HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use MNEXSPIKE safely and effectively. See full prescribing information for MNEXSPIKE.

MNEXSPIKE (COVID-19 Vaccine, mRNA) injectable suspension, for intramuscular use
2025-2026 Formula
Initial U.S. Approval: 2025

----------RECENT MAJOR CHANGES----------

Indications and Usage (1)	8/2025
Dosage and Administration, Dosing and Schedule (2.3)	8/2025
Warnings and Precautions, Myocarditis and Pericarditis (5.2)	6/2025

----------INDICATIONS AND USAGE----------

MNEXSPIKE is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

MNEXSPIKE is approved for use in individuals who are:

- 65 years of age and older, or
- 12 years through 64 years of age with at least one underlying condition that puts them at high risk for severe outcomes from COVID-19. (1)

----------DOSAGE AND ADMINISTRATION----------

- For intramuscular use.
- Administer MNEXSPIKE as a single 0.2 mL dose at least 3 months after the last dose of COVID-19 vaccine. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------

MNEXSPIKE is an injectable suspension.
A single dose is 0.2 mL. (3)

----------CONTRAINDICATIONS----------

Do not administer MNEXSPIKE to individuals with a known history of severe allergic reaction (e.g., anaphylaxis) to any component of MNEXSPIKE or to individuals who had a severe allergic reaction (e.g., anaphylaxis) following a previous dose of SPIKEVAX (COVID-19 Vaccine, mRNA) or any Moderna COVID-19 vaccine authorized for emergency use. (4)

----------WARNINGS AND PRECAUTIONS----------

Analyses of postmarketing data from use of authorized or approved mRNA COVID-19 vaccines have demonstrated increased risks of myocarditis and pericarditis, with onset of symptoms typically in the first week following vaccination. The observed risk has been highest in males 12 years through 24 years of age. (5.2)

----------ADVERSE REACTIONS----------

Most commonly reported adverse reactions following administration of MNEXSPIKE (≥10%):

- *Participants 12 years through 17 years of age*: pain at the injection site (up to 68.8%), headache (up to 54.5%), fatigue (up to 47.3%), myalgia (up to 39.2%), axillary swelling or tenderness (up to 34.6%), chills (up to 31.6%), arthralgia (up to 23.9%), and nausea/vomiting (up to 16.1%). (6)
- *Participants 18 years through 64 years of age*: pain at the injection site (up to 74.8%), fatigue (up to 54.3%), headache (up to 47.8%), myalgia (up to 41.6%), arthralgia (up to 32.4%), chills (up to 24.3%), axillary swelling or tenderness (up to 21.7%), and nausea/vomiting (up to 13.8%). (6)
- *Participants 65 years of age and older*: pain at the injection site (up to 54.6%), fatigue (up to 43.0%), headache (up to 33.1%), myalgia (up to 30.5%), arthralgia (up to 25.7%), chills (up to 16.5%), nausea/vomiting (up to 11.4%), and axillary swelling or tenderness (up to 10.7%). (6)

To report SUSPECTED ADVERSE REACTIONS, contact ModernaTX, Inc. at 1-866-663-3762 or VAERS at 1-800-822-7967 or https://vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 8/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

MNEXSPIKE is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

MNEXSPIKE is approved for use in individuals who are:

- 65 years of age and older, or
- 12 years through 64 years of age with at least one underlying condition that puts them at high risk for severe outcomes from COVID-19.

2 DOSAGE AND ADMINISTRATION

For intramuscular use.

2.1 Preparation for Administration

- Verify that the label on the prefilled syringe states 2025-2026 Formula.
- If prefilled syringes of MNEXSPIKE are frozen, thaw before use following the instructions below.

Table 1: Thawing Conditions and Times

	Thaw in Refrigerator 2°C to 8°C (36°F to 46°F)	**Thaw at Room Temperature 15°C to 25°C (59°F to 77°F)**
Carton of 10 syringes	Thaw for 2 hours and 40 minutes	Thaw for 1 hour and 20 minutes
Carton of 2 syringes	Thaw for 1 hour and 40 minutes	Thaw for 40 minutes
Carton of 1 syringe	Thaw for 1 hour and 40 minutes	Thaw for 40 minutes
One syringe (removed from carton)	Thaw for 1 hour and 40 minutes	Thaw for 40 minutes

- After thawing, do not refreeze.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.
- MNEXSPIKE is a white to off-white suspension. It may contain white or translucent product-related particulates. Do not administer if vaccine is discolored or contains other particulate matter.
- **Do not shake.**
- With tip cap upright, remove tip cap by twisting counterclockwise until tip cap releases.

Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe.
- Discard after single use.

2.2 Administration

Administer MNEXSPIKE intramuscularly.

2.3 Dosing and Schedule

Administer MNEXSPIKE as a single 0.2 mL dose.

For individuals previously vaccinated with any COVID-19 vaccine, administer the dose of MNEXSPIKE at least 3 months after the last dose of COVID-19 vaccine.

3 DOSAGE FORMS AND STRENGTHS

MNEXSPIKE is an injectable suspension.

A single dose is 0.2 mL.

4 CONTRAINDICATIONS

Do not administer MNEXSPIKE to individuals with a known history of severe allergic reaction (e.g., anaphylaxis) to any component of MNEXSPIKE *[see Description (11)]* or to individuals who had a severe allergic reaction (e.g., anaphylaxis) following a previous dose of SPIKEVAX (COVID-19 Vaccine, mRNA) or any Moderna COVID-19 vaccine authorized for emergency use.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment must be immediately available to manage potential anaphylactic reactions following administration of MNEXSPIKE.

5.2 Myocarditis and Pericarditis

Analyses of postmarketing data from use of authorized or approved mRNA COVID-19 vaccines have demonstrated increased risks of myocarditis and pericarditis, with onset of symptoms typically in the first week following vaccination. The observed risk has been highest in males 12 years through 24 years of age.

Based on analyses of commercial health insurance claims data from inpatient and outpatient settings, the estimated unadjusted incidence of myocarditis and/or pericarditis during the period

1 through 7 days following administration of the 2023-2024 Formula of mRNA COVID-19 vaccines was approximately 8 cases per million doses in individuals 6 months through 64 years of age and approximately 27 cases per million doses in males 12 years through 24 years of age.

Although some individuals with myocarditis and/or pericarditis following administration of mRNA COVID-19 vaccines have required intensive care support, available data suggest that individuals typically have resolution of symptoms within a few days with conservative management.

Follow-up information on cardiovascular outcomes in hospitalized patients who had been diagnosed with COVID-19 vaccine-associated myocarditis is available from a longitudinal retrospective observational study. Most of these patients had received a two-dose primary series of an mRNA COVID-19 vaccine prior to their diagnosis. In this study, at a median follow-up of approximately 5 months post-vaccination, persistence of abnormal cardiac magnetic resonance imaging (CMR) findings that are a marker for myocardial injury was common. The clinical and prognostic significance of these CMR findings is not known[1] *[see Adverse Reactions (6.2)]*.

Information is not yet available about potential long-term sequelae of myocarditis or pericarditis following administration of mRNA COVID-19 vaccines.

The Centers for Disease Control and Prevention (CDC) has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressive therapy, may have a diminished immune response to MNEXSPIKE *[see Use in Specific Populations (8.6)]*.

5.5 Limitations of Vaccine Effectiveness

MNEXSPIKE may not protect all vaccine recipients.

6 ADVERSE REACTIONS

Most commonly (≥10%) reported adverse reactions following administration of MNEXSPIKE:

- Participants 12 years through 17 years of age: pain at the injection site (up to 68.8%), headache (up to 54.5%), fatigue (up to 47.3%), myalgia (up to 39.2%), axillary swelling

or tenderness (up to 34.6%), chills (up to 31.6%), arthralgia (up to 23.9%), and nausea/vomiting (up to 16.1%).

- Participants 18 years through 64 years of age: pain at the injection site (up to 74.8%), fatigue (up to 54.3%), headache (up to 47.8%), myalgia (up to 41.6%), arthralgia (up to 32.4%), chills (up to 24.3%), axillary swelling or tenderness (up to 21.7%), and nausea/vomiting (up to 13.8%).

- Participants 65 years of age and older: pain at the injection site (up to 54.6%), fatigue (up to 43.0%), headache (up to 33.1%), myalgia (up to 30.5%), arthralgia (up to 25.7%), chills (16.5%), nausea/vomiting (up to 11.4%), and axillary swelling or tenderness (up to 10.7%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared with rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

Individuals 12 Years of Age and Older

Single Dose (Bivalent Original and Omicron BA.4/BA.5) in Vaccine-Experienced

The safety of MNEXSPIKE was evaluated in a randomized, observer-blind, active-controlled clinical trial conducted in the United States, United Kingdom, and Canada involving 11,417 participants 12 years of age and older who received a single dose of MNEXSPIKE (n=5,706) or comparator vaccine (Moderna COVID-19 Vaccine, Bivalent [Original and Omicron BA.4/BA.5] not U.S. licensed, authorized for emergency use; n=5,711) (Study 1, NCT05815498). MNEXSPIKE administered in the study contained 5 mcg mRNA encoding the membrane-bound, linked N-terminal domain (NTD) and receptor-binding domain (RBD) of the Spike (S) glycoprotein from SARS-CoV-2 Wuhan-Hu 1 strain (Original) and 5 mcg mRNA encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Omicron variant lineages BA.4 and BA.5. The comparator vaccine administered in the study contained 25 mcg mRNA encoding the S glycoprotein from SARS-CoV-2 Wuhan-Hu 1 strain (Original) and 25 mcg mRNA encoding the S glycoprotein from SARS-CoV-2 Omicron variant lineages BA.4 and BA.5. The median duration of follow-up for safety was 8.8 months.

