PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

SPIKEVAX™

Elasomeran mRNA vaccine

Dispersion for intramuscular injection

Multidose Vial, 0.20 mg / mL

Multidose Vial, 0.10 mg / mL

Active Immunizing Agent

SPIKEVAX 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 please refer to Health Canada's COVID-19 vaccines and treatments portal.

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RECENT MAJOR LABEL CHANGES

1. INDICATION	January 2023
4. DOSAGE AND ADMINISTRATION	January 2023
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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

SPIKEVAX (elasomeran 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.

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 include participants 65 years of age and older and their data contributes to the overall assessment of safety and efficacy (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.

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. Dose volume will be different depending on which presentation of the vaccine is being administered. Careful attention should be paid to the vial cap colour and the corresponding dose volumes.

Individuals ≥ 12 Years of Age: The primary series is a two-dose regimen of 100 mcg each.

Individuals 6 to 11 Years of Age: The primary series is a two-dose regimen of 50 mcg each.

Individuals 6 Months of Age to 5 Years of Age: The primary series is a two-dose regimen of 25 mcg each.

The SPIKEVAX booster dose for individuals 12 years of age or older is 50 mcg.

Age Range	Vaccination	Presentation	Vial Cap Colour	Label Border Colour	Dose	Dose Volume
18 years of age or older	Primary Series	0.20 mg/mL	Red	Light blue	100 mcg*	0.50 mL
	Booster Dose	0.20 mg/mL	Red	Light blue	50 mcg	0.25 mL
		0.10 mg/mL	Royal Blue	Purple		0.50 mL
12 to 17 years of age	Primary Series	0.20 mg/mL	Red	Light blue	100 mcg*	0.50 mL
	Booster Dose	0.20 mg/mL	Red	Light blue	50 mcg	0.25 mL
		0.10 mg/mL	Royal Blue	Purple		0.50 mL
6 to 11 years of age	Primary Series	0.20 mg/mL	Red	Light blue	50 mcg	0.25 mL
		0.10 mg/mL	Royal Blue	Purple		0.50 mL
6 months to 5 years of age	Primary Series	0.10 mg/mL	Royal Blue	Purple	25 mcg**	0.25 mL

*The 0.10 mg/mL presentation of SPIKEVAX with royal blue vial cap and purple label is not intended for preparation of the primary series 100 mcg dose.
**The 0.20 mg/mL presentation of SPIKEVAX with red vial cap and light blue label is not intended for preparation of the 25 mcg dose.

4.2 Recommended Dose and Dosage Adjustment

Primary Series

Individuals ≥ 12 Years of Age: SPIKEVAX is administered intramuscularly as a primary series of two doses of 100 mcg each given 4 weeks apart (see CLINICAL TRIALS).

Individuals 6 to 11 Years of Age: SPIKEVAX is administered intramuscularly as a primary series of two doses of 50 mcg each given 4 weeks apart (see CLINICAL TRIALS).

Individuals 6 Months of Age to 5 Years of Age: SPIKEVAX is administered intramuscularly as a primary series of two doses of 25 mcg each given 4 weeks apart (see CLINICAL TRIALS).

There are currently no data available from Moderna clinical trials on the interchangeability of SPIKEVAX with other COVID-19 vaccines to complete the primary vaccination series.

Booster Dose

A booster dose of 50 mcg may be administered intramuscularly at least 4 months after completion of the primary series in individuals 12 years of age or older.

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.

Presentation	Vial Cap Colour	Label Border Colour	Volume in vial	Number of 0.5 mL doses	Number of 0.25 mL doses
0.20 mg / mL	Red	Light blue	5 mL	10	20*
0.10 mg /mL	Royal blue	Purple	2.5 mL	5	10**

*Do not puncture the 5 mL vial more than 20 times

** Do not puncture the 2.5 mL vial more than 10 times

Thaw each vial before use.

Presentation	Vial Cap Colour	Label Border 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)
0.20 mg/mL	Red	Light blue	• 2 hours and 30 minutes *After thawing, let vial stand at room temperature for 15 minutes before administering.*	• 1 hour
0.10 mg/mL	Royal blue	Purple	• 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: The dose in the syringe should be used as soon as feasible and no later than 24 hours after the vial was first entered (needle-punctured).

