PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

SPIKEVAX™

Elasomeran mRNA vaccine

Dispersion for intramuscular injection

Multidose Vial, 100 mcg / 0.5mL

Active Immunizing Agent

ModernaTX, Inc.
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Cambridge, MA, USA, 02139

Imported and Distributed by:
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TABLE OF CONTENTS

Sections or subsections that are not applicable at the time of authorization are not listed.

TABLE OF CONTENTS 2

PART I: HEALTH PROFESSIONAL INFORMATION 4

1 INDICATIONS 4

1.1 Pediatrics 4

1.2 Geriatrics 4

2 CONTRAINDICATIONS 4

3 Serious warning and precautions 4

4 DOSAGE AND ADMINISTRATION 4

4.1 Dosing Considerations 4

4.2 Recommended Dose and Dosage Adjustment 4

4.3 Reconstitution 5

4.4 Administration 5

5 OVERDOSAGE 6

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING 6

7 WARNINGS AND PRECAUTIONS 7

7.1 Special Populations 8

7.1.1 Pregnant Women 8

7.1.2 Breast-feeding 8

7.1.3 Pediatrics 8

7.1.4 Geriatrics 8

8 ADVERSE REACTIONS 8

8.1 Adverse Reaction Overview 8

8.2 Clinical Trial Adverse Reactions 9

8.3 Less Common Clinical Trial Adverse Reactions 18

8.4 Post-Market Adverse Reactions 18

9 DRUG INTERACTIONS 18

10 CLINICAL PHARMACOLOGY 19

10.1 Mechanism of Action 19

11 STORAGE, STABILITY AND DISPOSAL 19

12 SPECIAL HANDLING INSTRUCTIONS 20
PART II: SCIENTIFIC INFORMATION 21
13 PHARMACEUTICAL INFORMATION 21
14 CLINICAL TRIALS 21
14.1 Trial Design and Study Demographics 21
14.2 Study Results 23
15 MICROBIOLOGY 25
16 NON-CLINICAL TOXICOLOGY 25
PATIENT MEDICATION INFORMATION 26

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 12 years of age and older.

1.1 Pediatrics

The safety and efficacy of SPIKEVAX in individuals under 12 years 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 WARNING 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. The SPIKEVAX primary series is a two-dose regimen of 0.5 mL (100 mcg) each.

The SPIKEVAX booster is one dose of 0.25 mL (50 mcg).

4.2 Recommended Dose and Dosage Adjustment

Vaccination Schedule
SPIKEVAX is administered intramuscularly as a primary series of two doses of 0.5 mL each (100 mcg) 4 weeks apart in individuals 12 years of age and older (see CLINICAL TRIALS).

A booster dose of 0.25 mL (50 mcg) may be administered intramuscularly at least 6 months after completion of the primary series in individuals 18 years of age or older.

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.

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 vial contains a volume of 5 mL supplied as a frozen dispersion that does not contain preservative. Ten (10) doses of 0.5 mL volume each or a maximum of twenty (20) doses of 0.25 mL volume each can be withdrawn from each multidose vial. Each vial must be thawed prior to administration.

Thaw each vial before use:

- Thaw in refrigerated conditions between 2°C to 8°C for 2 hours and 30 minutes. Let each vial stand at room temperature for 15 minutes before administering.
- Alternatively, thaw at room temperature between 15°C to 25°C for 1 hour.
- 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. 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. Do not puncture the vial more than 20 times.

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

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 (each of 5 mL) 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.

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

The clinical data available for SPIKEVAX are derived from the COVE Phase 3 study (Study P301) and Phase 1 and Phase 2 studies. Serious and unexpected adverse events may occur that have not been previously reported with SPIKEVAX use.

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.

A second dose of the vaccine should not be given to those who have experienced anaphylaxis to the first 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. These cases occurred more commonly after the second dose and in adolescents and young adults. Typically, the onset of symptoms has been within a few days following receipt of SPIKEVAX. Available short-term follow-up data suggest that the symptoms resolve in most individuals, 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.