In Study 1, the median age of the population was 56 years (range 12 through 96 years); 8.7% of participants were 12 years through 17 years, 62.6% were 18 years through 64 years, and 28.7% were 65 years and older. Overall, 45.7% of the participants were male, 54.3% were female, 13.2% were Hispanic or Latino, 82.2% were White, 11.2% were Black or African American, 3.6% were Asian, 0.4% were American Indian or Alaska Native, 0.1% were Native Hawaiian or Pacific Islander, 0.4% were other races, and 1.5% were Multiracial. Overall, 64.3% of study participants reported at least one CDC-defined high-risk condition for severe COVID-19. Demographic characteristics were similar between participants who received MNEXSPIKE and those who received the comparator vaccine.

All participants in the study, except one participant in the MNEXSPIKE group, had previously received at least one dose of a COVID-19 vaccine prior to the study with a median interval of 9.8 months since the last dose. Overall, 74.3% of participants (MNEXSPIKE=4,211; comparator vaccine=4,270) had evidence of prior SARS-CoV-2 infection at baseline (immunologic or virologic evidence of prior SARS-CoV-2 infection [defined as positive RT-PCR test and/or positive Elecsys immunoassay result at Day 1]).

Solicited Adverse Reactions

Local and systemic adverse reactions and use of antipyretic medication were solicited in an electronic diary for 7 days following injection (i.e., day of vaccination and the next 6 days) among participants who received MNEXSPIKE (n=5,702) and participants who received the comparator vaccine (n=5,706). Events that persisted for more than 7 days were followed until resolution.

The reported number and percentage of solicited local and systemic adverse reactions for 12 years through 17 years are presented in Table 2 and Table 3, 18 years through 64 years are presented in Table 4 and Table 5, and 65 years and older are presented in Table 6 and Table 7, respectively.

Table 2: Number and Percentage of Participants with Solicited Local Adverse Reactions Starting Within 7 Days* After Injection in Participants 12 Years Through 17 Years (Solicited Safety Set)

Local Adverse Reactions[a]	**MNEXSPIKE[b]** N=497 n (%)	**Comparator Vaccine[c]** N=495 n (%)
Pain[d]	342 (68.8)	390 (78.8)
Pain, Grade 3[d]	10 (2.0)	19 (3.8)
Axillary swelling or tenderness[d]	172 (34.6)	134 (27.1)
Axillary swelling or tenderness, Grade 3[d]	6 (1.2)	2 (0.4)
Swelling (hardness) ≥25 mm[e]	18 (3.6)	25 (5.1)
Swelling (hardness) >100 mm, Grade 3[e]	4 (0.8)	2 (0.4)
Erythema (redness) ≥25 mm[e]	6 (1.2)	13 (2.6)

* 7 days included day of vaccination and the subsequent 6 days. Events were collected in the electronic diary (e-diary).
N=Number of participants in the Solicited Safety Set.

n=Number of participants with listed solicited adverse reactions.
[a] Absence of rows for Grade 3 or Grade 4 adverse reactions indicates no events were reported.
[b] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Original and Omicron variant lineages BA.4/BA.5
[c] Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)
[d] Pain and axillary swelling or tenderness grading scale: no interference with activity (Grade 1); some interference with activity (Grade 2); prevents daily activity (Grade 3).
[e] Swelling and erythema grading scale: 25-50 mm / 2.5-5 cm (Grade 1); 51-100 mm / 5.1-10 cm (Grade 2); >100 mm / >10 cm (Grade 3).

Table 3: Number and Percentage of Participants with Solicited Systemic Adverse Reactions Starting Within 7 Days* After Injection in Participants 12 Years Through 17 Years (Solicited Safety Set)

Systemic Adverse Reactions[a]	**MNEXSPIKE[b]** N=497 n (%)	**Comparator Vaccine[c]** N=495 n (%)
Headache[d]	271 (54.5)	287 (58.0)
Headache, Grade 3[d]	35 (7.0)	20 (4.0)
Fatigue[d]	235 (47.3)	251 (50.7)
Fatigue, Grade 3[d]	34 (6.8)	22 (4.4)
Myalgia[d]	195 (39.2)	178 (36.0)
Myalgia, Grade 3[d]	28 (5.6)	17 (3.4)
Chills[e]	157 (31.6)	158 (31.9)
Chills, Grade 3[e]	6 (1.2)	1 (0.2)
Arthralgia[d]	119 (23.9)	117 (23.6)
Arthralgia, Grade 3[d]	10 (2.0)	6 (1.2)
Nausea/vomiting[f]	80 (16.1)	87 (17.6)
Nausea/vomiting, Grade 3[f]	0 (0)	2 (0.4)
Fever[g]	49 (9.9)	46 (9.3)
Fever, Grade 3[g]	4 (0.8)	2 (0.4)

Table 3: Number and Percentage of Participants with Solicited Systemic Adverse Reactions Starting Within 7 Days* After Injection in Participants 12 Years Through 17 Years (Solicited Safety Set)

Systemic Adverse Reactions[a]	MNEXSPIKE[b] N=497 n (%)	Comparator Vaccine[c] N=495 n (%)
Use of antipyretic or pain medication	186 (37.4)	211 (42.6)

* 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=Number of participants in the Solicited Safety Set.
n=Number of participants with listed solicited adverse reactions.
[a] No Grade 4 adverse reactions were reported.
[b] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Original and Omicron variant lineages BA.4/BA.5
[c] Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)
[d] Headache, fatigue, myalgia, arthralgia grading scale: no interference with activity (Grade 1); some interference with activity (Grade 2); prevents daily activity (Grade 3).
[e] Chills grading scale: no interference with activity (Grade 1); some interference with activity not requiring medical intervention (Grade 2); prevents daily activity and requires medical intervention (Grade 3).
[f] Nausea/vomiting grading scale: no interference with activity or 1-2 episodes/24 hours (Grade 1); some interference with activity or >2 episodes/24 hours (Grade 2); prevents daily activity, requires outpatient intravenous hydration (Grade 3).
[g] Fever grading scale: ≥38.0° – ≤38.4°C / ≥100.4° – ≤101.1°F (Grade 1); ≥38.5° – ≤38.9°C / ≥101.2°– ≤102.0°F (Grade 2); ≥39.0° – ≤40.0°C / ≥102.1° – ≤104.0°F (Grade 3).

Table 4: Number and Percentage of Participants with Solicited Local Adverse Reactions Starting Within 7 Days* After Injection in Participants 18 Years Through 64 Years (Solicited Safety Set)

Local Adverse Reactions[a]	MNEXSPIKE[b] N=3,573 n (%)	Comparator Vaccine[c] N=3,574 n (%)
Pain[d]	2,672 (74.8)	2,920 (81.7)
Pain, Grade 3[d]	38 (1.1)	49 (1.4)
Axillary swelling or tenderness[d]	777 (21.7)	749 (21.0)
Axillary swelling or tenderness, Grade 3[d]	11 (0.3)	15 (0.4)
Swelling (hardness) ≥25 mm[e]	140 (3.9)	246 (6.9)
Swelling (hardness) >100 mm, Grade 3[e]	11 (0.3)	19 (0.5)

Table 4: Number and Percentage of Participants with Solicited Local Adverse Reactions Starting Within 7 Days* After Injection in Participants 18 Years Through 64 Years (Solicited Safety Set)

Local Adverse Reactions[a]	MNEXSPIKE[b] N=3,573 n (%)	Comparator Vaccine[c] N=3,574 n (%)
Erythema (redness) ≥25 mm[e]	85 (2.4)	152 (4.3)
Erythema (redness) >100 mm, Grade 3[e]	9 (0.3)	17 (0.5)

* 7 days included day of vaccination and the subsequent 6 days. Events were collected in the electronic diary (e-diary).
N=Number of participants in the Solicited Safety Set.
n=Number of participants with listed solicited adverse reactions.
[a] No Grade 4 adverse reactions were reported.
[b] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Original and Omicron variant lineages BA.4/BA.5
[c] Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)
[d] Pain and axillary swelling or tenderness grading scale: no interference with activity (Grade 1); some interference with activity (Grade 2); prevents daily activity (Grade 3).
[e] Swelling and erythema grading scale: 25-50 mm / 2.5-5 cm (Grade 1); 51-100 mm / 5.1-10 cm (Grade 2); >100 mm / >10 cm (Grade 3).