SPIKEVAX is preservative free. Once the vial has been entered, it should be discarded after 24 hours. 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, (0.20 mg /mL) Elasomeran (mRNA), encoding the pre fusion stabilized Spike glycoprotein of 2019 novel Coronavirus (SARS-CoV-2) Multidose vial (5 mL)	• Acetic acid • Cholesterol • DSPC (1,2-distearoyl-sn-glycero-3-phosphocholine) • Lipid SM-102 • PEG2000-DMG (1,2-dimyristoyl-rac-glycerol,methoxy-polyethyleneglycol) • Sodium acetate trihydrate • Sucrose • Trometamol • Trometamol hydrochloride • Water for injection
Intramuscular injection	Dispersion, (0.10 mg /mL) Elasomeran (mRNA), encoding the pre fusion stabilized Spike glycoprotein of 2019 novel Coronavirus (SARS-CoV-2) Multidose vial (2.5 mL)	• Acetic acid • Cholesterol • DSPC (1,2-distearoyl-sn-glycero-3-phosphocholine) • Lipid SM-102 • PEG2000-DMG (1,2-dimyristoyl-rac-glycerol,methoxy-polyethyleneglycol) • Sodium acetate trihydrate • Sucrose • Trometamol

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

SPIKEVAX is provided as a white to off-white, sterile, preservative-free, frozen dispersion for intramuscular injection. SPIKEVAX contains lipid nanoparticle (LNP), comprised of a messenger ribonucleic acid (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 I glass vial with a 20 mm Fluro Tec-coated chlorobutyl elastomer stopper, 20 mm flip-off aluminum seal. 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 0.20 mg/mL multi-dose vial is supplied with a red flip-off plastic cap. The 0.10 mg/mL multi-dose vial is supplied with a royal blue flip-off plastic cap.

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. 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, particularly within the first week following receipt of the second primary series dose or first booster dose in male young adults. Available short-term follow-up data

suggest that the symptoms resolve in most individuals following standard treatment and rest, but information on long-term sequelae is lacking. 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. In these individuals, a third dose may be considered as part of the primary series.

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.

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to SPIKEVAX during pregnancy. Women who are vaccinated with SPIKEVAX during pregnancy are encouraged to enroll in the registry 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 include participants 65 years of age and older and their data contributes to the overall assessment of safety and efficacy (see ADVERSE REACTIONS and CLINICAL TRIALS sections).

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The safety profile in participants ≥ 18 years of age presented below is based on data generated from an ongoing Phase 3 placebo- controlled clinical study on subjects ≥ 18 years of age (Study P301, NCT 04470427).

Solicited adverse reactions were reported more frequently among subjects in the vaccine group than in the placebo group. The most frequently reported adverse reactions after any dose were pain at the injection site (92.0%), fatigue (70.0%), headache (64.7%), myalgia (61.5%) and chills (45.4%). The majority of local and systemic adverse reactions had a median duration of 1 to 3 days.

Overall, there was a higher reported rate of solicited adverse reactions in younger age groups; the incidence of lymphadenopathy (axillary swelling/tenderness), fatigue, headache, myalgia, arthralgia, chills, nausea/vomiting, fever was higher in adults 18 to 64 years of age than in those 65 years of age and above. Solicited adverse reactions were also more frequent after the second dose, compared to the first one, including grade 3 local and systemic adverse reactions (see Table 2, Table 3, Table 4 and Table 5 respectively).

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 (n=2,486) or placebo (n=1,240). Of these, 1,360 adolescents (vaccine=942, placebo=418) have been followed for at least 2 months (60 days) after the second dose of SPIKEVAX at the time of the analysis (cut-off date May 8, 2021). 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 6 and Table 7).

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%).

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; at the time of data snapshot (November 10, 2021) 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.

In Part 2, the median follow-up duration was 82 days after dose 1 and 51 days after dose 2. A total of 2,981 (99.15%) subjects in the SPIKEVAX group and 966 (97.1%) subjects in the placebo group have been followed for 28 days or more after dose 2. A total of 1,066 subjects in the SPIKEVAX group (35.3%) and 218 subjects in the placebo group (21.9%) 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 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 8 and Table 9).

