PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

SPIKEVAX®

COVID-19 mRNA vaccine

Dispersion for intramuscular injection

Multidose Vial, 0.1 mg / mL

Active Immunizing Agent

Omicron KP.2 variant

ATC Classification: J07BN01 (COVID-19, RNA-based Vaccine)

SPIKEVAX (COVID-19 mRNA vaccine) is indicated for:

- Active immunization against coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus in individuals 6 months of age and older.

SPIKEVAX has been issued marketing authorization with Terms and Conditions that need to be met by the Market Authorization Holder to ascertain the continued quality, safety and effectiveness of the vaccine.

Patients should be advised of the nature of the authorization. For further information for SPIKEVAX (COVID-19 mRNA vaccine) please refer to Health Canada's COVID-19 vaccines and treatments portal.

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Date of Initial Authorization:
September 12, 2023

Date of Revision:
September 17, 2024

Submission Control Number: 287904

RECENT MAJOR LABEL CHANGES

7 WARNINGS AND PRECAUTIONS	JAN 2024
6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING	JULY 2024

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

SPIKEVAX (COVID-19 mRNA vaccine) is indicated for active immunization against coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus in individuals 6 months of age and older.

The safety and effectiveness of SPIKEVAX for individuals 6 months of age and older is inferred from several studies of a primary series and booster dose of SPIKEVAX Bivalent (Original/Omicron BA.1) in individuals 6 months to 5 years of age, a booster dose study of SPIKEVAX Bivalent (Original/Omicron BA.1) in individuals >18 years of age, a booster dose study of SPIKEVAX XBB.1.5 in individuals > 18 years of age, as well as data from studies which evaluated the primary series and booster vaccination with SPIKEVAX (elasomeran).

The National Advisory Committee on Immunization (NACI) provides additional guidance on the use of the COVID-19 vaccines in Canada. Please refer to the COVID-19 vaccine: Canadian Immunization Guide and current vaccine statements.

1.1 Pediatrics

The safety and efficacy of SPIKEVAX in individuals under 6 months of age has not yet been established (see ADVERSE REACTIONS, and CLINICAL TRIALS sections).

1.2 Geriatrics

Clinical studies of SPIKEVAX Bivalent (Original/Omicron BA.1) that included participants 65 years of age and older and their data contribute to the overall assessment of safety and effectiveness of SPIKEVAX COVID-19 mRNA vaccine (see ADVERSE REACTIONS and CLINICAL TRIALS sections).

2 CONTRAINDICATIONS

SPIKEVAX is contraindicated in individuals who are hypersensitive to the active ingredient or to any ingredients in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.
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3 SERIOUS WARNINGS AND PRECAUTIONS

At the time of authorization, there are no known serious warnings or precautions associated with this product.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

SPIKEVAX is a dispersion for intramuscular injection that should be administered by a trained healthcare worker.

Individuals ≥ 12 Years of Age: One dose of 50 mcg.

Individuals 5 to 11 Years of Age: One dose of 25 mcg.

Individuals 6 Months to 4 Years of Age:

- Not previously vaccinated: Two (2) doses of 25 mcg each.
- Previously vaccinated with 1 or more doses: One dose of 25 mcg.

Age Range	COVID-19 Vaccination History	Presentation	Vial Cap Colour	Label Colour	Dose(s)	Dose Volume
12 years of age or older	Not previously vaccinated **OR** previously vaccinated	0.1 mg/mL	**Royal Blue**	**Coral Blue**	1 dose: 50 mcg	0.5 mL
5 to 11 years of age	Not previously vaccinated **OR** previously vaccinated	0.1 mg/mL	**Royal Blue**	**Coral Blue**	1 dose: 25 mcg	0.25 mL
6 months to 4 years of age	Not previously vaccinated	0.1 mg/mL	**Royal Blue**	**Coral Blue**	2 doses: 25 mcg	0.25 mL
	Previously vaccinated; *1 or more previous doses*	0.1 mg/mL	**Royal Blue**	**Coral Blue**	1 dose: 25 mcg	0.25 mL

4.2 Recommended Dose and Dosage Adjustment

4.2.1 Vaccination for Individuals 12 Years of Age and Older

A dose of 50 mcg SPIKEVAX is administered intramuscularly. If the individual has been previously vaccinated with a COVID-19 vaccine, SPIKEVAX is administered at least 6 months after receipt of a previous COVID-19 vaccine dose in individuals 12 years of age or older.

4.2.2 Vaccination for Individuals Aged 5 to 11 Years

A dose of 25 mcg SPIKEVAX is administered intramuscularly. If the individual has been previously vaccinated with a COVID-19 vaccine, SPIKEVAX is administered at least 6 months after receipt of a previous COVID-19 vaccine dose individuals 5 through 11 years of age.

4.2.3 Vaccination Schedule for Individuals Aged 6 Months to 4 Years

Children Not Previously Vaccinated
A two-dose series of 25 mcg SPIKEVAX is administered intramuscularly 4 weeks apart in children 6 months to 4 years of age.

Children Previously Vaccinated
In individuals who received 1 or more previous doses of COVID-19 vaccine, SPIKEVAX is administered intramuscularly as one dose of 25 mcg at least 6 months after receipt of the previous dose in individuals 6 months to 4 years of age.

If the child has received only 1 (one) prior dose of a COVID-19 vaccine, SPIKEVAX should be administered to complete the two-dose series.

4.3 Reconstitution

SPIKEVAX must not be reconstituted, mixed with other medicinal products, or diluted. No dilution is required prior to administration.

4.4 Administration

Use aseptic technique for preparation and administration.

Preparation
SPIKEVAX multidose vials are supplied as a frozen dispersion that does not contain preservative. Each vial must be thawed prior to administration.

Vaccination	Presentation	Volume in vial	Number of 0.5 mL doses	Number of 0.25 mL doses
SPIKEVAX	0.1 mg /mL	2.5 mL	5	10

Thaw each vial before use.

Presentation	Vial Cap Colour	Thaw time under refrigeration between 2° to 8°C (36° to 46°F)	Thaw time at room temperature between 15° to 25°C (59° to 77°F)
0.1 mg/mL	**Royal Blue**	• 2 hours *After thawing, let vial stand at room temperature for 15 minutes before administering.*	• 45 minutes

Do not re-freeze vials after thawing.

Swirl the vial gently after thawing and between each withdrawal. Do not shake.

Administration

SPIKEVAX is a white to off-white dispersion. It may contain white or translucent product-related particulates. Visually inspect SPIKEVAX vials for foreign particulate matter and/or discoloration prior to administration. If either of these conditions exists, the vaccine should not be administered.

Administer SPIKEVAX intramuscularly (IM) only. The preferred site is the deltoid muscle of the upper arm, or in infants and young children, the anterolateral aspect of the thigh. A needle length of ≥1 inch should be used as needles <1 inch may be of insufficient length to penetrate muscle tissue in some adults.

Do not inject the vaccine intravascularly, subcutaneously or intradermally.

Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab. Withdraw each dose of vaccine from the vial using a new sterile needle and syringe (preferentially a low dead-volume syringe and/or needle) for each injection. Pierce the stopper preferably at a different site each time.

After Vial Puncture: SPIKEVAX is preservative free. The dose in the syringe should be used as soon as feasible after the vial was first entered (needle-punctured).

Once the vial has been entered, it should be discarded as follows:

- after 24 hours if refrigerated, or
- after 12 hours if stored at room temperature.

Do not refreeze. Thawed vials and filled syringes can be handled in room light conditions.

Any unused vaccine or waste material should be disposed of in accordance with local requirements.

5 OVERDOSAGE

In the case of a suspected vaccine overdose, monitoring of vital functions and symptomatic treatment are recommended. Contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intramuscular injection	Dispersion, (0.1 mg /mL) Each 0.5 mL dose contains 50 mcg of mRNA encoding SARS-CoV-2 spike protein, 5'(m7G-5'-ppp-5'-Gm) cap, 100-nucleotide 3' poly(A) tail of the strain listed below. Multidose vial (2.5 mL)	• Acetic acid • Cholesterol • DSPC (1,2-distearoyl-sn-glycero-3-phosphocholine) • SM-102 (Heptadecan-9-yl 8-((2-hydroxyethyl) (6-oxo-6-(undecyloxy) hexyl) amino) octanoate) • PEG2000-DMG (1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000) • Sodium acetate trihydrate

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
		• Sucrose • Trometamol • Trometamol hydrochloride • Water for injection

Description

Each 0.5 mL dose of SPIKEVAX contains 50 micrograms of mRNA encoding SARS-CoV-2 spike protein. The mRNA encoding spike protein is derived from the Omicron variant KP.2.

SPIKEVAX is provided as a white to off-white, sterile, preservative-free, frozen dispersion for intramuscular injection. SPIKEVAX contains lipid nanoparticle (LNP), comprised of mRNA encoding the pre-fusion stabilized Spike glycoprotein (S) of SARS-CoV-2 virus, and four lipids, formulated with the non-medicinal ingredients listed in Table 1. SPIKEVAX does not contain any preservatives, antibiotics, adjuvants, or human- or animal-derived materials.

SPIKEVAX is supplied in a multi-dose 10R type 1 glass vial. The vial stopper does not contain natural rubber latex. Vials are packaged in a secondary carton containing a total of ten (10) SPIKEVAX vials per carton. The 0.1 mg/mL multi-dose vial is supplied with a royal blue flip-off plastic cap and has a vial label with the strength printed in coral blue.

To help ensure the traceability of vaccines for patient immunization record-keeping as well as safety monitoring, health professionals should record the time and date of administration, quantity of administered dose (if applicable), anatomical site and route of administration, brand name and generic name of the vaccine, the product lot number and expiry date.

7 WARNINGS AND PRECAUTIONS

As with any vaccine, vaccination with SPIKEVAX may not protect all recipients.

Hypersensitivity and Anaphylaxis

Anaphylaxis has been reported in individuals who have received SPIKEVAX (elasomeran). As with all vaccines, appropriate medical treatment, training for immunizers and supervision after immunization should always be readily available in case of a rare anaphylactic event following the administration of this vaccine.

Vaccine recipients should be kept under observation for at least 15 minutes after immunization; 30 minutes is a preferred interval when there is a specific concern about a possible vaccine reaction.

Subsequent doses of the vaccine should not be given to those who have experienced anaphylaxis to an earlier dose of SPIKEVAX.

Cardiovascular

Myocarditis and Pericarditis

Very rare cases of myocarditis and/or pericarditis following vaccination with SPIKEVAX have been reported during post-authorization use. There is an increased risk for myocarditis and pericarditis following vaccination with SPIKEVAX, primarily within 14 days of vaccination and more often in young male adults. These events have been observed more often after the second dose compared to the first dose and less often after subsequent doses.

Available data suggest that the symptoms resolve in most individuals following standard treatment and rest, but information on potential long-term sequelae is not yet available. Some reported cases required intensive care support. Although causality has not been established, fatal events have been very rarely reported. Post-authorization data indicate that myocarditis and pericarditis following vaccination is more commonly of shorter duration and less severe than infectious myocarditis or pericarditis. The decision to administer SPIKEVAX to an individual with a history of myocarditis or pericarditis should take into account the individual's clinical circumstances.

Healthcare professionals are advised to consider the possibility of myocarditis and/or pericarditis in their differential diagnosis if individuals present with chest pain, shortness of breath, palpitations or other signs and symptoms of myocarditis and/or pericarditis following immunization with a COVID-19 vaccine. This could allow for early diagnosis and treatment. Cardiology consultation for management and follow up should be considered. Vaccinees should be instructed to seek immediate medical attention if they develop the signs or symptoms indicative of myocarditis or pericarditis as described above.

Acute Illness

Consideration should be given to postponing immunization in persons with severe febrile illness or severe acute infection. Persons with moderate or severe acute illness should be vaccinated as soon as the acute illness has improved.

Hematologic-Bleeding

As with other intramuscular injections, SPIKEVAX should be given with caution in individuals with bleeding disorders, such as haemophilia, or individuals currently on anticoagulant therapy, to avoid the risk of haematoma following the injection, and when the potential benefit clearly outweighs the risk of administration.

Immune

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the vaccine.

Syncope

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. Procedures should be in place to prevent injury from fainting and manage syncopal reactions.

7.1 Special Populations

7.1.1 Pregnant Women

The safety and efficacy of SPIKEVAX in pregnant women have not yet been established.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/fetal development, parturition, or post-natal development (see NON-CLINICAL TOXICOLOGY).

Individuals who are vaccinated with SPIKEVAX during pregnancy are encouraged to report experienced adverse events by calling 1-866-MODERNA (1-866-663-3762).

7.1.2 Breast-feeding

It is unknown if SPIKEVAX is excreted in human milk. A risk to the newborns/infants cannot be excluded. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for immunization against COVID-19.

7.1.3 Pediatrics

The safety and efficacy of SPIKEVAX in children under 6 months of age have not yet been established.

7.1.4 Geriatrics

Clinical studies of SPIKEVAX Bivalent (Original/Omicron BA.1) that included participants 65 years of age and older and their data contribute to the overall assessment of safety and effectiveness of SPIKEVAX COVID-19 mRNA vaccine (see ADVERSE REACTIONS and CLINICAL TRIALS sections).

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The safety of SPIKEVAX COVID-19 mRNA vaccine for individuals 6 months of age and older is inferred from several studies of a primary series and booster dose of SPIKEVAX Bivalent (Original/Omicron BA.1) in individuals 6 months to 5 years of age, a booster dose study of SPIKEVAX Bivalent (Original/Omicron BA.1) in individuals >18 years of age, a booster dose study of SPIKEVAX XBB.1.5 in individuals > 18 years of age, as well as data from studies which evaluated the primary series and booster vaccination with SPIKEVAX (Original).

Participants 18 Years of Age and Older

The safety of a monovalent booster dose of SPIKEVAX XBB.1.5 was evaluated in a Phase 2/3 open-label study in adult participants (mRNA-1273-P205, Part J). The vaccines were administered as a fifth dose to adults (50 micrograms) who previously received a two-dose primary series and a booster dose of an original COVID-19 vaccine and a booster dose of a bivalent vaccine.

SPIKEVAX XBB.1.5 had a reactogenicity profile similar to prior doses of SPIKEVAX (original) and SPIKEVAX Bivalent Original / Omicron BA.4/5. The most frequently reported adverse reactions after the SPIKEVAX

XBB.1.5 50 mcg booster dose were pain (68.0%), fatigue (44.0%), myalgia (38.0%), headache (34.0%), arthralgia (28.0%), axillary swelling or tenderness (16.0%) and chills (14.0%).

The safety profile of SPIKEVAX Bivalent (Original/Omicron BA.1) in participants ≥ 18 years of age presented below is based on data generated from an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 437 participants received the SPIKEVAX Bivalent (Original/Omicron BA.1) 50 mcg booster dose (mRNA-1273.214, as 25 mcg elasomeran and 25 mcg imelasomeran), and 377 participants received the SPIKEVAX original 50 mcg booster dose (mRNA-1273).

Overall, the frequency of solicited adverse reactions after the SPIKEVAX Bivalent 50 mcg booster dose was similar to that observed following the SPIKEVAX (elasomeran) original 50 mcg booster dose. The most frequently reported adverse reactions after the SPIKEVAX Bivalent 50 mcg booster dose were pain (77.3%), fatigue (54.9%), headache (43.9%), myalgia (39.6%), arthralgia (31.1%) and axillary swelling or tenderness (17.4%). The median duration of local and systemic adverse reactions was 2 days. The most common adverse reactions after the SPIKEVAX original 50 µg booster dose was fatigue (51.4%), headache (41.1%), myalgia (38.6%), and arthralgia (31.7%). The median duration of local and systemic adverse reactions was 2 days.

Overall, after both the SPIKEVAX Bivalent 50 mcg booster dose and the SPIKEVAX original 50 mcg booster dose there was a higher reported rate of solicited adverse reactions in younger age groups. The incidence of pain, erythema, swelling/induration, lymphadenopathy (axillary swelling/tenderness), fatigue, headache, myalgia, arthralgia, and nausea/vomiting was higher in adults 18 to 64 years of age than in those 65 years of age and above (see Table 2, Table 3, Table 4 and Table 5 respectively).

Children and Adolescents 6 to 17 Years of Age

The safety and effectiveness of SPIKEVAX COVID-19 mRNA vaccine for individuals 6 through 17 years of age are inferred from studies of a primary series and booster dose of SPIKEVAX Bivalent (Original/Omicron BA.1) in individuals 6 months to 5 years of age, a booster dose of SPIKEVAX Bivalent (Original/Omicron BA.1) in individuals 18 years of age and older, as well as data from studies which evaluated the primary series and booster vaccination with SPIKEVAX.

Adolescents 12 to 17 Years of Age

Safety data in adolescents (12 to 17 years of age) were collected in an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind clinical trial (Study P203, NCT04649151) conducted in the United States involving 3,726 participants who received at least one dose of SPIKEVAX (elasomeran) (n=2,486) or placebo (n=1,240). Overall, solicited adverse reactions at any dose were reported more frequently among adolescents in the vaccine group than in the placebo group. The most frequently reported adverse reactions in adolescent subjects were pain at the injection site (97.2%), headache (78.4%), fatigue (75.2%), myalgia (54.3%), and chills (49.1%) (see Table 11 and Table 12).

This study transitioned to an open-label Phase 2/3 study in which 1,364 participants 12 years through 17 years of age received a booster dose of SPIKEVAX at least 5 months after the second dose of the primary series. The most common solicited local adverse reactions were pain (91%) and axillary swelling or tenderness (28%). The most common solicited systemic ARs were fatigue (59%), headache (57%), myalgia (40%), chills (31%), and arthralgia (24%).

Children 6 to 11 Years of Age

Safety data in children (6 years to 11 years of age) were collected in an ongoing Phase 2/3 two-part clinical trial (Study P204, NCT04796896) conducted in the United States and Canada. Part 1 is an open-label phase of the trial for safety, dose selection, and immunogenicity involving 380 participants who received at least one dose of SPIKEVAX (0.25 mL, 50 mcg). Part 2 is the placebo-controlled phase for safety, immunogenicity and efficacy and it included 4,002 participants 6 years to 11 years of age who received at least one dose (0.25 mL, 50 mcg) of SPIKEVAX (n=3,007) or placebo (n=995), and 2,988 SPIKEVAX participants and 973 placebo participants had received dose 2. No participants in Part 1 participated in Part 2.

Overall, solicited adverse reactions were reported more frequently among children in the vaccine group than in the placebo group. The most frequently reported adverse reactions in children 6 years to 11 years of age in Part 2 following administration of the primary series were pain at the injection site (94.8%), fatigue (64.5%), headache (54.3%), chills (30.3%) and myalgia (28.2%) (see Table 13 and Table 14).

The study protocol was amended to include an open label booster dose phase that included 1,294 participants 6 years through 11 years of age who received a booster dose of SPIKEVAX at least 6 months after the second dose of the primary series. No additional adverse reactions were identified in the open-label portion of the study.

Children 6 Months to 5 Years of Age

Safety data for SPIKEVAX COVID-19 mRNA vaccine is inferred from Study P306 where SPIKEVAX Bivalent (Original / Omicron BA.1) was evaluated for use in two-dose primary series vaccination (25 mcg). Data were collected in an ongoing Phase 3 open-label clinical trial conducted in the United States. Part 1 included data in 179 participants 6 months through 5 years of age who received at least one dose of SPIKEVAX Bivalent (Original / Omicron BA.1) (Study P306 Part 1, NCT05436834). As of the data cut-off date of December 5, 2022, the median duration of follow-up for safety was 68 days after Dose 2.

Safety data in children (6 months to 5 years of age) were collected in an ongoing Phase 2/3 two-part clinical trial (Study P204, NCT04796896) conducted in the United States and Canada. Part 1 is an open-label phase of the trial for safety, dose selection, and immunogenicity involving 225 participants who received at least one dose of SPIKEVAX (25 mcg). Part 2 is the placebo-controlled phase for safety, immunogenicity and efficacy; at the time of data snapshot (February 21, 2022), this trial involved 6,388 participants 6 months to 5 years of age who received at least one dose (25 mcg) of SPIKEVAX (n=4,792) or placebo (n=1,596) and 4,560 SPIKEVAX participants and 1,499 placebo participants had received dose 2.

In participants 6 months to less than 2 years of age in Part 2 the median follow-up duration was 98.0 days after dose 1 and 68.0 days after dose 2. A total of 1,470 (83.5%) subjects in the SPIKEVAX group and 482 (81.8%) subjects in the placebo group have been followed for 28 days or more after dose 2. A total of 1,138 subjects in the SPIKEVAX group (64.6%) and 368 subjects in the placebo group (62.5%) have been followed for 56 days or more after dose 2. In participants 2 years to less than 6 years of age in Part 2 the median follow-up duration was 103.0 days after dose 1 and 71.0 days after dose 2. A total of 2,713 (89.5%) subjects in the SPIKEVAX group and 892 (88.6%) subjects in the placebo group have been followed for 28 days or more after dose 2. A total of 2,180 subjects in the SPIKEVAX group (71.9%) and 710 subjects in the placebo group (70.5%) have been followed for 56 days or more after dose 2.

Overall, solicited adverse reactions were reported more frequently among children in the vaccine group than in the placebo group. The most frequently reported local and systemic adverse reactions in children 6 months to < 24 months of age in Part 2 following administration of the primary series were irritability/crying (64.3%), pain (46.2%), sleepiness (35.1%) and loss of appetite (32.1%). The most frequently reported local adverse reaction in children 2 years to 5 years of age in Part 2 following administration of the primary series was pain (71.4%). The most frequently reported systemic adverse reactions in children 24 months to ≤ 36 months of age in Part 2 following administration of the primary series were irritability/crying (54.3%), sleepiness (36.0%) and loss of appetite (30.5%) The most frequently reported systemic adverse reactions in children 37 months to 5 years of age in Part 2 following administration of the primary series was fatigue (48.8%).

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another vaccine. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse vaccine reactions in real-world use.

8.2.1 SPIKEVAX XBB.1.5

8.2.1.1 Participants 18 Years of Age and Older

8.2.1.1.1 Booster Dose

Solicited Adverse Reactions

The safety, reactogenicity, and immunogenicity of a monovalent booster dose of SPIKEVAX XBB.1.5 are evaluated in a Phase 2/3 open-label study in adult participants (mRNA-1273-P205, Part J). In this study, 50 participants received a monovalent booster dose of SPIKEVAX XBB.1.5 (50 micrograms), and 51 participants received a dose of an investigational bivalent vaccine (XBB.1.5/Omicron BA.4/5). The vaccines were administered as a fifth dose to adults who previously received a two-dose primary series and a booster dose of an original COVID-19 vaccine and a booster dose of a bivalent vaccine. Participants were followed for a median duration of 20 days.