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 (0.5 mL, 100 mcg) 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 12 years 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, 1360 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%).

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.

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 18-64 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	9908 (86.9)	2177 (19.1)	9873 (89.9)	2040 (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	1322 (11.6)	567 (5.0)	1775 (16.2)	470 (4.3)
Grade 3 or 4	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=3762	Placebo Group n (%) N=3748	SPIKEVAX Group n (%) N=3692	Placebo Group n (%) N=3648
Pain				
Any grade	2782 (74.0)	481 (12.8)	3070 (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	3	72	7

Solicited local AR	Dose 1		Dose 2	
	SPIKEVAX Group n (%) N=3762	Placebo Group n (%) N=3748	SPIKEVAX Group n (%) N=3692	Placebo Group n (%) N=3648
	(0.5)	(<0.1)	(2.0)	(0.2)
Axillary swelling/ Tenderness				
Any grade	231 (6.1)	155 (4.1)	315 (8.5)	97 (2.7)
Grade 3 or 4	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 18-64 Years of Age (Safety Analysis Set*)

Solicited Systemic AR	Dose 1		Dose 2	
	SPIKEVAX Group n (%) N=11406	Placebo Group n (%) N=11407	SPIKEVAX Group n (%) N=10985	Placebo Group n (%) N=10918
Fatigue				
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				

Solicited Systemic AR	Dose 1		Dose 2	
	SPIKEVAX Group n (%) N=11406	Placebo Group n (%) N=11407	SPIKEVAX Group n (%) N=10985	Placebo Group n (%) N=10918
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.
[h] Grade 3 fever: Defined as ≥39.0 – ≤40.0°C / ≥102.1 – ≤104.0°F.
[i] 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=3762	Placebo Group n (%) N=3748	SPIKEVAX Group n (%) N=3692	Placebo Group n (%) N=3648
Fatigue				
Any grade	1251 (33.3)	851 (22.7)	2152 (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)	1704 (46.2)	650 (17.8)
Grade 3[b]	52 (1.4)	34 (0.9)	106 (2.9)	33 (0.9)
Myalgia				
Any grade	742	443	1739	398

Solicited Systemic AR	Dose 1		Dose 2	
	SPIKEVAX Group n (%) N=3762	Placebo Group n (%) N=3748	SPIKEVAX Group n (%) N=3692	Placebo Group n (%) N=3648
	(19.7)	(11.8)	(47.1)	(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)	1291 (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)	1141 (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)
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 3, 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.[a] 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)[b,c]

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

* 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary).

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)[d,e]

	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[d]	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[e]	56 (2.3)	17 (1.4)	112 (4.5)	14 (1.1)
Grade 4[f]	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[g]	4 (0.2)	1 (<0.1)	11 (0.4)	0 (0)
Arthralgia				
Any grade	371 (15.0)	143 (11.6)	716 (28.9)	113 (9.3)
Grade 3[d]	15 (0.6)	5 (0.4)	57 (2.3)	2 (0.2)
Nausea/vomiting				
Any grade	281 (11.3)	110 (8.9)	591 (23.9)	106 (8.7)
Grade 3[h]	2 (<0.1)	0 (0)	2 (<0.1)	0 (0)
Grade 4[i]	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)

	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
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)

* 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary).

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.

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

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

[f] Grade 4 headache: Defined as requires emergency room visit or hospitalisation.

[g] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.

[h] Grade 3 nausea/vomiting: Defined as prevents daily activity, requires outpatient intravenous hydration.

[i] 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.

Booster Dose Study Participants

Study 3 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.

8.3 Less Common Clinical Trial Adverse Reactions

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

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

Nervous System Disorders: facial paralysis / Bell's palsy, hypoaesthesia, 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 -25° to -15°C (-13° to 5°F). Store in the original carton to protect from light.