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 (48.4%).

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.

Primary Series

Participants 18 Years of Age and Older

Solicited Adverse Reactions

The safety profile presented below is based on data generated in an ongoing Phase 3, placebo-controlled clinical study on 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 (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 2, Table 3, Table 4 and Table 5 respectively.

Table 2 – 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 n (%) N=11,406	Placebo Group n (%) N=11,407	SPIKEVAX Group n (%) N=10,985	Placebo Group n (%) N=10,918
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)	1389 (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 3 – 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 n (%) N=3,762	Placebo Group n (%) N=3,748	SPIKEVAX Group n (%) N=3,692	Placebo Group n (%) N=3,648
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 4 – 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 n (%) N=11,406	Placebo Group n (%) N=11,407	SPIKEVAX Group n (%) N=10,985	Placebo Group n (%) N=10,918
Fatigue				

Solicited Systemic AR	Dose 1		Dose 2	
	SPIKEVAX Group n (%) N=11,406	Placebo Group n (%) N=11,407	SPIKEVAX Group n (%) N=10,985	Placebo Group n (%) N=10,918
Any grade	4,384 (38.4)	3,282 (28.8)	7,430 (67.6)	2,687 (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 5 – 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 n (%) N=3,762	Placebo Group n (%) N=3,748	SPIKEVAX Group n (%) N=3,692	Placebo Group n (%) N=3,648
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 n (%) N=3,762	Placebo Group n (%) N=3,748	SPIKEVAX Group n (%) N=3,692	Placebo Group n (%) N=3,648
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 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 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.

Three serious adverse events were likely related to SPIKEVAX: 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, 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 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 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 group.

There were three reports of Bell's palsy in the SPIKEVAX 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.

Adolescents 12 to 17 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 adolescent participants receiving SPIKEVAX (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 6 and Table 7 respectively. Solicited local and systemic adverse reactions reported following administration of SPIKEVAX had a median duration of 1 to 3 days.

Table 6 – 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	7	0

	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
	(0.4)	(0)	(0.3)	(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 7 – 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				
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)

	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
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 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 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 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.

Children 6 to 11 Years of Age

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 (n=3,007) and participants receiving placebo (n=995) with at least 1 documented dose, and 2,988 participants receiving SPIKEVAX 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 8 and Table 9 respectively. The majority of solicited local adverse reactions following administration of SPIKEVAX occurred within the first 1 to 2 days after any dose and persisted for a median of 3 days.

Table 8 – 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	
	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
Pain				
Any grade	2,796 (93.1)	465 (46.8)	2,832 (94.8)	480 (49.5)
Grade 3[b]	28 (0.9)	0	81 (2.7)	2 (0.2)
Erythema (redness)				
Any grade	349 (11.9)	13 (1.3)	559 (18.7)	10 (1.0)
Grade 3[c]	16 (0.5)	1 (0.1)	33 (1.1)	1 (0.1)
Swelling (hardness)				
Any grade	354 (11.8)	12 (1.2)	507 (17.0)	12 (1.2)
Grade 3[c]	19 (0.6)	1 (0.1)	20 (0.7)	0 (0)
Axillary swelling/ tenderness				
Any grade	465 (15.5)	84 (8.5)	537 (18.0)	65 (6.7)
Grade 3[b]	3 (<0.1)	1 (0.1)	3 (0.1)	2 (0.2)