Table 5: Number and Percentage of Participants with Solicited Systemic Adverse Reactions Starting Within 7 Days* After Injection in Participants 18 Years Through 64 Years (Solicited Safety Set)

Systemic Adverse Reactions[a]	MNEXSPIKE[b] N=3,573 n (%)	Comparator Vaccine[c] N=3,574 n (%)
Fatigue[d]	1,939 (54.3)	1,876 (52.5)
Fatigue, Grade 3[d]	170 (4.8)	156 (4.4)
Headache[d]	1,708 (47.8)	1,583 (44.3)
Headache, Grade 3[d]	90 (2.5)	76 (2.1)
Myalgia[d]	1,485 (41.6)	1,469 (41.1)
Myalgia, Grade 3[d]	144 (4.0)	105 (2.9)
Arthralgia[d]	1,159 (32.4)	1,094 (30.6)

Table 5: Number and Percentage of Participants with Solicited Systemic Adverse Reactions Starting Within 7 Days* After Injection in Participants 18 Years Through 64 Years (Solicited Safety Set)

Systemic Adverse Reactions[a]	MNEXSPIKE[b] N=3,573 n (%)	Comparator Vaccine[c] N=3,574 n (%)
Arthralgia, Grade 3[d]	86 (2.4)	62 (1.7)
Chills[e]	867 (24.3)	760 (21.3)
Chills, Grade 3[e]	26 (0.7)	22 (0.6)
Nausea/vomiting[f]	492 (13.8)	424 (11.9)
Nausea/vomiting, Grade 3[f]	4 (0.1)	3 (<0.1)
Fever[g]	193 (5.4)	138 (3.9)
Fever, Grade 3[g]	27 (0.8)	17 (0.5)
Use of antipyretic or pain medication	1,243 (34.8)	1,226 (34.3)

* 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=Number of participants in the Solicited Safety Set.

n=Number of participants with listed solicited adverse reactions.

[a] No Grade 4 adverse reactions were reported.

[b] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Original and Omicron variant lineages BA.4/BA.5

[c] Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)

[d] Fatigue, headache, myalgia, arthralgia grading scale: no interference with activity (Grade 1); some interference with activity (Grade 2); prevents daily activity (Grade 3).

[e] Chills grading scale: no interference with activity (Grade 1); some interference with activity not requiring medical intervention (Grade 2); prevents daily activity and requires medical intervention (Grade 3).

[f] Nausea/vomiting grading scale: no interference with activity or 1-2 episodes/24 hours (Grade 1); some interference with activity or >2 episodes/24 hours (Grade 2); prevents daily activity, requires outpatient intravenous hydration (Grade 3).

[g] Fever grading scale: ≥38.0° – ≤38.4°C / ≥100.4° – ≤101.1°F (Grade 1); ≥38.5° – ≤38.9°C / ≥101.2°– ≤102.0°F (Grade 2); ≥39.0° – ≤40.0°C / ≥102.1° – ≤104.0°F (Grade 3).

Table 6: Number and Percentage of Participants with Solicited Local Adverse Reactions Starting Within 7 Days* After Injection in Participants 65 Years and Older (Solicited Safety Set)

Local Adverse Reactions[a]	MNEXSPIKE[b] N=1,632 n (%)	Comparator Vaccine[c] N=1,637 n (%)
Pain[d]	891 (54.6)	1,109 (67.7)
Pain, Grade 3[d]	12 (0.7)	7 (0.4)
Axillary swelling or tenderness[d]	174 (10.7)	164 (10.0)
Axillary swelling or tenderness, Grade 3[d]	2 (0.1)	2 (0.1)
Swelling (hardness) ≥25 mm[e]	48 (2.9)	88 (5.4)
Swelling (hardness), Grade 3[e]	1 (<0.1)	11 (0.7)
Erythema (redness) ≥25 mm[e]	32 (2.0)	60 (3.7)
Erythema (redness), Grade 3[e]	2 (0.1)	7 (0.4)

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

N=Number of participants in the Solicited Safety Set.

n=Number of participants with listed solicited adverse reactions.

[a] No Grade 4 adverse reactions were reported.

[b] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Original and Omicron variant lineages BA.4/BA.5

[c] Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)

[d] Pain and axillary swelling or tenderness grading scale: no interference with activity (Grade 1); some interference with activity (Grade 2); prevents daily activity (Grade 3).

[e] Swelling and erythema grading scale: 25-50 mm / 2.5-5 cm (Grade 1); 51-100 mm / 5.1-10 cm (Grade 2); >100 mm / >10 cm (Grade 3).

Table 7: Number and Percentage of Participants with Solicited Systemic Adverse Reactions Starting Within 7 Days* After Injection in Participants 65 Years and Older (Solicited Safety Set)

Systemic Adverse Reactions[a]	MNEXSPIKE[b] N=1,632 n (%)	Comparator Vaccine[c] N=1,637 n (%)
Fatigue[d]	702 (43.0)	671 (41.0)
Fatigue, Grade 3[d]	59 (3.6)	41 (2.5)
Headache[d]	540 (33.1)	479 (29.3)
Headache, Grade 3[d]	22 (1.3)	22 (1.3)
Myalgia[d]	498 (30.5)	467 (28.5)
Myalgia, Grade 3[d]	33 (2.0)	27 (1.6)
Arthralgia[d]	418 (25.6)	366 (22.4)
Arthralgia, Grade 3[d]	24 (1.5)	21 (1.3)
Chills[e]	269 (16.5)	209 (12.8)
Chills, Grade 3[e]	10 (0.6)	8 (0.5)
Nausea/vomiting[f]	119 (7.3)	114 (7.0)
Nausea/vomiting, Grade 3[f]	2 (0.1)	5 (0.3)
Fever[g]	75 (4.6)	70 (4.3)
Fever, Grade 3[g]	2 (0.1)	9 (0.6)
Fever, Grade 4[g]	0 (0)	1 (<0.1)
Use of antipyretic or pain medication	429 (26.3)	393 (24.0)

* 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=Number of participants in the Solicited Safety Set.
n=Number of participants with listed solicited adverse reactions.
[a] Absence of rows for Grade 4 adverse reactions indicates no events were reported.

[b] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Original and Omicron variant lineages BA.4/BA.5
[c] Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)
[d] Headache, fatigue, myalgia, arthralgia grading scale: no interference with activity (Grade 1); some interference with activity (Grade 2); prevents daily activity (Grade 3).
[e] Chills grading scale: no interference with activity (Grade 1); some interference with activity not requiring medical intervention (Grade 2); prevents daily activity and requires medical intervention (Grade 3).
[f] Nausea/vomiting grading scale: no interference with activity or 1-2 episodes/24 hours (Grade 1); some interference with activity or >2 episodes/24 hours (Grade 2); prevents daily activity, requires outpatient intravenous hydration (Grade 3).
[g] Fever grading scale: ≥38.0° – ≤38.4°C / ≥100.4° – ≤101.1°F (Grade 1); ≥38.5° – ≤38.9°C / ≥101.2°– ≤102.0°F (Grade 2); ≥39.0° – ≤40.0°C / ≥102.1° – ≤104.0°F (Grade 3); >40.0°C / >104.0°F (Grade 4).

Solicited local and systemic adverse reactions reported following vaccine administration had a median duration of 2 days for MNEXSPIKE and 2 to 3 days for the comparator vaccine.

Unsolicited Adverse Events

Participants were monitored for unsolicited adverse events for 28 days following injection. Serious adverse events and medically attended adverse events will be recorded for the entire study duration (1 year). Among the 11,417 participants who received MNEXSPIKE (n=5,706) or the comparator vaccine (n=5,711), unsolicited adverse events that occurred within 28 days following injection were reported by 12.3% of participants (n=701) who received MNEXSPIKE and 11.9% of participants (n=680) who received the comparator vaccine.

There were no notable patterns or numerical imbalances between treatment groups for specific categories of adverse events that would suggest a causal relationship to MNEXSPIKE.

Serious Adverse Events

Serious adverse events were reported by 2.7% of participants (n=156) who received MNEXSPIKE and 2.6% of participants (n=151) who received the comparator vaccine through a median follow-up of 8.8 months. There were no serious adverse events considered causally related to MNEXSPIKE.

There were no notable patterns or imbalances between treatment groups for specific categories of serious adverse events that would suggest a causal relationship to MNEXSPIKE.

Single Dose (Monovalent Omicron XBB.1.5) in Vaccine-Experienced

The safety of MNEXSPIKE was evaluated in a randomized, observer-blind, active-controlled clinical trial conducted in Japan involving 689 participants 12 years of age and older who received a single dose of MNEXSPIKE (n=343) or comparator vaccine (SPIKEVAX 2023-2024 Formula [n=346]) (Study 2). MNEXSPIKE administered in the study contained 10 mcg mRNA encoding the membrane-bound, linked N-terminal domain (NTD) and receptor-binding domain (RBD) of the Spike (S) glycoprotein from SARS-CoV-2 Omicron variant lineage XBB.1.5. The comparator vaccine administered in the study contained 50 mcg mRNA encoding the S glycoprotein from SARS-CoV-2 Omicron variant lineage XBB.1.5. The median duration of

follow-up for safety was 35 days.

In Study 2, the median age of the population was 52 years (range 12 through 83 years); 20.3% of participants were 12 years through 17 years, 58.8% were 18 years through 64 years, and 20.9% were 65 years of age and older. Overall, 65.7% were male, 34.3% were female, and all participants were Asian. All participants in the study had previously received at least one dose of a COVID-19 vaccine prior to the study with a median interval of 16.7 months since the last dose.

