of mRNA-1273 in Part 2
- **Pre-booster/third dose**: unless specified otherwise, is defined as the most recent non-missing measurement (scheduled or unscheduled) collected before the booster/third dose

For the summary statistics of all numerical variables unless otherwise specified, the display precision will follow programming standards. Please see Appendix A for variable display standards.

When count data are presented, the percentage will be suppressed when the count is zero in order to draw attention to the non-zero counts. A row denoted “Missing” will be included in count tabulations where specified on the shells to account for dropouts and missing values. The denominator for all percentages will be the number of subjects in that vaccination group within the analysis set of interest, unless otherwise specified.

Baseline SARS-CoV-2 Status:

- Baseline SARS-CoV-2 status for long-term analysis is determined by using virologic and serologic evidence of SARS-CoV-2 infection at the date of first mRNA-1273 (first dose of mRNA-1273 in the blinded phase or crossover first dose of mRNA-1273 in the open label).
  Negative SARS-CoV-2 status for long-term analysis is defined as a most recent negative RT-PCR test for SARS-CoV-2 and a most recent negative serology test based on bAb specific to SARS-CoV-2 nucleocapsid (as measured by Roche Elecsys Anti-SARS-CoV-2 assay) at the date of the first mRNA-1273 dose.

Positive SARS-CoV-2 status for long-term analysis is defined as a most recent positive RT-PCR test for SARS-CoV-2 at the date of the first mRNA-1273 dose, and/or a most recent positive serology test based on bAb specific to SARS-CoV-2 nucleocapsid (as measured by Roche Elecsys Anti-SARS-CoV-2 assay) at the date of the first mRNA-1273 dose.

- **Pre-booster/third dose SARS-CoV-2 Status**

  Pre-booster/third dose SARS-CoV-2 status is determined by using virologic and serologic evidence of SARS-CoV-2 infection at the date of booster/third dose (BD-Day 1).
  Pre-booster/third dose negative status is 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 (as measured by Roche Elecsys Anti-SARS-CoV-2 assay) at the date of booster/third dose.
  Else, Pre-booster/third dose positive SARS-CoV-2 status is defined as a positive RT-PCR test for SARS-CoV-2 at the date of booster/third dose, and/or a positive serology test based on bAb specific to SARS-CoV-2 nucleocapsid (as measured by Roche Elecsys Anti-SARS-CoV-2 assay) at the date of booster/third dose.

Study day relative to the first injection in Part 2 open-label phase will be calculated as below:

a) study day prior to the first injection will be calculated as: date of assessment/event – date of the first injection of mRNA-1273 in Part 2 open-label phase (Crossover Day 1);

b) study day on or after the date of the first injection will be calculated as: date of assessment/event – date of the first injection of mRNA-1273 in Part 2 open-label phase (Crossover Day 1) + 1;

Study day relative to the injection in booster/third dose analysis will be calculated as below:

a) study day prior to the booster/third dose will be calculated as: date of assessment/event – date of the injection in booster/third dose analysis;

b) study day on or after the date of the booster/third dose will be calculated as: date of assessment/event – date of the injection in booster/third dose analysis + 1;

Study day relative to the most recent injection will be calculated as below:

a) study day on or after the date of the first injection in Part 2 open-label phase (if applicable) but before the second injection in Part 2 open-label phase (if applicable) will be calculated as: date of assessment/event – date of the first injection of mRNA-1273 in Part 2 open-label phase + 1;

b) study day on or after the date of the second injection in Part 2 open-label phase (if applicable) but before the injection in booster dose analysis (if applicable) will be calculated as: date of assessment/event – date of the second injection of mRNA-1273 in Part 2 open-label phase + 1;

c) study day on or after the date of booster/third dose analysis (if applicable) will be calculated as: date of assessment/event – date of the injection in booster/third dose analysis + 1;

   if study day is on the same day as the injection, date and time will be compared with the injection date and time.

For calculation regarding antibody values in booster/third dose analysis, antibody values reported as below LLOQ will be replaced by 0.5 × LLOQ. Values that are greater than the upper limit of quantification (ULOQ) will be converted to the ULOQ if actual values are not available, and actual values will be used if available. Missing results will not be imputed.

The following analysis periods for Long-term and booster/third dose phase safety analyses will be used as applicable for specific subjects group in this study:

- Up to 28 days after any vaccination (mRNA-1273 primary series or booster/third dose): this stage starts at the day of each vaccination and continue through the earliest date of (the day of each vaccination and 27 subsequent days, next vaccination [if applicable]). This analysis period will be used as the primary analysis period for safety analyses including unsolicited AE, except for solicited AR, unless specified otherwise.

- Overall period or throughout the study: this analysis period starts at the first injection on Day 1 and continues through the earliest date of (study completion, discontinuation from the study, or death).

Long-term Analysis (including Part 2 Open-Label Phase)

For unsolicited AE or assessments that will be collected throughout the study after mRNA-1273 primary series, this analysis period starts from the first dose date of mRNA-1273 and continues until the earliest date of (booster dose, study completion, discontinuation from the study, or death).

Booster/Third Dose Analysis

For unsolicited AE or assessments that will be collected throughout the study, this analysis period starts from the booster/third dose date and continues until the earliest date of (study completion, discontinuation from the study, or death).

Unscheduled visits: Unscheduled visit measurements will be included in analysis as follows:

- In scheduled visit windows per specified visit windowing rules.
- In the derivation of baseline/last on-treatment measurements.
- In the derivation of maximum/minimum on-treatment values and maximum/minimum change from baseline values for safety analyses.
- In individual subject data listings as appropriate.

Visit windowing rules: The analysis visit windows for protocol-defined visits are provided in Appendix B.

Incomplete/missing data:

- Imputation rules for missing prior/concomitant medications, non-study vaccinations and procedures are provided in Appendix C.
- Imputation rules for missing AE dates are provided in Appendix D.
- For laboratory assessments, if majority of results are indefinite, imputation of these values will be considered. If the laboratory results are reported as below the LLOQ (e.g., <0.1), the numeric values will be imputed by 0.5 × LLOQ in the summary. If the laboratory results are reported as greater than the ULOQ (e.g., ">3000"), the numeric values will be imputed by ULOQ in the summary.
- Other incomplete/missing data will not be imputed, unless specified otherwise.

Treatment groups:

The following vaccination groups will be used for summary purposes:

- Long-term Analysis (Part 1 Open-Label Phase plus Part 2 Blinded and Open-Label Phase):
    - mRNA-1273: Participants from mRNA-1273 group in Part 1 open-label phase or Part 2 blinded phase
    - Placebo - mRNA-1273: Participants from Part 2 blinded phase placebo group who cross over and receive mRNA-1273 in Part 2 open-label phase
- Part 3, First Two Doses of Primary Series:
    - mRNA-1273 25 μg: Participants from mRNA-1273 group in Part 3 open-label phase
- Booster/Third Dose Analysis:
    - mRNA-1273 - mRNA-1273 Booster: Participants from the Part 1 open-label phase or Part 2 blinded phase mRNA-1273 group who reveived a booster dose of mRNA-1273 in Part 1 or Part 2
    - Placebo - mRNA-1273 - mRNA-1273 Booster: Participants from the Part 2 blinded phase placebo group who crossed over to receive mRNA-1273 in Part 2 open-label phase, and received a booster dose of mRNA-1273 in the booster phase
    - mRNA-1273 - mRNA-1273.214 Booster: Participants from the Part 1 open-label phase or Part 2 blinded phase mRNA-1273 group who received a booster dose of mRNA-1273.214 in Part 1 or Part 2
    - Placebo - mRNA-1273 - mRNA-1273.214 Booster: Participants from the Part 2 blinded phase placebo group who crossed over to receive mRNA-1273 in the Part 2 open-label phase, and received a booster dose of mRNA-1273.214 in booster phase
    - mRNA-1273 - mRNA-1273 Third Dose: Participants from the Part 3 open-label phase who received a third dose of mRNA-1273 in Part 3

Analysis periods

The following analysis periods and treatment groups will be used for long-term and booster dose analysis.

- Long-term Analysis (Part 1 Open-Label Phase plus Part 2 Blinded and Open-Label Phase, until Booster Dose)

Group	Category	Start Date	End Date
mRNA-1273	Safety	Date of First Dose of mRNA-1273	Earliest date of booster dose (exclusive), study discontinuation, study completion, death, or data cutoff
Placebo - mRNA-1273			
mRNA-1273	Efficacy/ Immunogenicity	Date of First Dose of mRNA-1273	Earliest date of booster dose (inclusive), study discontinuation, study completion, death, or data cutoff
Placebo - mRNA-1273			

- Long-term analysis (Part 1 Open-Label Phase plus Part 2 Blinded and Open-Label Phase, Regardless of Booster Dose) incidence rate will also be performed for the entire study period after the first dose of mRNA-1273 regardlesss of booster dose.

Group	Category	Start Date	End Date
mRNA-1273	Safety	Date of First Dose of mRNA-1273	Earliest date of study discontinuation, study completion, death, or data cutoff
Placebo - mRNA-1273			
mRNA-1273	Efficacy/ Immunogenicity	Date of First Dose of mRNA-1273	Earliest date of study discontinuation, study completion, death, or data cutoff
Placebo - mRNA-1273			

- Part 3, First Two Doses of Primary Series Analysis

Group	Category	Start Date	End Date
mRNA-1273 25 µg	Safety	Date of First Dose of mRNA-1273	Earliest date of third dose (exclusive), study discontinuation, study completion, death, or data cutoff

mRNA-1273 25 µg	Immunogenicity	Date of First Dose of mRNA-1273	Earliest date of third dose (inclusive), study discontinuation, study completion, death, or data cutoff

- Booster/Third Dose Analysis

Group	Category	Start	End
mRNA-1273 - mRNA-1273 Booster	Safety	Date of Booster/Third Dose	Earliest date of study discontinuation, study completion, death, or data cutoff
mRNA-1273 - mRNA-1273 Third Dose			
Placebo - mRNA-1273 - mRNA-1273 Booster			
mRNA-1273 - mRNA-1273.214 Booster			
Placebo - mRNA-1273 - mRNA-1273.214 Booster			
mRNA-1273 - mRNA-1273 Booster	Efficacy/ Immunogenicity	Date of Booster/Third Dose (considered as pre-booster/third dose data, exclusive)	Earliest date of study discontinuation, study completion, death, or data cutoff
mRNA-1273 - mRNA-1273 Third Dose			
Placebo - mRNA-1273 - mRNA-1273 Booster			

For mRNA-1273.214 Booster Dose, only safety analysis related to endpoints in section 3.3.1 will be performed.