SPIKEVAX XBB.1.5 had a reactogenicity profile similar to prior doses of SPIKEVAX (original) and SPIKEVAX Bivalent Original / Omicron BA.4/5. There were no Grade 4 local or systemic reactions and no fatal events or serious adverse events in this interim analysis. Reported solicited local and systemic adverse reactions are presented in Table 2 and Table 3 respectively.

Table 2 – Summary of Participants with Solicited Local Adverse Reactions within 7 Days After the Injection by Grade – 3rd Booster Dose: mRNA-1273.815, Participants 18 to 64 (Solicited Safety Set*)

	SPIKEVAX XBB.1.5 Group (mRNA-1273.815) **50 mcg** N=50 n (%)
Pain	
Any grade	34 (68.0)

	SPIKEVAX XBB.1.5 Group (mRNA-1273.815) 50 mcg N=50 n (%)
Grade 3[a]	0 (0)
Axillary swelling/ Tenderness	
Any grade	8 (16.0)
Grade 3[b]	0 (0)
Swelling (Hardness)	
Any grade	5 (10.0)
Grade 3[c]	0 (0)
Erythema (Redness)	
Any grade	2 (4.0)
Grade 3[c]	0 (0)

*Solicited Safety Set: All participants who received a dose and contributed any solicited Adverse Reaction data.
n= # of participants with specified reaction, percentages are based on n/N
N= number of exposed subjects who submitted any data for the event.
[a] Pain - Grade 3: any use of Rx pain reliever/prevents daily activity
[b]Axillary Swelling/Tenderness collected as solicited local adverse reaction (i.e., lymphadenopathy: localized axillary swelling or tenderness ipsilateral to the vaccination arm) - Grade 3: any use of Rx pain reliever/prevents daily activity
[c] Erythema and Swelling/Induration - Grade 3: >100mm/>10cm

Table 3 – Summary of Participants with Solicited Systemic Adverse Reactions within 7 Days After the Injection by Grade – 3rd Booster Dose: mRNA-1273.815, Participants 18 to 64 (Solicited Safety Set*)

	SPIKEVAX XBB.1.5 Group (mRNA-1273.815) 50 mcg N=50 n (%)
Fatigue	
Any grade	22 (44.0)
Grade 3[a]	0 (0)
Myalgia	
Any grade	19 (38.0)
Grade 3[a]	0 (0)
Headache	
Any grade	17 (34.0)
Grade 3[b]	0 (0)
Arthralgia	
Any grade	14 (28.0)
Grade 3[a]	0 (0)
Chills	
Any grade	7 (14.0)
Grade 3[c]	0 (0)
Nausea/vomiting	
Any grade	4 (8.0)
Grade 3[d]	0 (0.0)
Fever	
Any grade	3 (6.0)
Grade 3[e]	1 (2.0)

*Solicited Safety Set: All participants who received a dose and contributed any solicited Adverse Reaction data.
n= # of participants with specified reaction, percentages are based on n/N
N= number of exposed subjects who submitted any data for the event.
[a] Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.
[b] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.
[c] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.
[d] Grade 3 nausea/vomiting: Defined as prevents daily activity, requires outpatient intravenous hydration.
[e] Grade 3 fever: Defined as ≥39.0 – ≤40.0°C / ≥102.1 – ≤104.0°F.

Unsolicited Adverse Events

There were no fatal or serious adverse events and no adverse events of special interest reported in Study P205 Part J. All unsolicited adverse events were grade 1 or grade 2 in severity; no grade 3 or higher events were reported.

8.2.2 SPIKEVAX Bivalent Original / Omicron BA.4/5

8.2.2.1 Participants 18 Years of Age and Older

8.2.2.1.1 Booster Dose

Solicited Adverse Reactions

The safety, reactogenicity, and immunogenicity of a bivalent booster dose of SPIKEVAX Bivalent Original/Omicron BA.4-5 are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 511 participants received a second booster dose of SPIKEVAX Bivalent Original/Omicron BA.4/5 (50 micrograms), and 376 participants received a second booster dose of SPIKEVAX (original) (50 micrograms).

SPIKEVAX Bivalent Original/Omicron BA.4/5 had a reactogenicity profile similar to that of the SPIKEVAX (original) booster given as a second booster dose. The frequency of adverse reactions after immunisation with SPIKEVAX Bivalent Original/Omicron BA.4-5 was also similar or lower relative to that of a first booster dose of SPIKEVAX (original) (50 micrograms) and relative to the second dose of the SPIKEVAX (original) primary series (100 micrograms). No new safety signals were identified. The incidence of solicited adverse reactions did not appear to be increased in participants with prior SARS-CoV-2 infection when compared to participants without infection before receipt of the booster dose.

8.2.3 SPIKEVAX Bivalent (Original/Omicron BA.1)

8.2.3.1 Participants 18 Years of Age and Older

8.2.3.1.1 Booster Dose

Solicited Adverse Reactions

The safety, reactogenicity, and immunogenicity of a booster dose of SPIKEVAX Bivalent (Original/Omicron BA.1) are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 437 participants received the SPIKEVAX Bivalent 50 mcg booster dose (mRNA-1273.214, as 25 mcg elasomeran and 25 mcg imelasomeran), and 377

participants received the SPIKEVAX original 50 mcg booster dose (mRNA-1273). Participants were followed for a median duration of 43 days and 57 days for the SPIKEVAX Bivalent 50 mcg booster dose and SPIKEVAX 50 mcg booster dose, respectively. The safety profile of SPIKEVAX Bivalent (Original/Omicron BA.1) with a median follow-up period of 113 days was similar to the safety profile of SPIKEVAX (original) with a median follow up period of 127 days.

Solicited adverse reaction data were collected from Day 1 to Day 7 and reported by participants in an electronic diary (e-Diary) after each dose and on electronic case report forms. The reactogenicity observed for both local and systemic adverse reactions was similar for both groups with 380 (87%) of subjects in the mRNA-1273.214 group and 301 (85%) of subjects in the mRNA-1273 group experiencing any solicited adverse reactions (AR)s. The frequency of grade 3 adverse reactions was 8.0% in both groups. There were no grade 4 solicited ARs in either group. Reported solicited local and systemic adverse reactions are presented in Tables 4, 5, 6 and 7 respectively.

Table 4 – Summary of Participants with Solicited Local Adverse Reactions within 7 Days After the Injection by Grade – 2nd Booster Dose: mRNA-1273.214, mRNA-1273 Participants 18 to 64 (Solicited Safety Set*)

Solicited local AR	2nd Booster Dose	
	SPIKEVAX Bivalent (Original/Omicron BA.1) Group (mRNA-1273.214) 50 mcg N=263 n (%)	**SPIKEVAX Group (mRNA-1273) 50 mcg** N=211 n (%)
Pain		
Any grade	231 (87.8)	175 (82.9)
Grade 3[a]	2 (0.8)	4 (1.9)
Erythema		
Any grade	20 (7.6)	10 (4.7)
Grade 3[b]	7 (2.7)	1 (0.5)
Swelling/Induration		
Any grade	22 (8.4)	15 (7.1)
Grade 3[b]	4 (1.5)	2 (0.9)
Axillary swelling/ Tenderness		
Any grade	56 (21.3)	39 (18.5)
Grade 3[c]	0 (0)	4 (1.9)

*Solicited Safety Set: All participants who received a dose and contributed any solicited Adverse Reaction data.
n= # of participants with specified reaction, percentages are based on n/N
N= number of exposed subjects who submitted any data for the event.
[a] Pain - Grade 3: any use of Rx pain reliever/prevents daily activity
[b] Erythema and Swelling/Induration - Grade 3: >100mm/>10cm
[c] Axillary Swelling/Tenderness collected as solicited local adverse reaction (i.e., lymphadenopathy: localized axillary swelling or tenderness ipsilateral to the vaccination arm) - Grade 3: any use of Rx pain reliever/prevents daily activity

Table 5 – Summary of Participants with Solicited Local Adverse Reactions within 7 Days After the Injection by Grade – 2nd Booster Dose: mRNA-1273.214, mRNA-1273 Participants 65 Years of Age and Older (Solicited Safety Set*)

Solicited local AR	2nd Booster Dose	
	SPIKEVAX Bivalent (Original/Omicron BA.1) Group (mRNA-1273.214) 50 mcg N=174 n (%)	**SPIKEVAX Group (mRNA-1273) 50 mcg** N=140 n (%)
Pain		
Any grade	107 (61.5)	94 (67.1)
Grade 3 or 4[a]	2 (1.1)	0 (0)
Erythema		
Any grade	10 (5.7)	3 (2.1)
Grade 3[b]	2 (1.1)	1 (0.7)
Swelling/Induration		
Any grade	8 (4.6)	8 (5.7)
Grade 3[b]	1 (0.6)	3 (2.1)
Axillary swelling/ Tenderness		
Any grade	20 (11.5)	15 (10.7)
Grade 3[c]	1 (0.6)	0 (0)

*Solicited Safety Set: All participants who received a dose and contributed any solicited Adverse Reaction data.
n= # of participants with specified reaction, percentages are based on n/N
N= number of exposed subjects who submitted any data for the event.
[a] Pain - Grade 3: any use of Rx pain reliever/prevents daily activity
[b] Erythema and Swelling/Induration - Grade 3: >100mm/>10cm
[c] Axillary Swelling/Tenderness collected as solicited local adverse reaction (i.e., lymphadenopathy: localized axillary swelling or tenderness ipsilateral to the vaccination arm) - Grade 3: any use of Rx pain reliever/prevents daily activity

Table 6 – Summary of Participants with Solicited Systemic Adverse Reactions within 7 Days After the Injection by Grade – 2nd Booster Dose: mRNA-1273.214, mRNA-1273 Participants 18 to 64 (Solicited Safety Set*)

Solicited Systemic AR	2nd Booster Dose	
	SPIKEVAX Bivalent (Original/Omicron BA.1) Group (mRNA-1273.214) 50 mcg N=263 n (%)	**SPIKEVAX Group (mRNA-1273) 50 mcg** N=263 n (%)
Fatigue		
Any grade	154 (58.6)	115 (54.5)
Grade 3[a]	10 (3.8)	7 (3.3)
Headache		
Any grade	129 (49.0)	100 (47.4)
Grade 3[b]	4 (1.5)	1 (0.5)
Myalgia		

Solicited Systemic AR	2nd Booster Dose	
	SPIKEVAX Bivalent (Original/Omicron BA.1) Group (mRNA-1273.214) 50 mcg N=263 n (%)	**SPIKEVAX Group (mRNA-1273) 50 mcg** N=263 n (%)
Any grade	113 (43.0)	90 (42.7)
Grade 3[a]	9 (3.4)	8 (3.8)
Arthralgia		
Any grade	87 (33.1)	69 (32.7)
Grade 3[a]	3 (1.1)	2 (0.9)
Chills		
Any grade	64 (24.3)	54 (25.6)
Grade 3[c]	1 (0.4)	0 (0.0)
Nausea/vomiting		
Any grade	35 (13.3)	27 (12.8)
Grade 3[d]	0 (0.0)	0 (0.0)
Fever		
Any grade	10 (3.8)	10 (4.7)
Grade 3[e]	1 (0.4)	0 (0)
Use of antipyretic or pain medication	104 (39.5)	67 (31.8)

*Solicited Safety Set: All participants who received a dose and contributed any solicited Adverse Reaction data.
n= # of participants with specified reaction, percentages are based on n/N
N= number of exposed subjects who submitted any data for the event.
[a] Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.
[b] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.
[c] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.
[d] Grade 3 nausea/vomiting: Defined as prevents daily activity, requires outpatient intravenous hydration.
[e] Grade 3 fever: Defined as ≥39.0 – ≤40.0°C / ≥102.1 – ≤104.0°F.

Table 7 – Summary of Participants with Solicited Systemic Adverse Reactions within 7 Days After the Injection by Grade – 2nd Booster Dose: mRNA-1273.214, mRNA-1273 Participants 65 Years of Age and Older (Solicited Safety Set)

Solicited Systemic AR	2nd Booster Dose	
	SPIKEVAX Bivalent (Original/Omicron BA.1) Group (mRNA-1273.214) 50 mcg N=174 n (%)	**SPIKEVAX Group (mRNA-1273) 50 mcg** N= 140 n (%)
Fatigue		
Any grade	86 (49.4)	65 (46.8)
Grade 3[a]	5 (2.9)	4 (2.9)
Headache		
Any grade	63 (36.2)	44 (31.7)
Grade 3[b]	1 (0.6)	1 (0.7)
Myalgia		
Any grade	60 (34.5)	45 (32.4)
Grade 3[a]	1 (0.6)	5 (3.6)

Solicited Systemic AR	2nd Booster Dose	
	SPIKEVAX Bivalent (Original/Omicron BA.1) Group (mRNA-1273.214) 50 mcg N=174 n (%)	**SPIKEVAX Group (mRNA-1273) 50 mcg** N= 140 n (%)
Arthralgia		
Any grade	49 (28.2)	42 (30.2)
Grade 3[a]	1 (0.6)	1 (0.7)
Chills		
Any grade	40 (23.0)	20 (14.4)
Grade 3[c]	0 (0.0)	1 (0.7)
Nausea/vomiting		
Any grade	10 (5.7)	8 (5.8)
Grade 3[d]	1 (0.6)	0 (0.0)
Fever		
Any grade	9 (5.2)	2 (1.4)
Grade 3[e]	0 (0.0)	0 (0.0)
Use of antipyretic or pain medication	46 (26.4)	40 (28.6)

*Solicited Safety Set: All participants who received a dose and contributed any solicited Adverse Reaction data.
n= # of participants with specified reaction, percentages are based on n/N
N= number of exposed subjects who submitted any data for the event.
[a] Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.
[b] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.
[c] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.
[d] Grade 3 nausea/vomiting: Defined as prevents daily activity, requires outpatient intravenous hydration.
[e] Grade 3 fever: Defined as ≥39.0 – ≤40.0°C / ≥102.1 – ≤104.0°F.

Table 8 – Summary of Participants with Solicited Adverse Reactions Within 7 Days After the Injection by Grade and Pre-booster SARS-CoV-2 Status – 2nd Booster Dose: mRNA-1273.214; mRNA-1273 (Solicited Safety Set)

	2nd Booster Dose			
	SPIKEVAX Bivalent (Original/Omicron BA.1) Group mRNA-1273.214 50 µg		**SPIKEVAX Group mRNA-1273 50 µg**	
	Pre-booster SARS-CoV-2 Status		**Pre-booster SARS-CoV-2 Status**	
Solicited Adverse Reaction Category Grade*	**Negative (N=340) n (%)**	**Positive (N=96) n (%)**	**Negative (N=250) n (%)**	**Positive (N=92) n (%)**
Solicited adverse reactions - N1	340	96	250	92
Any grade solicited adverse reactions	299 (87.9)	80 (83.3)	217 (86.8)	77 (83.7)
95% CI	84.0, 91.2	74.4, 90.2	82.0, 90.7	74.5, 90.6
Grade 3	29 (8.5)	6 (6.3)	24 (9.6)	4 (4.3)
Solicited local adverse reactions - N1	340	96	250	92
Any grade solicited local adverse reactions	272 (80.0)	74 (77.1)	200 (80.0)	73 (79.3)
95% CI	75.3, 84.1	67.4, 85.0	74.5, 84.8	69.6, 87.1

Solicited Adverse Reaction Category Grade*	2nd Booster Dose			
	SPIKEVAX Bivalent (Original/Omicron BA.1) Group mRNA-1273.214 50 µg		SPIKEVAX Group mRNA-1273 50 µg	
	Pre-booster SARS-CoV-2 Status		Pre-booster SARS-CoV-2 Status	
	Negative (N=340) n (%)	Positive (N=96) n (%)	Negative (N=250) n (%)	Positive (N=92) n (%)
Grade 3	14 (4.1)	1 (1.0)	9 (3.6)	3 (3.3)
Pain - N1	340	96	250	92
Any grade	265 (77.9)	72 (75.0)	193 (77.2)	71 (77.2)
Grade 3	4 (1.2)	0	3 (1.2)	1 (1.1)
Erythema (redness)[a] - N1	340	96	250	92
Any grade	27 (7.9)	3 (3.1)	10 (4.0)	3 (3.3)
Grade 3	8 (2.4)	1 (1.0)	1 (0.4)	1 (1.1)
Swelling (hardness)- N1	340	96	250	92
Any grade	26 (7.6)	4 (4.2)	19 (7.6)	4 (4.3)
Grade 3	5 (1.5)	0	5 (2.0)	0
Axillary swelling or tenderness - N1	340	96	250	92
Any grade	58 (17.1)	18 (18.8)	35 (14.0)	18 (19.6)
Grade 3	1 (0.3)	0	3 (1.2)	1 (1.1)
Solicited systemic adverse reactions - N1	340	96	250	92
Any grade solicited systemic adverse reactions	244 (71.8)	63 (65.6)	171 (68.4)	57 (62.0)
95% CI	66.7, 76.5	55.2, 75.0	62.2, 74.1	51.2, 71.9
Grade 3	19 (5.6)	5 (5.2)	15 (6.0)	1 (1.1)
Fever[b] - N1	339	96	250	92
Any grade	16 (4.7)	3 (3.1)	10 (4.0)	2 (2.2)
Grade 3	1 (0.3)	0	0	0
Headache - N1	340	96	250	92
Any grade	154 (45.3)	38 (39.6)	106 (42.4)	37 (40.2)
Grade 3	5 (1.5)	0	2 (0.8)	0
Fatigue - N1	340	96	250	92
Any grade	194 (57.1)	46 (47.9)	134 (53.6)	42 (45.7)
Grade 3	11 (3.2)	4 (4.2)	10 (4.0)	1 (1.1)
Myalgia - N1	340	96	250	92
Any grade	137 (40.3)	36 (37.5)	93 (37.2)	40 (43.5)
Grade 3	10 (2.9)	0	13 (5.2)	0
Arthralgia - N1	340	96	250	92
Any grade	110 (32.4)	26 (27.1)	80 (32.0)	29 (31.5)
Grade 3	4 (1.2)	0	3 (1.2)	0
Nausea/vomiting - N1	340	96	250	92
Any grade	36 (10.6)	9 (9.4)	25 (10.0)	10 (10.9)
Grade 3	0	1 (1.0)	0	0
Chills - N1	340	96	250	92
Any grade	86 (25.3)	18 (18.8)	58 (23.2)	15 (16.3)
Grade 3	1 (0.3)	0	1 (0.4)	0

Abbreviations: CI = confidence interval; SARS-CoV-2 = severe acute respiratory infection coronavirus-2.
*No Grade 4 Solicited Adverse Reactions were observed.
N1 = number of exposed participants who submitted any data for the event. Any = Grade 1 or higher. Percentages are based on the number of exposed participants who submitted any data for the event (N1). The 95% CI is calculated using the Clopper-Pearson method.
[a] Toxicity grade for erythema (redness) is defined as: Grade 1 = 25 – 50 mm; Grade 2 = 51 – 100 mm; Grade 3 = greater than 100 mm.
[b] Toxicity grade for fever is defined as: Grade 1 = 38 – 38.4°C; Grade 2 = 38.5 – 38.9°C; Grade 3 = 39 – 40°C.

Overall, there were no safety concerns or differences identified in solicited adverse reactions based on pre-booster SARS-CoV-2 status. The frequency of solicited local ARs was similar among participants with a positive pre-booster SARS-CoV-2 status 74/96 [77.1%]) and participants with a negative pre-booster SARS-CoV-2 status (272/340 [80.0%])

Unsolicited Adverse Events

There were no important clinical differences between unsolicited events that occurred within 28 days for participants who received the SPIKEVAX Bivalent (Original/Omicron BA.1, mRNA-1273.214) 50 mcg booster dose when compared to participants who received the SPIKEVAX original (mRNA-1273) 50 mcg booster dose. There were 81/437 participants (18.5%) in the SPIKEVAX Bivalent group that reported unsolicited events, regardless of relationship to the vaccine, compared to 78/377 participants (20.7%) in the SPIKEVAX original group.

In both groups the majority of unsolicited events were consistent with reactogenicity events. The most commonly reported unsolicited events within 28 days after the SPIKEVAX Bivalent 50 mcg booster dose, regardless of causality were fatigue (11/437 [2.5%]); headache and arthralgia (7/437 [1.6%] each). The most commonly reported unsolicited events within 28 days after the SPIKEVAX original 50 mcg booster dose, regardless of causality were fatigue (12/377 [3.2%]), upper respiratory tract infection (9/377 [2.4%]), and coronavirus infection (i.e., coronaviruses other than SARS-CoV-2) (8/377 [2.1%]). There were no deaths reported in any of the two groups in the study.

Serious adverse events (SAE) were reported in 0.5% (2/437) of subjects who received the SPIKEVAX Bivalent 50 mcg booster dose; and 0.3% (1/377) of subjects who received the SPIKEVAX original 50 mcg booster dose, within 28 days after vaccination. Up to the data cut-off date (27 Apr 2022), one additional SAE occurred in the SPIKEVAX Bivalent 50 mcg booster dose group.

8.2.3.2 Participants 6 Months to 5 Years of Age

8.2.3.2.1 Primary Series

The safety of a primary series of SPIKEVAX Bivalent (Original/Omicron BA.1) are evaluated in an ongoing Phase 3 open-label clinical trial. In this study, 179 participants 6 months through 5 years of age who received at least one dose of bivalent vaccine (mRNA-1273.214, as 12.5 mcg elasomeran and 12.5 mcg imelasomeran). As of the data cutoff date of December 5, 2022, the median duration of follow-up for safety was 68 days after Dose 2.

Solicited Adverse Reactions

Local and systemic adverse reactions and use of antipyretic medication were solicited in an electronic diary for 7 days following each injection (i.e., day of vaccination and the next 6 days) among participants receiving bivalent vaccine (Original and Omicron BA.1) with at least 1 documented dose. Events that persisted for more than 7 days were followed until resolution.

The solicited local and systemic adverse reactions in participants 6 months through 36 months of age following administration of a primary series with SPIKEVAX Bivalent (Original / Omicron BA.1) included irritability/crying (55.2%), pain at the injection site (50.6%), sleepiness (43.7%), loss of appetite (36.8%), fever (20.7%), axillary (or groin) swelling/tenderness (6.9%), erythema at the injection site (6.9%), and swelling at the injection site (5.7%). The solicited local and systemic adverse reactions in participants 37 months through 5 years of age following administration of a primary series with SPIKEVAX Bivalent (Original / Omicron BA.1) included pain at the injection site (52.2%), fatigue (41.8%), myalgia (22.0%), headache (17.6%), fever (17.4%), arthralgia (16.5%), chills (11.0%), nausea/vomiting (9.9%), axillary (or groin) swelling/tenderness (9.8%), and erythema at the injection site (2.2%).