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 9 – 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	
	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
Fever				
Any grade	99 (3.3)	15 (1.5)	714 (23.9)	19 (2.0)
Grade 3 (≥39.0° – ≤40.0°C)	17 (0.6)	2 (0.2)	113 (3.8)	2 (0.2)
Headache				
Any grade	938 (31.2)	306 (30.8)	1,622 (54.3)	275 (28.4)
Grade 3[b]	18 (0.6)	4 (0.4)	119 (4.0)	8 (0.8)
Fatigue				
Any grade	1,298 (43.2)	334 (33.6)	1,925 (64.5)	335 (34.6)
Grade 3[b]	31 (1.0)	8 (0.8)	191 (6.4)	8 (0.8)
Myalgia				
Any grade	438 (14.6)	96 (9.7)	843 (28.2)	105 (10.8)
Grade 3[b]	11 (0.4)	1 (0.1)	71 (2.4)	1 (0.1)
Arthralgia				
Any grade	260 (8.7)	75 (7.6)	482 (16.1)	84 (8.7)
Grade 3[b]	3 (<0.1)	1 (0.1)	25 (0.8)	0 (0)
Nausea/vomiting				
Any grade	325 (10.8)	107 (10.8)	716 (24.0)	97 (10.0)
Grade 3[c]	5 (0.2)	0 (0)	19 (0.6)	0 (0)
Chills				
Any grade	309 (10.3)	67 (6.7)	904 (30.3)	74 (7.6)
Grade 3[b]	3 (<0.1)	0 (0)	19 (0.6)	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 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 (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 and 25.1% of participants (n=995) who received placebo. Unsolicited adverse events that occurred in ≥ 1% of study participants who received SPIKEVAX 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 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 group.

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

Children 6 Months to 5 Years of Age

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. 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 (n=4,792) and participants receiving placebo (n=1,596) with at least 1 documented dose, and 4,561 participants receiving SPIKEVAX 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 10 and Table 11 respectively. The majority of solicited local and systemic adverse reactions following administration of SPIKEVAX 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 12. 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 13 and 14, respectively. The majority of solicited local and systemic adverse reactions following administration of SPIKEVAX occurred within the first 1 to 2 days after any dose and persisted for a median of 2 days.

Table 10 – 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 11 – 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	11	3	7	6

	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 (%)
(≥39.6°C to ≤40°C)	(0.6)	(0.5)	(0.4)	(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 12 – 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 (0.1)	0 (0)	11 (0.4)	0 (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)

	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 (%)
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 13 – 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 (54.5)	163 (51.1)	523 (54.3)	148 (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	71	294	69

	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 (%)
	(23.9)	(22.3)	(30.5)	(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 14 – 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)
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	2	6	0

	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 (%)
	(0.3)	(0.3)	(0.3)	(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 (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 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 (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 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 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 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 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 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, 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.

Booster Dose

Participants 18 Years of Age and Older

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 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 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, there were no serious adverse events reported from the booster dose through 29 days after the booster dose.

Adolescents 12 to 17 Years of Age

Safety data for a booster dose of SPIKEVAX 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 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 Events

Local and systemic adverse reactions (ARs) were solicited in an electronic diary for 7 days following the injection among participants receiving SPIKEVAX 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.

8.3 Less Common Clinical Trial Adverse Reactions

The following events were reported in the ongoing Phase 3, placebo-controlled clinical study 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.

8.4 Post-Market Adverse Reactions

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

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.

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 sequence 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 protein undergoes post-translational modification and trafficking resulting in properly folded, fully functional Spike protein that is inserted into the cellular membrane of the expressing cell(s). The Spike protein is 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 30 days prior to first use.
- Unpunctured vials may be stored between 8° to 25°C (46° to 77°F) for up to 24 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 12 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)
0.20 mg/mL	Red	• 2 hours and 30 minutes *After thawing, let vial stand at room temperature for 15 minutes before administering.*	• 1 hour
0.10 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 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: Elasomeran (mRNA vaccine)

Chemical name: mRNA-1273 LS (Large Scale) Lipid Nanoparticle (LNP)

Product Characteristics

SPIKEVAX is an mRNA-lipid complex [lipid nanoparticle (LNP)] dispersion that contains elasomeran (mRNA CX-024414) that encodes for the pre-fusion stabilized Spike glycoprotein of 2019-novel Coronavirus (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 at 0.20 mg/mL or 0.10 mg/mL for intramuscular administration. SPIKEVAX is in a 10R clear Type 1 glass vial with a rubber serum stopper and an aluminum seal with flip-off plastic cap.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

14.1.1 Participants 18 Years of Age and Older

The safety and efficacy of SPIKEVAX 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 15 – 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
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)	1309 (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	9023 (63.8)	8916 (63.4)	17,939 (63.6)
Communities of color	5088 (36.0)	5132 (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 (eg, 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.

14.1.2 Adolescents 12 to 17 Years of Age

Safety, efficacy and immunogenicity data for SPIKEVAX 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 (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 Children 6 to 11 Years of Age

Safety, efficacy and immunogenicity data for SPIKEVAX in children 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. 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 (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.