For Part 3 mRNA-1273 Third Dose, only safety and immune analysis related to endpoints in section 3.3 will be performed.

Subgroup Analysis

Safety, efficacy and immunogenicity endpoints may be analyzed in select subgroups specified below as applicable:

- Baseline SARS-CoV-2 Status (Positive, Negative)
- Pre-booster/third dose SARS-CoV-2 Status (Positive, Negative)
- Age (6 Months to < 2 Years, 2 Years to < 6 Years, and 6 Years to < 12 Years)
- Sex (Female, Male)

- Race
- Ethnicity
- Obesity status (Obesity is defined as BMI >= 95th percentile for age based on WHO growth reference data)

All analyses and data summaries/displays will be provided by vaccination group for each age group (6 months to < 2 years, 2 years to < 6 years, and 6 years to < 12 years), unless otherwise specified.

All analyses will be conducted using SAS Version 9.4 or higher.

6.2. Background Characteristics

6.2.1. Subject Disposition

The number and percentage of subjects in the following categories will be summarized by age and vaccination group as defined in Section 6.1 based on specific analysis datasets for Part 2 Open-label Phase, and Booster Dose Analysis separately:

For mRNA-1273 Primary Series Long-term and mRNA-1273 Booster:

- Full Analysis Set (Long-term Analysis)
- Full Analysis Set (Booster Dose Analysis)
- Immunogenicity Subset (Long-term Analysis)
- Immunogenicity Subset (Booster Dose Analysis)
- PP Immunogenicity Subset (Long-term Analysis)
- PP Immunogenicity Subset (Booster Dose Analysis)
- PP Immunogenicity Subset - Pre-booster SARS-CoV-2 Negative (Booster Dose Analysis)
- mITT1 Set (Long-term Analysis)
- mITT1 Set (Booster Dose Analysis)
- Solicited Safety Set (Booster Dose Analysis)
- Safety Set (Long-term Analysis)

- Safety Set (Booster Dose Analysis)

For mRNA-1273.214 Booster:

- Full Analysis Set (Booster Dose Analysis)
- Safety Set (Booster Dose Analysis)

For Part 3 First Two Doses of Primary Series, and Third Dose Analysis separately:

- Full Analysis Set
- Full Analysis Set (Third Dose Analysis)
- Solicited Safety Set
- Solicited Safety Set (Third Dose Analysis)
- Safety Set
- Safety Set (Third Dose Analysis)
- Immunogenicity Subset
- Immunogenicity Subset (Third Dose Analysis)
- PP Immunogenicity Subset
- PP Immunogenicity Subset (Third Dose Analysis)

The percentage will be based on subjects in that age and vaccination group within the Full Analysis Set for long-term analysis and booster/third dose analysis separately, except the Solicited Safety Set and Safety Set for which the percentages will be based on the age and vaccination group in the Safety Set (as treated) for long-term analysis and booster/third dose separately.

The number and percentage of subjects in each of the following disposition categories will be summarized by age and vaccination group based on the Randomization Set in Part 2:

- Received each dose of IP in Part 2 blinded phase
- Continuing and unblinded in Part 2 open-label phase
- Received each cross-over dose of IP in Part 2 open-label phase
- Prematurely discontinued study vaccine during Part 2 open-label phase and the reason for discontinuation

- Received mRNA-1273 booster dose in booster dose analysis for Part 2
- Received mRNA-1273.214 booster dose in booster dose analysis for Part 2
- Completed study
- Prematurely discontinued the study and the reason for discontinuation (for the entire study period, and for study parts in applicable subjects group)

The number and percentage of subjects in each of the following disposition categories will be summarized by age and vaccination group based on the Full Analysis Set for booster/third dose analysis:

- Received mRNA-1273 booster/third dose in booster/third dose analysis
- Received mRNA-1273.214 booster dose in booster dose analysis
- Completed study
- Prematurely discontinued the study and the reason for discontinuation

A subject disposition listing will be provided, including informed consent date, subjects who completed the study injection schedule, subjects who completed study, subjects who discontinued from study vaccine or who discontinued from participation in the study, with reasons for discontinuation.

A subject from Part 1 or Part 2 who completed 12 months of follow up after the last injection received is considered to have completed the study if not received booster dose. For subject who completed 12 months of follow up after the booster injection received is considered to have completed the study if received booster dose. For Part 3 subjects who completed 12 months of follow up after the third injection received is considered to have completed the study.

6.2.2. Demographics

Descriptive statistics will be calculated for the following continuous demographic and baseline characteristics: age (years), weight (kg, z-score), height (cm, z-score), and body mass index (BMI) (kg/m^2, z-score). Number and percentage of subjects will be provided for categorical variables such as gender, race, ethnicity. The summaries will be presented by age and vaccination group as defined in Section 6.1 if applicable, based on the Safety Set, FAS, mITT1 Set, Immunogenicity Subset, and PP Immunogenicity Subset (by pre-booster/third dose SARS-CoV-2 status and overall for booster/third dose analysis).

6.2.3. Medical History

Medical history data will be coded by system organ class (SOC) and preferred term (PT) using the Medical Dictionary for Regulatory Activities (MedDRA).

The number and percentage of participants with any medical history will be summarized by SOC and PT based on the Safety Set. A participant will be counted only once for multiple events within each SOC and PT. SOC will be displayed in internationally agreed order. PT will be displayed in descending order of frequency and then alphabetically within SOC.

Medical history data will be presented in a listing.

Medical history data for participants who entered study in Part 1 open-label phase or Part 2 blinded phase will be provided in Part 1 open-label phase and Part 2 blinded Phased analysis.

6.2.4. Prior and Concomitant Medications

Prior and concomitant medications and non-study vaccination will be coded using the World Health Organization (WHO) drug dictionary (WHODD). The summary of concomitant medications will be based on the Safety Set (Booster/Third Dose Analysis). Categorization of prior, concomitant, and post medications is summarized in Appendix C Table 5.

The number and percentage of subjects using concomitant medications and non-study vaccination during the 7-day follow-up period (i.e., on the day of injection and the 6 subsequent days) and during the 28-day follow-up period after booster/third dose injection in booster/third dose analysis (i.e., on the day of injection and the 27 subsequent days) will be summarized by vaccination groups as defined in Section 6.1 as follows:

- Any concomitant medications and non-study vaccination within 7 Days Post Injection
- Any concomitant medications and non-study vaccination within 28 Days Post Injection
- Seasonal influenza vaccine within 28 Days Post Injection
- Antipyretic or analgesic medication within 28 Days Post Injection

A summary table of concomitant medications and non-study vaccination that continued or newly received at or after the first injection through 28 days after the booster/third injection will be provided by PT in descending frequency in the mRNA-1273 group.

Medications taken to prevent pain or fever will be collected on eDiary and summaries will be provided based on the Solicited Safety Set by vaccination group as defined in Section 6.1 for booster/third injection, including within 7 days after injection, beyond 7 days after injection.

Concomitant and post medications and non-study vaccination will be presented in a listing.

6.2.5. Study Exposure

Study IP administration data will be presented in a listing for Part 2 open-label phase and booster dose analysis and Part 3 third dose analysis separately.

Long-term analysis study duration will be summarized as earliest date of (study discontinuation, study completion, death, and data cutoff date) - first dose of mRNA-1273 + 1.

Booster/Third dose analysis study duration will be summarized as earliest date of (study discontinuation, study completion, death, and data cutoff date) – date of booster/third injection +1.

6.2.6. Major Protocol Deviations

Major protocol deviations are a subset of protocol deviations that may significantly impact the completeness, accuracy, or reliability of the study data or that may significantly affect a subject's rights, safety, or well-being. Major protocol deviations rules will be developed and finalized before database lock.

The number and percentage of the subjects with each major protocol deviation type will be provided by age and vaccination group as defined in Section 6.1 based on the FAS (Booster/Third Dose Analysis).

Major protocol deviations will be presented in a listing.

6.3. Safety Analysis

Safety and reactogenicity will be assessed by clinical review of all relevant parameters including solicited ARs (local and systemic), unsolicited AEs, SAEs, MAAEs, AESI, AEs leading to withdrawal from study vaccine and/or study participation, and physical

examination findings. Unsolicited AEs will be coded by SOC and PT according to the MedDRA. Two modified versions of The Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventative Vaccine Clinical Trials (DHHS 2007) are used in this study for solicited ARs as presented in protocol section 7.4.3's Table 8 and 9; Table 8 is the pediatric toxicity scale used for children older than 36 months and < 12 years, and Table 9 is the infant/toddler toxicity scale used for children 6 to 36 months of age, inclusive.

All safety analyses will be based on the Safety Set, except summaries of solicited ARs which will be based on the Solicited Safety Set. All safety analyses will be provided by age and vaccination group unless otherwise specified.

6.3.1. Adverse Events

A treatment-emergent AE (TEAE) is defined as any event occurring during the study not before exposure to study vaccine or any event already present that worsens after exposure to study vaccine. [Note: worsening of a pre-existing condition after vaccination will be reported as a new AE.]