The reported number and percentage of the solicited local and systemic adverse reactions by dose in participants 6 months through 36 months of age are presented in Table 9 and participants 37 months to 5 years are presented in Table 10.

Table 9 – Number and Percentage of Participants With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days After Each Dose of SPIKEVAX Bivalent (Original / Omicron BA.1) in Participants 6 Months Through 36 Months (Solicited Safety Set, Dose 1 and Dose 2)*

	SPIKEVAX Bivalent (Original / Omicron BA.1) Primary Series	
	Dose 1 (N=87) n (%)	**Dose 2** (N=70) n (%)
Local Adverse Reactions		
Pain	29 (33.3)	28 (40.0)
Axillary (or groin) swelling/tenderness	5 (5.7)	2 (2.9)
Erythema (redness) ≥5 mm	2 (2.3)	4 (5.7)
Erythema (redness), Grade 3: >50 mm	1 (1.1)	0 (0)
Swelling (hardness) ≥5 mm	2 (2.3)	3 (4.3)
Swelling (hardness), Grade 3: >50 mm	1 (1.1)	0 (0)
Systemic Adverse Reactions		
Irritability/crying	35 (44.3)	29 (41.4)
Irritability/crying, Grade 3[a]	0 (0)	1 (1.4)
Sleepiness	24 (30.4)	22 (31.4)
Loss of appetite	20 (25.3)	19 (27.1)
Loss of appetite, Grade 3[b]	0 (0)	1 (1.4)
Fever >38.0°C / >100.4°F	8 (9.2)	10 (14.3)
Use of antipyretic or pain medication	22 (25.3)	15 (21.4)

* 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary). Absence of rows for Grade 3 or Grade 4 adverse reactions indicates no events were reported.

[a] Grade 3 irritability/crying: Defined as lasting >3 hours or inconsolable.

[b] Grade 3 loss of appetite: Defined as missed >2 feeds/meals completely or refuses most feeds/meals.

Table 10 – Number and Percentage of Participants With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days After Each Dose of SPIKEVAX Bivalent (Original / Omicron BA.1) in Participants 37 Months Through 5 Years (Solicited Safety Set, Dose 1 and Dose 2)*

	SPIKEVAX Bivalent (Original / Omicron BA.1) Primary Series	
	Dose 1 (N=92) n (%)	**Dose 2** (N=71) n (%)
Local Adverse Reactions		
Pain	32 (34.8)	34 (47.9)
Axillary (or groin) swelling/tenderness	6 (6.5)	3 (4.2)
Erythema (redness) ≥25 mm	1 (1.1)	1 (1.4)
Systemic Adverse Reactions		
Fatigue	23 (25.6)	24 (33.8)
Fatigue, Grade 3[a]	1 (1.1)	0
Headache	10 (11.1)	8 (11.3)
Fever ≥38.0°C	8 (8.7)	9 (12.7)
Fever, Grade 3: 39.0° - 40.0°C	2 (2.2)	2 (2.8)
Myalgia	11 (12.2)	11 (15.5)
Chills	4 (4.4)	6 (8.5)
Nausea/vomiting	5 (5.6)	5 (7.0)
Arthralgia	7 (7.8)	9 (12.7)
Use of antipyretic or pain medication	13 (14.1)	22 (31.0)

* 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary). Absence of rows for Grade 3 or Grade 4 adverse reactions indicates no events were reported.

[a] Grade 3 fatigue: Defined as prevents daily activity.

Solicited local and systemic adverse reactions reported following administration of bivalent vaccine (Original and Omicron BA.1) had a median duration of 2 days for participants 6 months through 5 years of age.

Unsolicited Adverse Events

Participants were monitored for unsolicited adverse events for up to 28 days following each dose and follow-up is ongoing. Serious adverse events and medically attended adverse events will be recorded for the entire study duration. As of December 5, 2022, among participants 6 months through 5 years of age who had received at least 1 dose of SPIKEVAX Bivalent (Original / Omicron BA.1) (n=179), unsolicited adverse events that occurred within 28 days following each vaccination were reported by 30.7% of participants (n=55). In these analyses, 60.3% of participants had at least 28 days of follow-up after Dose 2. No new safety concerns were identified.

8.2.4 SPIKEVAX (Original)

8.2.4.1 Participants 18 Years of Age and Older

8.2.4.1.1 Primary Series

Solicited Adverse Reactions

The safety profile presented below is based on data generated in an ongoing Phase 3, placebo-controlled clinical study of SPIKEVAX (elasomeran) in subjects ≥ 18 years of age in which pre-specified cohorts of subjects who were either ≥ 65 years of age or 18 to 64 years of age with comorbid medical conditions were included. At the time of the analysis, the safety analysis set included a total of 30,351 subjects who received at least one dose of SPIKEVAX (elasomeran) (n=15,181) or placebo (n=15,170). Subjects were followed for a median of 92 days from first injection and 63 days from second injection.

Solicited adverse reaction data were collected from Day 1 to Day 7 and reported by participants in an electronic diary (e-Diary) after each dose and on electronic case report forms. Reported solicited local and systemic adverse reactions are presented in Table 11, Table 12, Table 13 and Table 14 respectively.

Table 11 – Solicited Local Adverse Reactions Within 7 Days After First and Second Injection by Grade- Participants 18 to 64 Years of Age (Safety Analysis Set*)

Solicited local AR	Dose 1		Dose 2	
	SPIKEVAX Group 100 mcg N=11,406 n (%)	**Placebo Group** N=11,407 n (%)	**SPIKEVAX Group 100 mcg** N=10,985 n (%)	**Placebo Group** N=10,918 n (%)
Pain				
Any grade	9,908 (86.9)	2,177 (19.1)	9,873 (89.9)	2,040 (18.7)
Grade 3 or 4[a]	366 (3.2)	23 (0.2)	506 (4.6)	22 (0.2)
Erythema				
Any grade	344 (3.0)	47 (0.4)	982 (8.9)	43 (0.4)
Grade 3 or 4[b]	34 (0.3)	11 (<0.1)	210 (1.9)	12 (0.1)
Swelling/Induration				
Any grade	767 (6.7)	34 (0.3)	1,389 (12.6)	36 (0.3)
Grade 3 or 4[b]	62 (0.5)	3 (<0.1)	182 (1.7)	4 (<0.1)
Axillary swelling/ Tenderness				
Any grade	1,322 (11.6)	567 (5.0)	1,775 (16.2)	470 (4.3)
Grade 3 or 4[c]	37 (0.3)	13 (0.1)	46 (0.4)	11 (0.1)

*Safety Analyses Set: all randomized participants who received ≥1 vaccine or control dose.
n= # of participants with specified reaction, percentages are based on n/N
N= number of exposed subjects who submitted any data for the event.
[a] Pain - Grade 3: any use of Rx pain reliever/prevents daily activity; Grade 4: requires E.R. visit or hospitalization
[b] Erythema and Swelling/Induration - Grade 3: >100mm/>10cm; Grade 4: necrosis/exfoliative dermatitis

[c] Axillary Swelling/Tenderness collected as solicited local adverse reaction (i.e., lymphadenopathy: localized axillary swelling or tenderness ipsilateral to the vaccination arm) - Grade 3: any use of Rx pain reliever/prevents daily activity; Grade 4: requires E.R. visit or hospitalization.

Table 12 – Solicited Local Adverse Reactions Within 7 Days After First and Second Injection by Grade - Participants 65 Years of Age and Older (Safety Analysis Set*)

Solicited local AR	Dose 1		Dose 2	
	SPIKEVAX Group 100 mcg N=3,762 n (%)	**Placebo Group** N=3,748 n (%)	**SPIKEVAX Group 100 mcg** N=3,692 n (%)	**Placebo Group** N=3,648 n (%)
Pain				
Any grade	2,782 (74.0)	481 (12.8)	3,070 (83.2)	437 (12.0)
Grade 3 or 4[a]	50 (1.3)	32 (0.9)	98 (2.7)	18 (0.5)
Erythema				
Any grade	86 (2.3)	20 (0.5)	275 (7.5)	13 (0.4)
Grade 3 or 4[b]	8 (0.2)	2 (<0.1)	77 (2.1)	3 (<0.1)
Swelling/Induration				
Any grade	165 (4.4)	18 (0.5)	400 (10.8)	13 (0.4)
Grade 3 or 4[b]	20 (0.5)	3 (<0.1)	72 (2.0)	7 (0.2)
Axillary swelling/ Tenderness				
Any grade	231 (6.1)	155 (4.1)	315 (8.5)	97 (2.7)
Grade 3 or 4[c]	12 (0.3)	14 (0.4)	21 (0.6)	8 (0.2)

*Safety Analyses Set: all randomized participants who received ≥1 vaccine or control dose.
n= # of participants with specified reaction, percentages are based on n/N
N= number of exposed subjects who submitted any data for the event.
[a] Pain - Grade 3: any use of Rx pain reliever/prevents daily activity; Grade 4: requires E.R. visit or hospitalization
[b] Erythema and Swelling/Induration - Grade 3: >100mm/>10cm; Grade 4: necrosis/exfoliative dermatitis
[c] Axillary Swelling/Tenderness collected as solicited local adverse reaction (i.e., lymphadenopathy: localized axillary swelling or tenderness ipsilateral to the vaccination arm) - Grade 3: any use of Rx pain reliever/prevents daily activity; Grade 4: requires E.R. visit or hospitalization.

Table 13 – Solicited Systemic Adverse Reactions Within 7 Days After First and Second Injection by Grade - Participants 18 to 64 Years of Age (Safety Analysis Set*)

Solicited Systemic AR	Dose 1		Dose 2	
	SPIKEVAX Group 100 mcg N=11,406 n (%)	**Placebo Group** N=11,407 n (%)	**SPIKEVAX Group 100 mcg** N=10,985 n (%)	**Placebo Group** N=10,918 n (%)
Fatigue				
Any grade	4,384	3,282	7,430	2,687

Solicited Systemic AR	Dose 1		Dose 2	
	SPIKEVAX Group 100 mcg N=11,406 n (%)	**Placebo Group** N=11,407 n (%)	**SPIKEVAX Group 100 mcg** N=10,985 n (%)	**Placebo Group** N=10,918 n (%)
	(38.4)	(28.8)	(67.6)	(24.6)
Grade 3[a]	120 (1.1)	83 (0.7)	1,174 (10.7)	86 (0.8)
Grade 4[b]	1 (<0.1)	0 (0)	0 (0)	0 (0)
Headache				
Any grade	4,030 (35.3)	3,304 (29.0)	6,898 (62.8)	2,760 (25.3)
Grade 3[c]	219 (1.9)	162 (1.4)	553 (5.0)	129 (1.2)
Myalgia				
Any grade	2,699 (23.7)	1,628 (14.3)	6,769 (61.6)	1,411 (12.9)
Grade 3[a]	73 (0.6)	38 (0.3)	1,113 (10.1)	42 (0.4)
Arthralgia				
Any grade	1,893 (16.6)	1,327 (11.6)	4,993 (45.5)	1,172 (10.7)
Grade 3[a]	47 (0.4)	29 (0.3)	647 (5.9)	37 (0.3)
Grade 4[b]	1 (<0.1)	0 (0)	0 (0)	0 (0)
Chills				
Any grade	1,051 (9.2)	730 (6.4)	5,341 (48.6)	658 (6.0)
Grade 3[d]	17 (0.1)	8 (<0.1)	164 (1.5)	15 (0.1)
Nausea/vomiting				
Any grade	1,068 (9.4)	908 (8.0)	2,348 (21.4)	801 (7.3)
Grade 3[e]	6 (<0.1)	8 (<0.1)	10 (<0.1)	8 (<0.1)
Fever				
Any grade	105 (0.9)	37 (0.3)	1,908 (17.4)	39 (0.4)
Grade 3[f]	10 (<0.1)	1 (<0.1)	184 (1.7)	2 (<0.1)
Grade 4[g]	4 (<0.1)	4 (<0.1)	12 (0.1)	2 (<0.1)
Use of antipyretic or pain medication	2,656 (23.3)	1,523 (13.4)	6,292 (57.3)	1,248 (11.4)

*Safety Analyses Set: all randomized participants who received ≥1 vaccine or control dose.
n= # of participants with specified reaction, percentages are based on n/N
N= number of exposed subjects who submitted any data for the event.
[a] Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.
[b] Grade 4 fatigue, arthralgia: Defined as requires emergency room visit or hospitalization.
[c] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.

[d] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.
[e] Grade 3 nausea/vomiting: Defined as prevents daily activity, requires outpatient intravenous hydration.
[f] Grade 3 fever: Defined as ≥39.0 – ≤40.0°C / ≥102.1 – ≤104.0°F.
[g] Grade 4 fever: Defined as >40.0°C / >104.0°F.

Table 14 – Solicited Systemic Adverse Reactions Within 7 Days After First and Second Injection by Grade - Participants 65 Years of Age and Older (Safety Analysis Set*)

Solicited Systemic AR	Dose 1		Dose 2	
	SPIKEVAX Group 100 mcg N=3,762 n (%)	**Placebo Group** N=3,748 n (%)	**SPIKEVAX Group 100 mcg** N=3,692 n (%)	**Placebo Group** N=3,648 n (%)
Fatigue				
Any grade	1,251 (33.3)	851 (22.7)	2,152 (58.3)	716 (19.6)
Grade 3[a]	30 (0.8)	22 (0.6)	254 (6.9)	20 (0.5)
Headache				
Any grade	921 (24.5)	723 (19.3)	1,704 (46.2)	650 (17.8)
Grade 3[b]	52 (1.4)	34 (0.9)	106 (2.9)	33 (0.9)
Myalgia				
Any grade	742 (19.7)	443 (11.8)	1,739 (47.1)	398 (10.9)
Grade 3[a]	17 (0.5)	9 (0.2)	205 (5.6)	10 (0.3)
Arthralgia				
Any grade	618 (16.4)	456 (12.2)	1,291 (35.0)	397 (10.9)
Grade 3[a]	13 (0.3)	8 (0.2)	123 (3.3)	7 (0.2)
Chills				
Any grade	202 (5.4)	148 (4.0)	1,141 (30.9)	151 (4.1)
Grade 3[c]	7 (0.2)	6 (0.2)	27 (0.7)	2 (<0.1)
Nausea/vomiting				
Any grade	194 (5.2)	166 (4.4)	437 (11.8)	133 (3.6)
Grade 3[d]	4 (0.1)	4 (0.1)	10 (0.3)	3 (<0.1)
Grade 4[e]	0 (0)	0 (0)	1 (<0.1)	0 (0)
Fever				
Any grade	10 (0.3)	7 (0.2)	370 (10.0)	4 (0.1)
Grade 3[f]	1 (<0.1)	1 (<0.1)	18 (0.5)	0 (0)
Grade 4[g]	0 (0)	2 (<0.1)	1 (<0.1)	1 (<0.1)

Solicited Systemic AR	Dose 1		Dose 2	
	SPIKEVAX Group 100 mcg N=3,762 n (%)	**Placebo Group** N=3,748 n (%)	**SPIKEVAX Group 100 mcg** N=3,692 n (%)	**Placebo Group** N=3,648 n (%)
Use of antipyretic or pain medication	673 (17.9)	477 (12.7)	1546 (41.9)	329 (9.0)

*Safety Analyses Set: all randomized participants who received ≥1 vaccine or control dose.
n= # of participants with specified reaction, percentages are based on n/N
N= number of exposed subjects who submitted any data for the event.
[a] Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.
[b] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.
[c] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.
[d] Grade 3 Nausea/vomiting: Defined as prevents daily activity, requires outpatient intravenous hydration.
[e] Grade 4 Nausea/vomiting: Defined as requires emergency room visit or hospitalization for hypotensive shock.
[f] Grade 3 fever: Defined as ≥39.0 – ≤40.0°C / ≥102.1 – ≤104.0°F.
[g] Grade 4 fever: Defined as >40.0°C / >104.0°F.

Unsolicited Adverse Events

Serious Adverse Events

Serious adverse events were reported in 0.6% of participants who received SPIKEVAX (elasomeran) and 0.6% of participants who received a placebo, from the first dose until 28 days following the last vaccination. Serious adverse events were reported in 1% of participants who received SPIKEVAX (elasomeran) and 1% of participants who received a placebo, from the first dose until the last observation (cut-off date November 25, 2020). In these analyses, 87.9% of study participants had at least 28 days of follow-up after dose 2, and the median follow-up time for all participants was 9 weeks after dose 2.

There were no other notable patterns or numerical imbalances between treatment groups for specific categories of adverse events (including other neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to SPIKEVAX (elasomeran).

Three serious adverse events were likely related to SPIKEVAX (elasomeran): two cases of facial swelling occurring within 7 days of receiving Dose 2, in female patients aged 46 and 51; one case of nausea and vomiting with headaches and fever occurring within 7 days after Dose 2 and requiring in-hospital treatment in a 61-year-old female, with past medical history of headaches with nausea and vomiting requiring hospitalization. One case of Bell's palsy, which occurred 32 days following receipt of vaccine, was classified as a serious adverse event. Currently available information on Bell's palsy is insufficient to determine a causal relationship with the vaccine.

No deaths related to the vaccine were reported in the study.

Non-Serious Adverse Events

In the COVE Phase 3 study, unsolicited adverse events occurring within 28 days after each vaccination were reported by 23.9% of subjects who received SPIKEVAX (elasomeran), and 21.6% of subjects who received the placebo. These adverse events were predominantly solicited adverse reactions occurring outside of the conventional 7-day monitoring period after the injection (injection site pain, fatigue, headaches, myalgia, etc.).

Unsolicited adverse events that occurred in ≥ 1% of study participants who received SPIKEVAX (elasomeran) and at a rate at least 1.5-fold higher rate than placebo, were lymphadenopathy related events (1.1% of versus 0.6%) and delayed injection site reactions reported >7 days after vaccination (1.2% versus 0.4%). All of the lymphadenopathy events are similar to the axillary swelling/tenderness in the injected arm reported as solicited adverse reactions. Delayed injection site reactions included one or more of the following: erythema, pain and swelling, and are likely related to vaccination. Hypersensitivity events were reported in 1.5% of the SPIKEVAX (elasomeran) group compared to 1.1% of the placebo group, but this imbalance was mostly due to injection site rash and injection site erythema/swelling occurring more frequently in the SPIKEVAX (elasomeran) group.

There were three reports of Bell's palsy in the SPIKEVAX (elasomeran) group (one of which was a serious adverse event), which occurred 22, 29, and 32 days after the second dose of vaccine, and one in the placebo group which occurred 17 days after the first dose of saline. Currently available information on Bell's palsy is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including neurologic, musculoskeletal or inflammatory events) that would suggest a causal relationship to SPIKEVAX (elasomeran).

8.2.4.1.2 Booster Dose

Study P201 Part B is an ongoing Phase 2, randomized, observer-blind, placebo-controlled, dose-confirmation study to evaluate the safety, reactogenicity, and immunogenicity of SPIKEVAX (elasomeran) in participants 18 years of age and older (NCT04405076). In an open-label phase of this study, 171 participants received a single booster dose (50 mcg) at least 6 months after receiving the second dose (100 mcg) of the SPIKEVAX (elasomeran) primary series. At the time of analysis, participants were followed-up for safety for one month after receiving the booster.

The solicited adverse reaction profile for the booster dose was similar to that after the second dose in the primary series. The most common solicited local adverse reactions (ARs) were pain at injection site (84%) and axillary swelling or tenderness (20%). The most common solicited systemic ARs were fatigue (59%), headache (55%), myalgia (49%), arthralgia (41%), and chills (35%). The local and systemic ARs were transient, and most resolved by Day 4. The frequency and severity of solicited ARs was numerically comparable between age cohorts (18 to <55; ≥55 years of age). The most common unsolicited AEs were headache (2.3%) and fatigue (2.3%); these were also solicited AEs that extended beyond Day 7. All unsolicited AEs were mild or moderate in severity. Of the 171 participants who received a booster dose of SPIKEVAX (elasomeran), there were no serious adverse events reported from the booster dose through 29 days after the booster dose.

8.2.4.2 Adolescents 12 to 17 Years of Age

8.2.4.2.1 Primary Series

Solicited Adverse Reactions

Data on solicited local and systemic adverse reactions and use of antipyretic medication were collected on a daily basis in an electronic diary for 7 days following each injection (i.e., day of vaccination and the next 6 days) among adolescent participants receiving SPIKEVAX (elasomeran) (n=2,482) and participants

receiving placebo (n=1,238) with at least 1 documented dose. Events that persisted for more than 7 days were followed until resolution.

The reported number and percentage of the solicited local and systemic adverse reactions in participants 12 through 17 years of age by dose are presented in Table 15 and Table 16 respectively. Solicited local and systemic adverse reactions reported following administration of SPIKEVAX (elasomeran) had a median duration of 1 to 3 days.

Table 15 – Solicited Local Adverse Reactions Within 7 Days After First and Second Injection by Grade – Participants 12 to 17 Years of Age (Solicited Safety Analysis Set)

	Dose 1		Dose 2	
	Vaccine Group n (%) N=2,482	**Placebo Group**[a] n (%) N=1,238	**Vaccine Group** n (%) N=2,478	**Placebo Group**[a] n (%) N=1,220
Pain				
Any grade	2,310 (93.1)	431 (34.8)	2,290 (92.4)	370 (30.3)
Grade 3[b]	133 (5.4)	1 (<0.1)	126 (5.1)	3 (0.2)
Axillary swelling/ tenderness				
Any grade	578 (23.3)	101 (8.2)	519 (21.0)	61 (5.0)
Grade 3[b]	10 (0.4)	0 (0)	7 (0.3)	0 (0)
Swelling (hardness)				
≥25 mm	403 (16.2)	12 (1.0)	509 (20.5)	12 (1.0)
Grade 3[c]	27 (1.1)	0 (0)	56 (2.3)	0 (0)
Erythema (redness)				
≥25 mm	334 (13.5)	8 (0.6)	484 (19.5)	11 (0.9)
Grade 3[c]	21 (0.8)	0 (0)	72 (2.9)	0 (0)

n= # of participants with specified reaction, percentages are based on n/N.
N= number of exposed subjects who submitted any data for the event.
[a] Placebo was a saline solution.
[b] Grade 3 pain and axillary swelling/tenderness: Defined as any use of prescription pain reliever; prevents daily activity.
[c] Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.