Participants were monitored for unsolicited adverse events for 28 days following injection. Among the 689 participants who received MNEXSPIKE (n=343) or the comparator vaccine (n=346), unsolicited adverse events that occurred within 28 days following injection were reported by 7.0% of participants (n=24) who received MNEXSPIKE and 6.9% of participants (n=24) who received the comparator vaccine. There were no notable patterns or numerical imbalances between treatment groups for specific categories of adverse events that would suggest a causal relationship to MNEXSPIKE. No serious adverse events were reported.

In addition, in a separate portion of Study 1, vaccine-experienced participants 12 years of age and older (n=617), including 53 participants 65 years of age and older, received a single dose of MNEXSPIKE (Monovalent Omicron XBB.1.5). Participants were monitored for serious adverse events through 6 months following injection. There were no serious adverse events considered causally related to MNEXSPIKE.

Single Dose (Monovalent Omicron XBB.1.5) in Vaccine-Naïve

In a separate randomized, observer-blind, active-controlled portion of Study 1 conducted in the United States, 782 COVID-19 vaccine-naïve participants 12 years of age and older received a single dose of MNEXSPIKE (n=396) or comparator vaccine (SPIKEVAX 2023-2024 Formula [n=386]). The vaccine formula of MNEXSPIKE administered in the study contained 10 mcg mRNA encoding the membrane-bound, linked N-terminal domain (NTD) and receptor-binding domain (RBD) of the Spike (S) glycoprotein from SARS-CoV-2 Omicron variant lineage XBB.1.5. The comparator vaccine administered in the study contained 50 mcg mRNA encoding the S glycoprotein from SARS-CoV-2 Omicron variant lineage XBB.1.5. The median duration of follow-up for safety was 5.8 months.

Among vaccine-naïve participants in this study, the median age was 38 years (range 12 through 81 years); 12.4% of participants were 12 years through 17 years, 79.4% were 18 years through 64 years, and 8.2% were 65 years and older. Overall, 46.9% of the participants were male, 53.1% were female, 36.6% were Hispanic or Latino, 53.5% were White, 42.8% were Black or African American, 0.1% were Asian, 0.9% were American Indian or Alaska Native, 0.3% were other races, and 1.5% were Multiracial. Demographic characteristics were similar between participants who received MNEXSPIKE and those who received the comparator vaccine.

Solicited Adverse Reactions

Local and systemic adverse reactions and use of antipyretic medication were solicited in an electronic diary for 7 days following injection (i.e., day of vaccination and the next 6 days)

among participants who received MNEXSPIKE (n=396) and participants who received the comparator vaccine (n=386). Events that persisted for more than 7 days were followed until resolution.

The reported number and percentage of solicited local and systemic adverse reactions for vaccine-naïve participants 12 years of age and older are presented in Table 8 and Table 9.

Table 8: Number and Percentage of Participants with Solicited Local Adverse Reactions Starting Within 7 Days* After Injection in Participants 12 Years and Older (Solicited Safety Set)

Local Adverse Reactions[a]	**MNEXSPIKE**[b] N=396 n (%)	**Comparator Vaccine**[c] N=386 n (%)
Pain[d]	145 (36.6)	183 (47.4)
Pain, Grade 3[d]	7 (1.8)	9 (2.3)
Axillary swelling or tenderness[d]	69 (17.4)	79 (20.5)
Axillary swelling or tenderness, Grade 3[d]	2 (0.5)	4 (1.0)
Swelling (hardness) ≥25 mm[e]	6 (1.5)	13 (3.4)
Swelling (hardness) >100 mm, Grade 3[e]	2 (0.5)	3 (0.8)
Erythema (redness) ≥25 mm[e]	5 (1.3)	9 (2.3)
Erythema (redness) ≥100 mm, Grade 3[e]	3 (0.8)	3 (0.8)

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

N=Number of participants in the Solicited Safety Set.

n=Number of participants with listed solicited adverse reactions.

[a] No Grade 4 adverse reactions were reported.

[b] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Omicron variant lineage XBB.1.5

[c] SPIKEVAX 2023-2024 Formula

[d] Pain and axillary swelling or tenderness grading scale: no interference with activity (Grade 1); some interference with activity (Grade 2); prevents daily activity (Grade 3).

[e] Swelling and erythema grading scale: 25-50 mm / 2.5-5 cm (Grade 1); 51-100 mm / 5.1-10 cm (Grade 2); >100 mm / >10 cm (Grade 3).

Table 9: Number and Percentage of Participants with Solicited Systemic Adverse Reactions Starting Within 7 Days* After Injection in Participants 12 Years and Older (Solicited Safety Set)

Systemic Adverse Reactions[a]	MNEXSPIKE[b] N=396 n (%)	Comparator Vaccine[c] N=386 n (%)
Headache[d]	119 (30.1)	104 (26.9)
Headache, Grade 3[d]	7 (1.8)	4 (1.0)
Fatigue[d]	110 (27.8)	98 (25.4)
Fatigue, Grade 3[d]	10 (2.5)	4 (1.0)
Myalgia[d]	99 (25.0)	101 (26.2)
Myalgia, Grade 3[d]	10 (2.5)	9 (2.3)
Arthralgia[d]	82 (20.7)	82 (21.2)
Arthralgia, Grade 3[d]	6 (1.5)	6 (1.6)
Chills[e]	58 (14.6)	63 (16.3)
Chills, Grade 3[e]	4 (1.0)	0 (0)
Nausea/vomiting[f]	52 (13.1)	49 (12.7)
Nausea/vomiting, Grade 3[f]	2 (0.5)	1 (0.3)
Fever[g]	15 (3.8)	11 (2.8)
Fever, Grade 3[g]	4 (1.0)	4 (1.0)
Use of antipyretic or pain medication	84 (21.2)	56 (14.5)

* 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=Number of participants in the Solicited Safety Set.

n=Number of participants with listed solicited adverse reactions.

[a] No Grade 4 adverse reactions were reported.

[b] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Omicron variant lineage XBB.1.5

[c] SPIKEVAX 2023-2024 Formula

[d] Headache, fatigue, myalgia, arthralgia grading scale: no interference with activity (Grade 1); some interference with activity (Grade 2); prevents daily activity (Grade 3).
[e] Chills grading scale: no interference with activity (Grade 1); some interference with activity not requiring medical intervention (Grade 2); prevents daily activity and requires medical intervention (Grade 3).
[f] Nausea/vomiting grading scale: no interference with activity or 1-2 episodes/24 hours (Grade 1); some interference with activity or >2 episodes/24 hours (Grade 2); prevents daily activity, requires outpatient intravenous hydration (Grade 3).
[g] Fever grading scale: ≥38.0° – ≤38.4°C / ≥100.4° – ≤101.1°F (Grade 1); ≥38.5° – ≤38.9°C / ≥101.2°– ≤102.0°F (Grade 2); ≥39.0° – ≤40.0°C / ≥102.1° – ≤104.0°F (Grade 3).

Solicited local and systemic adverse reactions reported following vaccine administration had a median duration of 2 to 3 days for both MNEXSPIKE and the comparator vaccine. In analyses of solicited adverse reactions by age groups in vaccine-naïve participants 12 years through 17 years of age (n=51), 18 years through 64 years of age (n=310), and 65 years of age and older (n=35) who received MNEXSPIKE, the most commonly occurring solicited adverse reactions (≥10%) were reported in a similar or lower percentage of participants compared with those reported in the respective age groups in MNEXSPIKE vaccine-experienced participants (refer to Tables 2 through 7), with the exception of nausea/vomiting reported in 11.4% of vaccine-naïve participants 65 years of age and older who received MNEXSPIKE.

Unsolicited Adverse Events

Participants were monitored for unsolicited adverse events for 28 days following injection. Serious adverse events and medically attended adverse events were recorded for the entire study duration (6 months). Among the 782 vaccine-naïve participants who received MNEXSPIKE (n=396) or the comparator vaccine (n=386), unsolicited adverse events that occurred within 28 days following injection were reported by 4.3% of participants (n=17) who received MNEXSPIKE and 6.2% of participants (n=24) who received the comparator vaccine.

There were no notable patterns or numerical imbalances between treatment groups for specific categories of adverse events that would suggest a causal relationship to MNEXSPIKE.

Serious Adverse Events

Serious adverse events were reported by 1.5% of vaccine-naïve participants (n=6) who received MNEXSPIKE and 3.1% of vaccine-naïve participants (n=12) who received the comparator vaccine through a median follow-up of 5.8 months. There were no serious adverse events considered causally related to MNEXSPIKE.

There were no notable patterns or imbalances between treatment groups for specific categories of serious adverse events that would suggest a causal relationship to MNEXSPIKE.

6.2 Postmarketing Experience

Postmarketing data with authorized or approved mRNA COVID-19 vaccines have demonstrated increased risks of myocarditis and pericarditis *[see Warnings and Precautions (5.2)]*.