Additional Storage Information Not Displayed on the Vial Labels and Cartons

- Do not store on dry ice or below -40°C (-40°F).
- 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 -25° to -15°C (-13° 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.

Thawed under refrigeration: Thaw in refrigerated conditions between 2° to 8°C (36° to 46°F) for 2 hours and 30 minutes. After thawing, let vial stand at room temperature for 15 minutes before administering.

Thawed at room temperature: Alternatively, thaw at room temperature between 15° to 25°C (59° to 77°F) for 1 hour.

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.

The four lipids are: SM-102 (a custom-manufactured, ionizable lipid (Heptadecan-9-yl 8-((2-hydroxyethyl) (6-oxo-6-(undecyloxy) hexyl) amino)octanoate)); PEG2000-DMG (1,2-dimyristoyl-rac-glycerol,methoxy-polyethyleneglycol); 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC) and cholesterol.

SPIKEVAX is supplied as a multidose liquid ready-to-use dispersion at 0.20 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.

Each vial contains 1.26 mg of CX-024414 mRNA and 24.38 mg of SM-102 LNP as a white to off-white dispersion in preservative-free diluent buffer at pH 7.5.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

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 8 – 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	6768 (47.9)	6611 (47.0)	13,379 (47.4)
Male	7366 (52.1)	7462 (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	3583 (25.4)	3552 (25.2)	7135 (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	1385 (9.8)	1349 (9.6)	2734 (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	2789 (19.7)	2780 (19.8)	5569 (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	3593 (25.4)	3581 (25.4)	7174 (25.4)
High Risk Condition**			
One high risk condition present	2616 (18.5)	2591 (18.4)	5207 (18.5)
Two or more high risk conditions present	590 (4.2)	576 (4.1)	1166 (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	8189 (57.9)	8200 (58.3)	16,389 (58.1)
18 to <65 years and at risk	2367 (16.7)	2324 (16.5)	4691 (16.6)
≥ 65 years	3578 (25.3)	3549 (25.2)	7127 (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.

14.2 Study Results

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 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 group~~s~~, 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.

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 mRNA COVID-19 Vaccine 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%).

Immunogenicity in Adolescents (12 – 17 Years of Age)

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 mRNA-1273 COVID-19 Vaccine 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).

Immunogenicity in Booster Dose Participants

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=1055).

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 post-booster in Study P201 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 9.

Table 9 – Neutralizing Antibody Geometric Mean Titers (ID50) Against a Pseudovirus Expressing the SARS-CoV-2 Spike Protein at 28 Days After a Booster Dose in Study P201 Part B vs 28 Days After Completion of the Primary Series in Study P301, Participants ≥18 Years of Age, Per-Protocol Immunogenicity Set

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

* Per-Protocol Immunogenicity Set included all subjects who had both baseline (or Study P201 Part B Day 1) and post-vaccination immunogenicity samples, did not have SARS-CoV-2 infection at baseline (or Study P201 Part B Day 1), did not have a

major protocol deviation that impacted immune response, and had post-injection immunogenicity assessment at timepoint of primary interest (Day 29 for Study P201 Part B and Day 57 for Study P301).
[a]Number of subjects with non-missing data at the corresponding timepoint.
[b]Given the lack of randomization in Study P201 Part 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

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, 0.2mL 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 12 years 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.

Individuals may not be optimally protected until after receiving the second dose of the vaccine.

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 of 10 doses. Each dose in the primary vaccination series is 0.5 mL and contains 100 micrograms of elasomeran (mRNA). The dose for the booster is 0.25 mL and contains 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 0.5 mL 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.

The booster dose is given as one 0.25 mL injection. The booster dose may be given on a separate visit at least 6 months after completion of the primary vaccination series in individuals 18 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)
- dizziness

Non-severe allergic reactions (such as rash, itching, hives or swelling of the face), severe allergic reactions and facial paralysis / Bell's palsy have been reported.

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 ModernaTX, Inc. 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 ModernaTX, Inc.

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