Table 16 – Solicited Systemic Adverse Reactions Within 7 Days After First and Second Injection by Grade – Participants 12 to 17 Years of Age (Solicited Safety Analysis Set)

	Dose 1		Dose 2	
	Vaccine Group n (%) N=2,482	**Placebo Group**[a] n (%) N=1,238	**Vaccine Group** n (%) N=2,478	**Placebo Group**[a] n (%) N=1,220
Fatigue				

	Dose 1		Dose 2	
	Vaccine Group n (%) N=2,482	**Placebo Group**[a] n (%) N=1,238	**Vaccine Group** n (%) N=2,478	**Placebo Group**[a] n (%) N=1,220
Any grade	1,188 (47.9)	453 (36.6)	1,679 (67.8)	353 (28.9)
Grade 3[b]	33 (1.3)	18 (1.5)	188 (7.6)	10 (0.8)
Headache				
Any grade	1,106 (44.6)	477 (38.5)	1,739 (70.2)	370 (30.3)
Grade 3[c]	56 (2.3)	17 (1.4)	112 (4.5)	14 (1.1)
Grade 4[d]	0 (0)	0 (0)	1 (<0.1)	0 (0)
Myalgia				
Any grade	668 (26.9)	205 (16.6)	1,154 (46.6)	153 (12.5)
Grade 3[d]	24 (1.0)	10 (0.8)	129 (5.2)	3 (0.2)
Chills				
Any grade	456 (18.4)	138 (11.1)	1,066 (43.0)	97 (8.0)
Grade 3[e]	4 (0.2)	1 (<0.1)	11 (0.4)	0 (0)
Arthralgia				
Any grade	371 (15.0)	143 (11.6)	716 (28.9)	113 (9.3)
Grade 3[d]	15 (0.6)	5 (0.4)	57 (2.3)	2 (0.2)
Nausea/vomiting				
Any grade	281 (11.3)	110 (8.9)	591 (23.9)	106 (8.7)
Grade 3[f]	2 (<0.1)	0 (0)	2 (<0.1)	0 (0)
Grade 4[g]	0 (0)	0 (0)	1 (<0.1)	0 (0)
Fever				
Any grade	63 (2.5)	12 (1.0)	302 (12.2)	12 (1.0)
Grade 3 (≥39.0° – ≤40.0°C)	9 (0.4)	1 (<0.1)	46 (1.9)	1 (<0.1)
Grade 4 (>40.0°C)	0 (0)	0 (0)	1 (<0.1)	1 (<0.1)
Use of antipyretic or analgesic medications	748 (30.1)	118 (9.5)	1,242 (50.1)	108 (8.9)

n= # of participants with specified reaction, percentages are based on n/N.

N= number of exposed subjects who submitted any data for the event.

[a] Placebo was a saline solution.

[b] Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.

[c] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.

[d] Grade 4 headache: Defined as requires emergency room visit or hospitalisation.
[e] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.
[f] Grade 3 nausea/vomiting: Defined as prevents daily activity, requires outpatient intravenous hydration.
[g] Grade 4 nausea/vomiting: Defined as requires emergency room visit or hospitalisation for hypotensive shock.

Unsolicited Adverse Events

Participants (12 to 17 years of age) were monitored for unsolicited adverse events for up to 28 days following each dose and follow-up is ongoing. Serious adverse events and medically attended adverse events will be recorded for the entire study duration. As of May 8, 2021, 3,726 participants (vaccine=2,486, placebo=1,240) had received at least 1 dose and 97.3% of the study participants had at least 28 days of follow-up after Dose 2. The median follow-up time for all participants was 53 days after Dose 2.

Unsolicited adverse events that occurred within 28 days following each vaccination were reported by 20.5% of participants (n=510) who received SPIKEVAX (elasomeran) and 15.9% of participants (n=197) who received placebo. Imbalances in unsolicited adverse events up to 28 days after any injection are primarily attributable to events related to local reactogenicity such as lymphadenopathy.

Serious adverse events within 28 days of any injection were reported by < 0.1% (n=2) of participants who received SPIKEVAX (elasomeran) and < 0.1% (n=1) of participants who received placebo. As of May 8, 2021, serious adverse events during the overall study period were reported by 0.2% (n=6) of participants who received SPIKEVAX (elasomeran) and 0.2% (n=2) of participants who received placebo. No SAEs during the study were assessed by the investigator as related to study vaccine.

8.2.4.2.2 Booster Dose

Safety data for a booster dose of SPIKEVAX (elasomeran) in adolescents were collected in an ongoing Phase 2/3 clinical trial (Study P203, NCT04649151) with multiple parts. The open-label booster portion of the study involved 1,364 participants 12 years through 17 years of age who received a booster dose (50 mcg) of SPIKEVAX (elasomeran) at least 5 months after the second dose of the primary series (100 mcg). As of the data cutoff date of May 16, 2022, the median duration of follow-up for safety was 116 days after the booster dose.

Solicited Adverse Reactions

Local and systemic adverse reactions (ARs) were solicited in an electronic diary for 7 days following the injection among participants receiving SPIKEVAX (elasomeran) as a booster dose. Solicited ARs were reported by most (95.1%) participants after the booster dose (N=1,312); 11.0% reported a Grade 3 solicited AR. The solicited local ARs were pain (91%), axillary swelling or tenderness (28%), swelling (hardness) (14%) and erythema (redness) (9%). The solicited systemic ARs were fatigue (59%), headache (57%), myalgia (40%), chills (31%), arthralgia (24%), nausea/vomiting (18%) and fever (6%). The median duration of solicited local and systemic adverse reactions was 3 days.

Unsolicited Adverse Events

Participants were monitored for unsolicited adverse events for up to 28 days following the booster dose. As of May 16, 2022, among the 1,364 participants who had received a booster dose, unsolicited adverse

events that occurred within 28 days following vaccination were reported by 14.2% of participants (n=194). In these analyses, 97.4% of study participants had at least 28 days of follow-up after the booster dose.

Serious Adverse Events

Through the cut-off date of May 16, 2022, with a median follow-up duration of 116 days after booster, no serious adverse events following the booster dose were reported.

8.2.4.3 Children 6 to 11 Years of Age

8.2.4.3.1 Primary Series

Solicited Adverse Reactions

Data on solicited local and systemic adverse reactions were collected on a daily basis in an electronic diary for 7 days following each injection (i.e., day of vaccination and the next 6 days) among pediatric participants aged 6 to 11 years receiving SPIKEVAX (elasomeran) (n=3,007) and participants receiving placebo (n=995) with at least 1 documented dose, and 2,988 participants receiving SPIKEVAX (elasomeran) and 973 participants in the placebo group had received dose 2 in Study P204 Part 2. For events that persisted for more than 7 days the caregiver was prompted to continue to record until resolution.

The reported number and percentage of the solicited local and systemic adverse reactions in participants 6 through 11 years of age by dose are presented in Table 17 and Table 18 respectively. The majority of solicited local adverse reactions following administration of SPIKEVAX (elasomeran) occurred within the first 1 to 2 days after any dose and persisted for a median of 3 days.

Table 17 – Solicited Local Adverse Reactions Within 7 Days After First and Second Injection by Grade – Participants 6 to 11 of Age in Study P204 Part 2 (Solicited Safety Analysis Set)

	Dose 1		Dose 2		Dose 3
	Vaccine Group 50 mcg n (%) N=3,004	**Placebo Group**[a] n (%) N=993	**Vaccine Group 50 mcg** n (%) N=2,988	**Placebo Group**[a] n (%) N=969	**Vaccine Group 25 mcg** n (%) N=1,280
Pain					
Any grade	2,796 (93.1)	465 (46.8)	2,832 (94.8)	480 (49.5)	1152 (90.1)
Grade 3[b]	28 (0.9)	0	81 (2.7)	2 (0.2)	24 (1.9)
Erythema (redness)					
Any grade	349 (11.9)	13 (1.3)	559 (18.7)	10 (1.0)	137 (10.7)
Grade 3[c]	16 (0.5)	1 (0.1)	33 (1.1)	1 (0.1)	4 (0.3)
Swelling (hardness)					
Any grade	354 (11.8)	12 (1.2)	507 (17.0)	12 (1.2)	139 (10.9)

Grade 3[c]	19 (0.6)	1 (0.1)	20 (0.7)	0 (0)	4 (0.3)
Axillary swelling/ tenderness					
Any grade	465 (15.5)	84 (8.5)	537 (18.0)	65 (6.7)	355 (27.8)
Grade 3[b]	3 (<0.1)	1 (0.1)	3 (0.1)	2 (0.2)	4 (0.3)

n= # of participants with specified reaction, percentages are based on n/N.
N= number of exposed subjects who submitted any data for the event.
[a] Placebo was a saline solution.
[b] Grade 3 pain and axillary swelling/tenderness: Defined as prevents daily activity.
[c] Grade 3 swelling and erythema: Defined as >100 mm / >10 cm

Table 18 – Solicited Systemic Adverse Reactions Within 7 Days After First and Second Injection by Grade – Participants 6 to 11 Years of Age in Study P204 Part 2 (Solicited Safety Analysis Set)

	Dose 1		**Dose 2**		**Dose 3**
	Vaccine Group 50 mcg n (%) N=3,004	**Placebo Group[a]** n (%) N=993	**Vaccine Group 50 mcg** n (%) N=2,988	**Placebo Group[a]** n (%) N=969	**Vaccine Group 25 mcg n (%)** N=1,280
Fever					
Any grade	99 (3.3)	15 (1.5)	714 (23.9)	19 (2.0)	108 (8.5)
Grade 3 (≥39.0° – ≤40.0°C)	17 (0.6)	2 (0.2)	113 (3.8)	2 (0.2)	16 (1.3)
Grade 4 (>40.0°C)	0	0	0	0	1 (<0.1)
Headache					
Any grade	938 (31.2)	306 (30.8)	1,622 (54.3)	275 (28.4)	489 (38.2)
Grade 3[b]	18 (0.6)	4 (0.4)	119 (4.0)	8 (0.8)	22 (1.7)
Fatigue					
Any grade	1,298 (43.2)	334 (33.6)	1,925 (64.5)	335 (34.6)	625 (48.9)
Grade 3[b]	31 (1.0)	8 (0.8)	191 (6.4)	8 (0.8)	47 (3.7)
Myalgia					
Any grade	438 (14.6)	96 (9.7)	843 (28.2)	105 (10.8)	269 (21.0)
Grade 3[b]	11 (0.4)	1 (0.1)	71 (2.4)	1 (0.1)	19 (1.5)
Arthralgia					
Any grade	260 (8.7)	75 (7.6)	482 (16.1)	84 (8.7)	160 (12.5)
Grade 3[b]	3 (<0.1)	1 (0.1)	25 (0.8)	0 (0)	12 (0.9)
Nausea/vomiting					

Any grade	325 (10.8)	107 (10.8)	716 (24.0)	97 (10.0)	168 (13.1)
Grade 3[c]	5 (0.2)	0 (0)	19 (0.6)	0 (0)	6 (0.5)
Chills					
Any grade	309 (10.3)	67 (6.7)	904 (30.3)	74 (7.6)	179 (14.0)
Grade 3[b]	3 (<0.1)	0 (0)	19 (0.6)	0 (0)	4 (0.3)

n= # of participants with specified reaction, percentages are based on n/N.
N= number of exposed subjects who submitted any data for the event.
[a] Placebo was a saline solution.
[b] Grade 3 headache, fatigue, myalgia, arthralgia and chills: Defined as prevents daily activity.
[c] Grade 3 nausea/vomiting: Defined as prevents daily activity.

Unsolicited Adverse Events

Participants (6 to 11 years of age) were monitored for unsolicited adverse events for up to 28 days following each dose. Serious adverse events and medically attended adverse events will be recorded for the entire study duration. As of November 10, 2021, overall safety data are available for the 4,382 participants enrolled in Study P204 Part 1 and Part 2 which includes data from 3,387 participants who received at least one 50 mcg dose of SPIKEVAX (elasomeran) (Part 1=380; Part 2=3,007) and 995 placebo participants in Part 2.

Unsolicited adverse events that occurred within 28 days following each vaccination were reported by 29.6% of participants (n=3,007) who received SPIKEVAX (elasomeran) and 25.1% of participants (n=995) who received placebo. Unsolicited adverse events that occurred in ≥ 1% of study participants who received SPIKEVAX (elasomeran) and at a rate at least 1.5-fold higher rate than placebo, were injection site erythema (3.0% versus 0.1%) and injection site lymphadenopathy (1.7% vs 0.4%). Hypersensitivity events were reported in 4.7% of the SPIKEVAX (elasomeran) group compared to 2.5% of the placebo group, but this imbalance was mostly due to injection site rash and urticaria occurring more frequently in the SPIKEVAX (elasomeran) group.

Serious adverse events (SAE) within 28 days of any injection were reported by <0.1% (n=4) of participants who received SPIKEVAX (elasomeran). No SAEs during the study were assessed by the investigator as related to study vaccine.

8.2.4.3.2 Booster Dose

Safety data for a booster dose of SPIKEVAX (elasomeran) in individuals 6 years through 11 years of age were collected in an ongoing Phase 2/3 clinical trial with multiple parts. The open-label booster portion of the study involved 1,294 participants 6 years through 11 years of age who received a booster dose of SPIKEVAX (elasomeran) at least 6 months after the second dose of the primary series (Study P204, NCT04796896). As of the data cutoff date of May 23, 2022, the median duration of follow-up for safety was 29 days after the booster dose. No additional adverse reactions were identified in the open-label portion of the study.

Solicited Adverse Reactions

The most common solicited local adverse reactions (ARs) were pain (90 %) and axillary swelling or tenderness (28 %). The most common solicited systemic ARs were fatigue (49%), headache (38%), myalgia (21%), and chills (14%). The median duration of solicited local and systemic adverse reactions was 3 days.

Unsolicited Adverse Events

Participants were monitored for unsolicited adverse events for up to 28 days following the booster dose. Serious adverse events and medically attended adverse events will be recorded for the entire study duration. As of May 23, 2022, among the 1,294 participants who had received a booster dose, unsolicited adverse events that occurred within 28 days following vaccination were reported by 13.1% of participants (n=169). In these analyses, 55.4% of study participants had at least 28 days of follow-up after the booster dose. Serum sickness-like reaction with onset 10 days following administration of a booster dose was reported in an 8-year-old participant. This event was assessed as related to vaccination. After initiation of treatment with antihistamines and steroids, symptoms resolved within 15 days with the exception of intermittent urticaria that was ongoing 31 days after the onset of the reaction.

Serious Adverse Events

As of May 23, 2022, with a median follow-up duration of 29 days after booster, there was one serious adverse event of abdominal pain reported 16 days following booster dose by a 7-year-old participant. Currently available information is insufficient to determine a causal relationship with the vaccine.

8.2.4.4 Children 6 Months to 5 Years of Age

8.2.4.4.1 Primary Series

The safety profile presented below is based on data generated in an ongoing Phase 2/3, placebo controlled clinical study on subjects 6 months to 5 years of age in which pre-specified cohorts of subjects who were either 6 months to < 2 years of age or 2 years to 5 years of age (Study P204). At the time of the analysis, the safety analysis set included 375 subjects who were 6 months to < 1 year of age, 1,373 subjects who were 1 to < 2 years of age, and 3,007 subjects who were 2 to 5 years of age.

Solicited Adverse Reactions

Data on solicited local and systemic adverse reactions and use of antipyretic medication were collected on a daily basis in an electronic diary for 7 days following each injection (i.e., day of vaccination and the next 6 days) among pediatric participants aged 6 months to 5 years of age receiving SPIKEVAX (elasomeran) (n=4,792) and participants receiving placebo (n=1,596) with at least 1 documented dose, and 4,561 participants receiving SPIKEVAX (elasomeran) and 1,498 participants in the placebo group had received dose 2 in Study P204 Part 2. For events that persisted for more than 7 days the caregiver was prompted to continue to record until resolution.

The reported number and percentage of the solicited local and systemic adverse reactions in participants 6 months to less than 2 years by dose are presented in Table 19 and Table 20 respectively. The majority of solicited local and systemic adverse reactions following administration of SPIKEVAX (elasomeran) occurred within the first 2 days after any dose and persisted for a median of 2 to 3 days.

The reported number and percentage of the solicited local adverse reactions in participants 2 years to 5 years by dose are presented in Table 21. The reported number and percentage of the solicited systemic adverse reactions in participants 24 months to less than or equal to 36 months and in participants 37 months to 5 years by dose are presented in Table 22 and Table 23, respectively. The majority of solicited local and systemic adverse reactions following administration of SPIKEVAX (elasomeran) occurred within the first 1 to 2 days after any dose and persisted for a median of 2 days.

Table 19 – Solicited Local Adverse Reactions Within 7 Days After First and Second Injection by Grade – Participants 6 Months to < 24 Months of Age in Study P204 Part 2 (Solicited Safety Analysis Set)

	Dose 1		Dose 2	
	Vaccine Group 25 µg N=1,746 n (%)	**Placebo[a]** N=582 n (%)	**Vaccine Group 25 µg** N=1,596 n (%)	**Placebo[a]** N=526 n (%)
Pain				
Any	652 (37.4)	175 (30.1)	738 (46.2)	135 (25.7)
Grade 3[b]	0 (0)	0 (0)	0 (0)	0 (0)
Erythema (redness)				
Any	150 (8.6)	24 (4.1)	215 (13.5)	20 (3.8)
Grade 3[c]	5 (0.3)	2 (0.3)	13 (0.8)	0 (0)
Swelling (hardness)				
Any	146 (8.4)	15 (2.6)	243 (15.2)	11 (2.1)
Grade 3[c]	5 (0.3)	0 (0)	14 (0.9)	0 (0)
Axillary (or groin) swelling or tenderness				
Any	102 (5.9)	26 (4.5)	148 (9.3)	28 (5.3)
Grade 3[b]	0 (0)	0 (0)	0 (0)	0 (0)

n= # of participants with specified reaction, percentages are based on n/N.
N= number of exposed subjects who submitted any data for the event.
[a] Placebo was a saline solution.
[b] Grade 3 pain and axillary swelling/tenderness: Defined as prevents daily activity.
[c] Grade 3 swelling and erythema: Defined as >50 mm / >5 cm

Table 20 – Solicited Systemic Adverse Reactions Within 7 Days After First and Second Injection by Grade – Participants 6 Months to < 24 Months of Age in Study P204 Part 2 (Solicited Safety Analysis Set)

	Dose 1		Dose 2	
	Vaccine Group 25 µg N=1,746 n (%)	**Placebo[a]** N=582 n (%)	**Vaccine Group 25 µg** N=1,596 n (%)	**Placebo[a]** N=526 n (%)
Fever				
Any	191 (11.0)	49 (8.4)	232 (14.6)	44 (8.4)
Grade 3 (≥39.6°C to ≤40°C)	11 (0.6)	3 (0.5)	7 (0.4)	6 (1.1)
Grade 4 (>40.0°C)	1 (<0.1)	1 (0.2)	3 (0.2)	0 (0)
Use of antipyretic or analgesic medications[c]	482 (27.6)	141 (24.2)	543 (34.0)	111 (21.1)
Irritability/crying				
Any	1,175 (67.6)	361 (62.1)	1,021 (64.3)	307 (58.5)
Grade 3[b]	24 (1.4)	6 (1.0)	25 (1.6)	5 (1.0)
Sleepiness				
Any	645 (37.1)	217 (37.3)	558 (35.1)	175 (33.3)
Grade 3[b]	4 (0.2)	1 (0.2)	1 (< 0.1)	1 (0.2)
Loss of appetite				
Any	524 (30.2)	152 (26.2)	510 (32.1)	132 (25.1)
Grade 3[b]	10 (0.6)	1 (0.2)	16 (1.0)	2 (0.4)

n= # of participants with specified reaction, percentages are based on n/N.
N= number of exposed subjects who submitted any data for the event.
[a] Placebo was a saline solution.
[b] Grade 3 irritability/crying, sleepiness and loss of appetite: Defined as prevents daily activity

Table 21 – Solicited Local Adverse Reactions Within 7 Days After First and Second Injection by Grade – Participants 2 to 5 Years of Age in Study P204 Part 2 (Solicited Safety Analysis Set)

	Dose 1		Dose 2	
	Vaccine Group 25 µg N = 2,957 n (%)	**Placebo[a]** N = 970 n (%)	**Vaccine Group 25 µg** N = 2,938 n (%)	**Placebo[a]** N = 959 n (%)
Pain				
Any	1,813 (61.4)	382 (39.4)	2,099 (71.4)	395 (41.2)
Grade 3 [b]	4	0	11	0

	Dose 1		Dose 2	
	Vaccine Group 25 µg N = 2,957 n (%)	**Placebo[a]** N = 970 n (%)	**Vaccine Group 25 µg** N = 2,938 n (%)	**Placebo[a]** N = 959 n (%)
	(0.1)	(0)	(0.4)	(0)
Erythema (redness)				
Any	164 (5.5)	14 (1.4)	259 (8.8)	15 (1.6)
Grade 3[c]	12 (0.4)	3 (0.3)	12 (0.4)	0 (0)
Swelling (hardness)				
Any	134 (4.5)	17 (1.8)	240 (8.2)	11 (1.1)
Grade 3[c]	10 (0.3)	2 (0.2)	13 (0.4)	0 (0)
Axillary (or groin) swelling or tenderness				
Any	205 (6.9)	56 (5.8)	267 (9.1)	31 (3.2)
Grade 3[b]	0 (0)	0 (0)	1 (< 0.1)	0 (0)
Use of antipyretic or analgesic medications[d]	498 (16.8)	121 (12.5)	800 (27.2)	105 (10.9)

n= # of participants with specified reaction, percentages are based on n/N.
N= number of exposed subjects who submitted any data for the event.
[a] Placebo was a saline solution.
[b] Grade 3 pain and axillary swelling/tenderness: Defined as prevents daily activity.
[c] Grade 3 swelling and erythema: Defined as >100 mm / >10 cm
[d] Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary).