Adverse events will also be evaluated by the investigator for the coexistence of MAAE which is defined as an AE that leads to an unscheduled visit to a healthcare practitioner.

Unsolicited AEs will be coded by PT and SOC using MedDRA and summarized by age and vaccination group, and stage (up to 28 days after any vaccination, follow-up analysis period and overall stage; see Section 6.1 for definitions of vaccination group and stage).

All summary tables (except for the overall summary of AEs) for unsolicited AEs will be presented by SOC and PT for TEAEs with counts of subjects included. SOC will be displayed in internationally agreed order. PT will be displayed in descending order of frequency of total mRNA-1273 group with all dose level combined in Part 1 and in Part 2 correspondingly and then alphabetically within SOC. When summarizing the number and percentage of subjects with an event, subjects with multiple occurrences of the same AE or a continuing AE will be counted once. Subjects will be presented according to the highest severity (the strongest relationship) in the summaries by severity (of related AEs), if subjects reported multiple events under the same SOC and/or PT.

Percentages will be based upon the number of subjects in the Safety Set for specified analysis (long-term analysis or booster/third dose analysis) within each age and vaccination group.

6.3.1.1. Incidence of Adverse Events

An overall summary of unsolicited TEAEs including the number and percentage of subjects who experience the following will be presented:

- Any unsolicited TEAEs
- Any serious TEAEs
- Any fatal TEAEs
- Any unsolicited medically-attended TEAEs
- Any unsolicited TEAEs leading to discontinuation from study vaccine
- Any unsolicited TEAEs leading to discontinuation from participation in the study
- Any unsolicited Grade 3/Severe TEAEs
- Any unsolicited Grade 3 or higher TEAEs
- Any unsolicitd Non-serious TEAEs
- Any unsolicited Non-serious and Grade 3/Severe TEAEs
- Any unsolicited Non-serious and Grade 3 or higher TEAEs
- Any AESI of MIS-C
- Any AESI of myocarditis and/or pericarditis
- Any AESI other than MIS-C and myocarditis and/or pericarditis

The table will also include number and percentage of subjects with unsolicited TEAEs that are treatment-related in each of the above categories. Safety summary tables for booster/third dose analysis will be provided separately.

In addition, listings containing individual subject adverse event data for unsolicited AEs, unsolicited TEAEs leading to discontinuation from study vaccine, unsolicited TEAEs leading to discontinuation from participation in the study, serious AEs, unsolicited medically-attended AEs, AESI other than MIS-C and myocarditis and/or pericarditis, AESI of MIS-C and AESI of myocarditis and/or pericarditis will be provided separately for placebo-mRNA-1273 group in Part 2 open-label phase and the group receiving booster/third dose in booster/third dose analysis. In Part 2, the safety data for the original

mRNA-1273 group in open-label will be included in blinded listings with a flag for open-label phase.

6.3.1.2.TEAEs by System Organ Class and Preferred Term

The following summary tables of TEAEs will be provided by SOC and PT using frequency counts and percentages (i.e., number and percentage of subjects with an event):

- All unsolicited TEAEs
- All unsolicited TEAEs that are treatment-related
- All serious TEAEs
- All serious TEAEs that are treatment-related
- All unsolicited TEAEs leading to discontinuation from study vaccine
- All unsolicited TEAEs leading to discontinuation from participation in the study
- All unsolicited Severe TEAEs
- All unsolicited Severe TEAEs that are treatment-related
- All unsolicited medically-attended TEAEs
- All unsolicited medically-attended TEAEs that are treatment-related
- All AESI of MIS-C
- All AESI other than MIS-C
- All AESI other than MIS-C and myocarditis and/or pericarditis

6.3.1.3.TEAEs by System Organ Class, Preferred Term and Severity (Any vs. Grade >= 3)

The following summary tables of TEAEs will be provided by SOC, PT, and maximum severity (mild < moderate < severe) using frequency counts and percentages:

- Summary tables of TEAEs by SOC, PT, and severity (Any vs. Grade >= 3) will be provided as well.

6.3.2. Solicited Adverse Reactions

An AR is any AE for which there is a reasonable possibility that the test product caused the AE. The term "Solicited Adverse Reactions" refers to selected signs and symptoms occurring after injection administration during a specified post-injection follow-up period (day of injection and 6 subsequent days). The solicited ARs are recorded by the subject in eDiary. The occurrence and intensity of selected signs and symptoms is actively solicited from the participant during a specified post-injection follow-up period (day of injection and 6 subsequent days), using a pre-defined checklist (i.e., solicited ARs).

The following systemic ARs will be solicited by the eDiary in booster/third dose analysis: headache, fatigue, myalgia (muscle aches all over the body), arthralgia (aching in several joints), nausea/vomiting, fever, chills, irritability/crying, sleepiness, and loss of appetite.

The AR categories are different for younger population between Age 37 months to <12 years and Age 6 months to ≤ 36 months. Details presented in Table 8 and 9 in the protocol.

The solicited ARs will be graded based on the grading scales presented in Table 8 and 9 in the protocol, modified from the Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventative Vaccine Clinical Trials (DHHS 2007). Investigator will assess Grade 4 events (with exception of fever).

If a solicited local or systemic AR continues beyond 7 days post injection, the participant's parent(s)/ LAR(s) will be prompted to capture details of the solicited local or systemic AR in the eDiary until it resolves or the next IP injection occurs, whichever occurs first.

All solicited ARs (local and systemic) will be considered causally related to injection.

After booster doses with mRNA-1273.214, local or systemic ARs will only be reported if they are medically attended, considered serious or lead to discontinuation from the study. No eDiaries will be used after booster doses with mRNA-1273.214.

Analyses of solicited ARs will be provided by age and treatment group for each injection (mRNA-1273 booster or third dose) based on the associated subset of Solicited Safety Set, i.e. Booster/Third Injection Solicited Safety Set, unless otherwise specified.

The number and percentage of subjects who reported each individual solicited local AR (has a severity grade of Grade 1 or greater) and solicited systemic AR (has a toxicity grade of Grade 1 or greater) during the 7-day follow-up period after booster/third dose will be tabulated by age group, vaccination group, toxicity grade, and injection. The number and

percentage of subjects who reported each individual solicited AR will also be summarized by age group, vaccination group, toxicity grade, days of reporting and injection.

The number and percentage of subjects experiencing fever (a temperature greater than or equal to 38.0°C/100.4°F by the oral, axillary, or tympanic route) by toxicity grade will be provided.

A two-sided 95% exact confidence interval (CI) using the Clopper-Pearson method will be provided for the percentage of subjects who reported any solicited local AR, solicited systemic AR, or any solicited AR.

The onset of individual solicited AR is defined as the time point after each injection at which the respective solicited AR first occurred. The number and percentage of subjects with onset of individual solicited AR will be summarized by age group, vaccination group, study day relative to the corresponding injection (Day 1 through Day 7), and injection.

The duration will be calculated as the end date/day of the solicited AR event – start date/day of the solicited AR event + 1, regardless of whether it is intermittent or continued. If the solicited AR continues beyond 7 days, the days a solicited AR is reported after 7 days will be included (e.g., an event that lasted 5 days in the first 7 days post injection and 3 days beyond 7 days post injection, the duration will be reported as 8 (5+3) days.)

6.3.3. Pregnancy Tests

A point-of-care urine pregnancy test will be performed at the Screening Visit (Day 0) and before each vaccine dose. At any time, a pregnancy test either via blood or point-of-care urine can be performed, at the discretion of the investigator.

A by-subject listing will be provided for pregnancy tests for Part 2 open-label phase and booster/third dose analysis separately.

6.4. Immunogenicity Analysis

The analyses of immunogenicity in long-term analysis at Day 1, Day 57, Day 209 and Day 394 (as applicable) will be based on the PP Immunogenicity Subset (Long-term Analysis) and Immunogenicity Subset (Long-term Analysis).

The analyses of immunogenicity in mRNA-1273 booster/third dose analysis will be based on

- PP Immunogenicity Subset with Pre-booster SARS-CoV-2 Negative for booster dose Analysis.

- PP Immunogenicity Subset (including Pre-booster/third dose SARS-CoV-2 Negative and Positive) for booster/third dose Analysis.

The PP Immunogenicity Subset with pre-booster SARS-CoV-2 negative will be used in the primary and secondary immunogenicity analyses for Part 1 and Part 2 booster dose analysis (Not applicable for Part 3 third dose analysis). And PP Immunogenicity Subset will be used for Part 3 third dose analysis, unless otherwise specified. The PP Immunogenicity Subset will be used in the immunogenicity analyses by pre-booster/third dose SARS-CoV-2 status (negative vs. positive).

The GMT and geometric mean (GM) level will be calculated using the following formula:

$$10^{\left\{\frac{\sum_{i=1}^{n}\log_{10}(t_i)}{n}\right\}}$$

where $t_1, t_2, \ldots, t_n$ are n observed immunogenicity values or levels.

The geometric mean fold-rise (GMFR) measures the changes in immunogenicity values or levels within subjects. The GMFR will be calculated using the following formula:

$$10^{\left\{\frac{\sum_{i=1}^{n}\log_{10}\left(v_{ij}/v_{ik}\right)}{n}\right\}} = 10^{\left\{\frac{\sum_{i=1}^{n}\log_{10}(v_{ij})-\log_{10}(v_{ik})}{n}\right\}}$$

where, for n subjects, v_{ij} and v_{ik} are observed immunogenicity values for subject i at time points j and k, $j \neq k$

6.4.1. Immunogenicity Assessments

There will be two types of immunogenicity assessments in booster/third dose analysis:

- Serum nAb value against SARS-CoV-2 as measured by pseudovirus and/or live virus neutralization assays.
- Serum bAb value as measured by enzyme-linked immunosorbent assay specific to the SARS-CoV-2 S protein.