Cardiovascular Outcomes in Patients Diagnosed with mRNA COVID-19 Vaccine-associated Myocarditis

In a longitudinal retrospective observational cohort study across 38 hospitals in the U.S., information on cardiovascular outcomes was collected on 333 patients 5 years through 29 years of age who had been diagnosed with COVID-19 vaccine-associated myocarditis. Among these patients, 322 were confirmed to have received an mRNA COVID-19 vaccine encoding the S glycoprotein of the Original SARS-CoV-2. Of 331 patients, 278 had onset of symptoms following the second dose of a primary series, 33 following the first dose of a primary series, and 20 following a first booster dose[1].

Among 307 patients who had been diagnosed with COVID-19 vaccine-associated myocarditis for whom follow-up information was available, 89 reported cardiac symptoms at a median follow-up of 91 days (interquartile range 25-186 days) post-vaccination[1].

Initial gadolinium-enhanced cardiac magnetic resonance imaging (CMR) was performed on 216 patients, of whom 177 had late gadolinium enhancement (LGE), a marker of myocardial injury. Among 161 patients who had LGE on initial CMR and who had a follow-up gadolinium-enhanced CMR at a median follow-up of 159 days (interquartile range 78-253 days), 98 had persistence of LGE. Overall, the severity of LGE decreased during follow-up. The clinical and prognostic significance of these CMR findings is not known[1].

Limitations of this study include potential selection bias towards patients with more severe myocarditis who are more likely to be hospitalized and have CMR, variability in diagnostic testing, and variability in follow-up[1].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on MNEXSPIKE administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study was performed where female rats were administered a vaccine formulation containing 80 mcg of nucleoside-modified messenger ribonucleic acid (mRNA) (which is 8 times the amount of nucleoside-modified mRNA in a full human dose of MNEXSPIKE [encoding the N-terminal domain (NTD) and receptor-binding domain (RBD) of the spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu 1 strain]) twice prior to mating and twice during gestation. The study revealed no evidence of harm to the fetus due to the vaccine. The study also revealed no evidence of effects on female fertility (*see Animal Data*).

Data

Animal Data

A developmental toxicity study was conducted to assess the effects of MNEXSPIKE on pregnant/lactating female rats, as well as the development of the embryo/fetus and offspring following exposure to the female to the vaccine from implantation through the end of pregnancy, with follow-up of the offspring through weaning. In this study, 0.2 mL of a vaccine formulation containing 80 mcg of nucleoside-modified mRNA per dose (which is 8 times the amount of mRNA in a full human dose of MNEXSPIKE [10 mcg of nucleoside-modified mRNA; encoding the N-terminal domain (NTD) and receptor-binding domain (RBD) of the spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu 1 strain]). Each dose of the vaccine formulation administered to rats also contained the following ingredients: a total lipid content of 1.8 mg (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), 0.48 mg tromethamine, 17 mg sucrose, and 0.1 mg sodium acetate). MNEXSPIKE 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 fetal malformations or variations and no adverse effect on postnatal development were observed in the study. The study also revealed no evidence of effects on female fertility.

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk

Pregnant individuals infected with SARS-CoV-2 are at increased risk of severe COVID-19 compared with non-pregnant individuals.

8.2 Lactation

Risk Summary

It is not known whether MNEXSPIKE is excreted in human milk. Data are not available to assess the effects of MNEXSPIKE on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for MNEXSPIKE and any potential adverse effects on the breastfed infant from MNEXSPIKE or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of MNEXSPIKE in individuals 12 years through 17 years of age with at least one underlying condition that puts them at high risk for severe outcomes from COVID-19 is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14)]*. The safety and effectiveness of MNEXSPIKE have not been established in individuals younger than 12 years of age.

8.5 Geriatric Use

Clinical studies of MNEXSPIKE included approximately 1,801 participants 65 years of age and older and 348 participants 75 years of age and older *[see Adverse Reactions (6.1) and Clinical Studies (14)]*.

Some local and systemic adverse reactions were reported in a lower proportion of participants 65 years of age and older compared with participants 18 years through 64 years of age *[see Adverse Reactions (6.1)]*.

Relative vaccine efficacy was similar among participants 65 years of age and older and participants 18 years through 64 years *[see Clinical Studies (14)]*.

8.6 Immunocompromised Individuals

The Centers for Disease Control and Prevention has published considerations related to COVID-19 vaccination for individuals who are moderately to severely immunocompromised (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html).

11 DESCRIPTION

MNEXSPIKE (COVID-19 Vaccine, mRNA) is a sterile white to off-white injectable suspension for intramuscular use.

Each 0.2 mL dose of MNEXSPIKE (2025-2026 Formula) contains 10 mcg nucleoside-modified messenger RNA (mRNA) encoding the N-terminal domain (NTD) and receptor-binding domain (RBD) of the Spike glycoprotein of the SARS-CoV-2 Omicron variant sublineage LP.8.1. Each dose also contains the following ingredients: a total lipid content of 0.2 mg (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), 0.09 mg tromethamine, 0.51 mg tromethamine hydrochloride, and 17 mg sucrose.

MNEXSPIKE does not contain a preservative.

The rubber tip cap and plunger used for the single-dose syringes are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in MNEXSPIKE is formulated in lipid particles, which enable delivery of the nucleoside-modified mRNA into host cells to allow expression of the N-terminal domain (NTD) and receptor-binding domain (RBD) of the Spike (S) glycoprotein of SARS-CoV-2. The vaccine elicits an immune response which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

MNEXSPIKE has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility in animals. *[see Use in Specific Populations (8.1)]*.

14 CLINICAL STUDIES

14.1 Adults and Adolescents 12 Years of Age and Older

Efficacy and Immunogenicity of Single Dose (Bivalent Original and Omicron BA.4/BA.5) in Vaccine-Experienced

Study 1 is a Phase 3 randomized, observer-blind, active-controlled clinical trial that evaluated the relative vaccine efficacy, safety, and immunogenicity of MNEXSPIKE in participants 12 years of age and older in the United States, United Kingdom, and Canada. Randomization was stratified by age: 12 years through 17 years, 18 years through 64 years, and 65 years of age and older. The study allowed for the inclusion of participants with stable pre-existing medical conditions, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 2 months before enrollment, as well as participants with stable human immunodeficiency virus (HIV) infection. A total of 11,454 participants were randomized in a 1:1 ratio to receive MNEXSPIKE (n=5,728), a vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Original and Omicron variant lineages BA.4/BA.5, or comparator vaccine (Moderna COVID-19 Vaccine, Bivalent [Original and Omicron BA.4/BA.5] not U.S. licensed, authorized for emergency use; n=5,726). All participants in the study, except one participant in the MNEXSPIKE group, had previously received at least one dose of a COVID-19 vaccine prior to the study with a median interval of 9.8 months since the last dose.

The primary efficacy analysis population (referred to as the Per-Protocol Set for Efficacy) included 11,366 participants who received either MNEXSPIKE (n=5,679) or Moderna COVID-19 Vaccine, Bivalent (n=5,687). In the Per-Protocol Set for Efficacy, 45.7% of participants were male, 54.3% were female, 13.1% were Hispanic or Latino, 82.2% were White, 11.1% were Black or African American, 3.6% were Asian, 0.4% were American Indian or Alaska Native, 0.1% were Native Hawaiian or Pacific Islander, 0.3% were other races, and 1.5% were Multiracial. The median age of participants was 56 years (range 12 through 96 years) and 28.7% of participants were 65 years of age and older. There were no notable differences in demographics between participants who received MNEXSPIKE and those who received the comparator vaccine.

The population for the relative vaccine efficacy analysis included participants 12 years of age and older who were enrolled from March 28, 2023, and followed for the development of COVID-19 through January 31, 2024. The median length of follow-up was 8 months.

The primary efficacy objective in this study was to demonstrate the noninferior vaccine efficacy

against COVID-19 starting 14 days after MNEXSPIKE compared with that after the comparator vaccine. The case definition of COVID-19 was the presence of at least one symptom from a list of COVID-19 symptoms and a positive NP swab 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, and diarrhea. The statistical criterion to demonstrate noninferiority (lower bound of the 99.4% CI >-10%) for relative vaccine efficacy was met (Table 10).

Table 10: Relative Vaccine Efficacy Against COVID-19* in Participants 12 Years of Age and Older† Starting 14 Days After a Single Dose of MNEXSPIKE or Comparator Vaccine – Per-Protocol Set for Efficacy

MNEXSPIKE[a]			Comparator Vaccine[b]			
Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 Per 100 Person-Months[c]	Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 Per 100 Person-Months[c]	Relative Vaccine Efficacy (99.4% CI)[d]
5,679	560	1.4	5,687	617	1.5	9.3% (-6.6%, 22.8%)[e]

***** Presence of at least one symptom from a list of COVID-19 symptoms and a positive NP swab 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, and diarrhea.

† Participants had previously received at least one dose of a COVID-19 vaccine prior to the study.

[a] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Original and Omicron variant lineages BA.4/BA.5

[b] Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)

[c] Person-months is defined as the total months from study injection date to the date of event (COVID-19), date of off-study COVID-19 vaccine, last date of study participation, death date or efficacy data cutoff date, whichever is the earliest.

[d] Relative Vaccine Efficacy (rVE) = 1-hazard ratio (MNEXSPIKE vs comparator vaccine). Hazard ratio and CI are estimated using a stratified Cox proportional hazard model (stratified by age group per randomization) with Efron's method of tie handling and with the treatment group as a fixed effect. Alpha-adjusted 2-sided (99.4%) confidence level is calculated using Lan-DeMets O'Brien-Fleming spending function (nominal one-sided alpha = 0.0028).