Table 22 – Solicited Systemic Adverse Reactions Within 7 Days After First and Second Injection by Grade – Participants 24 Months to ≤ 36 Months of Age in Study P204 Part 2 (Solicited Safety Analysis Set)

	Dose 1		Dose 2	
	Vaccine Group 25 µg N = 944 n (%)	**Placebo[a]** N = 320 n (%)	**Vaccine Group 25 µg** N = 963 n (%)	**Placebo[a]** N = 330 n (%)
Fever				
Any	106 (11.3)	25 (7.8)	182 (18.9)	35 (10.6)
Grade 3 (≥39.6°C to ≤40°C)	3 (0.3)	3 (0.3)	12 (1.2)	0 (0)
Grade 4 (>40.0°C)	3 (0.3)	1 (0.3)	3 (0.3)	0 (0)
Irritability/crying				
Any	513	163	523	148

	Dose 1		Dose 2	
	Vaccine Group 25 µg N = 944 n (%)	**Placebo[a]** N = 320 n (%)	**Vaccine Group 25 µg** N = 963 n (%)	**Placebo[a]** N = 330 n (%)
	(54.5)	(51.1)	(54.3)	(44.8)
Grade 3[b]	12 (1.3)	6 (1.9)	10 (1.0)	2 (0.6)
Sleepiness				
Any	285 (30.3)	92 (28.8)	347 (36.0)	89 (27.0)
Grade 3[b]	2 (0.2)	0 (0)	1 (0.1)	0 (0)
Loss of appetite				
Any	225 (23.9)	71 (22.3)	294 (30.5)	69 (20.9)
Grade 3[b]	7 (0.7)	1 (0.3)	8 (0.8)	0 (0)

n= # of participants with specified reaction, percentages are based on n/N.
N= number of exposed subjects who submitted any data for the event.
[a] Placebo was a saline solution.
[b] Grade 3 irritability/crying, sleepiness and loss of appetite: Defined as prevents daily activity.

Table 23 – Solicited Systemic Adverse Reactions Within 7 Days After First and Second Injection by Grade – Participants 37 Months to 5 Years of Age in Study P204 Part 2 (Solicited Safety Analysis Set)

	Dose 1		Dose 2	
	mRNA-1273 25 µg N = 2,013 n (%)	**Placebo[a]** N = 650 n (%)	**mRNA-1273 25 µg** (N = 1,975 n (%)	**Placebo[a]** N = 629 n (%)
Fever				
Any	155 (7.7)	33 (5.1)	316 (16.0)	28 (4.5)
Grade 3 (≥39°C to ≤40°C)	23 (1.1)	4 (0.6)	58 (2.9)	2 (0.3)
Grade 4 (>40.0°C)	1 (<0.1)	1 (0.2)	4 (0.2)	0 (0)
Headache				
Any	232 (11.5)	78 (12.0)	310 (15.7)	51 (8.1)
Grade 3[b]	5 (0.2)	2 (0.3)	8 (0.4)	1 (0.2)
Fatigue				
Any	807 (40.1)	236 (36.3)	956 (48.4)	185 (29.4)
Grade 3[b]	21 (1.0)	11 (1.7)	45 (2.3)	8 (1.3)
Myalgia				
Any	200 (9.9)	60 (9.2)	310 (15.7)	47 (7.5)

	Dose 1		Dose 2	
	mRNA-1273 25 µg N = 2,013 n (%)	**Placebo[a]** N = 650 n (%)	**mRNA-1273 25 µg** (N = 1,975 n (%)	**Placebo[a]** N = 629 n (%)
Grade 3[b]	5 (0.2)	2 (0.3)	9 (0.5)	3 (0.5)
Arthralgia				
Any	124 (6.2)	32 (4.9)	168 (8.5)	28 (4.5)
Grade 3[b]	2 (< 0.1)	1 (0.2)	3 (0.2)	0 (0)
Nausea/vomiting				
Any	137 (6.8)	50 (7.7)	194 (9.8)	30 (4.8)
Grade 3[b]	7 (0.3)	2 (0.3)	6 (0.3)	0 (0)
Chills				
Any	129 (6.4)	40 (6.2)	245 (12.4)	31 (4.9)
Grade 3[b]	1 (< 0.1)	0 (0)	10 (1.0)	2 (0.6)

n= # of participants with specified reaction, percentages are based on n/N.
N= number of exposed subjects who submitted any data for the event.
[a] Placebo was a saline solution.
[b] Grade 3 headache, fatigue, myalgia, arthralgia, nausea/vomiting and chills: Defined as prevents daily activity.

Unsolicited Adverse Events

Participants (6 months to 5 years of age) were monitored for unsolicited adverse events for up to 28 days following each dose. Serious adverse events and medically attended adverse events will be recorded for the entire study duration. As of February 21, 2022, among participants 2 through 5 years of age who had received at least 1 dose of SPIKEVAX (elasomeran) (25 mcg) or placebo (SPIKEVAX=3,031, placebo=1,007), unsolicited adverse events that occurred within 28 days following each vaccination were reported by 40.0% of participants (n=1,212) who received SPIKEVAX (elasomeran)and 37.5% of participants (n=378) who received placebo. In these analyses, 89.3% of study participants 2 through 5 years of age had at least 28 days of follow-up after Dose 2.

Among participants 6 through 23 months of age who had received at least 1 dose of SPIKEVAX (elasomeran) (25 mcg) or placebo (SPIKEVAX=1,761, placebo=589), unsolicited adverse events that occurred within 28 days following each vaccination were reported by 49.3% of participants (n=869) who received SPIKEVAX (elasomeran) and 48.2% of participants (n=284) who received placebo. In these analyses, 83.1% of study participants 6 through 23 months of age had at least 28 days of follow-up after Dose 2. Among participants 2 through 5 years of age, one unsolicited adverse event of injection site erythema (1.3% versus 0.2%) occurred in ≥ 1% of study participants who received SPIKEVAX (elasomeran) and at a rate at least 1.5-fold higher rate than placebo. Among participants 6 months through 23 months of age, unsolicited adverse events that occurred in ≥ 1% of study participants who received SPIKEVAX (elasomeran) and at a rate at least 1.5-fold higher rate than placebo, were otitis media acute (1.4% versus 0.7%), injection site lymphadenopathy (1.4% versus 0.2%) and injection site erythema (1.1% versus 0.2%).

As of February 21, 2022, serious adverse events were reported by 0.3% (n=9) of participants who received SPIKEVAX (elasomeran) and 0.2% (n=2) participants who received placebo who were 2 through 5 years of age, and by 0.9% (n=15) of participants who received SPIKEVAX (elasomeran) and 0.2% (n=1) participants who received placebo who were 6 through 23 months of age. In these analyses, 89.3% of study participants 2 through 5 years of age had at least 28 days of follow-up after Dose 2, and the median follow-up time for all participants was 71 days after Dose 2. In these analyses, 83.1% of study participants 6 through 23 months of age had at least 28 days of follow-up after Dose 2, and the median follow-up time for all participants was 68 days after Dose 2. In participants 2 through 5 years of age who received SPIKEVAX (elasomeran), none of the events were considered related to vaccine. In participants 6 through 23 months of age who received the vaccine, a 1-year-old female experienced serious adverse events of a Grade 3 fever 6 hours after Dose 1 and a febrile convulsion 2 days after Dose 1. These events were considered related to vaccination.

8.2.4.4.2 Booster Dose

Safety data for a booster dose of SPIKEVAX (elasomeran) in individuals 6 months through 5 years of age were collected in an ongoing Phase 2/3 clinical trial with multiple parts. The open-label booster portion of the study involved 145 participants 6 months through 5 years of age who received a 10 mcg booster dose of SPIKEVAX (elasomeran) at least 6 months after the second dose of the primary series (Study P204). As of the data cut-off date of August 18, 2022, the median duration of follow-up for safety was 99 days after the booster dose.

Solicited Adverse Reactions

The most common solicited local adverse reactions (ARs) reported in participants 17 to 36 months of age were pain (42 %), erythema (11%) and swelling (11 %). The most common solicited local adverse reactions (ARs) reported in participants 37 months to 5 years of age were pain (56 %), swelling (12%) and erythema (4%). The most common solicited systemic ARs in participants 17 to 36 months of age were irritability/crying (53%), sleepiness (27%), loss of appetite (23%) and fever (10%). The most common solicited systemic ARs in participants 37 months to 5 years of age were fatigue (32%), headache (20%), myalgia (12%), arthralgia (8%), chills (8%) and nausea (4%). The median duration of solicited local and systemic adverse reactions was 3 days.

Unsolicited Adverse Events

Participants were monitored for unsolicited adverse events for up to 28 days following the booster dose. Serious adverse events and medically attended adverse events will be recorded for the entire study duration. As of August 18, 2022, among the 145 participants who had received a booster dose, unsolicited adverse events that occurred within 28 days following vaccination were reported by 24.1% of participants (n=35). In these analyses, 99.3% of study participants had at least 28 days of follow-up after the booster dose. Through the cut-off date, there were no unsolicited adverse events not already captured as solicited local and systemic reactions that were considered causally related to the vaccine.

Serious Adverse Events

As of August 18, 2022, with a median follow-up duration of 99 days after booster, there were no serious adverse events reported following the booster dose.

8.3 Less Common Clinical Trial Adverse Reactions

The following events were reported in the ongoing Phase 3, placebo-controlled clinical study of SPIKEVAX (elasomeran) in participants ≥ 18 years of age:

Nervous System Disorders: Acute peripheral facial paralysis†

Skin and Subcutaneous Tissue Disorders: Rash.

General Disorders and Administration Site Conditions: Injection site pruritus, injection site rash, injection site swelling, injection site erythema, injection site urticaria, facial swelling.§

† Throughout the safety follow-up period, acute peripheral facial paralysis (or palsy) was reported by three participants in the SPIKEVAX group and one participant in the placebo group. Onset in the vaccine group participants was 22 days, 28 days, and 32 days after Dose 2.
§ There were two serious adverse events of facial swelling in vaccine recipients with a history of injection of dermatological fillers. The onset of swelling was reported on Day 1 and Day 3, respectively, relative to day of vaccination.

8.5 Post-Market Adverse Reactions

The following adverse reactions have been identified during post-authorization use of SPIKEVAX (elasomeran).

Immune System Disorders: Anaphylaxis, hypersensitivity.

Cardiac Disorders: Myocarditis and/or pericarditis (see WARNINGS AND PRECAUTIONS).

Skin and Subcutaneous Tissue Disorders: Erythema multiforme, acute and delayed urticaria.

Nervous System Disorders: facial paralysis / Bell's palsy, hypoaesthesia / paraesthesia, dizziness.

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to product exposure.

9 DRUG INTERACTIONS

No interaction studies have been performed.

Other Vaccines
Do not mix SPIKEVAX with other vaccines/products in the same syringe.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

SPIKEVAX encodes for the pre-fusion stabilized Spike (S) protein of SARS-CoV-2 . After intramuscular injection, cells take up the lipid nanoparticle, effectively delivering the mRNA sequences into cells for expression of the SARS-CoV-2 S antigen. The delivered mRNA does not enter the cellular nucleus or

interact with the genome, is nonreplicating, and is expressed transiently. The proteins undergo post-translational modification and trafficking resulting in properly folded, fully functional Spike proteins that are inserted into the cellular membrane of the expressing cell(s). The Spike proteins are membrane bound, mimicking the presentation of natural infection. The vaccine induces both neutralizing antibody and cellular immune responses (T-cell and B-cell) to the Spike (S) antigen, which may contribute to protection against COVID-19 disease.

11 STORAGE, STABILITY AND DISPOSAL

Storage Prior to Use

As Displayed on the Vial Labels and Cartons

The SPIKEVAX multidose vials are stored frozen between -50° to -15°C (-58° to 5°F). Store in the original carton to protect from light.

Additional Storage Information Not Displayed on the Vial Labels and Cartons

- Vials can be stored refrigerated between 2° to 8°C (36° to 46°F) for up to 50 days prior to first use.
- Unpunctured vials may be stored between 8° to 25°C (46° to 77°F) for up to 12 hours.
- Do not refreeze once thawed.

Transportation of Thawed Vials in Liquid State at 2° to 8°C (36° to 46°F)

If transport at -50° to -15°C (-58° to 5°F) is not feasible, available data support transportation of one or more thawed vials in liquid state for up to 36 hours at 2° to 8°C (36° to 46°F) when shipped using shipping containers which have been qualified to maintain 2° to 8°C (36° to 46°F) and under routine road and air transport conditions with shaking and vibration minimized. Precautions should be taken (packaging/dunnage) to minimize vibration of vials when transporting at this temperature. Once thawed and transported in liquid state at 2° to 8°C (36° to 46°F), vials should not be refrozen and should be stored at 2° to 8°C (36° to 46°F) until use.

Thawing Vials Prior To Use

The SPIKEVAX multidose vial contains a frozen dispersion that does not contain a preservative and must be thawed prior to administration. Remove the required number of vial(s) from storage and thaw each vial before use.

Presentation	Vial Cap Colour	Thaw time under refrigeration between 2° to 8°C (36° to 46°F)	Thaw time at room temperature between 15° to 25°C (59° to 77°F)
0.1 mg/mL	**Royal Blue**	• 2 hours *After thawing, let vial stand at room temperature for 15 minutes before administering.*	• 45 minutes

After thawing, do not refreeze.

Storage After Use (Punctured Vials)

SPIKEVAX is preservative-free. Once the vial has been entered (needle-punctured), it can be stored at:

- room temperature but must be discarded after 12 hours, or

- refrigerated, but must be discarded after 24 hours.

Do not refreeze.

12 SPECIAL HANDLING INSTRUCTIONS

SPIKEVAX must not be mixed with other medicinal products or diluted. Any unused vaccine or waste material should be disposed of in accordance with local requirements.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: COVID-19 mRNA vaccine

Medicinal ingredient: mRNA encoding SARS-CoV-2 spike protein, 5'(m7G-5'-ppp-5'-Gm) cap, 100-nucleotide 3' poly(A) tail

Product Characteristics

SPIKEVAX is an mRNA-lipid complex [lipid nanoparticle (LNP)] dispersion that contains mRNA encoding the pre-fusion stabilized Spike glycoprotein (S) of SARS-CoV-2, and four lipids which act as protectants and carriers of the mRNA.

SPIKEVAX is supplied as a multidose liquid ready-to-use dispersion for intramuscular administration. The 0.1 mg/mL presentation of SPIKEVAX is supplied in a 10R clear Type 1 glass vial.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

The safety and effectiveness of SPIKEVAX COVID-19 mRNA vaccine for children 6 months to 11 years of age are inferred from studies of a primary series of SPIKEVAX Bivalent (Original/Omicron BA.1) in individuals 6 months to 5 years of age and older. Safety data from SPIKEVAX primary series studies in individuals ≥18 years of age and studies from SPIKEVAX Bivalent as a booster dose in individuals ≥18 years of age and individuals 6 months to 5 years of age are also considered supportive. The safety and effectiveness of SPIKEVAX for children 6 to 11 years of age and adolescents 12 through 17 years of age are also inferred from studies of a booster dose of SPIKEVAX Bivalent (Original/Omicron BA.1) in individuals 18 years of age and older, as well as data from studies which evaluated the primary series and booster vaccination with SPIKEVAX. The safety of SPIKEVAX in adolescents 12 through 17 years of age is inferred from safety data from studies of a booster dose of SPIKEVAX in adolescents 12 through 17 years of age and from the safety profile of SPIKEVAX administered as a booster dose in children 6 to 11 years of age. Safety data from studies in individuals ≥18 years of age using SPIKEVAX Bivalent (50 mcg) are also considered supportive.

The safety of SPIKEVAX is based on safety data from clinical trials which evaluated primary and booster vaccination with SPIKEVAX (see CLINICAL TRIALS, Clinical Trial Adverse Reactions) and post marketing safety data. Safety data accrued with SPIKEVAX and SPIKEVAX Bivalent in individuals ≥18 years of age are relevant to the SPIKEVAX vaccine in individuals 6 through 17 years of age because these vaccines are manufactured using the same process.

Table 24 – Summary of SPIKEVAX, SPIKEVAX Bivalent and SPIKEVAX XBB.1.5 Clinical Trials

Study #	Study Drug	Study Design	Dosage, route of administration and duration	Study subjects[a] (n)
P301	SPIKEVAX	Randomized, placebo-controlled study in adults 18 years of age and older	100 mg, IM, 2 doses 29 days apart	14,134
P201 Part B	SPIKEVAX	Open-label study arm assessing immunogenicity in participants 18 years of age and older	50 mcg booster dose, IM, at least 6 months following primary series	171
P203 Part 1C-1	SPIKEVAX	Open-label study arm assessing immunogenicity and safety in participants 12 to 17 years of age and older	50 mcg booster dose, IM, at least 5 months following primary series	1346
P204	SPIKEVAX	Open-label study assessing immunogenicity and safety in participants 6 months to 11 years of age and older	10 mcg or 25 mcg booster dose, IM	1439
P205 Part G	SPIKEVAX Bivalent (Original/ Omicron BA.1)	Open-label Phase 2/3 assessing immunogenicity and safety in participants 18 years of age and older	50 mcg second booster dose, IM	437
P205 Part H	SPIKEVAX Bivalent Original/ Omicron BA.4/5	Open-label Phase 2/3 assessing immunogenicity and safety in participants 18 years of age and older	50 mcg second booster dose, IM	511
P205 Part J	SPIKEVAX XBB.1.5	Open-label Phase 2/3 assessing safety, reactogenicity and immunogenicity in participants 18 years of age and older	50 mcg administered as fifth dose in adults who previously received 2-dose primary series, a booster dose and a bivalent booster dose, IM	101
P306 Part 1	SPIKEVAX Bivalent (Original/ Omicron BA.1)	Open-label Phase 3 assessing safety and immunogenicity of bivalent 2-dose primary series in participants 6 months to 5 years of age	25 mcg, IM, 2 doses 28 days apart	142
P306 Part 2	SPIKEVAX Bivalent (Original/ Omicron BA.1)	Open-label Phase 3 assessing safety and immunogenicity of a booster dose in participants 6 months to 5 years of age	10 mcg booster dose, IM, at least 4 months following primary series	539

[A] Total vaccinated subjects; does not include placebo population.

14.1.1 SPIKEVAX XBB.1.5

14.1.1.1 Participants 18 Years of Age and Older

The safety, reactogenicity, and immunogenicity of SPIKEVAX XBB.1.5 are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (Study P205, Part J). In this study 50 participants received a 50 mcg dose of SPIKEVAX XBB.1.5, and 51 participants received a dose of an investigational bivalent vaccine (XBB.1.5/Omicron BA.4/5). Overall, of the SPIKEVAX XBB.1.5 group 60.0% were female and 40.0% were male. The mean age was 51.6 years (range: 21 to 84 years) and 22.0% of participants were ≥ 65 years of age. The interval between the fourth dose (SPIKEVAX Bivalent Original/Omicron BA.4/5) and the fifth dose of SPIKEVAX XBB.1.5 was a median of 8.2 months.

14.1.2 SPIKEVAX Bivalent (Original / Omicron BA.1)

14.1.2.1 Participants 18 Years of Age and Older

14.1.2.1.1 Booster Dose

The safety, reactogenicity, and immunogenicity of the SPIKEVAX Bivalent (Original / Omicron BA.1) booster dose are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (Study P205). In this study 437 participants received the SPIKEVAX Bivalent 50 mcg booster dose and 377 participants received the SPIKEVAX (Original) 50 mcg booster dose. Overall, of the SPIKEVAX Bivalent group 59.0% were female, 41.0% were male, 89.2% were White, and 10.8% were Hispanic or Latino. The median age was 60 years (range: 20 to 88 years) and 39.8% of participants were ≥ 65 years of age. Demographic and baseline characteristics were similar between the SPIKEVAX Bivalent 50 mcg and SPIKEVAX 50 mcg groups.

In Study P205 SPIKEVAX Bivalent was administered as a second booster dose. The median time between a first booster dose and the second booster dose with SPIKEVAX Bivalent was 136 days (range: 88 to 408 days). At baseline, 22.0% of subjects receiving SPIKEVAX Bivalent as a second booster dose had evidence of prior SARS-CoV-2 infection.

14.1.2.2 Participants 6 Months to 5 Years of Age

14.1.2.2.1 Primary Series

The safety, reactogenicity and effectiveness of SPIKEVAX Bivalent (Original / Omicron BA.1) for use as a primary series (2 doses of 25 mcg) are evaluated in an ongoing, Phase 3, open-label study in participants 6 months to 5 years of age (Study P306 Part 1). SPIKEVAX Bivalent (Original / Omicron BA.1) was administered to vaccine-naïve children compared with recipients of SPIKEVAX (original) in the same group in Study P204. In this study as of the data cut-off (05 Dec 2022) 142 subjects received two doses of SPIKEVAX Bivalent, and 179 subjects received at least 1 dose. The per-protocol immunogenicity set was 71 participants that were compared to 632 subjects who received the SPIKEVAX (original) two-dose primary series in Study P204. Overall, of the SPIKEVAX Bivalent group 54.7% were male, 45.3% were female, 65.4% were White, 25.7% were Black and 11.7% were Hispanic or Latino. The median age was 3 years. At baseline, 63.4% of subjects receiving SPIKEVAX Bivalent had evidence of prior SARS-CoV-2 infection. Participants will be followed for occurrence of COVID-19 and safety until 1 year after the last dose.

14.1.2.2.2 Booster Dose

The safety and immunogenicity of the SPIKEVAX Bivalent (Original / Omicron BA.1) booster dose are evaluated in an ongoing, Phase 3, open-label study in participants 6 months to 5 years of age (Study P306 Part 2). SPIKEVAX Bivalent was administered as a single 10 mcg booster dose to participants who had received a SPIKEVAX (original) two-dose primary series at least 4 months prior. As of the data cut-off (05 Dec 2022), 539 subjects had received a booster dose. The median time between dose 2 of the primary series and the SPIKEVAX Bivalent booster dose was 7.85 months.

14.1.3 SPIKEVAX (Original)

14.1.3.1 Participants 18 Years of Age and Older

14.1.3.1.1 Primary Series

The safety and efficacy of SPIKEVAX (elasomeran) were evaluated in Study P301, a Phase 3 randomized, placebo-controlled, multicentre study in participants 18 years of age and older (COVE Study). A total of 30,351 (15,181 in the SPIKEVAX group and N=15,170 in the placebo group) participants were randomized equally to receive 2 doses of SPIKEVAX or placebo separated by 28 days. Randomization was stratified by age and risk of severe COVID-19 as follows: ≥ 65 years old, < 65 years old and at increased risk for the complications of COVID-19, and < 65 years old and not at increased risk for the complications of COVID-19.

Pregnant or breastfeeding women and individuals with known history of SARS-CoV-2 infection, immunosuppressive or immunodeficient state, asplenia or recurrent severe infections were excluded from the study. The primary efficacy was symptomatic* COVID-19 infection confirmed by Polymerase Chain Reaction (PCR) and by a clinical adjudication committee. The population for the analysis of the primary efficacy endpoint included participants who did not have evidence of prior infection with SARS-CoV-2 through 14 days after the second dose. Participants are planned to be followed for up to 24 months for assessments of safety and efficacy against COVID-19 disease.