14.1.4 Children > 6 Months of Age to 5 Years of Age

Safety, efficacy and immunogenicity data for SPIKEVAX in children 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 225 participants 6 months through 5 years of age who received at least 1 dose (25 mcg) of SPIKEVAX. 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 (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 and those who received placebo.

14.1.5 Booster Dose (Participants ≥ 18 Years of Age)

A booster dose of SPIKEVAX was evaluated in Study P201 Part B, an open-label part assessing immunogenicity following administration of a 50 mcg 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%).

14.1.6 Booster Dose (Participants 12 to 17 Years of Age)

A booster dose of SPIKEVAX 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 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.

14.2 Study Results

14.2.1 Efficacy in Participants ≥ 18 Years of Age (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 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 group and 3273.7 person years in the placebo group.

There were 11 confirmed COVID-19 cases identified in the SPIKEVAX group and 185 in placebo groups, respectively, for the primary efficacy analysis. Compared to placebo, efficacy of SPIKEVAX 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 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 group.

14.2.2 Efficacy and Immunogenicity in Adolescents 12 to 17 Years of Age (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 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 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).

14.2.3 Immunogenicity and Efficacy in Children 6 to 11 Years of Age (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 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 16).

Table 16 – 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 (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 Immunogenicity and Efficacy in Children 6 Months of Age to 5 Years of Age (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 (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 17).

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 17 – 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 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 18 and Table 19, respectively. No cases of severe COVID-19 were reported in the study.

Table 18 – 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 19 for footnotes.

Table 19 – 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.

14.2.5 Immunogenicity in Participants ≥ 18 Years of Age – After Booster Dose

Effectiveness of the single booster dose of 50 mcg of SPIKEVAX in adults 18 years of age and older who received a 2-dose primary series with 100 mcg SPIKEVAX 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 to participants primed with 100 mcg doses of SPIKEVAX. Participants with negative baseline SARS-CoV-2 status were randomly selected from Study P301 participants in the SPIKEVAX 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=1,055).

In participants who were primed with a 2-dose series of 100 mcg of SPIKEVAX, single booster dose of 50 mcg of SPIKEVAX 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 20.

Table 20 – 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]=1,053 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

14.2.6 SPIKEVAX Immunogenicity in Participants 12 to 17 Years of Age – After Booster Dose

Effectiveness of a booster dose of 50 mcg of SPIKEVAX 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 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. 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 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 21.

Table 21 – 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 and 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).

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, 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. 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™

Elasomeran 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.

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. The primary vaccination series will require two doses given 4 weeks apart.

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: Elasomeran (mRNA)

Non-medicinal ingredients:
- acetic acid
- cholesterol
- DSPC (1,2-distearoyl-sn-glycero-3-phosphocholine)
- PEG2000-DMG (1,2-dimyristoyl-rac-glycerol,methoxy-polyethyleneglycol)
- lipid SM-102
- 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. For individuals 12 years of age and older each dose in the primary vaccination series is 100 micrograms of elasomeran (mRNA). For children 6 to 11 years of age each dose in the primary vaccination series is 50 micrograms of elasomeran. For children > 6 months of age to 5 years of age each dose in the primary vaccination series is 25 micrograms of elasomeran.

The dose for the booster in individuals 12 years of age and older is 50 micrograms of elasomeran.

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 no 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:
SPIKEVAX will be given to you as two injections (called the primary vaccination series). Each injection will be given on a separate visit 1 month apart. It is very important that you return for the second

injection, or the vaccine may not work as well.

- For individuals 12 years of age and older, each dose is 100 micrograms.
- For children 6 to 11 years of age, each dose is 50 micrograms.
- For children >6 months of age to 5 years of age, each dose is 25 micrograms.

The booster dose is given as one 50 microgram injection. The booster dose may be given on a separate visit at least 4 months after completion of the primary vaccination series in individuals 12 years of age and older.

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
- headache
- muscle ache and stiffness
- chills
- fever
- swelling or redness at the injection site
- 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. Myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) have been reported following SPIKEVAX administration.

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 Corporation 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 Corporation.

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