6.4.2. Primary Analysis of Antibody-Mediated Immunogenicity Endpoints

Part 1 or Part 2 booster dose:

For Part 1 or Part 2 booster dose primary immunogenicity analysis of GM in children receiving mRNA 1273 booster dose, an analysis of covariance (ANCOVA) model will be performed to assess the difference in the immune response (Ab level) between BD-Day 29 in children receiving mRNA-1273 booster dose in Study P204 and Day 57 in young adults (≥18 to 25 years of age) receiving mRNA-1273 primary series in Study P301. In the analysis of covariance model, antibody values at BD-Day 29 for P204 and Day 57 for P301 will be a dependent variable, and a group variable (children in Study P204 and young adults in Study P301) will be the fixed effect. The GMT will be estimated by the GLSM from the model, and its corresponding 95% CI will be provided for each group. The GMR (ratio of GMTs) for children in Study P204 with respect to young adults in Study P301 will be estimated by the ratio of GLSM from the model, and the corresponding 95% CIs will be provided. The 95% CI for GMR will be used to assess the between-group difference in immune response at BD-Day 29 in children in Study P204 compared with Day 57 after the primary vaccine series in young adults in Study P301. The noninferiority of post booster GM in children will be considered demonstrated if the lower bound of the 95% CI of the GMR is > 0.667 based on the noninferiority margin of 1.5. The estimated GMT with 95% CI and GMR with 95% CI will also be provided using t-distribution.

For Part 1 or Part 2 booster dose primary immunogenicity analysis of seroresponse in children receiving mRNA-1273 booster dose, the SRR with 95% CI (using Clopper-Pearson method) will be summarized. The SRR difference with 95% CI (using Miettinen-Nurminen score method) to compare post-booster SRR at BD-Day 29 in children in Study P204 with the primary series SRR at Day 57 (28 days after Dose 2) in adults (≥18 to 25 years of age) in Study P301 will be computed. The SRR is defined as a value change from baseline (pre-Dose 1) below the LLOQ to ≥ 4 × LLOQ, or at least a 4-fold rise if baseline is ≥ LLOQ. The noninferiority of SRR in children receiving mRNA-1273 booster dose will be considered demonstrated if the lower bound of the 95% CI of the SRR difference is > -10% based on the noninferiority margin of 10%.

Booster dose primary immunogenicity objective for an age group in Part 2 will be considered to be met if the noninferiority in the age group compared with the young adults (≥18 to 25 years of age) is demonstrated based on both coprimary endpoints.

Part 3:

For Part 3 primary series primary immunogenicity analysis of Ab GM in children 6 years to < 12 years of age receiving mRNA-1273 25 µg which is half of the 50 µg dose level

used in Part 2 for the same age group, the GM in children compared with young adults ≥18 to 25 years of age from Study P301 will be assessed using ANCOVA model. The estimated GMT with 95% CI and GMR with 95% CI will also be provided using t-distribution.

For Part 3 third dose primary immunogenicity analysis of GM in children receiving a third mRNA-1273 dose, an ANCOVA model will be performed to assess the difference in the immune response at BD-Day 29 in children receiving mRNA-1273 third dose in Study P204 compared with Day 57 in young adults (≥18 to 25 years of age) receiving mRNA-1273 primary series in Study P301. In the ANCOVA model, antibody values at BD-Day 29 in P204 children and values at Day 57 in P301 young adults will be a dependent variable, and a group variable (children in Study P204 and adults in Study P301) will be the fixed effect.

The P301 comparator in SAP for Part 3 immunogenicity analysis is young adults ≥18 to 25 years of age instead of protocol P301 comparator ≥18 years of age, because the originally planned hypothesis testing in protocol for part 3 will not be performed due to the small number of participants enrolled in Part 3, which is insufficient to power the hypothesis testing. All the immunogenicity analyses for Part 3 will be descriptive. In these descriptive analyses, the comparator will be young adults ≥18 to 25 years of age from P301 instead of ≥18 years of age to be consistent with the comparator group in immunogenicity analyses in part 1 and part 2 of the study.

The GMT will be estimated by the GLSM from the model and its corresponding 95% CI will be provided for each group. The GMR for children in Study P204 with respect to adults in Study P301 will be estimated by the ratio of GLSM from the model and the corresponding 95% CIs will be provided. The 95% CI for GMR will be used to assess the between-group difference in immune response at BD-Day 29 in children in Study P204 compared with Day 57 following the primary vaccine series in young adults in Study P301.

For Part 3 third dose primary immunogenicity analysis of seroresponse in children receiving a third dose of mRNA-1273, the SRR with (1-alpha) CI (using Clopper-Pearson method) will be summarized, where the 1-alpha can be 95% depending on the alpha level of 0.05. The SRR difference with (1-alpha)% CI (using Miettinen-Nurminen score method) to compare post-third dose SRR at BD-Day 29 in children in Study P204 with the primary series SRR at Day 57 (28 days after Dose 2) in young adults (>=18 to 25 years of age) in Study P301 will be computed.

6.4.3. Secondary Analysis of Antibody-Mediated Immunogenicity Endpoints

In the booster dose analysis for Part 1 and Part 2, the noninferiority of secondary endpoints will be assessed and tested using the same method as primary series of mRNA-1273 in part 1 open-label phase and part 2 blinded phase.

6.4.4. Exploratory Analysis of Antibody-Mediated Immunogenicity Endpoints

For each group applicable, the following evaluations will be performed at each time point at which blood samples are collected for immunogenicity antibody tests against SAS-CoV-2 prototype or variants of interest as applicable.

- GM level of SARS-CoV-2-specific Ab levels with corresponding 95% CI will be provided at each time point (e.g., Baseline [Pre-dose 1], Day 57, Day 209, Pre-booster/third dose, and BD-Day 29). The 95% CIs will be calculated based on the t-distribution of the log-transformed values then back transformed to the original scale for presentation. GM level will be plotted at each timepoint using boxplot. The following descriptive statistics will be also provided at each time point: the number of subjects (n), median, minimum and maximum.
- GM fold-rise of SARS-CoV-2-specific Ab levels with corresponding 95% CI will be provided at each timepoint over baseline (pre-dose 1) level, and post-booster/third dose timepoint over pre-dose 1 level and pre-booster/third dose level. The 95% CIs will be calculated based on the t-distribution of the log-transformed values then back transformed to the original scale for presentation. The following descriptive statistics will be also provided at each time point: the number of subjects (n), median, minimum and maximum.
- Proportion of subjects with seroresponse due to vaccination relative to pre-dose 1 will be tabulated with 2-sided 95% Clopper-Pearson CIs at each timepoint.

Multiplicity adjustment:

Please refer to SAP section 6.4.2 in Part 1 open-label phase and Part 2 blinded phase for the hierarchical hypothesis testing to adjust mulplicity to to preserve the family-wise Type I error rate (alpha = 0.05) in part 1 open-label phase and part 2 blinded phase.

The hypothesis testing for the two coprimary endpoints (geometric mean titer [GMT] and SRR) for the primary series of mRNA-1273 in part 2 blinded phase was completed and statistically significant based on data snapshot dated 10 Nov 2021 for 6-<12 years age

group, and was also statistically significant based on data snapshot dated 21 Feb 2022 for 2-<6 years and 6 months -<2 years age group for pseudovirus neutralizing antibody. Thus the alpha level of 0.05 may be passed to Part 2 booster dose analysis hypothesis testing.

In booster phase, the hypothesis testing for the two coprimary endpoints after BD of mRNA-1273 will be tested first at alpha level of 0.05. The alpha 0.05 is preserved for the hypothesis testing for the booster dose primary immunogenicity endpoint in Part 2, starting in the older age group (6 years to < 12 years of age), then the younger age group (2 years to < 6 years and 6 months to <2 years of age combind, at the same dose level). The testing will continue through the sequence only until an endpoint is not statistically significant (did not meet specified noninferiority success criteria of any primary endpoint) in Part 2, in which case the testing will stop. There will be no hypothesis testing for Part 3 due to enrollment early discontinuation, and thus no type I error will be used in Part 3.

6.5. Efficacy Analysis

Exploratory analyses of incidence rates in COVID-19, SARS-CoV-2 infection, and asymptomatic infection will be performed using mITT1 Set. The mITT1 Set for the long-term analysis will be used for the incidence rate analysis in the long term including both the blinded and open-label phases; the mITT1 Set for the booster dose analysis will be used for the incidence analysis in the booster dose phase, unless otherwise specified. Subjects will be included in the vaccination group as defined in Section 6.1. As protocol amendment 9 was implemented in October 2022, no surveillance was conducted thereafter, and, therefore, no incidence rates will be calculated after October 2022.

6.5.1. Endpoint Definition/Derivation

6.5.1.1.Derivation of SARS-CoV-2 Infection

This is a secondary efficacy endpoint, which is a combination of COVID-19 and asymptomatic SARS-CoV-2 infection for participants with negative SARS-CoV-2 status at baseline (for mRNA-1273 group in long-term analysis), pre-dose 1 of mRNA-1273 (for Placebo-mRNA-1273 group in long-term analysis), or pre-booster dose (for booster dose analysis), the incidence of SARS-CoV-2 infection counted starting 14 days after the second dose of mRNA-1273 in Part 2 open-label phase, and cases counted starting 14 days after the booster dose of mRNA 1273 in booster dose analysis. SARS-CoV-2 infection will be defined in participants with negative SARS-CoV-2 at baseline of each part (pre-dose 1 of mRNA-1273 for long-term analysis or pre-booster dose for booster dose):

- bAb level against SARS-CoV-2 nucleocapsid protein negative (as measured by *Roche Elecsys*) at baseline of each part that becomes positive (as measured by *Roche Elecsys*) post-baseline, OR
- Positive RT-PCR post-baseline.

Derivation of this secondary efficacy endpoint is summarized in Table 1 below.