* Symptomatic COVID-19 case definition: At least two of the following systemic symptoms: fever (≥38ºC), 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 the participant must have at least one NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) positive for SARS- CoV-2 by RT-PCR. COVID-19 cases were adjudicated by a Clinical Adjudication Committee.

Table 25 – Demographic Characteristics – Subjects ≥ 18 Years of Age Without Evidence of Infection Prior to 14 Days After Dose 2 – Evaluable Efficacy Population (Data Accrued Through November 21, 2020)

	SPIKEVAX Group (N=14,134) n (%)	**Placebo Group** (N=14,073) n (%)	**Total** (N=28,207) n (%)
Sex			
Female	6,768 (47.9)	6,611 (47.0)	13,379 (47.4)
Male	7,366 (52.1)	7,462 (53.0)	14,828 (52.6)
Age (years)			
Mean (SD)	51.6 (15.44)	51.6 (15.54)	51.6 (15.49)
Median	53.0	52.0	53.0

	SPIKEVAX Group (N=14,134) n (%)	Placebo Group (N=14,073) n (%)	Total (N=28,207) n (%)
Min, max	18, 95	18, 95	18, 95
Age – Subgroups (years)			
18 to <65	10,551 (74.6)	10,521 (74.8)	21,072 (74.7)
65 and older	3,583 (25.4)	3,552 (25.2)	7,135 (25.3)
Race			
American Indian or Alaska Native	108 (0.8)	111 (0.8)	219 (0.8)
Asian	620 (4.4)	689 (4.9)	1,309 (4.6)
Black or African American	1,385 (9.8)	1,349 (9.6)	2,734 (9.7)
Native Hawaiian or Other Pacific Islander	35 (0.2)	31 (0.2)	66 (0.2)
White	11,253 (79.6)	11,174 (79.4)	22,427 (79.5)
Other	299 (2.1)	295 (2.1)	594 (2.1)
Ethnicity			
Hispanic or Latino	2,789 (19.7)	2,780 (19.8)	5,569 (19.7)
Not Hispanic or Latino	11,212 (79.3)	11,165 (79.3)	22,377 (79.3)
Race and Ethnicity			
Non-Hispanic White	9,023 (63.8)	8,916 (63.4)	17,939 (63.6)
Communities of color	5,088 (36.0)	5,132 (36.5)	10,220 (36.2)
Occupational Risk*	11,586 (82.0)	11,590 (82.4)	23,176 (82.2)
Healthcare worker	3,593 (25.4)	3,581 (25.4)	7,174 (25.4)
High Risk Condition**			
One high risk condition present	2,616 (18.5)	2,591 (18.4)	5,207 (18.5)
Two or more high risk conditions present	590 (4.2)	576 (4.1)	1,166 (4.1)
No high risk condition	10,928 (77.3)	10,906 (77.5)	21,834 (77.4)
Age and Health Risk for Severe COVID-19***			
18 to <65 years and not at risk	8,189 (57.9)	8,200 (58.3)	16,389 (58.1)
18 to <65 years and at risk	2,367 (16.7)	2,324 (16.5)	4,691 (16.6)
≥ 65 years	3,578 (25.3)	3,549 (25.2)	7,127 (25.3)

* Occupational risk includes: Healthcare Workers; Emergency Response; Retail/Restaurant Operations; Manufacturing and Production; Operations, Warehouse Shipping and Fulfillment centers, Transportation and Delivery Services, Border Protection and Military Personnel Personal care and in-home services; Hospitality and Tourism Workers, Pastoral; Social or Public Health Workers; and Educators and Students.

** High risk for severe COVID-19 is defined as patients who meet at least one of the following criteria (protocol-defined):

- Chronic lung disease (e.g., emphysema and chronic bronchitis, idiopathic pulmonary fibrosis, and cystic fibrosis) or moderate to severe asthma
- Significant cardiac disease (e.g., heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and
- pulmonary hypertension)
- Severe obesity (body mass index ≥ 40 kg/m2)
- Diabetes (Type 1, Type 2 or gestational)
- Liver disease
- Human immunodeficiency virus (HIV) infection

*** Age and health risk for severe COVID-19 is used as stratification factor for randomization.

14.1.3.1.2 Booster Dose

A booster dose of SPIKEVAX (elasomeran) was evaluated in Study P201 Part B, an open-label part assessing immunogenicity following administration of a 50 ug booster dose in participants 18 years of age and older (N=171) who had received a SPIKEVAX primary series in Study P201 Part A. Participants were predominantly female (60.8%), had a mean age of approximately 52 years and were predominantly white (95.9%).

14.1.3.2 Adolescents 12 to 17 Years of Age

14.1.3.2.1 Primary Series

Safety, efficacy, and immunogenicity data for SPIKEVAX (elasomeran) in adolescents were collected in an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind clinical trial (Study P203) conducted in the United States involving 3,726 participants 12 through 17 years of age who received at least one dose of SPIKEVAX (elasomeran) (n=2,486) or placebo (n=1,240). Overall, 51.4% were male, 48.6% were female, 11.6% were Hispanic or Latino, 83.9% were White, 3.4% were African American, 5.9% were Asian, 0.5% were American Indian or Alaska Native, <0.1% were Native Hawaiian or Pacific Islander, 1.0% were other races, and 4.5% were multiracial. Demographic characteristics were similar among participants who received SPIKEVAX and those who received placebo.

14.1.3.2.2 Booster Dose

A booster dose of SPIKEVAX (elasomeran) was evaluated in an ongoing Phase 2/3 clinical trial (Study P203, NCT04649151) with multiple parts. The open-label booster portion of the study involved 1,364 participants 12 years through 17 years of age who received a 50 mcg booster dose of SPIKEVAX (elasomeran) at least 5 months after the second dose of the primary series. The median time from the second dose of the primary series to the booster dose was 316 days (range: 274 to 422 days). Overall, 51.2% were male, 48.8% were female, 13.1% were Hispanic or Latino, 84.9% were White, 3.2% were African American, 4.8% were Asian, 0.5% were American Indian or Alaska Native, <0.1% were Native Hawaiian or Pacific Islander, 0.7% were other races, and 5.2% were Multiracial.

14.1.3.3 Children 6 to 11 Years of Age

14.1.3.3.1 Primary Series

Safety, efficacy and immunogenicity data for SPIKEVAX (elasomeran) in children 6 through 11 years of age were collected in an ongoing Phase 2/3 two-part clinical trial conducted in the United States and Canada. Part 1 is an open-label phase of the trial for safety, dose selection, and immunogenicity and included 380 participants 6 through 11 years of age who received at least 1 dose (0.25 mL, 50 mcg) of SPIKEVAX (elasomeran). Part 2 is the placebo-controlled phase for safety, immunogenicity and efficacy, and included 4,002 participants 6 through 11 years of age who received at least one dose of SPIKEVAX (elasomeran) (n=3,007) or placebo (n=995). No participants in Part 1 participated in Part 2. Overall, in Part 2 50.8% were female and 49.2% male, 18.5% were Hispanic or Latino, 65.6% were White, 10.0% were African American, 9.9% were Asian, 0.4% were American Indian or Alaska Native, <0.1% were Native Hawaiian or Pacific Islander, 2.1% were other races and 10.6% were multiracial. Demographic characteristics were similar among participants who received Moderna COVID-19 Vaccine and those who received placebo.

14.1.3.3.2 Booster Dose

A booster dose of SPIKEVAX (elasomeran) was evaluated in participants 6 through 11 years of age in an ongoing Phase 2/3 clinical trial with multiple parts. The open-label booster portion of the study involved 1,294 participants 6 years through 11 years of age who received a 25 mcg booster dose of SPIKEVAX (elasomeran) at least 6 months after the second dose of the primary series (Study P204, NCT04796896). Overall, 51.9%% were male, 48.1% were female, 15.6% were Hispanic or Latino, 65.7% were White, 11.0% were African American, 7.8% were Asian, 0.5% were American Indian or Alaska Native, <0.1% were Native Hawaiian or Pacific Islander, 1.9% were other races, and 11.8% were Multiracial.

14.1.3.4 Children 6 months to 5 Years of Age

14.1.3.4.1 Primary Series

Safety, efficacy and immunogenicity data for SPIKEVAX (elasomeran) in children 6 months through 5 years of age were collected in an ongoing Phase 2/3 two-part clinical trial (Study P204). Part 1 is an open-label phase of the trial for safety, dose selection, and immunogenicity and included 225 participants 6 months through 5 years of age who received at least 1 dose (25 mcg) of SPIKEVAX (elasomeran). Part 2 is the placebo-controlled phase for safety, immunogenicity and efficacy, and included 6,388 participants 6 months through 5 years of age who received at least one dose of SPIKEVAX (elasomeran) (n=4,792) or placebo (n=1,596). No participants in Part 1 participated in Part 2. Overall, in Part 2 50.9% were male, 49.1% were female, 13.9% were Hispanic or Latino, 77.4% were White, 4.0% were African American, 5.6% were Asian, 0.3% were American Indian or Alaska Native, 0.2% were Native Hawaiian or Pacific Islander, 1.5% were other races, and 10.5% were multiracial. Demographic characteristics were similar among participants who received SPIKEVAX (elasomeran) and those who received placebo.

14.1.3.4.2 Booster Dose

Safety data for a booster dose of SPIKEVAX (elasomeran) in individuals 6 months through 5 years of age were collected in an ongoing Phase 2/3 clinical trial with multiple parts. The open-label booster portion of the study involved 145 participants 6 months through 5 years of age who received a 10 mcg booster dose of SPIKEVAX (elasomeran) at least 6 months after the second dose of the primary series (Study P204). Overall, 55.2% were male, 44.8% were female, 10.3% were Hispanic or Latino, 80.0% were White, 2.8% were African American, 6.2% were Asian, 0.7% were American Indian or Alaska Native, 0.0% were Native Hawaiian or Pacific Islander, 2.8% were other races, and 7.6% were Multiracial.

14.2 Study Results

14.2.1 SPIKEVAX XBB.1.5

14.2.1.1 Participants 18 Years of Age and Older

The safety, reactogenicity, and immunogenicity of SPIKEVAX XBB.1.5 is evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (Study P205 Part J). In this study, 50

participants received a 50 mcg dose of SPIKEVAX XBB.1.5 and 51 participants receive a dose of an investigational bivalent vaccine (XBB.1.5/Omicron BA.4/5, 50 mcg).

Study P205 Part J evaluated the safety, reactogenicity and immunogenicity of SPIKEVAX XBB.1.5 when administered as a fifth dose to adults to previously received 2 doses of SPIKEVAX (original) (100 mcg) as a primary series, a first booster dose of SPIKEVAX (original) (50 mcg) and a second booster dose of SPIKEVAX Bivalent Original/Omicron BA.4/5 (50 mcg). The evaluation of the safety and reactogenicity of SPIKEVAX XBB.1.5 was a primary objective. In addition, the evaluation of the Day 15 immunogenicity against variants contained in the vaccine was also a primary objective. All analysis were descriptive.

The median follow-up time in the interim analysis was 20 days (data cutoff date of 16 May 2023). SPIKEVAX XBB.1.5 elicited neutralizing responses at Day 15 against the SARS-CoV-2 variants assessed, including XBB.1.5, XBB.1.16, BA.4/5, BQ.1.1 and D614G. When assessed against XBB.1.5 the neutralising antibody geometric mean titre (GMT) and corresponding 95% CI was 2579.0 (1809.1, 3676.7) 15 days after the SPIKEVAX XBB.1.5 dose, and the GMFR (95% CI) was 16.7 (12.8, 21.7). When SPIKEVAX XBB.1.5 was assessed against BA.4/5, the GMT (95% CI) was 9673.4 (6965.6, 13433.8) and the GMFR (95% CI) was 6.3 (4.8, 8.2). Reactogenicity was similar to prior doses of the original SPIKEVAX vaccine and SPIKEVAX Bivalent Original/Omicron BA.4/5.

14.2.2 SPIKEVAX Bivalent Original / Omicron BA.4/5

14.2.2.1 Participants 18 Years of Age and Older

14.2.2.1.1 Booster Dose – Immunogenicity

The safety, reactogenicity, and immunogenicity of a SPIKEVAX Bivalent Original/Omicron BA.4/5 booster dose are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (Study P205 Part H). In this study, 511 participants received the SPIKEVAX Bivalent Original/Omicron BA.4-5 50 mcg booster dose, and 376 participants received the SPIKEVAX (original) 50 mcg booster dose.

Study P205 Part H evaluated the safety, reactogenicity and immunogenicity of SPIKEVAX Bivalent Original/Omicron BA.4/5 when administered as a second booster dose to adults who previously received 2 doses of SPIKEVAX (original) (100 mcg) as a primary series and a first booster dose of SPIKEVAX (original) (50 mcg). In Study P205 Part F, study participants received SPIKEVAX (original) (50 mcg) as a second booster dose and the Part F group serves as a within-study, non-contemporaneous comparator group to the SPIKEVAX Bivalent Original/Omicron BA.4/5 group.

The primary immunogenicity analysis was based on the primary immunogenicity set which includes participants with no evidence of SARS-CoV-2 infection at baseline (pre-booster). In the primary analysis, the original SARS-CoV-2 estimated neutralising antibody geometric mean titre (GMT) and corresponding 95% CI was 87.9 (72.2, 107.1) and 2324.6 (1921.2, 2812.7) 28 days after the SPIKEVAX Bivalent Original/Omicron BA.4/5 and SPIKEVAX (original) booster doses, respectively. The Day 29 GMR for SPIKEVAX Original/Omicron BA.4/5 50 mcg booster dose versus the SPIKEVAX (original) 50 mcg booster dose was 6.29 (5.27, 7.51), meeting the pre-specified criterion for superiority (lower bound of CI >1).

The estimated neutralising antibody GMTs (95% CI) against Omicron BA.4/BA.5 adjusted for pre-booster titre and age group were 2747.3 (2399.2, 3145.9) and 436.7 (389.1, 490.0) 28 days after SPIKEVAX Bivalent Original/Omicron BA.4/5 and SPIKEVAX (original) booster doses, respectively, and the GMR (95% CI) was 6.29 (5.27, 7.51), meeting the pre-specified criterion for non-inferiority (lower bound of CI >0.667).

14.2.3 SPIKEVAX Bivalent (Original / Omicron BA.1)

14.2.3.1 Participants 18 Years of Age and Older

14.2.3.1.1 Booster Dose – Immunogenicity

The safety, reactogenicity, and immunogenicity of the SPIKEVAX Bivalent (Original/Omicron BA.1) booster dose are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (Study P205). For the purpose of this clinical indication, data from Part G and Part F of the study are considered. Part G consisted of participants that were administered SPIKEVAX Bivalent vaccine as a second booster dose (50 mcg, mRNA-1273.214 [25 mcg elasomeran and 25 mcg imelasomeran]). The comparator group is from Part F, where study participants received SPIKEVAX original (50 mcg, mRNA-1273) as a second booster dose.

Immunobridging analyses compared the neutralizing antibody titers (ID50) 29 days following the second booster dose (P205 Part G; N=334) to the corresponding titers 29 days following the second booster dose (P205 Part F; N=260) against the Omicron BA.1 subvariant.

In this study, the primary analysis was based on the immunogenicity set, which included participants with no evidence of SARS-CoV-2 infection at baseline (pre-second booster dose).

The estimated Day 29 neutralising antibody GMTs against Omicron were 2479.9 (95%CI: 2264.5, 2715.8) and 1421.2 (95%CI: 1283.0, 1574.4) in the SPIKEVAX Bivalent (Part G) and SPIKEVAX original (Part F) second booster groups, respectively, and the GMR was 1.75 (97.5% CI: 1.49, 2.04). The Omicron SRRs were 100% (95%CI: 98.9, 100) and 99.2% (95%CI: 97.2, 99.9), 29 days in the mRNA-1273.214 and mRNA-1273 groups, respectively, and the SRR difference was 1.5% (97.5%CI: -1.1, 4.0). The findings are summarized in Table 26.

Table 26 – Ancestral SARS-CoV-2 (D614G) and Omicron Neutralizing Antibody Titres (ID_{50}) - SPIKEVAX Bivalent (mRNA-1273.214) 50 µg and SPIKEVAX (mRNA-1273) 50 µg Administered as Second Booster Doses

	Omicron variant		Ancestral SARS-CoV-2	
	P205 Part G	P205 Part F	P205 Part G	P205 Part F
Antibody: PsVNA nAb ID_{50} titres	SPIKEVAX Bivalent (Original/Omicron BA.1) mRNA-1273.214 50 µg (N=334)	SPIKEVAX mRNA-1273 50 µg (N=260)	SPIKEVAX Bivalent (Original/Omicron BA.1) mRNA-1273.214 50 µg (N=334)	SPIKEVAX mRNA-1273 50 µg (N=260)
Pre-booster, n	334	260	334	260
Observed GMT (95% CI)[a]	298.13 (258.75, 343.49)	332.02 (282.05, 390.85)	1266.74 (1120.19, 1432.47)	1521.00 (1352.77, 1710.15)
Day 29, n	334	260	334	260
Observed GMT (95% CI)[a]	2372.42 (2070.63, 2718.20)	1473.46 (1270.85, 1708.38)	5977.26 (5321.90, 6713.32)	5649.33 (5056.85, 6311.23)
Observed GMFR (95% CI)[a]	7.96 (7.18, 8.82)	4.44 (3.97, 4.96)	4.72 (4.36, 5.11)	3.71 (3.42, 4.03)
GLSM [estimated GMT] (95% CI)[b]	2479.89 (2264.47, 2715.80)	1421.24 (1282.98, 1574.41)	6422.32 (5990.12, 6885.71)	5286.63 (4887.07, 5718.86)
GMR (97.5% CI)[b]	**1.75 (1.49, 2.04)**		**1.22 (1.08, 1. 37)**	
Seroresponse, N1	333	258	334	260
Seroresponse rate, n (%)[c]	333 (100)	256 (99.2)	334 (100)	260 (100)
95% CI[d]	(98.9, 100.0)	(97.2, 99.9)	(98.9, 100.0)	(98.6, 100.0)
Difference in seroresponse rates (97.5%)[e]	**1.5 (-1.1, 4.0)**		**0**	

Abbreviations: CI = confidence interval; GLSM = geometric least squares mean; GMFR = geometric mean fold-rise; GMR = geometric mean ratio; GMT = geometric mean titre; ID_{50} = 50% inhibitory dilution; LLOQ = lower limit of quantification; nAb = neutralising antibodies; PsVNA = pseudotyped virus neutralisation assay; SARS-CoV-2 = severe acute respiratory syndrome-2; n = number of participants with non-missing data at the corresponding timepoint; N1 = number of participants with non-missing data at pre-vaccination baseline and the corresponding timepoint.

[a] 95% CI is calculated based on the t-distribution of the log-transformed values or the difference in the log-transformed values for GM value and GM fold-rise, respectively, then back transformed to the original scale for presentation.

[b] Based on ANCOVA modeling; the model includes adjustment for treatment group, pre-booster antibody titres, and age groups.

[C] Seroresponse at a participant level is defined as a change from below the LLOQ to equal or above 4 x LLOQ if the participant's baseline is below the LLOQ, or at least a 4-fold rise if the baseline is equal to or above the LLOQ. For participants without pre-Dose 1 antibody titer information, seroresponse is defined as >= 4*LLOQ for participants with negative SARS-CoV-2 status at their pre-dose 1 of the primary series, and these titers are imputed as <LLOQ at pre-dose 1 of primary series. For participants without SARS-CoV-2 status information at pre-dose 1 of primary series, their pre-booster SARS-CoV-2 status is used to impute their SARS-CoV-2 status at their pre-dose 1 of primary series.

[d] 95% CI is calculated using the Clopper-Pearson method.

[e] 97.5% CI was calculated by stratified Miettinen-Nurminen method adjusted by age group. The SRR difference is a calculated common risk difference using inverse-variance stratum weights and the middle point of Miettinen-Nurminen confidence limits of each one of the stratum risk differences. The stratified Miettinen-Nurminen estimate of the CI cannot be calculated when the seroresponse rate in both groups is 100%, absolute difference is reported.

14.2.3.2 Three-month Antibody Persistence of SPIKEVAX Bivalent (Original/Omicron BA.1) Booster

Participants in Study P205 Part G were sequentially enrolled to receive 50 micrograms of SPIKEVAX (original) (n = 376) or SPIKEVAX Bivalent Original/Omicron BA.1 (n = 437) as second booster doses. In participants with no pre-booster incidence of SARS-CoV-2, SPIKEVAX Bivalent Original/Omicron BA.1 elicited Omicron-BA.1-neutralising antibody titres (observed GMT) that were significantly higher (964.4 [834.4, 1114.7]) than those of SPIKEVAX (original) (624.2 [533.1, 730.9]) and similar between boosters against ancestral SARS-CoV-2 at three months.

14.2.3.2.1 SPIKEVAX Bivalent (Original/Omicron BA.1) Observed Neutralising Antibody Titres for Omicron Subvariant BA.4/5

In an exploratory analysis, additional analytical testing of SPIKEVAX Bivalent (Original/Omicron BA.1) was conducted to assess neutralizing antibody response against the dominant circulating SARS-CoV-2 Omicron subvariants BA.4/5 in July 2022.

For all participants regardless of prior SARs-CoV-2 infection the estimated Day 29 neutralising antibody GMTs against Omicron BA. 4/5 were 985.38 (95%CI: 914.77, 1061.434) and 588.36 (95%CI: 544.08, 636.24) in the SPIKEVAX Bivalent (Part G) and SPIKEVAX original (Part F) second booster groups, respectively, and the GMR was 1.68 (95%CI: 1.52, 1.84).

For participants without prior SARs-CoV-2 infection, the estimated Day 29 neutralising antibody GMTs against Omicron BA. 4/5 were 776.45 (95%CI: 719.49, 837.92) and 458.28 (95%CI: 420.62, 499.32) in the SPIKEVAX Bivalent (Part G) and SPIKEVAX original (Part F) second booster groups, respectively, and the GMR was 1.69 (95%CI: 1.51, 1.90).

For participants with prior SARs-CoV-2 infection, the estimated Day 29 neutralising antibody GMTs against Omicron BA. 4/5 were 2246.25 (95%CI: 1975.52, 2554.09) and 1406.89 (95%CI: 1227.88, 1612.01) in the SPIKEVAX Bivalent (Part G) and SPIKEVAX original (Part F) second booster groups, respectively, and the GMR was 1.60 (95%CI: 1.34, 1.91).