[e] The success criterion for the primary efficacy endpoint was that the lower limit of the 2-sided CI for rVE was >-10%.

A descriptive analysis of incidence of COVID-19 in participants 12 years of age and older by age subgroup was conducted (Table 11).

Table 11: Descriptive Analysis of Incidence of COVID-19* in Participants 12 Years of Age and Older† by Age Subgroup Starting 14 Days After a Single Dose of MNEXSPIKE or Comparator Vaccine – Per-Protocol Set for Efficacy

Age Subgroup (Years)	MNEXSPIKE[a]			Comparator Vaccine[b]			Descriptive rVE[d] (95% CI)[e]
	Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 Per 100 Person-Months[c]	Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 Per 100 Person-Months[c]	
12 to <18	491	29	1.0	490	23	0.8	-29.2%[f] (-123.3%, 25.3%)
18 to <65	3,558	382	1.4	3,562	422	1.6	9.7% (-3.8%, 21.3%)
≥65	1,630	149	1.3	1,635	172	1.5	13.5% (-7.7%, 30.6%)

***** Presence of at least one symptom from a list of COVID-19 symptoms and a positive NP swab 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, and diarrhea.

† Participants had previously received at least one dose of a COVID-19 vaccine prior to the study.

[a] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Original and Omicron variant lineages BA.4/BA.5

[b] Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)

[c] Person-months is defined as the total months from study injection date to the date of event (COVID-19), date of off-study COVID-19 vaccine, last date of study participation, death date or efficacy data cutoff date, whichever is the earliest.

[d] rVE=relative vaccine efficacy

[e] Descriptive relative vaccine efficacy means that these endpoints were not hypothesis-tested and do not necessarily make valid inferences about vaccine efficacy.

[f] VE cannot be reliably estimated due to the low number of cases accrued in this age group.

In Study 1, 60.8% of participants 12 years through 64 years of age reported at least one CDC-defined high-risk condition for severe COVID-19. The type and frequency of high-risk conditions reported in participants were generally representative of high-risk conditions in the U.S. general population 12 years through 64 years of age. A descriptive analysis of the incidence of COVID-19 in participants 12 years through 64 years of age with at least one CDC-defined high-risk condition for severe COVID-19 after a single dose of MNEXSPIKE or the comparator vaccine is presented in Table 12. In this analysis, 7.2% of participants were 12 years through 17 years of age and the remaining 92.8% of participants were 18 years through 64 years of age.

Table 12: Descriptive Analysis of Incidence of COVID-19* in Participants 12 Years Through 64 Years of Age† with at Least One CDC-Defined High-Risk Condition for Severe COVID-19‡ Starting 14 Days After a Single Dose of MNEXSPIKE or Comparator Vaccine – Per-Protocol Set for Efficacy

MNEXSPIKE[a]			Comparator Vaccine[b]			
Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 Per 100 Person-Months[c]	Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 Per 100 Person-Months[c]	Descriptive rVE[d] (95% CI)[e]
2,469	243	1.3	2,466	287	1.6	15.7% (0, 29.0%)[e]

* Presence of at least one symptom from a list of COVID-19 symptoms and a positive NP swab 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, and diarrhea.

† Participants had previously received at least one dose of a COVID-19 vaccine prior to the study.

‡ CDC-defined high-risk condition for severe COVID-19: https://www.cdc.gov/covid/hcp/clinical-care/underlying-conditions.html

[a] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Original and Omicron variant lineages BA.4/BA.5

[b] Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)

[c] Person-months is defined as the total months from study injection date to the date of event (COVID-19), date of off-study COVID-19 vaccine, last date of study participation, death date or efficacy data cutoff date, whichever is the earliest.

[d] Descriptive relative Vaccine Efficacy (rVE) = 1-hazard ratio (MNEXSPIKE vs comparator vaccine). Hazard ratio and CI are estimated using a stratified Cox proportional hazard model (stratified by age group per randomization) with Efron's method of tie handling and with the treatment group as a fixed effect.

[e] Descriptive relative vaccine efficacy means that these endpoints were not hypothesis-tested and do not necessarily make valid inferences about vaccine efficacy.

The primary immunogenicity analysis population included 621 participants who received MNEXSPIKE and 568 participants who received the comparator vaccine. Among participants assessed for immunogenicity, 45.3% were male, 54.7% were female, 13.5% were Hispanic or Latino, 80.7% were White, 11.9% were Black or African American, 4.0% were Asian, <0.1% were American Indian or Alaska Native, <0.1% were Native Hawaiian or Pacific Islander, 0.3% were other races, and 2.1% were Multiracial.

The primary immunogenicity analyses evaluated the ratio of neutralizing antibody geometric mean concentrations (GMC) and the difference in seroresponse rate (SRR) against a pseudovirus expressing Omicron BA.4/BA.5 and the original SARS-CoV-2 Spike protein (D614G) following vaccination with MNEXSPIKE compared with vaccination with the comparator vaccine. MNEXSPIKE met the pre-specified noninferiority criterion of the lower bound of the 95% CI of GMC ratio >0.667, and the pre-specified noninferiority criterion of the lower bound of the 95% CI of the SRR-difference >-10%. These analyses are summarized in Table 13 and Table 15. Descriptive analyses of GMC and SRR by age subgroup are summarized in Table 14 and Table 16.

Table 13: Comparison of Geometric Mean Concentration 28 Days After a Single Dose of MNEXSPIKE vs 28 Days After a Single Dose of Comparator Vaccine – Per-Protocol Immunogenicity Subset*

Assay[a]	MNEXSPIKE[b] GMC N=621 (95% CI)[c]	Comparator Vaccine[d] GMC N=568 (95% CI)[c]	GMC Ratio (MNEXSPIKE/ Comparator Vaccine) (95% CI)[c]
Omicron BA.4/BA.5	2340.9 (2167.0, 2528.8)	1753.8 (1618.2, 1900.7)	1.3 (1.2, 1.5)
Original SARS-CoV-2 (D614G)	10631.9 (9960.2, 11348.9)	8576.5 (8012.5, 9180.1)	1.2 (1.1, 1.4)

N=Number of participants with non-missing data at the corresponding timepoint(s).

* Per-Protocol Immunogenicity Subset included a randomly selected subset of subjects (Immunogenicity Subset) who received study vaccine, did not have a major protocol deviation that impacted immune response, and had both pre-dose and post-dose immunogenicity assessment at timepoint of primary interest (28 days post-dose). Participants had previously received at least one dose of a COVID-19 vaccine prior to the study.

[a] Geometric mean concentration (GMC) was determined using a SARS-CoV-2 Spike-Pseudotyped Virus Neutralization Assay. Quantification of SARS-CoV-2 neutralizing antibodies utilizes SARS-CoV-2 Reporter Virus Particles which express GFP for quantitative measurement of infection by counting the number of green fluorescent cells (assay readout [count] is Foci Forming Units [FFUs]). The serum antibody concentration (Ab[C]) of the neutralizing antibodies was determined by interpolating the mean of the replicate FFU values off the fitted reference standard curve (AU/mL).

[b] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Original and Omicron variant lineages BA.4/BA.5

[c] The log-transformed antibody levels are analyzed using an analysis of covariance (ANCOVA) model with the group variable (MNEXSPIKE vs comparator vaccine) as fixed effect, adjusted by SARS-CoV-2 infection status at baseline, randomization age group, number of prior COVID-19 boosters (0, 1, 2, ≥3), and type of last prior COVID-19 vaccine. Coefficients for Least Square Means use margins by level. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.

[d] Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)

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.

Table 14: Descriptive Analysis of Geometric Mean Concentration by Age Subgroup 28 Days After a Single Dose of MNEXSPIKE vs 28 Days After a Single Dose of Comparator Vaccine – Per-Protocol Immunogenicity Subset*

Assay[a]	Age Subgroup (Years)	MNEXSPIKE[b] GMC (95% CI)[c]	Comparator Vaccine[d] GMC (95% CI)[c]	GMC Ratio (MNEXSPIKE/ Comparator Vaccine) (95% CI)[c]
Omicron BA.4/BA.5	12 to <18	N=91 3561.4 (3037.5, 4175.7)	N=93 3398.9 (2908.9, 3971.4)	1.0 (0.8, 1.3)
	18 to <65	N=378 2120.6 (1917.3, 2345.6)	N=316 1661.0 (1487.8, 1854.4)	1.3 (1.1, 1.5)
	≥65	N=152 2339.5 (1984.3, 2758.3)	N=159 1326.8 (1130.0, 1557.7)	1.8 (1.4, 2.2)
Original SARS-CoV-2 (D614G)	12 to <18	N=91 13617.7 (12006.3, 15445.3)	N=93 12404.3 (10966.5, 14030.6)	1.1 (0.9, 1.3)
	18 to <65	N=378 9734.8 (8938.8, 10601.7)	N=316 8251.3 (7517.2, 9057.1)	1.2 (1.0, 1.3)
	≥65	N=152 11451.1 (9936.3, 13196.9)	N=159 7463.3 (6499.4, 8570.1)	1.5 (1.3, 1.9)

N=Number of participants in the corresponding age group.