Table 1. Derivation for SARS-CoV-2 Infection

	Post-baseline assessments		
Baseline SARS-CoV-2 Status	PCR test post baseline	bAb levels against SARS-CoV-2 Nucleocapsid	**Endpoint**: SARS-CoV-2 infection
Negative at Baseline of each part	**Positive** (either at nasal swab test, or at symptom-prompt nasal swab test)		Case
Negative at Baseline of each part		**Positive** (at post-baseline visits) as measured by *Roche Elecsys*	Case

The date of documented infection will be the earlier of:

- Date of positive post-baseline RT-PCR result, or
- Date of positive serology test result based on bAb specific to SARS-CoV-2 nucleocapsid

In long-term analysis (including Part 2 Open-Label Phase), SARS-CoV-2 infection cases will be counted starting 14 days after the second injection of mRNA-1273, i.e. date of documented infection - date of the 2nd injection ≥ 14. SARS-CoV-2 infection cases will also be summarized based on tests performed at least 14 days after first dose of IP.

In booster dose analysis, SARS-CoV-2 infection cases will be counted starting 14 days after the booster dose of mRNA-1273, i.e. date of documented infection ‑ date of the booster injection ≥ 14.

6.5.1.2.Derivation of Asymptomatic SARS-CoV-2 Infection

This is a secondary efficacy endpoint: the incidence of asymptomatic SARS-CoV-2 infection measured by RT-PCR and/or serology tests obtained at post-baseline visits counted starting 14 days after the second injection of mRNA-1273 in Part 2 open-label

Phase, and cases counted starting 14 days after the booster dose of mRNA 1273 in booster dose analysis, in participants with negative SARS-COV-2 status at baseline of each part.

Asymptomatic SARS-CoV-2 infection is identified by absence of symptoms and infections as detected by RT-PCR or serology tests. Specifically:

- Absent of COVID-19 symptoms
- AND at least one from below:
    - bAb level against SARS-CoV-2 nucleocapsid protein negative (as measured by Roche Elecsys) at baseline of each part that becomes positive (as measured by Roche Elecsys) post-baseline, OR
    - Positive RT-PCR test post-baseline (at scheduled or unscheduled/illness visits)

The date of documented asymptomatic infection is the earlier date of positive serology test result based on bAb specific to SARS-CoV-2 nucleocapsid due to infection, or positive RT-PCR at scheduled visits, with absence of symptoms.

6.5.1.3. Derivation of CDC Case Definition of COVID-19

This is a secondary efficacy endpoint: the incidence of CDC Case Definition of COVID-19 starting 14 days after the second dose of mRNA-1273 in Part 2 open-label phase, and cases counted starting 14 days after the booster dose of mRNA 1273 in booster dose analysis. COVID-19 is defined as symptomatic disease based on the criteria specified in table listed below. Cases are defined as participants meeting clinical criteria based on both symptoms for COVID-19 and positive RT-PCR test results.

While Part 2 is still blinded for any age group, surveillance for COVID-19 symptoms will be conducted via biweekly telephone calls or eDiary. Subjects reporting CDC Case Definition of COVID-19 symptoms, as defined in Section 7.3.2 of the protocol, will be arranged an illiness visit to collect a nasal swab for SARS-CoV-2.

Once the trial is unblinded for all age groups and thus no placebo comparator group is available going forward, COVID-19 surveillance will be discontinued, and COVID-19 cases will be reported under standard AE reporting per SoA only.

For this efficacy endpoint, a CDC Case Definition of COVID-19 case will be identified as a positive post-baseline RT-PCR test result, together with eligible symptoms, i.e. a positive PCR result of the eligible symptoms summarized below.

Derivation for CDC Case Definition of COVID-19

	COVID-19
Post-baseline PCR results	Positive, **AND**
Systemic Symptoms	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
Respiratory symptoms	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).

6.5.1.4.Derivation of COVID-19 (P301 Primary Definition)

This is a secondary efficacy endpoint: the incidence of P301 primary definition of COVID-19 starting 14 days after the second dose of mRNA-1273 in Part 2 open-label phase, and cases counted starting 14 days after the booster dose of mRNA 1273 in booster dose analysis.

The P301 primary definition of COVID-19 is defined by the following criteria:

- At least TWO of the following systemic symptoms: Fever (≥ 38ºC/≥ 100.4ºF), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s), OR
- The participant must have experienced at least ONE of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, OR clinical or radiographical evidence of pneumonia; AND
- At least one positive RT-PCR test for SARS CoV-2

The date of documented COVID-19 (P301 Primary Definition) will be the later date of :

- Date of the positive RT-PCR test (prompt by symptom)
- Date of eligible symptom(s), defined as earliest of
  - Respiratory symptom: earliest date of an eligible respiratory symptom is reported
  - Systemic symptoms: earliest date of the eligible systemic symptoms are reported

and the two dates should be within 14 days of each other.

6.5.2. Analysis Method

The number and percentage of subjects who had an event will be summarized in the mITT1 Set for the long-term analysis and booster dose phase anlaysis

The incidence rate will be provided by age and vaccination group if applicable, calculated as the number of cases divided by the total person-time. The 95% CI of the incidence rate will be calculated using the exact method (Poisson distribution) and adjusted by person-time.

Person-time is defined as the total time from date of the 1st dose of each part to the date of event, dose date in next part, last date of study participation, censoring time, or efficacy data cutoff date, whichever is earlier.

Incidence rate will also be analyzed by time period or by calendar month.

6.5.3. Sensitivity Analysis

Sensitivity analysis for these efficacy endpoints may be performed with the same methods described above based on the FAS, and with cases counted starting at different time points as applicable.

For the sensitivity analysis of efficacy endpoints in the long-term analysis and booster dose analysis, in addition to the efficacy endpoint COVID-19 (CDC Case Definition) and secondary case (P301 Primary Definition) COVID-19 based on eligible symptoms and confirmed positive RT-PCR results (central lab or local diagnostic test) originally defined in SAP, a sensitivity analysis using efficacy endpoint COVID-19 (CDC Case Definition) and secondary case (P301 Primary Definition) COVID-19 based on both RT-PCR results and other COVID-19 test results including home antigen tests will also be derived. Specifically, each COVID-19 case will be based on eligible symptom(s) and all positive COVID-19 test results including RT-PCR (central lab or local diagnostic test) and (home) antigen test results (refer to section 6.5.1. for the derivation of COVID-19 cases in SAP for Part 1 open-label phase and Part 2 blinded phase)

6.5.4. Exploratory Analysis of SARS-CoV-2 Exposure and Symptoms

SARS-CoV-2 reported exposure history and symptoms assessment will be assessed during the study.

SARS-CoV-2 reported exposure history and symptoms assessment will be provided in a listing for Part 2 Open-label Phase and booster dose Analysis separately as applicable.

6.6. Interim Analysis

Please refer to SAP for Part 1 open-label phase and Part 2 blinded phase

6.7. Final Analysis

The final analysis of all applicable endpoints will be performed after all participants have completed all planned study procedures. Results of this analysis will be presented in a final CSR, including individual listings.

7. References

Department of Health and Human Services (DHHS), Food and Drug Administration, Center for Biologics Evaluation and Research (US). Guidance for industry: Toxicity

grading scale for healthy adult and adolescent volunteers enrolled in preventative vaccine clinical trials. September 2007 [cited 2019 Apr 10] [10 screens].

Available from:
https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/ucm091977.pdf.List of Appendices

8. List of Appendices

8.1. Appendix A Standards for Safety and Immunogenicity Variable Display in TFLs

Continuous Variables: The precision for continuous variables will be based on the precision of the data itself. The mean and median will be presented to one decimal place more than the original results; the SD will be presented to two decimal places more than the original results; the minimum and maximum will be presented to the same precision as the original results.

Categorical Variables: Percentages will be presented to 1 decimal place.

8.2. Appendix B Analysis Visit Windows for Safety and Immunogenicity Analysis

Safety and Immunogenicity Analysis will be summarized using the following analysis visit window for post injection assessments:

Step 1: If the safety and immunogenicity assessments are collected at scheduled visit, i.e. nominal scheduled visit, the data collected at scheduled visit will be used.

Step 2: If the safety and immunogenicity assessments are not collected at the scheduled visit, assessments collected at unscheduled visit will be used using the analysis visit windows described in Table 4 below.

If a subject has multiple assessments within the same analysis visit, the following rule will be used:

- If multiple assessments occur within a given analysis visit, the assessment closest to the target study day will be used.
- If there are 2 or more assessments equal distance to the target study day, the last assessment will be used.