14.2.3.3 Children 6 Months to 5 Years of Age

14.2.3.3.1 Primary Series – Efficacy (Based on Cut-off Date of December 5, 2022)

Study P306 Part 1 is an ongoing Phase 3 open-label clinical trial to evaluate the safety and immunogencity of SPIKEVAX Bivalent (Original / Omicron BA.1) in individuals ages 6 months to 5 years of age. Participants with a known history of SARS-CoV-2 infection within 90 days of study vaccination were excluded from the study. A total of 179 participants were enrolled to receive 2 doses of SPIKEVAX Bivalent (Original /Omicron BA.1) (25 mcg per dose, mRNA-1273.214 [12.5 mcg elasomeran and 12.5 mcg imelasomeran] 1 month apart. Of the 179 participants, 142 had received 2 doses at the time of the data cut, of whom 108 had at least 28 days of follow-up after Dose 2.

Effectiveness in individuals 6 months through 5 years of age is based on a comparison of immune responses in this age group in Study P306 Part 1 to individuals 6 months through 5 years of age who received a primary series of SPIKEVAX (original) (25 mcg per dose) in Study P204.

In Study P306 Part 1, the neutralizing antibody concentrations against a pseudovirus expressing the original SARS-CoV-2 Spike protein (D614G) and a pseudovirus expressing the Omicron BA.1 Spike protein were evaluated. Primary immunogenicity analyses compared the GMC ratios 28 days after Dose 2 with SPIKEVAX Bivalent (Original / Omicron BA.1) to those following Dose 2 with SPIKEVAX (original). Analyses of GMC ratios met predefined success criteria for superiority against Omicron BA.1 and noninferiority against the Original strain (Table 27).

Table 27 – Summary of Geometric Mean Concentration Ratio 28 Days After Dose 2 with SPIKEVAX Bivalent (Original / Omicron BA.1) or SPIKEVAX (original) in Participants 6 Months Through 5 Years of Age – Per-Protocol Immunogenicity Set*

Assay	Bivalent Vaccine (Original and Omicron BA.1) N=71 GMC[a] (95% CI)	Moderna COVID-19 Vaccine N=632 GMC[a] (95% CI)	GMR[a] (Bivalent Vaccine [Original and Omicron BA.1]/Moderna COVID-19 Vaccine) (97.5% CI)	Met Success Criteria
Omicron BA.1	1889.7 (1520.4, 2348.7)	74.3 (68.5, 80.8)	25.4 (20.1, 32.1)	Lower limit of 95% CI >1 Criterion: Yes[b]
Original SARS-CoV-2 (D614G)	1432.9 (1173.4, 1749.7)	1732.5 (1620.9, 1851.8)	0.8 (0.7, 1.0)	Lower limit of 95% CI >0.667 Criterion: Yes[c]

* Per-Protocol Immunogenicity Set included all subjects who received the planned doses of study vaccine per schedule, had Day 57 neutralizing antibody data available, and had no major protocol deviations that impact key or critical data.

[a] The log-transformed antibody levels are analyzed using an analysis of covariance (ANCOVA) model with the group variable (children in Study P306 and in Study P204) as fixed variable, adjusted by age group (two age groups: 6 months through 23 months, 2 years through 5 years), and by the baseline SARS-CoV-2 infection status. Coefficients for Least Squares Means use margins by level. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.

[b] Superiority is declared if the lower limit of the 2-sided 95% CI for the GMC ratio is >1.

[c] Non-inferiority is declared if the lower limit of the 2-sided 95% CI for the GMC ratio is ≥0.667.

Note: Antibody values < the lower limit of quantitation (LLOQ) are replaced by 0.5 × LLOQ. Values > the upper limit of quantitation (ULOQ) are replaced by the ULOQ if actual values are not available.

14.2.4 SPIKEVAX (Original)

14.2.4.1 Participants 18 Years of Age and Older

14.2.4.1.1 Primary Series - Efficacy (Based on Cut-off Date of November 21, 2020)

The analysis of the primary efficacy endpoint in the COVE Study (P301) included 28,207 participants 18 years of age and older (14,134 in the SPIKEVAX [elasomeran] group and 14,073 in the placebo group). At the time of the final primary efficacy analysis, participants had been followed for symptomatic COVID-19 disease for a median of 2 months after the second dose, corresponding to 3304.9 person years for the SPIKEVAX (elasomeran) group and 3273.7 person years in the placebo group.

There were 11 confirmed COVID-19 cases identified in the SPIKEVAX (elasomeran) group and 185 in placebo group, respectively, for the primary efficacy analysis. Compared to placebo, efficacy of SPIKEVAX (elasomeran) in participants with first COVID-19 occurrence from 14 days after Dose 2 was

94.1% (two-sided 95% confidence interval of 89.3% to 96.8%). In participants 65 years of age and older, efficacy of SPIKEVAX (elasomeran) was 86.4% (two-sided 95% confidence interval of 61.4%% to 95.5%). At the time of primary efficacy analysis, there was a total of 30 severe COVID-19 cases reported in the placebo group starting 14 days after Dose 2, per adjudication committee assessment. No cases of severe COVID-19 were reported in the SPIKEVAX (elasomeran) group.

14.2.4.1.2 Booster Dose - Immunogenicity

Effectiveness of the single booster dose of 50 mcg of SPIKEVAX (elasomeran) in adults 18 years of age and older who received a 2-dose primary series with 100 mcg SPIKEVAX (elasomeran) at least 6 months prior to booster was inferred by comparing the antibody titers from Study P201 Part B to the pivotal adult Study P301.

Study P201 Part B was an open-label study assessing immunogenicity responses following administration of a 50 mcg booster of SPIKEVAX (elasomeran) to participants primed with 100 mcg doses of SPIKEVAX (elasomeran). Participants with negative baseline SARS-CoV-2 status were randomly selected from Study P301 participants in the SPIKEVAX (elasomeran) group to form an Immunogenicity Subset in Study P301, which was used as the comparator arm for the Study P201 Part B immunobridging analysis.

Immunobridging analyses compared the neutralizing antibody titers (ID50) 28 days following the booster dose (201 Part B; N=149) to the corresponding titers 28 days after completion of the primary series in a random subset of participants 18 years of age and older from the Phase 3 efficacy study (P301; N=1055).

In participants who were primed with a 2-dose series of 100 mcg of SPIKEVAX (elasomeran), single booster dose of 50 mcg of SPIKEVAX (elasomeran) demonstrated a geometric mean fold rise of 12.99 (95% CI: 11.04, 15.29) from pre-booster values of neutralizing antibodies as compared to 28 days after the booster dose. The geometric mean ratio (comparing the antibody levels on Day 29 in Study P201 Part B vs. the antibody levels on Day 57 after the priming series in Study P301) was 1.76 (95% CI: 1.50, 2.06), successfully meeting the pre-specified non-inferiority criterion of 0.67 corresponding to non-inferiority margin of 1.5. The analysis is summarized in Table 28.

Table 28 – Neutralizing Antibody Geometric Mean Titers (ID50) Against a Pseudovirus Expressing the SARS-CoV-2 Spike Protein at 28 Days After a Booster Dose in Study P201 Part B vs 28 Days After Completion of the Primary Series in Study P301, Participants ≥18 Years of Age, Per-Protocol Immunogenicity Set

Study P201 Part B Booster Dose N[a]=149 GMT[b] (95% CI)	Study P301 Primary Series N[a]=1053 GMT[b] (95% CI)	GMT Ratio (Study P201 Part B/ Study P301)	Met Success Criteria[c]
1802 (1548, 2099)	1027 (968, 1089)	1.76 (1.50, 2.06)	Lower limit of 95% CI ≥0.67 Criterion: Yes Point Estimate ≥1.0 Criterion: Yes

* Per-Protocol Immunogenicity Set included all subjects who had both baseline (or Study P201 Part B Day 1) and post-vaccination immunogenicity samples, did not have SARS-CoV-2 infection at baseline (or Study P201 Part B Day 1), did not have a major protocol deviation that impacted immune response, and had post-injection immunogenicity assessment at timepoint of primary interest (Day 29 for Study P201 Part B and Day 57 for Study P301).

[a] Number of subjects with non-missing data at the corresponding timepoint.

[b] The statistical analysis plan pre-specified an analysis of covariance model for estimating the geometric mean titer that adjusts for differences in age groups (<65 years, ≥65 years).

[c] Immunobridging is declared if the lower limit of the 2-sided 95% CI for the GMR is >0.67 and the point estimate of the GLSM ratio is ≥1.0.
Note: Antibody values < the lower limit of quantitation (LLOQ) are replaced by 0.5 × LLOQ. Values > the upper limit of quantitation (ULOQ) are replaced by the ULOQ if actual values are not available.
GLSM = Geometric least squares mean
GMR = Geometric mean ratio

14.2.4.2 Adolescents 12 to 17 Years of Age

14.2.4.2.1 Primary Series - Efficacy and Immunogenicity (Based on Cut-off Date of May 8, 2021)

The vaccine safety, efficacy and immunogenicity in participants 12 to 17 years of age was evaluated in Study P203, an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind, clinical trial. Participants with a known history of SARS-CoV-2 infection were excluded from the study. A total of 3,732 participants were randomised 2:1 to receive 2 doses of SPIKEVAX (elasomeran) or 2 doses of saline placebo 28 days apart. Participants will be followed for efficacy and safety until 1 year after the second dose.

There were 0 confirmed COVID-19 cases identified in the mRNA-1273 COVID-19 Vaccine (N=2,162) and 4 in placebo groups (N=1,073), respectively, for the vaccine efficacy analysis. Compared to placebo, efficacy of mRNA-1273 COVID-19 Vaccine in participants with first COVID-19 occurrence from 14 days after Dose 2 was 100% (two-sided 95% confidence interval of 28.9% to 100%).

An analysis of SARS-CoV-2 50% neutralising titers in randomly selected subsets of participants was performed to demonstrate non-inferior immune responses (within 1.5-fold) comparing adolescents 12 to 17 years of age (from Study P203) to participants 18 to 25 years of age (from Study P301) who had no serological or virological evidence of past SARS-CoV-2 infection. The immune response to SPIKEVAX (elasomeran) in adolescents 12 to 17 years of age (n=340) was non-inferior to the immune response in participants 18 to 25 years of age (n=305), based on results for SARS-CoV-2 neutralizing titers at 28 days after the second dose. The geometric mean titers (GMT) ratio of the adolescents 12 to 17 years of age group to the participants 18 to 25 years of age group was 1.08, with a 2-sided 95% CI of 0.93 to 1.24, meeting the 1.5-fold non-inferiority criterion (the lower bound of the 2-sided 95% CI for the geometric mean ratio [GMR] >0.67).

14.2.4.2.2 Booster Dose – Immunogenicity

Effectiveness of a booster dose of 50 mcg of SPIKEVAX (elasomeran) in participants 12 years through 17 years of age was inferred by comparing the post-booster antibody titers from Study P203 to those following the primary series in adults 18 through 25 years of age in the pivotal adult Study P301.

In an open-label phase of Study P203, participants 12 years through 17 years of age received a single booster dose at least 5 months after completion of the primary series (two doses 28 days apart). The primary immunogenicity analysis population included 257 booster dose participants from Study P203 and a random subset of 295 participants from Study P301 (ages ≥18 to ≤25 years) who previously completed a primary vaccination series of two doses 28 days apart of SPIKEVAX (elasomeran). Study P301 and Study P203 participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively. The median time from Dose 2 of the primary series to the booster dose in the primary immunogenicity analysis set in Study P203 was 295 days (range: 274 to 357 days).

In the 257 participants from Study P203, pre-booster (booster dose-Day 1) nAb GMC was 400.4 (95% CI: 370.0, 433.4); on booster dose-Day 29, the GMC was 7172.0 (95% CI: 6610.4, 7781.4). Post-booster booster dose-Day 29 GMC increased approximately 18-fold from pre-booster GMC.

The primary immunogenicity analyses of the GMC ratio and difference in seroresponse rates following the booster dose in Study P203 compared to after the primary series in Study P301 met the pre-defined immunobridging success criteria. Seroresponse for a participant was defined as achieving a ≥4-fold rise of neutralizing antibody concentration from baseline (before the first dose of the primary series in Study P301 and Study P203). These analyses are summarized in Table 29.

Table 29 – Comparison of Geometric Mean Concentration and Seroresponse Rate Against a Pseudovirus Expressing the SARS-CoV-2 Spike Protein at 28 Days After a Booster Dose in Study P203 (Participants 12 Years Through 17 Years of Age) vs 28 Days After Completion of the Primary Series in Study P301 (Participants 18 through 25 Years of Age) - Per-Protocol Immunogenicity Sets

Study P203* Booster Dose N[a]=257	Study P301† Primary Series N[a]=294		Met Success Criteria
GMC (95% CI)	**GMC (95% CI)**	**GMC Ratio (Study P203/Study P301)**	
7172 (6610, 7781)	1400 (1273, 1541)	5.1 (4.5, 5.8)	Yes[b]
Seroresponse[c] n/N1 (%) (95% CI)[d]	**Seroresponse[c] n/N1 (%) (95% CI)[d]**	**Difference in Seroresponse Rate (Study P203-Study P301) % (95% CI)[e]**	
257/257 (100) (98.6, 100)	292/294 (99.3) (97.6, 99.9)	0.7 (-0.8, 2.4)	Yes[f]

* Per-Protocol Immunogenicity Subset – Pre-Booster SARS-CoV-2 Negative for Study P203 included all subjects who had both pre-booster and post-booster immunogenicity samples, did not have SARS-CoV-2 infection at pre-booster, did not have a major protocol deviation that impacted immune response, and had post-booster immunogenicity assessment at timepoint of primary interest (28 days post-Booster Dose).

† Per-Protocol Immunogenicity Subset for Study P301 included all subjects who had both baseline (pre-vaccination) and post-vaccination immunogenicity samples, did not have SARS-CoV-2 infection at baseline, did not have a major protocol deviation that impacted immune response, and had post-injection immunogenicity assessment at timepoint of primary interest (28 days post-Dose 2).

[a] Number of subjects with non-missing data at the corresponding timepoint.

[b] Immunobridging success is declared if the lower limit of the 2-sided 95% CI for the GMC Ratio is ≥0.667 and the point estimate of the GMC Ratio is ≥0.8.

[c] Seroresponse is defined as ≥4-fold rise of pseudovirus neutralizing antibody concentration from baseline (pre-Dose 1 of primary series in Study P203 and Study P301), where baseline concentration < LLOQ is set to LLOQ for the analysis.

N1=number of participants with non-missing data at pre-vaccination baseline and 28 days post-Booster Dose for Study P203 or 28 days post-Dose 2 for Study P301.

n=number of participants who achieved seroresponse at 28 days post-Booster Dose for Study P203 or 28 days post-Dose 2 for Study P301.

[d] 95% CI is calculated using the Clopper-Pearson method.

[e] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

[f] Immunobridging success is declared if the lower limit of the 2-sided 95% CI for the percentage difference is ≥ -10%.

Note: Antibody values < the lower limit of quantitation (LLOQ) are replaced by 0.5 × LLOQ. Values > the upper limit of quantitation (ULOQ) are replaced by the ULOQ if actual values are not available.

A descriptive analysis evaluated seroresponse rates using pre-booster neutralizing antibody concentration in Study P203 participants. The booster dose seroresponse rate, with seroresponse defined as at least a 4-fold rise relative to the pre-booster concentration, was 96.5%. In this post-hoc analysis, the difference in seroresponse rates was -2.8% (96.5 % in Study P203 - 99.3% in Study P301) with the 95% CI of (-5.9, -0.6).

14.2.4.3 Children 6 to 11 Years of Age

14.2.4.3.1 Primary Series – Immunogenicity and Efficacy (Based on Cut-off Date of November 10, 2021

The vaccine safety, efficacy and immunogenicity in participants 6 to 11 years of age was evaluated in Study P204 Part 2, an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind, clinical trial. Participants with a known history of SARS-CoV-2 infection within 2 weeks of study vaccination were excluded from the study. A total of 4,016 participants were randomised 3:1 to receive 2 doses (0.25 mL, 50 mcg) of SPIKEVAX (elasomeran) or saline placebo 28 days apart. Participants will be followed for efficacy and safety until 1 year after the second dose. In Part 2, the median length of follow-up at the data cutoff date of November 10, 2021 was 82 days after dose 1 and 51 days after dose 2.

Efficacy in children 6 to 11 years of age is primarily based upon a comparison of immune responses in this age group to adults 18 to 25 years of age.

An immunobridging analysis evaluating SARS-CoV-2 50% neutralising titers and seroresponse rates 28 days after Dose 2 was conducted in subset of children aged 6 to 11 in the paediatric study (Study P204; N=320) and in participants 18 through 25 years of age from the Phase 3 efficacy study (Study P301; N=295). Subjects had no immunologic or virologic evidence of prior SARS-CoV-2 infection at baseline. The GMR of the neutralising antibody titers in children 6 to 11 years of age compared to the 18- to 25-year-olds was 1.239 (95% CI: 1.072, 1.432). The difference in seroresponse rate was 0.1% (95% CI: -1.9, 2.1). Non-inferiority criteria (lower bound of the 95% CI for GMR > 0.67 and lower bound of the 95% CI of the seroresponse rate difference > -10%) were met (see Table 30).

Table 30 – Immunogenicity Analysis, Neutralizing Antibody Geometric Mean Titers (ID50), Study P204 and Study P301 – Comparison of Children 6 Years to < 12 Years of Age to Participants 18 Through 25 Years of Age

	Study P204 6 years to < 12 Years SPIKEVAX 50 mcg N=320	**Study P301 18 to ≤ 25 Years SPIKEVAX 100 mcg N=295**
Baseline GMT	9.250	9.285
GMT Observed at Day 57	1610.203	1299.855
GMR at Day 57 (Study P204 vs P301; model based)(95% CI)[a]	1.239 (1.072, 1.432)	
Participants achieving seroresponse, %[b] at Day 57	99.1	99.0
Difference in seroresponse rate (Study P204 vs P301), % (95% CI)[c]	0.1 (-1.9, 2.1)	

Abbreviations: CI = confidence interval; GMR = geometric mean ratio; GMT = geometric mean titer (noted as observed or model based, which is estimated by geometric least squares mean); ID50 = 50% inhibitory dose.
[a] The log-transformed antibody levels are analyzed using an ANCOVA model with the group variable (children in P204 and young adults in P301) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.
[b] Seroresponse at a participant level is defined as a change from below the LLOQ to equal or above 4 × LLOQ, or at least a 4-fold rise if baseline is equal to or above the LLOQ. Percentages are based on the number of participants with non-missing data at baseline and the corresponding timepoint.
[c] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

An exploratory efficacy analysis evaluating confirmed COVID-19 cases that accrued up to the data cutoff date of November 10, 2021 was performed in 3,497 participants who received two doses of either SPIKEVAX (elasomeran) (n=2,644) or placebo (n=853), and had a negative baseline SARS-CoV-2 status. There were 3 confirmed cases in each arm, with the incidence rate per 1000 person-years being smaller in the vaccine arm (5.04) than in the placebo arm (16.26).

14.2.4.3.2 Booster Dose – Immunogenicity

Effectiveness of a booster dose of 25 mcg of SPIKEVAX (elasomeran) in participants 6 years through 11 years of age was inferred by comparing the post-booster antibody titers from Study P204 to those following the primary series in adults 18 through 25 years in the pivotal adult Study P301.

In an open-label phase of Study P204, participants 6 years through 11 years of age received a single booster dose at least 6 months after completion of the primary series (two doses 1 month apart). The primary immunogenicity analysis population included 95 booster dose participants in Study P204 and a random subset of 295 participants 18 through 25 years from Study P301 who received two doses of SPIKEVAX (elasomeran) 1 month apart. Study P301 and P204 participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively.

In the 95 participants, on booster dose-Day 29, the GMC was 5847.5 (95% CI: 4999.6, 6839.1) and the SRR was 100 (95% CI: 95.9, 100.0). Serum nAb levels for children 6 through 11 years in the Per-Protocol immunogenicity subset with pre-booster SARS-CoV-2 negative status and the comparison with those from young adults (18 to 25 years of age) were studied. The GMR of booster dose Day 29 GMC compared to young adults Day 57 GMC was 4.2 (95% CI [3.5, 5.0]), meeting the noninferiority criteria (i.e., lower bound of the 95% CI > 0.667); the SRR difference was 0.7% (95% CI: -3.5, 2.4), meeting the noninferiority criteria (lower bound of the 95% of the SRR difference >-10%).
The primary immunogenicity analyses of the GMC ratio and difference in seroresponse rates following the booster dose in Study P204 compared to following the primary series in Study P301 met the pre-defined immunobridging success criteria. Seroresponse for a participant was defined as achieving a ≥4-fold rise of neutralizing antibody concentration from baseline (before the first dose of the primary series in Study P204 and Study P301). These analyses are summarized in Table 31.

Table 31 – Comparison of Geometric Mean Concentration and Seroresponse Rate Against a Pseudovirus Expressing the SARS-CoV-2 Spike Protein at 28 Days After a Booster Dose in Study P204 (Participants 6 Years Through 11 Years of Age) vs 28 Days After Completion of the Primary Series in Study P301 (Participants 18 through 25 Years of Age) - Per-Protocol Immunogenicity Sets

Study P204* Booster Dose N[a]=95	Study P301† Primary Series N[a]=294		Met Success Criteria
GMC (95% CI)	**GMC (95% CI)**	**GMC Ratio (Study P204/ Study P301)**	
5848 (5000, 6839)	1400 (1273, 1541)	4.2 (3.5, 5.0)	Yes[b]
Seroresponse[c] n/N1 (%) (95% CI)[d]	**Seroresponse[c] n/N1 (%) (95% CI)[d]**	**Difference in Seroresponse Rate (Study P204-Study P301) % (95% CI)[e]**	
88/88 (100) (95.9, 100)	292/294 (99.3) (97.6, 99.9)	0.7 (-3.5, 2.4)	Yes[f]

* Per-Protocol Immunogenicity Subset – Pre-Booster SARS-CoV-2 Negative for Study 4 included all subjects who had both pre-booster and post-booster immunogenicity samples, did not have SARS-CoV-2 infection at pre-booster, did not have a major protocol deviation that impacted immune response, and had post-booster immunogenicity assessment at timepoint of primary interest (28 days post-Booster Dose).

† Per-Protocol Immunogenicity Subset for Study 1 included all subjects who had both baseline (pre-vaccination) and post-vaccination immunogenicity samples, did not have SARS-CoV-2 infection at baseline, did not have a major protocol deviation that impacted immune response, and had post-injection immunogenicity assessment at timepoint of primary interest (28 days post-Dose 2).