* Per-Protocol Immunogenicity Subset included a randomly selected subset of subjects (Immunogenicity Subset) who received study vaccine, did not have a major protocol deviation that impacted immune response, and had both pre-dose and post-dose immunogenicity assessment at timepoint of primary interest (28 days post-dose). Participants had previously received at least one dose of a COVID-19 vaccine prior to the study.

[a] Geometric mean concentration (GMC) was determined using a SARS-CoV-2 Spike-Pseudotyped Virus Neutralization Assay. Quantification of SARS-CoV-2 neutralizing antibodies utilizes SARS-CoV-2 Reporter Virus Particles which express GFP for quantitative measurement of infection by counting the number of green fluorescent cells (assay readout [count] is Foci Forming Units [FFUs]). The serum antibody concentration (Ab[C]) of the neutralizing antibodies was determined by interpolating the mean of the replicate FFU values off the fitted reference standard curve (AU/mL).

[b] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Original and Omicron variant lineages BA.4/BA.5

[c] The log-transformed antibody levels are analyzed using an analysis of covariance (ANCOVA) model with the group variable (MNEXSPIKE vs comparator vaccine) as fixed effect, adjusted by SARS-CoV-2 infection status at baseline, number of prior COVID-19 boosters (0, 1, 2, ≥3), and type of last prior COVID-19 vaccine. Coefficients for Least Square Means use margins by level. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.

[d] Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)

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.

Table 15: Comparison of Seroresponse Rate 28 Days After a Single Dose of MNEXSPIKE vs 28 Days After a Single Dose of Comparator Vaccine – Per-Protocol Immunogenicity Subset*

Assay	MNEXSPIKE[a] Seroresponse Rate[b] N=621 % (95% CI)[c]	Comparator Vaccine[d] Seroresponse Rate[b] N=568 % (95% CI)[c]	Difference in Seroresponse Rate (MNEXSPIKE-Comparator Vaccine) % (95% CI)[e]
Omicron BA.4/BA.5	79.9 (76.5, 83.0)	65.5 (61.4, 69.4)	14.4 (9.3, 19.4)
Original SARS-CoV-2 (D614G)	83.6 (80.4, 86.4)	72.9 (69.0, 76.5)	10.7 (6.0, 15.4)

N=Number of participants with non-missing data at the corresponding timepoint(s).

* Per-Protocol Immunogenicity Subset included a randomly selected subset of subjects (Immunogenicity Subset) who received study vaccine, did not have a major protocol deviation that impacted immune response, and had both pre-dose and post-dose immunogenicity assessment at timepoint of primary interest (28 days post-dose). Participants had previously received at least one dose of a COVID-19 vaccine prior to the study.

[a] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Original and Omicron variant lineages BA.4/BA.5

[b] Seroresponse is defined as an antibody value change from baseline below the LLOQ to ≥4 × LLOQ, or at least a 4-fold rise if baseline is ≥ LLOQ and <4 × LLOQ, or at least a 2-fold rise if baseline is ≥4 × LLOQ, where baseline refers to pre-dose.

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

[d] Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)

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

Table 16: Descriptive Analysis of Seroresponse Rate by Age Subgroup 28 Days After a Single Dose of MNEXSPIKE vs 28 Days After a Single Dose of Comparator Vaccine – Per-Protocol Immunogenicity Subset*

Assay	Age Subgroup (Years)	MNEXSPIKE[a] Seroresponse Rate[b] % (95% CI)[c]	Comparator Vaccine[d] Seroresponse Rate[b] % (95% CI)[c]	Difference in Seroresponse Rate (MNEXSPIKE-Comparator Vaccine) % (95% CI)[e]
Omicron BA.4/BA.5	12 to <18	N=91 87.9 (79.4, 93.8)	N=93 80.6 (71.1, 88.1)	7.3 (-3.4, 18.0)
	18 to <65	N=378 79.6 (75.2, 83.6)	N=316 63.6 (58.0, 68.9)	16.0 (9.3, 22.7)
	≥65	N=152 75.7 (68.0, 82.2)	N=159 60.4 (52.3, 68.0)	15.3 (4.9, 25.3)
Original SARS-CoV-2 (D614G)	12 to <18	N=91 85.7 (76.8, 92.2)	N=93 74.2 (64.1, 82.7)	11.5 (-0.1, 23.1)
	18 to <65	N=378 83.1 (78.9, 86.7)	N=316 75.9 (70.8, 80.6)	7.1 (1.1, 13.2)
	≥65	N=152 83.6 (76.7, 89.1)	N=159 66.0 (58.1, 73.4)	17.5 (8.0, 26.9)

N=Number of participants in the corresponding age group.

* Per-Protocol Immunogenicity Subset included a randomly selected subset of subjects (Immunogenicity Subset) who received study vaccine, did not have a major protocol deviation that impacted immune response, and had both pre-dose and post-dose immunogenicity assessment at timepoint of primary interest (28 days post-dose). Participants had previously received at least one dose of a COVID-19 vaccine prior to the study.

[a] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Original and Omicron variant lineages BA.4/BA.5

[b] Seroresponse is defined as an antibody value change from baseline below the LLOQ to ≥4 × LLOQ, or at least a 4-fold rise if baseline is ≥ LLOQ and <4 × LLOQ, or at least a 2-fold rise if baseline is ≥4 × LLOQ, where baseline refers to pre-dose.

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

[d] Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)

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

Immunogenicity of Single Dose (Monovalent Omicron XBB.1.5) in Vaccine-Experienced

Study 2 is a Phase 3 randomized, observer-blind, active-controlled clinical trial that evaluated the immunogenicity and safety of MNEXSPIKE in participants 12 years of age and older in Japan. Randomization was stratified by age: 12 years through 17 years, 18 years through 64 years, and 65 years of age and older. The study allowed for the inclusion of participants with stable pre-existing medical conditions, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 2 months before enrollment, as well as

participants with stable human immunodeficiency virus (HIV) infection. A total of 692 participants were randomized in a 1:1 ratio to receive MNEXSPIKE (n=344), a vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Omicron XBB.1.5 lineage, or comparator vaccine (SPIKEVAX 2023-2024 Formula [n=348]). All participants had previously received at least one dose of a COVID-19 vaccine prior to the study with a median interval of 16.7 months since the last dose.

The primary immunogenicity analysis population included 334 participants who received MNEXSPIKE and 334 participants who received the comparator vaccine. Among participants assessed for immunogenicity, 65.0% were male, 35.0% were female, and all participants were Asian. The median age of participants was 52 years (range 12 through 83 years) and 20.7% of participants were 65 years of age and older.

The primary immunogenicity analyses evaluated the ratio of neutralizing antibody geometric mean concentrations (GMC) against a pseudovirus expressing Omicron XBB.1.5 SARS-CoV-2 Spike protein following vaccination with MNEXSPIKE compared to vaccination with the comparator vaccine. MNEXSPIKE met the pre-specified noninferiority criterion of the lower bound of the 95% CI of the GMC ratio >0.667 (Table 17). A descriptive analysis of the difference in seroresponse rates is summarized in Table 18.

Table 17: Comparison of Geometric Mean Concentration 28 Days After a Single Dose of MNEXSPIKE vs 28 Days After a Single Dose of Comparator Vaccine – Per-Protocol Immunogenicity Set*

Assay[a]	MNEXSPIKE[b] GMC (95% CI)[c] N=334	Comparator Vaccine[d] GMC (95% CI)[c] N=334	GMC Ratio (MNEXSPIKE/ Comparator Vaccine) (95% CI)[c]
Omicron XBB.1.5	1757.2 (1580.1, 1954.3)	1470.4 (1322.4, 1635.0)	1.2 (1.0, 1.4)

N=Number of participants with non-missing data at baseline and the corresponding timepoint(s).

* Per-Protocol Immunogenicity Set included subjects who received study vaccine, did not have a major protocol deviation that impacted immune response, and had both pre-dose and post-dose immunogenicity assessment at timepoint of primary interest (28 days post-dose). Participants had previously received at least one dose of a COVID-19 vaccine prior to the study.

[a] Geometric mean concentration (GMC) was determined using a SARS-CoV-2 Spike-Pseudotyped Virus Neutralization Assay. Quantification of SARS-CoV-2 neutralizing antibodies utilizes SARS-CoV-2 Reporter Virus Particles which express GFP for quantitative measurement of infection by counting the number of green fluorescent cells (assay readout [count] is Foci Forming Units [FFUs]). The serum antibody concentration (Ab[C]) of the neutralizing antibodies was determined by interpolating the mean of the replicate FFU values off the fitted reference standard curve (AU/mL).

[b] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Omicron XBB.1.5

[c] The log-transformed antibody levels are analyzed using an analysis of covariance (ANCOVA) model with the group variable (MNEXSPIKE vs comparator vaccine) as fixed effect, adjusted by SARS-CoV-2 infection status at baseline, randomization age group, number of prior COVID-19 boosters (0, 1, 2, ≥3), and type of last prior COVID-19 vaccine. LS means are based on the observed margins. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.

[d] SPIKEVAX 2023-2024 Formula

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.