Table 4. Visit Window

Visit	Target Study Day	Visit Window in Study Day
Nasal Swabs for SARS-CoV-2 for Part 1 and Part 2 Booster mRNA-1273 Dose:		

BD-Day 1	1 (Date of Injection in booster dose Analysis) relative to BD-Day 1	≤1 and VISIT is BD-Day 1
BD-Day 29	29 relative to BD-Day 1	[2, 105]
BD-Day 181	181 relative to BD-Day 1	≥106
Nasal Swabs for SARS-CoV-2 for Part 3 First Two Doses of Primary Series:		
Day 1	1 (Date of First Injection)	1, Pre-first-dose
Day 29 (Month 1)	29 (Date of Second Injection)	[2, 43]
Day 57 (Month 2)	57	≥44
Nasal Swabs for SARS-CoV-2 for Part 3 Third Dose:		
BD-Day 1 (Month 5)	1 (Date of Injection in Thrid Dose Analysis) relative to BD-Day 1	≤1 and VISIT is BD-Day 1
BD-Day 29 (Month 6)	29 relative to BD-Day 1	[2, 105]
BD-Day 181 (Month 11)	181 relative to BD-Day 1	[106, 274]
BD-Day 366 (Month 17)	366 relative to BD-Day 1	≥275
Immunogenicity for Part 1 and Part 2 Booster mRNA-1273 Dose:		
BD-Day 1	1 (Date of Injection in Booster dose Analysis) relative to BD-Day 1	≤1 and VISIT is BD-Day 1
BD-Day 29	29 relative to BD-Day 1	[2, 105]
BD-Day 181	181 relative to BD-Day 1	[106, 274]
BD-Day 366	366 relative to BD-Day 1	≥275
Immunogenicity for Part 3 First Two Doses of Primary Series:		
Day 1	1 (Date of First Injection)	1, Pre-first-dose
Day 57 (Month 2)	57	[44,133]
Immunogenicity for Part 3 Third Dose:		
BD-Day 1 (Month 5)	1 (Date of Injection in Booster dose Analysis) relative to BD-Day 1	≤1 and VISIT is BD-Day 1

BD-Day 29 (Month 6)	29 relative to BD-Day 1	[2, 105]
BD-Day 181 (Month 11)	181 relative to BD-Day 1	[106, 274]
BD-Day 366 (Month 17)	366 relative to BD-Day 1	≥275

8.3. Appendix C Imputation Rules for Missing Prior/Concomitant Medications and Non-Study Vaccinations

Imputation rules for missing or partial medication start/stop dates are defined below:

1. Missing or partial medication start date:
   - If only Day is missing, use the first day of the month, unless:
     - The medication end date is after the date of first injection or is missing AND the start month and year of the medication coincide with the start month and year of the first injection. In this case, use the date of first injection
   - If Day and Month are both missing, use the first day of the year, unless:
     - The medication end date is after the date of first injection or is missing AND the start year of the medication coincide with the start year of the first injection. In this case, use the date of first injection
   - If Day, Month and Year are all missing, the date will not be imputed, but the medication will be treated as though it began prior to the first injection for purposes of determining if status as prior or concomitant.
2. Missing or partial medication stop date:
   - If only Day is missing, use the earliest date of (last day of the month, study completion, discontinuation from the study, or death).
   - If Day and Month are both missing, use the earliest date of (last day of the year, study completion, discontinuation from the study, or death).
   - If Day, Month and Year are all missing, the date will not be imputed, but the medication will be flagged as a continuing medication.

In summary, the prior, concomitant or post categorization of a medication is described in Table 5 below.

Table 5. Prior, Concomitant, and Post Categorization of Medications and Non-study Vaccinations

	Medication Stop Date		
Medication Start Date	**< First Injection Date of IP**	**≥ First Injection Date and ≤ 28 Days After Last Injection**	**≥ 28 Days After Last Injection [2]**
< First injection date of IP [1]	P	P, C	P, C, A
≥ First injection date and ≤ 28 days after last injection	-	C	C, A
> 28 days after last injection	-	-	A

A: Post; C: Concomitant; P: Prior
[1] includes medications with completely missing start date
[2] includes medications with completely missing end date

8.4. Appendix A Imputation Rules for Missing AE dates

Imputation rules for missing or partial AE start dates and stop dates are defined below:

1. Missing or partial AE start date:

   - If only Day is missing, use the first day of the month, unless:
     - The AE end date is after the date of first injection or is missing AND the start month and year of the AE coincide with the start month and year of the first injection. In this case, use the date and time of first injection, even if time is collected.
   - If Day and Month are both missing, use the first day of the year, unless:

- The AE end date is after the date of first injection or is missing AND the start year of the AE coincides with the start year of the first injection. In this case, use the date of first injection

- If Day, Month and Year are all missing, the date will not be imputed. However, if the AE end date is prior to the date of first injection, then the AE will be considered a pre-treatment AE. Otherwise, the AE will be considered treatment-emergent.

2. Missing or partial AE end dates will not be imputed.

8.5. Appendix E: Schedule of Assessments for Placebo Recipient Cross-Over Vaccination with mRNA-1273 if any COVID-19 Vaccine is Authorized or Licensed for Participant's Age Group[1]

Schedule of Assessments for Placebo Recipient Cross-Over Vaccination	Cross-Over D1	D29 (+ 7)[2]	D36 (+ 3)	D57 (+ 7)	Remainder of Study Visits
Days Since Most Recent Injection		28	7	28	
Study injection (including 30-minute post-dose observation period)	X	X			
Safety follow-up call			X	X	
Pregnancy test[3]	X	X			
Recording of unsolicited AEs	X	X	X	X	
Recording of MAAEs and concomitant medications relevant to or for the treatment of the MAAE	X	X	X	X	X
Recording of SAEs and concomitant medications relevant to or for the treatment of the SAE	X	X	X	X	X
Recording of AESIs (eg, MIS-C and myocarditis and/or pericarditis)	X	X	X	X	X

Abbreviations: AE = adverse event; AESI = adverse event of special interest; COVID-19 = coronavirus disease 2019; D = day; MAAE = medically attended adverse event; MIS-C = multisystem inflammatory syndrome in children; SAE = serious adverse event.

1. Authorized or licensed in participant's age group.
2. Refer to Protocol Section 6.1.1 for individual participant criteria for delay of study vaccination.
3. Pregnancy test prior to study injections on D1 and D29 will be a point-of-care urine test and will be performed if deemed appropriate by the investigator. At the discretion of the investigator, a pregnancy test either via blood or point-of-care urine test can be performed at any time during the study.

8.6. Appendix F: Schedule of Assessments for Optional Booster Doses with mRNA-1273 for Parts 1 and 2, Study Arms 1 Through 9 under Protocol Amendment 7

Visit Number	BD-1	BD-2	BD-2A	BD-3			BD-4	BD-5	BD-6
Type of Visit	C	SC	C	C	SFU		C	SC	C
					eDiary	SC			
Study Visit Day	BD-D1[1]	7 days after BD-D1 (BD-D8)	14 days after BD-D1 (Sub-Cohort E only and optional) BD-D15	BD-D29	Every 4 weeks BD-D43 – BD-D155	Every 4 weeks BD-D57 – BD-D169	BD-D181	270 days after BD-1 (BD-D271)	BD-D366
Window Allowance (Days)	0	+ 3	+ 3	-3/+14	± 3	± 3	-3/+14	+ 3	-3/+14
Days Since Most Recent Vaccination	0	7	14	28			180	270	365
Confirm informed consent /assent form booster addendum signing	X								
Physical examination[2]	X			X			X		X
Pregnancy testing[3]	X								
Immunogenicity Assessment									
Pre-booster blood for immunologic analysis[4] (or CMI with exploratory serology, as applicable) [5]	X								
Post-booster blood for immunologic analysis (or CMI with exploratory serology, as applicable) [5]			X	X			X		X
Dosing									
Study injection (including 30-minute post-dosing observation period[6])	X								
Unscheduled Visits[7]	X	X	X	X	X	X	X	X	X

Visit Number	BD-1	BD-2	BD-2A	BD-3			BD-4	BD-5	BD-6
Type of Visit	C	SC	C	C	SFU		C	SC	C
					eDiary	SC			
Study Visit Day	BD-D1[1]	7 days after BD-D1 (BD-D8)	14 days after BD-D1 (Sub-Cohort E only and optional) BD-D15	BD-D29	Every 4 weeks BD-D43 – BD-D155	Every 4 weeks BD-D57– BD-D169	BD-D181	270 days after BD-1 (BD-D271)	BD-D366
Window Allowance (Days)	0	+ 3	+ 3	-3/+14	± 3	± 3	-3/+14	+ 3	-3/+14
Days Since Most Recent Vaccination	0	7	14	28			180	270	365
Nasal swab[8]	X			X			X		
Safety Assessments									
Follow-up safety call[9]		X						X	
eDiary activation for recording solicited ARs (7 days)[10]	X								
Review of eDiary data[10]		X		X					
Recording of unsolicited AEs, concomitant medications and nonstudy vaccinations	X	X	X	X					
Recording of AE leading to withdrawal and concomitant medications relevant for AE leading to withdrawal	X	X	X	X	X	X	X	X	X
Recording of SAEs, AESI and MAAEs and concomitant medications relevant to or for the treatment of the SAE, AESI or MAAE[11]	X	X	X	X	X	X	X	X	X

Abbreviations: AE = adverse event; AESI = adverse event of special interest; AR = adverse reaction; BD = booster dose; C = clinic visit; CMI = cell-mediated immunity; COVID-19 = coronavirus disease 2019; D = day; eDiary = electronic diary; FDA = Food and Drug Administration; MAAE = medically attended AE;

mRNA = messenger RNA; RT-PCR = reverse transcriptase polymerase chain reaction; SAE = serious adverse event; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SC = safety (phone) call; SFU = safety follow up.

Note: In accordance with FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency (DHHS 2020), investigators may convert study site visits to home visits or telemedicine visits with the approval of the Sponsor.