[a] Number of subjects with non-missing data at the corresponding timepoint.

[b] Immunobridging success is declared if the lower limit of the 2-sided 95% CI for the GMC Ratio is ≥0.667.

[c] Seroresponse is defined as ≥4-fold rise of pseudovirus neutralizing antibody concentration from baseline (pre-Dose 1 of primary series in Study 4 and Study 1), where baseline concentration < LLOQ is set to LLOQ for the analysis.

N1=number of participants with non-missing data at pre-vaccination baseline and 28 days post-Booster Dose for Study 4 or 28 days post-Dose 2 for Study 1.

n=number of participants who achieved seroresponse at 28 days post-Booster Dose for Study 4 or 28 days post-Dose 2 for Study 1.

[d] 95% CI is calculated using the Clopper-Pearson method.

[e] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

[f] Immunobridging success is declared if the lower limit of the 2-sided 95% CI for the percentage difference is ≥ -10%.

Note: Antibody values < the lower limit of quantitation (LLOQ) are replaced by 0.5 × LLOQ. Values > the upper limit of quantitation (ULOQ) are replaced by the ULOQ if actual values are not available.

A descriptive analysis evaluated seroresponse rates using pre-booster neutralizing antibody concentration in study P204 participants. The booster dose seroresponse rate, with seroresponse defined as at least a 4-fold rise relative to the pre-booster concentration, was 92.6%. In this post-hoc analysis, the difference in seroresponse rates was -6.7% (95% CI -13.8, -2.7).

14.2.4.4 Children 6 Months to 5 Years of Age

14.2.4.4.1 Primary Series – Immunogenicity and Efficacy (Based on Cut-off date of February 21, 2022)

The vaccine safety, efficacy and immunogenicity in participants 6 months to 5 years of age was evaluated in Study P204 Part 2, an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind, clinical trial in healthy children 6 months to through 11 years of age. The study enrolled children in 3 age groups: 6 years through 11 years; 2 years through 5 years; and 6 months through 23 months. Participants with a known history of SARS-CoV-2 infection within 2 weeks of study vaccination were excluded from the study.

A total of 6,403 participants 6 months through 5 years of age were randomised 3:1 to receive 2 doses (25 mcg) of SPIKEVAX (elasomeran) (n=4,802) or saline placebo (n=1,601) 28 days apart. Participants will be followed for efficacy and safety until 1 year after the second dose. In Part 2, the median length of follow-up at the data cut-off date of February 21, 2022, was 71 days for participants 2 through 5 years of age and 68 days for participants 6 months through 23 months of age.

Immunogenicity

Efficacy in participants 6 months to 5 years of age is primarily based on a comparison of immune responses in this age group to adults 18 to 25 years of age. An immunobridging analysis was conducted of SARS-CoV-2 50% neutralizing titers and seroresponse rates 28 days after Dose 2 in a random subset of children 6 months to 5 years of age in the paediatric Study P204 and participants 18 through 25 years of age from the Phase 3 efficacy Study P301; subjects had no immunologic or virologic evidence of prior SARS-CoV-2 at baseline (referred to as the Per-Protocol Immunogenicity Set). Noninferior immune responses as assessed by geometric mean 50% neutralizing titers and seroresponse rates were demonstrated in a comparison of children 2 to 5 years of age to participants 18 through 25 years of age and children 6 months to < 2 years of age to participants 18 through 25 years of age (Table 32).

For children aged 2 years to 5 years of age, comparison of Day 57 nAb responses in the Per Protocol Immunogenicity Subset to those of adults 18 through 25 years of age demonstrated a GMR of 1.014 (95% CI: 0.881, 1.167), meeting the prespecified noninferiority success criteria (i.e., lower bound of the 95% CI for GMR ≥ 0.67; point estimate ≥ 0.8). The difference in seroresponse rates (SRR) between the children and adults was 0.4% (95% CI: 2.7, 1.5), also meeting the prespecified noninferiority success criterion (lower bound of the 95% CI of the SRR difference ≥ -10%; point estimate of the SSR difference ≥ -5%).

For infants and toddlers from 6 months to < 2 years of age, comparison of Day 57 nAb responses in the Per Protocol Immunogenicity Subset to those of adults 18 through 25 years of age demonstrated a GMR of 1.280 (95% CI: 1.115, 1.470), meeting the prespecified noninferiority success criterion (i.e., lower bound of the 95% CI for GMR ≥ 0.67; point estimate ≥ 0.8). The difference in SRR rates between the infants/toddlers and young adults was 0.7% (95% CI: -1.0, 2.5), also meeting the prespecified noninferiority success criteria (lower bound of the 95% CI of the seroresponse rate difference > 10%).

Table 32 – Immunogenicity Analysis, Neutralizing Antibody Geometric Mean Concentration, Study P204 and Study P301 – Comparison of Children 6 months to 5 Years of Age to Participants 18 Through 25 Years of Age

	Study P204 6 months to < 2 Years SPIKEVAX 25 mcg N=230	**Study P204 2 years to 5 Years SPIKEVAX 25 mcg N=264**	**Study P301 18 to ≤ 25 Years SPIKEVAX 100 mcg N=291**
Baseline GMC	7.9	7.7	11.1
GMC Observed at Day 57	1780.658	1410.015	1390.781
GMR at Day 57 (Study P204 vs P301; model based)(95% CI)[a]	1.280 (1.115, 1.470)	1.014 (0.881, 1.167)	n/a
Participants achieving seroresponse, %[b] at Day 57	100	98.9	99.3
Difference in seroresponse rate (Study P204 vs P301), % (95% CI)[c]	0.7 (-1.0, 2.5)	-0.4 (-2.7, 1.5)	n/a

Abbreviations: CI = confidence interval; GMR = geometric mean ratio; GMC = geometric mean concentration (noted as observed or model based, which is estimated by geometric least squares mean).

[a] The log-transformed antibody levels are analyzed using an ANCOVA model with the group variable (children in P204 and young adults in P301) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.

[b] Seroresponse at a participant level is defined as a change from below the LLOQ to equal or above 4 × LLOQ, or at least a 4-fold rise if baseline is equal to or above the LLOQ. Percentages are based on the number of participants with non-missing data at baseline and the corresponding timepoint.

[c] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Efficacy

A descriptive efficacy analysis evaluating confirmed COVID-19 cases that accrued up to the data cutoff date of February 21, 2022, was performed in 5,476 participants who received two doses of either SPIKEVAX (elasomeran) or placebo, and had a negative baseline SARS-CoV-2 status (referred to as the Per-Protocol Set for Efficacy) (for participants 6 months through 23 months, 1,511 participants in the vaccine group, 513 in the placebo group; for participants 2 years through 5 years, 2,594 in the vaccine group, 858 in the placebo group).

Vaccine efficacy was evaluated during the period when the B.1.1.529 (Omicron) variant was the predominant variant in circulation.

The efficacy information in children 2 through 5 years of age and 6 through 23 months of age are presented in Table 33 and Table 34, respectively. No cases of severe COVID-19 were reported in the study.

Table 33 – Efficacy analysis: COVID-19 and SARS-CoV-2 infections in participants 2 through 5 years of age starting 14 days after dose 2 – per-protocol set for efficacy

	SPIKEVAX N=2,594		Placebo N=858		% Vaccine efficacy (95% CI)*
	Cases (n)	Incidence rate of COVID-19 per 1,000 person-years	Cases (n)	Incidence rate of COVID-19 per 1,000 person-years	
COVID-19 cases - definition 1[a]	71	103.761	43	193.528	46.4 (19.8, 63.8)
COVID-19 cases - definition 2[b]	119	175.023	61	276.980	36.8 (12.5, 54.0)

See end of Table 21 for footnotes.

Table 34 – Efficacy analysis: COVID-19 and SARS-CoV-2 infections in participants 6 through 23 months of age starting 14 days after dose 2 – per protocol set for efficacy

	SPIKEVAX N=1,511		Placebo N=513		% Vaccine efficacy (95% CI)*
	Cases (n)	Incidence rate of COVID-19 per 1,000 person-years	Cases (n)	Incidence rate of COVID-19 per 1,000 person-years	
COVID-19 cases - definition 1[a]	37	99.981	18	146.042	31.5 (-27.7, 62.0)
COVID-19 cases - definition 2[b]	51	138.239	34	279.822	50.6 (21.4, 68.6)

N = Number of participants at risk at 14 days after Dose 1 for specific efficacy endpoint.
* Vaccine efficacy defined as 1 — ratio of incidence rate (SPIKEVAX vs. placebo). The 95% CI of the ratio is calculated using the exact method conditional upon the total number of cases, adjusting for person-years.
[a] 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 the participant must have at least one NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalised) positive for SARS-CoV-2 by RT-PCR.
[b] Presence of at least one symptom from a list of COVID-19 symptoms and a positive NP swab or saliva sample for SARS-CoV-2 by RT-PCR. Listed symptoms were fever (temperature >38°C / ≥100.4°F), or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle aches, or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea, or vomiting or diarrhea.

14.2.4.4.2 Booster Dose

Effectiveness of a booster dose of 10 mcg of SPIKEVAX (elasomeran) in participants 6 months through 5 years of age is based on a comparison of immune responses, as assessed by neutralizing antibody concentration against a pseudovirus expressing the SARS-CoV-2 Spike protein from a USA_WA1/2020 isolate carrying the D614G mutation, following the booster dose in participants 6 months through 5 years of age in Study P204 to that following the primary series in adults 18 years through 25 years of age in the pivotal adult Study P301.

In an open-label phase of Study P204, participants 6 months through 5 years of age received a single booster dose of SPIKEVAX (elasomeran) (10 micrograms mRNA) at least 6 months after completion of a SPIKEVAX (elasomeran) primary series (two doses 1 month apart). The primary immunogenicity analysis population included 56 booster dose participants in Study P204 and a random subset of 295 participants 18 through 25 years from the adult study who had completed primary vaccination with two doses of SPIKEVAX (elasomeran) 1 month apart. Study P301 and P204 participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively. Among the 56 participants in the primary immunogenicity analysis population, the median age for receipt of the booster dose was 2.3 years (range 1.4 to 5.6 years).

The primary immunogenicity analyses of the GMC ratio and difference in seroresponse rates following the booster dose in Study P204 compared to following the primary series in Study P301 met the pre-defined immunobridging success criteria. Seroresponse for a participant was defined as achieving a ≥4-fold rise of neutralising antibody concentration from baseline (before the first dose of the primary series in this study and the adult Study). These analyses are summarised in Table 35.

Table 35 – Comparison of GMC and seroresponse rate against a pseudovirus expressing the SARS-CoV-2 spike protein at 28 days after a booster dose (children 17 months - 5 years of age) vs 28 days after completion of the primary series (participants 18 years – 25 years of age) – per-protocol immunogenicity subsets

6 months – 5 years* booster dose N[a]=56 GMC (95% CI)	**Adult study† primary series N[a]=294 GMC (95% CI)**	**GMC ratio (6 months – 5 years/adult study)**	**Met success criterion**
5 713 (4 604, 7 089)	1 400 (1 275, 1 539)	4.1 (3.2, 5.2)	Yes[b]
6 months – 5 years booster dose seroresponse[c] N=56 n/N1 (%) (95% CI)[d]	**Adult study primary series seroresponse[c] N=294 n/N1 (%) (95% CI)[d]**	**Difference in seroresponse rate (6 months – 5 years/adult study)% (95% CI)[e]**	**Met Success Criterion**
53/53 (100) (93.3, 100.0)	292/294 (99.3) (97.6, 99.9)	0.7 (-6.1, 2.4)	Yes[f]

* Per-protocol immunogenicity subset – pre-booster SARS-CoV-2 negative for this study included all subjects who had both pre-booster and post-booster immunogenicity samples, did not have SARS-CoV-2 infection at pre-booster, did not have a major protocol deviation that impacted immune response, and had post-booster immunogenicity assessment at timepoint of primary interest (28 days post-booster dose).

† Per-protocol immunogenicity subset for the adult study included all subjects who had both baseline (pre-vaccination) and post-vaccination immunogenicity samples, did not have SARS-CoV-2 infection at baseline, did not have a major protocol deviation that impacted immune response, and had post-injection immunogenicity assessment at timepoint of primary interest (28 days post-dose 2).

[a] Number of subjects with non-missing data at the corresponding timepoint.

[b] Immunobridging success is declared if the lower limit of the 2-sided 95% CI for the GMC Ratio is ≥0.667.

[c] Seroresponse is defined as ≥4-fold rise of pseudovirus neutralising antibody concentration from baseline (pre-dose 1 of primary series in this study and the adult study), where baseline concentration < LLOQ is set to LLOQ for the analysis.
N1 = number of participants with non-missing data at pre-vaccination baseline and 28 days post-booster dose for this study or 28 days post-dose 2 for the adult study.
n = number of participants who achieved seroresponse at 28 days post-booster dose for this study or 28 days post-dose 2 for the adult study.
[d] 95% CI is calculated using the Clopper-Pearson method.
[e] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.
[f] Immunobridging success is declared if the lower limit of the 2-sided 95% CI for the percentage difference is ≥ -10%.
Note: Antibody values < the lower limit of quantitation (LLOQ) are replaced by 0.5 × LLOQ. Values > the upper limit of quantitation (ULOQ) are replaced by the ULOQ if actual values are not available.

In a descriptive analysis, the booster dose seroresponse rate among participants 17 months through 5 years of age, with seroresponse defined as at least a 4-fold rise relative to the pre-booster concentration, was 94.6%. The difference in seroresponse rates (this study participants minus adult study participants) in this post-hoc analysis was -4.7% (95% CI -14.0, -0.9).

15 MICROBIOLOGY

No microbiological information is required for this vaccine product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology: Intramuscular administration of SPIKEVAX (or other Moderna mRNA investigational vaccines) at doses ranging from 9 to 150 mcg/dose administered once every 2 weeks for up to 6 weeks resulted in transient injection site erythema and edema, body temperature increases, and a generalized systemic inflammatory response. Transient hepatocyte vacuolation and/or Kupffer cell hypertrophy, often observed without liver enzyme elevations, was observed and considered secondary to the systemic inflammatory response. In general, all changes resolved within 2 weeks.

Carcinogenicity: SPIKEVAX has not been evaluated for carcinogenicity in animals, as carcinogenicity studies were not considered relevant to this vaccine.

Genotoxicity: SM-102, a proprietary lipid component of SPIKEVAX, SPIKEVAX Bivalent, SPIKEVAX Bivalent Original/Omicron BA.4/5 and SPIKEVAX XBB.1.5 is not genotoxic in the bacterial mutagenicity and the human peripheral blood lymphocytes chromosome aberration assays. Two intravenous in vivo micronucleus assays were conducted with mRNA therapies using the same lipid nanoparticle (LNP) formulation as SPIKEVAX Bivalent (Original/Omicron BA.1). Equivocal results observed at high systemic concentrations were likely driven by micronuclei formation secondary to elevated body temperature induced by a LNP-driven systemic inflammatory response. The genotoxic risk to humans is considered to be low due to minimal systemic exposure following intramuscular administration, limited duration of exposure, and the negative in vitro results.

Reproductive and Developmental Toxicology: In a pre- and post-natal developmental toxicity study, 0.2 mL of a vaccine formulation containing the same quantity of mRNA (100 mcg) and other ingredients included in a single human dose of SPIKEVAX was administered to female rats by the intramuscular route on four occasions: 28 and 14 days prior to mating, and on gestation days 1 and 13. No vaccine-related adverse effects on female fertility, fetal development or postnatal development were reported in the study.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

SPIKEVAX

COVID-19 mRNA vaccine, Dispersion for Intramuscular Injection

Read this carefully before you start taking **SPIKEVAX**. This leaflet is a summary and will not tell you everything about this vaccine. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **SPIKEVAX**.

What is SPIKEVAX used for?
SPIKEVAX is a vaccine used to prevent the coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 virus. It can be given to people aged 6 months and older.

The safety and effectiveness of SPIKEVAX COVID-19 mRNA vaccine for individuals 6 months of age and older is inferred from several studies of a primary series and booster dose of SPIKEVAX Bivalent (Original/Omicron BA.1) in individuals 6 months to 5 years of age, a booster dose of SPIKEVAX Bivalent (Original/Omicron BA.1) in individuals >18 years of age, a booster dose study of SPIKEVAX XBB.1.5 in individuals > 18 years of age as well as data from studies which evaluated the primary series and booster vaccination with SPIKEVAX (Original).

How does SPIKEVAX work?
SPIKEVAX works by causing the body to produce its own protection (antibodies) against the SARS-CoV-2 virus that causes the COVID-19 infection. SPIKEVAX uses a molecule called messenger ribonucleic acid (mRNA, the genetic code for a piece of the virus) to deliver the set of instructions that cells in your body can use to make antibodies to help fight the virus that causes COVID-19. The vaccine is given by injection with a needle in the upper arm.

You cannot get COVID-19 from this vaccine.

As with any vaccine, SPIKEVAX may not fully protect all those who receive it. Even after you have had the vaccine, continue to follow the recommendations of local public health officials to prevent spread of COVID-19.

What are the ingredients in SPIKEVAX?
Medicinal ingredients:
Each 0.5 mL dose of SPIKEVAX contains 50 micrograms of mRNA encoding SARS-CoV-2 spike protein.

The mRNA encoding spike protein is derived from Omicron variant KP.2**.**

Non-medicinal ingredients:
- acetic acid
- cholesterol
- DSPC (1,2-distearoyl-sn-glycero-3-phosphocholine)
- PEG2000-DMG (1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000)
- SM-102 (Heptadecan-9-yl 8-((2-hydroxyethyl) (6-oxo-6-(undecyloxy) hexyl) amino) octanoate)

- sodium acetate trihydrate
- sucrose
- trometamol
- trometamol hydrochloride
- water for injection

SPIKEVAX comes in the following dosage forms:
White to off-white dispersion for injection provided in a multidose vial.

Do not receive SPIKEVAX if:
- you are allergic to the active substance or any of the other ingredients of this vaccine (see What are the ingredients in SPIKEVAX?)
- you have had an allergic reaction to a previous dose of SPIKEVAX
- you currently have symptoms that could be due to COVID-19. Talk with your healthcare professional about your symptoms and getting a COVID-19 test. Your healthcare professional will advise you when you are able to receive the vaccine.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take SPIKEVAX. Talk about any health conditions or problems you may have, including if you:
- have any allergies
- have had previous problems following administration of SPIKEVAX such as an allergic reaction or breathing problems
- have a weakened immune system due to a medical condition or are on a medicine that affects your immune system
- have a bleeding problem, bruise easily or use a blood thinning medication
- have a high fever or severe infection
- have any serious illness
- have previously had episodes of myocarditis (inflammation of the heart muscle) and/or pericarditis (inflammation of the lining outside the heart)
- are pregnant, think you may be pregnant or plan to become pregnant
- are breastfeeding or plan to breastfeed

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

There is limited information on the use of SPIKEVAX with other vaccines. Tell your healthcare professional if you have recently received any other vaccine.

How is SPIKEVAX given:
- Your doctor, pharmacist or nurse will inject the vaccine into a muscle (intramuscular injection) in your upper arm.
- During and after each injection of the vaccine, your doctor, pharmacist or nurse will watch over you for around 15 minutes to monitor for signs of an allergic reaction.

Usual dose:
- 12 years of age and older: One (1) dose of SPIKEVAX is 50 micrograms.
- 5 to 11 years of age: One (1) dose of SPIKEVAX is 25 micrograms.

- 6 months to 4 years of age:
  - *If the child has not been previously vaccinated*: Two (2) doses of SPIKEVAX of 25 micrograms each.
  - *If the child has had 1 or more COVID-19 vaccine doses previously*: One (1) dose of SPIKEVAX is 25 micrograms.

Overdose:

In the event of suspected overdose with SPIKEVAX, contact your regional poison control centre.

Missed Dose:
If you forget to go back to your healthcare professional at the scheduled time for your next dose, ask your healthcare professional for advice.

What are possible side effects from using SPIKEVAX?
Like all vaccines, SPIKEVAX can cause side effects.

The following are common or very common side effects of SPIKEVAX. Most of these side effects are mild and do not last long. Tell your doctor if you have side effects that bother you:
- pain at the injection site
- tiredness, sleepiness
- headache
- muscle ache and stiffness
- chills
- fever
- swelling or redness at the injection site
- decreased appetite
- nausea and/or vomiting
- enlarged lymph nodes
- hypoaesthesia (decreased sense of touch or sensation, numbness) or paraesthesia (tingling, itching or pricking sensation)
- dizziness

Non-severe allergic reactions (such as rash, itching, hives or swelling of the face), severe allergic reactions, erythema multiforme (red round patches on the skin) and facial paralysis / Bell's palsy have been reported with the administration of SPIKEVAX.

Myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) have been reported following SPIKEVAX administration. Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as shortness of breath, palpitations and chest pain, and seek immediate medical attention should these occur. These conditions can develop within just a few days after vaccination and have primarily occurred within 14 days. They have been observed more often in younger males, and more often after the second dose compared to the first dose. Most cases of myocarditis and pericarditis recover. Some cases required intensive care support and fatal cases have been seen.

These are not all the possible side effects you may have when taking SPIKEVAX. If you experience any side effects not listed here, tell your healthcare professional.

Should you develop any serious symptoms or symptoms that could be an allergic reaction, seek medical attention right away. Symptoms of an allergic reaction include:

- hives (bumps on the skin that are often very itchy)
- swelling of the face, tongue or throat
- difficulty breathing

If you experience a severe allergic reaction, call 9-1-1, or go to the nearest hospital.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Suspected Side Effects for Vaccines

For the general public: Should you experience a side effect following immunization, please report it to your healthcare professional.

Should you require information related to the management of the side effect, please contact your healthcare professional. The Public Health Agency of Canada, Health Canada and Moderna Biopharma Canada Corp. cannot provide medical advice.

For healthcare professionals: If a patient experiences a side effect following immunization, please complete the Adverse Events Following Immunization (AEFI) Form appropriate for your province/territory (https://www.canada.ca/en/public-health/services/immunization/reporting-adverse-events-following-immunization/form.html) and send it to your local Health Unit.

Storage:
Your doctor or pharmacist is responsible storing, supplying and administering SPIKEVAX, as well as disposing of any unused product correctly.

Keep out of reach and sight of children.

If you want more information about SPIKEVAX:

- Talk to your healthcare professional.

- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website https://www.modernacovid19global.com/ca/, or by calling 1-866-MODERNA (1-866-663-3762).

This leaflet was prepared by Moderna Biopharma Canada Corp.

Last Revised September 17, 2024