Table 18: Comparison of Seroresponse Rate 28 Days After a Single Dose of MNEXSPIKE vs 28 Days After a Single Dose of Comparator Vaccine – Per-Protocol Immunogenicity Set*

Assay	MNEXSPIKE[a] Seroresponse Rate[b] % (95% CI)[c] N=334	Comparator Vaccine[d] Seroresponse Rate[b] % (95% CI)[c] N=334	Difference in Seroresponse Rate (MNEXSPIKE-Comparator Vaccine) % (95% CI)[e]
Omicron XBB.1.5	92.2 (88.8, 94.9)	86.8 (82.7, 90.3)	5.4 (0.8, 10.2)

N=Number of participants with non-missing data at baseline and the corresponding timepoint(s).

* Per-Protocol Immunogenicity Set included subjects who received study vaccine, did not have a major protocol deviation that impacted immune response, and had both pre-dose and post-dose immunogenicity assessment at timepoint of primary interest (28 days post-dose). Participants had previously received at least one dose of a COVID-19 vaccine prior to the study.

[a] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Omicron XBB.1.5

[b] Seroresponse is defined as an antibody value change from baseline below the LLOQ to ≥4 × LLOQ, or at least a 4-fold rise if baseline is ≥ LLOQ and <4 × LLOQ, or at least a 2-fold rise if baseline is ≥4 × LLOQ, where baseline refers to pre-dose.

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

[d] SPIKEVAX 2023-2024 Formula

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

Immunogenicity of Single Dose (Monovalent Omicron XBB.1.5) in Vaccine-Naïve

In a separate observer-blind, active-controlled portion of Study 1, the immunogenicity of MNEXSPIKE was evaluated in participants 12 years of age and older in the United States. The study allowed for the inclusion of participants with stable pre-existing medical conditions, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 2 months before enrollment, as well as participants with stable human immunodeficiency virus (HIV) infection. A total of 1,056 participants (COVID-19 vaccine-naïve [n=400] and COVID-19 vaccine-experienced [n=656]) received MNEXSPIKE, a vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Omicron variant lineage XBB.1.5.

The immunogenicity analysis population included 371 vaccine-naïve participants and 617 vaccine-experienced participants who received MNEXSPIKE. Among vaccine-naïve participants assessed for immunogenicity, 48.2% were male, 51.8% were female, 36.4% were Hispanic or Latino, 55.3% were White, 43.1% were Black or African American, 0.5% were American Indian or Alaska Native, and 0.3% were Multiracial. The median age of participants was 38 years (range 12 through 81 years) and 8.1% of participants were 65 years of age and older. Among vaccine-experienced participants assessed for immunogenicity, 46.0% were male, 54.0% were female, 14.1% were Hispanic or Latino, 73.3% were White, 17.2% were Black or African

American, 2.9% were Asian, 0.5% were American Indian or Alaska Native, 0.2% were Native Hawaiian or Pacific Islander, 0.2% were other races, and 5.7% were Multiracial. The median age of participants was 16 years (range 12 years through 83 years) and 8.6% of participants were 65 years of age and older.

Descriptive immunogenicity analyses evaluated the ratio of neutralizing antibody geometric mean concentrations (GMC) and the difference in seroresponse rate (SRR) against a pseudovirus expressing Omicron XBB.1.5 SARS-CoV-2 Spike protein following vaccination with MNEXSPIKE in vaccine-naïve participants compared with vaccine-experienced participants (Table 19 and Table 20).

Table 19: Descriptive Analysis of Geometric Mean Concentration 28 Days After a Single Dose of MNEXSPIKE in COVID-19 Vaccine-Naïve vs COVID-19 Vaccine-Experienced Participants – Per-Protocol Immunogenicity Subset*

	MNEXSPIKE[a]		
Assay[b]	**Vaccine-Naïve GMC N=371 (95% CI)[c]**	**Vaccine-Experienced GMC N=617 (95% CI)[c]**	**GMC Ratio (Vaccine-Naïve/ Vaccine-Experienced) (95% CI)[c]**
Omicron XBB.1.5	2934.9 (2559.3, 3365.6)	2640.3 (2386.8, 2920.8)	1.1 (0.9, 1.3)

N=Number of participants with non-missing data at the corresponding timepoint(s).

* Per-Protocol Immunogenicity Subset included a randomly selected subset of subjects (Immunogenicity Subset) who received study vaccine, and did not have a major protocol deviation that impacted immune response and had both pre-dose and post-dose immunogenicity assessment at timepoint of primary interest (28 days post-dose).

[a] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Omicron variant lineage XBB.1.5

[b] Geometric mean concentration (GMC) was determined using a SARS-CoV-2 Spike-Pseudotyped Virus Neutralization Assay. Quantification of SARS-CoV-2 neutralizing antibodies utilizes SARS-CoV-2 Reporter Virus Particles which express GFP for quantitative measurement of infection by counting the number of green fluorescent cells (assay readout [count] is Foci Forming Units [FFUs]). The serum antibody concentration (Ab[C]) of the neutralizing antibodies was determined by interpolating the mean of the replicate FFU values off the fitted reference standard curve (AU/mL).

[c] The log-transformed antibody levels are analyzed using an analysis of covariance (ANCOVA) model with the group variable (vaccine-naïve vs vaccine-experienced) as fixed effect, adjusted by randomization age group. Least Square Means use observed margins. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.

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.

Table 20: Descriptive Analysis of Seroresponse Rate 28 Days After a Single Dose of MNEXSPIKE in COVID-19 Vaccine-Naïve vs COVID-19 Vaccine-Experienced Participants – Per-Protocol Immunogenicity Subset*

Assay	MNEXSPIKE[a]		
	Vaccine-Naïve Seroresponse Rate[b] N=371 % (95% CI)[c]	Vaccine-Experienced Seroresponse Rate[b] N=617 % (95% CI)[c]	Difference in Seroresponse Rate (Vaccine-Naïve-Vaccine-Experienced) % (95% CI)[d]
Omicron XBB.1.5	91.1 (87.7, 93.8)	86.5 (83.6, 89.1)	4.6 (0.4, 8.4)

N=Number of participants with non-missing data at the corresponding timepoint(s).
* Per-Protocol Immunogenicity Subset included a randomly selected subset of subjects (Immunogenicity Subset) who received study vaccine, and did not have a major protocol deviation that impacted immune response and had both pre-dose and post-dose immunogenicity assessment at timepoint of primary interest (28 days post-dose).
[a] A vaccine encoding the membrane-bound, linked NTD and RBD of the S glycoprotein from SARS-CoV-2 Omicron variant lineage XBB.1.5
[b] Seroresponse is defined as an antibody value change from baseline below the LLOQ to ≥4 × LLOQ, or at least a 4-fold rise if baseline is ≥ LLOQ and <4 × LLOQ, or at least a 2-fold rise if baseline is ≥4 × LLOQ, where baseline refers to pre-dose.
[c] 95% CI is calculated using the Clopper-Pearson method.
[d] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

15 REFERENCES

1. Jain SS, Anderson SA, Steele JM, et al. Cardiac manifestations and outcomes of COVID-19 vaccine-associated myocarditis in the young in the USA: longitudinal results from the Myocarditis After COVID Vaccination (MACiV) multicenter study. Lancet. 2024;76:1-13. https://doi.org/10.1016/j.eclinm.2024.102809

16 HOW SUPPLIED/STORAGE AND HANDLING

MNEXSPIKE (2025-2026 Formula) is supplied as follows:

NDC 80777-400-62	Carton of 1 single-dose prefilled syringe containing 1 dose of 0.2 mL (NDC 80777-400-17)
NDC 80777-400-61	Carton of 2 single-dose prefilled syringes, each syringe containing 1 dose of 0.2 mL (NDC 80777-400-17)
NDC 80777-400-60	Carton of 10 single-dose prefilled syringes, each syringe containing 1 dose of 0.2 mL (NDC 80777-400-17)

Storage
Store frozen between -40°C to -15°C (-40°F to 5°F).

During storage and after thawing, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

After thawing, MNEXSPIKE may be stored refrigerated between 2°C to 8°C (36°F to 46°F) for up to 90 days or up to the expiration date printed on the carton, whichever comes first.

After thawing, MNEXSPIKE may be stored between 8°C to 25°C (46°F to 77°F) for up to 24 hours.

Do not refreeze once thawed.

Thawed syringes can be handled in room light conditions.

Transportation of Thawed Syringes at 2°C to 8°C (36°F to 46°F)
Thawed prefilled syringes can be transported at 2°C to 8°C (36°F to 46°F) in shipping containers qualified to maintain 2°C to 8°C (36°F to 46°F). Once thawed and transported at 2°C to 8°C (36°F to 46°F), prefilled syringes should not be refrozen and should be stored at 2°C to 8°C (36°F to 46°F) until use.

17 PATIENT COUNSELING INFORMATION

Advise the vaccine recipient or caregiver to read the FDA-approved patient labeling.

Inform the vaccine recipient or caregiver of the potential benefits and risks of vaccination with MNEXSPIKE.

Instruct the vaccine recipient or caregiver to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and https://vaers.hhs.gov.

Manufactured for:
Moderna US, Inc.
Princeton, NJ 08540

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