1. A BD may be administered to Part 1 participants (all ages) and 6 to < 12 year old Part 2 participants provided there are no current contraindications for further dosing. A participant who is currently in the Convalescent Period may come in for a BD-1 visit and receive a BD as long they are at least 90 days from initial diagnosis of COVID-19. Applicable participants will be offered a booster at least 6 months (Participants in part 1 and participants 6 to < 12 year old in Part 2) after Dose 2.
2. Symptom-directed physical examination will be performed at the BD-D1. On dosing day before injection, the arm receiving the injection should be examined and the associated lymph nodes should be evaluated. At visits BD-3 (BD-D29), BD-4 (BD-D181) and BD-6 (BD-D366), a symptom-directed physical examination may be performed at the discretion of the investigator. Any clinically significant finding identified during a study visit should be reported as a MAAE. An oral or tympanic temperature should be taken on the day of injection (BD-D1). Participants who are febrile (body temperature ⩾ 38.0°C/100.4°F) before dosing (BD-D1) must be rescheduled to receive the injection. Afebrile participants with minor illnesses can be vaccinated at the discretion of the investigator.
3. Pregnancy test at BD- D1 before the booster dose injection will be a point-of-care urine test and will be performed if deemed appropriate by the investigator. At the discretion of the investigator, a pregnancy test either via blood or point-of-care urine test can be performed at any time during the study.
4. Sample should be collected prior to dosing on BD-D1.
5. Selected subgroups only; for details, see Appendix G. Participants in sub-Cohort E original mRNA-1273 will have a blood sample for CMI and exploratory serology
6. Post-dosing, participants will have a 30-minute observation period. If any concerning symptoms occur, investigator may check vital signs during this period (however, no routine vital signs necessary after vaccination, except temperature as per 30-minute eDiary, if no concerning symptoms).
7. An unscheduled visit may be prompted by reactogenicity issues or new or ongoing AEs.
8. The nasal swab sample must be collected prior to injection at the BD-1 visit.
9. Trained study personnel will call all participants to collect information relating to any unsolicited AEs, MAAEs (including any signs and symptoms of COVID-19), AESI, AEs leading to withdrawal, SAEs, information on concomitant medications associated with those events, and any nonstudy vaccinations.
10. Age at time of enrollment determines which eDiary the participant will use. Diary entries will be recorded by the participant at approximately 30 minutes after injection while at the study site with instruction provided by study staff. Study participants will continue to record entries in the eDiary each day after they leave the study site, preferably in the evening, on the day of injection and for 6 days following injection. If a solicited local or systemic AR continues beyond Day 7 after vaccination, the participant will be prompted to capture details of the solicited local or systemic AR in the eDiary until the AR resolves; capture of details of ARs in the eDiary should not exceed 28 days after vaccination. Adverse reactions recorded in eDiaries beyond Day 7 should be reviewed either via telephone call or at the following study visit. Review of eDiary will occur on BD-D8 and BD-D29.
11. All concomitant medications relevant to or for the treatment of an SAE, AESI, or MAAE will be recorded from screening through the final visit. Non-study COVID-19 vaccines will be recorded through EOS.

8.7. Appendix G: Phlebotomy Schedule for Participants Opting for Booster Dose with mRNA-1273 under Amendment 7 by Part and Age Group

		BD-Day 1	Post-booster Blood Samples
Part 1 participants			
6 - < 12 years[1]	Study Arm 1	X	BD-Day 29 for immunogenicity
	Study Arm 2	X	None
2 to < 6 years[1]	Study Arm 3	X	None
	Study Arm 4	X	None
	Study Arm 7	X	BD-Day 29 for immunogenicity
6 months to < 2 years[1]	Study Arm 5	X	BD-Day 29 for immunogenicity
Part 2 participants			
Part 2, 6 to <12 years[1,2]			
	Sub-Cohort A	X	None
	Sub-Cohort B	X	None
	Sub-Cohort C	X	BD-Day 29 for immunogenicity
	Sub-Cohort D	X	Enrolled 8/11/21-8/13/21 (~ 600) - BD-Day 29 Enrolled 8/14/21 -8/17/21 (~600) - BD-Day 181 Enrolled August 8/18-8/21 (~600) - BD-Day 366 Enrolled after 8/21/21: None
	Sub-Cohort E[3,5]	X	(Optional BD-Day 15[4]), BD-Day 181

Abbreviations: BD = booster dose.
[1] Age at time of enrollment
[2] Participants who were 5 years old at enrollment but turned 6 years old prior to booster dose will only require a BD-Day1 blood draw.
[3] Participants who originally received placebo will not require any post-booster dose blood draws and will only have one blood draw on BD-Day 1 for immunogenicity.
[4] BD-Day 15 is optional for participants in Sub-Cohort E.
[5] CMI samples and exploratory serology for participants originally receiving mRNA-1273.

8.8. Appendix H: Schedule of Assessments for Part 3, Study Arm 14

Visit Number	0	1	2	3	4	5			6	6A	6B			7	8
Type of Visit	C	C	TMV	C	TMV	C	SFU		C	TMV	C	SFU		C	C
Month Time Point		M0		M1		M2	eDiary	SC	M5		M6	eDiary	SC	M11	M17
Study Visit Day	D-28 to D-1 (Screening)[1]	D1 (Baseline)	D8	D29[2]	D36[2]	D57[2, 3]	Every 4 weeks D71 – D183[2, 4]	Every 4 weeks D85– D197[2,5]	D149 (BD-D1)	D156 (BD-D8)	D177 (BD-D29)	Every 4 weeks D191 (BD-D43)– D303 (BD-155)[2,4]	Every 4 weeks D205 (BD-D57)– D317 BD-D169)[2,5]	D329 (BD -D181)[2, 5]	D514 (BD-D366)
Window Allowance (Days)	-	-	+ 3	+ 7	+ 3	+ 7	± 3	± 3	± 28	+ 3	+7	± 3	± 3	± 14	± 14
Days Since Most Recent Injection	-	0	7	28	7	28	-	-	120/0	127/7	148/28	-	-	305/180	485/365
Informed consent/assent form, demographics, concomitant medications, medical history	X														
Review of inclusion and exclusion criteria	X	X							X						
Physical examination including body temperature, length/height, weight, and BMI[6]	X	X		X		X			X					X	X
Pregnancy test[7]	X	X		X					X						
Randomization		X													
Study injection (including 30-minute post-dose observation period)		X		X					X						
Blood sample for vaccine immunogenicity (Part 3)[8,9]		X				X			X[9]		X			X[10]	X[11]
Nasal swab sample for SARS-CoV-2[12]		X		X		X			X		X			X	X
Unscheduled visit[13]			X	X	X	X	X	X	X	X	X	X	X	X	X

Visit Number	0	1	2	3	4	5			6	6A	6B			7	8
Type of Visit	C	C	TMV	C	TMV	C	SFU		C	TMV	C	SFU		C	C
Month Time Point		M0		M1		M2	eDiary	SC	M5		M6	eDiary	SC	M11	M17
Study Visit Day	D-28 to D-1 (Screening)[1]	D1 (Baseline)	D8	D29[2]	D36[2]	D57[2, 3]	Every 4 weeks D71 – D183[2, 4]	Every 4 weeks D85– D197[2,5]	D149 (BD-D1)	D156 (BD-D8)	D177 (BD-D29)	Every 4 weeks D191 (BD-D43)– D303 (BD-155)[2,4]	Every 4 weeks D205 (BD-D57)– D317 BD-D169)[2,5]	D329 (BD -D181)[2, 5]	D514 (BD-D366)
Window Allowance (Days)	-	-	+ 3	+ 7	+ 3	+ 7	± 3	± 3	± 28	+ 3	+7	± 3	± 3	± 14	± 14
Days Since Most Recent Injection	-	0	7	28	7	28	-	-	120/0	127/7	148/28	-	-	305/180	485/365
eDiary activation for recording solicited ARs (7 days)[15]		X		X					X						
Review of eDiary data			X		X					X					
Follow-up safety telephone calls[16]								X					X		
Recording of unsolicited AEs		X	X	X	X	X			X	X	X				
Recording of MAAEs, SAEs, and AESIs (eg, MIS-C, myocarditis/pericarditis) and concomitant medications and procedures relevant to or for the treatment of the MAAE, AESI and SAE[17]		X	X	X	X	X	X		X	X	X	X		X	X
Recording of concomitant medications and procedures and nonstudy vaccinations[18]		X	X	X	X	X			X	X	X				
Study completion															X

Abbreviations: AE = adverse event; AESI = adverse event of special interest; AR = adverse reaction; BD = booster (third) dose; BMI = body mass index; C = clinic visit; COVID-19 = coronavirus disease 2019; D = day; eCRF = electronic case report form; EDC = electronic data capture; eDiary = electronic diary; FDA = Food and Drug Administration; IP = investigational product; IRB = institutional review board; LAR = legally

authorized representative; M = month; MAAE = medically attended adverse event; MIS-C = multisystem inflammatory syndrome in children; RT-PCR = reverse transcriptase polymerase chain reaction; SAE = serious adverse event; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SC = safety (telephone) call; SFU = safety follow-up; TMV = telemedicine visit.

Note: In accordance with FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency (FDA March 2020), investigators may convert study site visits to home visits or telemedicine visits (with the exception of Screening, Day 1, Day 29, and Day 149) with the approval of the Sponsor.

1. Screening Visit and Day 1 may be combined on the same day. Additionally, the Screening Visit may be performed over multiple visits if performed within the 28-day screening window.
2. If the visit for the second dose (Day 29) is disrupted and cannot be completed at Day 29 (+7 days) as a result of the COVID-19 pandemic (self-quarantine or disruption of study site activities following business continuity plans and/or local government mandates for "stay at home" or "shelter in place"), the visit window may be extended to Day 29 + 21 days. When the extended visit window is used, the remaining study visits should be rescheduled to follow the intervisit interval from the actual date of the second dose. Refer to protocol section 6.1.1 for individual participant criteria for delay of study vaccination.
3. All scheduled study visits should be completed within the respective visit windows. If the participant is not able to attend a study site visit as a result of the COVID-19 pandemic (self-quarantine or disruption of study site activities following business continuity plans and/or local government mandates for "stay at home" or "shelter in place"), a telemedicine visit should be conducted in place of the study site visit. The telemedicine visit should encompass all scheduled visit assessments that can be completed remotely, such as assessment for AEs and concomitant medications (eg, as defined in scheduled safety telephone calls). Home visits will be permitted for all nondosing visits, with the exception of Screening, if a participant cannot visit the study site as a result of the COVID-19 pandemic. Home visits must be permitted by the study site IRB and the participant's parent(s)/LAR(s) via informed consent and have prior approval from the Sponsor (or its designee).
4. Safety follow-up via an eDiary questionnaire will be performed every 4 weeks from Day 71 to Day 183 and again from Day 191 to Day 303.
5. Safety follow-up via a safety telephone call will be performed every 4 weeks from Day 85 to Day 197 and again from Day 205 to Day 317.
6. A full physical examination, including body temperature (oral [for participants > 4 years of age] or tympanic [for participants ≤ 4 years of age]), length/height, and weight, will be performed at the Screening Visit or on Day 1. Symptom-directed physical examination will be performed on Day 1, Day 29, Day 57, Day 149, Day 329, and Day 514 and may be performed at other time points at the discretion of the investigator. Body mass index will be calculated only at Screening Visit. Body temperature (oral/tympanic) should be measured on each injection day prior to injection. On each injection day before injection and again 7 days after injection, the injection site should be examined. Any clinically significant finding identified during a study visit should be reported as an MAAE. Participants who are febrile (body temperature ≥ 38.0°C/≥ 100.4°F) before injection on Day 1 Day 29, or Day 149 must have the visit rescheduled within the relevant visit window to receive the injection. Afebrile participants with minor illnesses may be injected at the discretion of the investigator.
7. Pregnancy test at Screening and Day 1 and before the second and third study injection will be a point-of-care urine test and will be performed if deemed appropriate by the investigator. At the discretion of the investigator, a pregnancy test either via blood or point-of-care urine test can be performed at any time during the study.
8. On Day 1, sample must be collected prior to randomization and dosing. If a Day 1 (baseline) blood sample cannot be obtained in Part 3, the participant will be considered either a screen failure due to inability to satisfy inclusion criterion 3 or could be scheduled for rescreening. Participants may be rescreened 1 time. If the participant is rescreened and a blood sample still cannot be obtained, then he/she will be considered a screen failure due to inability to satisfy inclusion criterion 3.

9. On Day 149, sample must be collected prior to dosing.
10. Sub-Cohort F only, see Appendix I for details.
11. Sub-Cohort G only, see Appendix I for details.
12. The nasal swab sample (collected before dosing on injection day) will be used to ascertain the presence of SARS-CoV-2 via RT-PCR.
13. An unscheduled visit may be prompted by reactogenicity issues, or new or ongoing AEs.
14. A convalescent visit may be scheduled approximately 28 days (+7 days) after diagnosis of COVID-19 if there are any doubts about initial diagnosis (at investigator's discretion). At this visit, a blood sample for potential immunologic assessment of SARS-CoV-2 infection will be collected.
15. At each injection visit, participants' parent(s)/LAR(s) will record data into the eDiary starting approximately 30 minutes after injection under the supervision of the study site staff to ensure successful entry of assessment. Participants' parent(s)/LAR(s) will continue to record entries in the eDiary after they leave the study site, preferably in the evening and at the same time each day, on the day of injection and for 6 days following injection. If a solicited local or systemic AR continues beyond Day 7 after vaccination, the participant's parent(s)/LAR(s) will be prompted to capture details of the solicited local or systemic AR in the eDiary until the AR is resolved or the next IP injection occurs, whichever occurs first. Capturing details of ARs in the eDiary should not exceed 28 days after each vaccination. Adverse reactions recorded in eDiaries beyond Day 7 should be reviewed by the study site staff either during the next scheduled telephone call or at the next study site visit.
16. Trained study site personnel will call all participants to collect information relating to any MAAEs, SAEs, AEs leading to study withdrawal and information on concomitant medications associated with those events and any nonstudy vaccinations. In addition, study personnel will collect information on known participant exposure to someone with known COVID-19 or SARS-CoV-2 infection and on any COVID-19 symptoms the participant may experience.
17. All concomitant medications and procedures and nonstudy vaccinations will be recorded through 28 days after each injection; all concomitant medications relevant to or for the treatment of an SAE, AESI or MAAE will be recorded from Day 1 through the final visit (Day 514).
18. In addition to MIS-C and myocarditis and/or pericarditis, a list of AESIs pertinent to this study may be referenced in the list of AESIs that is maintained by the Sponsor and provided to each investigator. All SAEs and AESIs will be reported to the Sponsor or designee immediately and in all circumstances within 24 hours of becoming aware of the event via the EDC system. If a site receives a report of a new SAE or AESI from a study participant or receives updated data on a previously reported SAE or AESI and the eCRF has been taken offline, then the site can report this information on a paper SAE or AESI form using the SAE Mailbox, the SAE Hotline, or the SAE Fax line (see protocol section 7.4.11).

8.9. Appendix I: Phlebotomy Schedule for Serology for Part 3

Sub-Cohort	Number of Subjects	Study Visit Day					
		D1[1,2]	D57	D149[1]	D177	D329	D514
F	First 150 participants	X	X	X	X	X	
G	Next 150 participants	X	X	X	X		X

Abbreviations: D = day.

[1.] On Day 1, sample must be collected prior to randomization and dosing. On Day 149, sample must be collected prior to dosing.
Note: If a Day 1 (baseline) blood sample cannot be obtained in Part 3, the participant will be considered either a screen failure due to inability to satisfy inclusion criterion 3 or could be scheduled for rescreening. Participants may be rescreened 1 time. If the participant is rescreened and a blood sample still cannot be obtained, then he/she will be considered a screen failure due to inability to satisfy inclusion criterion 3.

8.10. Appendix J: Schedule of Assessments for Optional Booster Doses with mRNA-1273.214 for Previously Unboosted Participants from Part 1 and Part 2 under Protocol Amendment 9

Visit Number	BD-1	BD-2	BD-3	SFU	BD-4
Type of Visit	C	SC	C		C
				SC	
Study Visit Day	BD-D1[1]	7 days after BD-D1 (BD-D8)	BD-D29	Every 4 weeks BD-D57– BD-D169	BD-D181 (EOS)
Window Allowance (Days)	0	+ 3	-3/+14	± 3	-3/+14
Days Since Most Recent Vaccination	0	7	28		180
Confirm informed consent /assent form booster addendum signing	X				
Physical examination[2]	X		X		X
Pregnancy testing[3]	X				
Immunogenicity Assessment					

Visit Number	BD-1	BD-2	BD-3	SFU	BD-4
Type of Visit	C	SC	C		C
				SC	
Study Visit Day	BD-D1[1]	7 days after BD-D1 (BD-D8)	BD-D29	Every 4 weeks BD-D57– BD-D169	BD-D181 (EOS)
Window Allowance (Days)	0	+ 3	-3/+14	± 3	-3/+14
Days Since Most Recent Vaccination	0	7	28		180
Pre-booster blood for immunologic analysis[4]	X				
Dosing					
Study injection (including 30-minute post-dosing observation period[5])	X				
Unscheduled visits[6]	X	X	X	X	X
Nasal swab[7]	X		X		X
Safety Assessments					
Follow-up safety call[8]		X			
Recording of AE leading to withdrawal and concomitant medications relevant for AE leading to withdrawal	X	X	X	X	X
Recording of SAEs, AESI and MAAEs and concomitant medications relevant to or for the treatment of the SAE, AESI or MAAE[9]	X	X	X	X	X

Abbreviations: AE = adverse event; AESI = adverse event of special interest; AR = adverse reaction; BD = booster dose; C = clinic visit; CMI = cell-mediated immunity; COVID-19 = coronavirus disease 2019; D = day; eDiary = electronic diary; FDA = Food and Drug Administration; MAAE = medically attended AE; mRNA = messenger RNA; RT-PCR = reverse transcriptase polymerase chain reaction; SAE = serious adverse event; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SC = safety (phone) call; SFU = safety follow up.

Note: In accordance with FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency (DHHS 2020), investigators may convert study site visits to home visits or telemedicine visits with the approval of the Sponsor.

1. A BD may be administered to all Part 2 participants provided there are no current contraindications for further dosing and have not received any booster doses outside of the trial. A participant who is currently in the Convalescent Period may come in for a BD-1 visit and receive a BD as long they are at least 90 days from initial diagnosis of COVID-19. Applicable participants will be offered a booster at least 3 months after Dose 2.
2. Symptom-directed physical examination will be performed at the BD-D1. On dosing day before injection, the arm receiving the injection should be examined and the associated lymph nodes should be evaluated. At visits BD-3 (BD-D29), BD-4 (BD-D181) and BD-6 (BD-D366), a symptom-directed physical examination may be performed at the discretion of the investigator. Any clinically significant finding identified during a study visit should be reported as a MAAE. An oral or tympanic temperature should be taken on the day of injection (BD-D1) prior to dosing. Participants who are febrile (body temperature ≥ 38.0°C/100.4°F) before dosing (BD-D1) must be rescheduled to receive the injection. Afebrile participants with minor illnesses can be vaccinated at the discretion of the investigator.
3. Pregnancy test at BD-D1 before the booster dose injection will be a point-of-care urine test and will be performed if deemed appropriate by the investigator. At the discretion of the investigator, a pregnancy test either via blood or point-of-care urine test can be performed at any time during the study.
4. Sample should be collected prior to dosing on BD-D1.
5. Post-dosing, participants will have a 30-minute observation period. If any concerning symptoms occur, investigator may check vital signs during this period (however, no routine vital signs necessary after vaccination if no concerning symptoms).
6. An unscheduled visit may be prompted by reactogenicity issues, or new or ongoing AEs.
7. The nasal swab sample must be collected prior to injection at the BD-1 visit.
8. Trained study personnel will call all participants to collect information relating to any MAAEs (including any signs and symptoms of COVID-19), AESI, AEs leading to withdrawal, SAEs, information on concomitant medications associated with those events, and any non-study vaccinations. Any solicited AR or AE that meets any of the following criteria must be entered into the participant's eCRF:1) An Event, including local or systemic AR, that results in a visit to a healthcare practitioner (HCP) (MAAE). 2) An Event, including local or systemic AR, leading to the participant withdrawing from the study or the participant being withdrawn from the study by the Investigator (AE leading to withdrawal) 3) An Event, including local or systemic AR, that otherwise meets the definition of an SAE. 4) Any AESI.
9. All concomitant medications relevant to or for the treatment of an SAE, AESI, or MAAE will be recorded from screening through the final visit. Non-study COVID-19 vaccines will be recorded through EOS.