EU Risk Management Plan for Spikevax, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5 and Spikevax XBB.1.5 (Elasomeran, elasomeran/imelasomeran, elasomeran/davesomeran and andusomeran)

Risk Management Plan (RMP) version to be assessed as part of this application:

RMP version number: 8.3

Data lock point for this RMP: 30 November 2023

Date of final sign off: 11 June 2024

Rationale for submitting an updated RMP:

Removal of the myocarditis/pericarditis follow-up questionnaire upon EMA feedback

Summary of significant changes in this RMP:

Compared to the previously approved Spikevax, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5, and Spikevax XBB.1.5, European Union (EU) RMP version 8.2, this RMP version 8.3 has been updated:

To remove the myocarditis/pericarditis follow-up questionnaire from Part III.1, Part V.3 and Annex 4

RMP Module:	Significant Changes:
Part I Product Overview	No changes.
Part II Safety Specification	
Module SI Epidemiology of the indication(s) and target population(s)	No changes.
Module SII Non-clinical part of the safety specification	No changes.
Module SIII Clinical trial exposure	No changes.
Module SIV Populations not studied in clinical trials	No changes.
Module SV Post-authorisation experience	No changes.
Module SVI Additional EU requirements for the safety specification	No changes.
Module SVII Identified and potential risks	No changes.
Module SVIII Summary of the safety concerns	No changes.
Part III Pharmacovigilance plan	Removed the myocarditis/pericarditis follow-up questionnaire from Part III.1.

RMP Module:	Significant Changes:
Part IV Plans for post-authorisation efficacy studies	No changes.
Part V Risk minimisation measures	Removed the myocarditis/pericarditis follow-up questionnaire in Part V.3.
Part VI Summary of the risk management plan	No changes.
Part VII Annexes	Annex 4 – Removed the myocarditis/pericarditis follow-up questionnaire. Annex 7 – Updated references. Annex 8 – Updated to reflect the changes made to the RMP.

Other RMP versions under evaluation:

N/A

Details of the currently approved RMP:

Version number: 8.2

Approved with procedure: EMEA/H/C/005791/II/0120

Date of approval (opinion date): 11 April 2024

EU QPPV name[1] : Marie-Pierre Caby-Tosi, EU QPPV

QPPV oversight declaration: The content of this RMP has been reviewed and approved by the Moderna's EU QPPV. The electronic signature is available on file.

[1] EU QPPV name will not be redacted in case of an access to documents request; see HMA/EMA Guidance document on the identification of commercially confidential information and personal data within the structure of the marketing-authorisation application; available on EMA website http://www.ema.europa.eu

Table of Contents

List of Tables

LIST OF ABBREVIATIONS

Acronym	Definition
2019-nCoV	2019 novel coronavirus
Ab	Antibody
ADR	Adverse drug reaction
AE	Adverse event
AESI	Adverse event of special interest
AI/ID	Autoimmune and/or inflammatory disease
AR	Adverse reaction
ARDS	Acute respiratory distress syndrome
BD	Booster dose
BLA	Biologics License Application
CEAC	Cardiac Event Adjudication Committee
CHMP	Committee for Medicinal Products for Human Use
CI	Confidence interval
CMV	Cytomegalovirus
COVID-19	Disease caused by the novel 2019 coronavirus
CoV	Coronaviruses
CSR	Clinical Study Report
DLP	Data lock point
DSPC	1,2-distearoyl-sn-glycero-3-phosphocholine
ECDC	European Centre for Disease Prevention and Control
EMA	European Medicines Agency
EPAR	European Public Assessment Report
ERD	Enhanced respiratory disease
ERVISS	European Respiratory Virus Surveillance System
EU/EEA	European Union/European Economic Area
EUA	Emergency Use Authorization
FDA	Food and Drug Administration
ICSR	Individual case safety report
Ig	Immunoglobulin
IM	Intramuscular(ly)
INN	International nonproprietary name
IP	Investigational product
IR	Incidence rate
IRR	Incidence rate ratio
IRT	Interactive response technology
KPSC	Kaiser Permanente Southern California
LPLV	Last participant last visit
LNP	Lipid nanoparticle
LSLV	Last subject last visit
MAAE	Medically attended adverse event
MedDRA	Medical Dictionary for Regulatory Activities
MedHx	Medical history
MERS	Middle East respiratory syndrome

MIS	Multisystem inflammatory syndrome
MIS-C	Multisystem inflammatory syndrome in children
mRNA	Messenger ribonucleic acid
MSSR	Monthly Summary Safety Report
nAb	Neutralizing antibody(ies)
NHP	Nonhuman primate
NP	Nasopharyngeal
NTD	N-terminal domain
O/E	Observed to expected
PL	Patient leaflet
PEG2000-DMG	1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000
PSUR	Periodic Safety Update Report
RBD	Receptor binding domain
RMP	Risk management plan
RSV	Respiratory syncytial virus
RT-PCR	Reverse transcription polymerase chain reaction
SAE	Serious adverse event
SARS	Severe acute respiratory syndrome
sBLA	Supplemental Biologic License Application
SCRI	Self-controlled risk interval
SmPC	Summary of Product Characteristics
SSR	Summary of Safety Report
TEAE	Treatment emergent adverse event
Th	T helper
TTO	Time to onset
VAED	Vaccine associated enhanced disease
VAERD	Vaccine-associated enhanced respiratory disease
VAERS	Vaccine Adverse Event Reporting System
WHO	World Health Organization

Throughout the document, both elasomeran and mRNA-1273 (only for clinical trials titles) are used to identify the product.

Throughout the document, elasomeran/imelasomeran and mRNA-1273.214 are used to identify the bivalent vaccine Spikevax bivalent Original/Omicron BA.1.

Throughout the document, elasomeran/davesomeran and mRNA-1273.222 are used to identify the bivalent vaccine Spikevax bivalent Original/Omicron BA.4-5.

Throughout the document, Spikevax bivalent is used to identify the bivalent vaccine Spikevax bivalent Original/Omicron BA.1.

Throughout the document, andusomeran is used to identify the Spikevax XBB.1.5 vaccine.

Part I: Products Overview

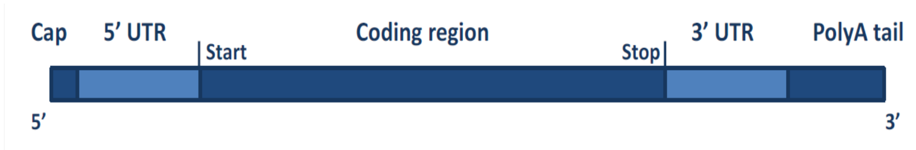
Table 1: Product Overview

Active substance(s) (INN or common name)	Elasomeran, elasomeran/imelasomeran, elasomeran/davesomeran and andusomeran
Pharmacotherapeutic group(s) (ATC Code)	Pharmacotherapeutic group: Vaccine, COVID-19 vaccines (J07BN01)
Marketing Authorisation Holder	MODERNA BIOTECH SPAIN, S.L. Calle del Príncipe de Vergara 132 Plt 12 Madrid 28002 Spain
Medicinal products to which this RMP refers	4
Invented name(s) in the European Economic Area	Spikevax, Spikevax bivalent/ Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5 and Spikevax XBB.1.5
Marketing authorisation procedure	Centralised
Brief description of the product	**Chemical class** The mRNA drug substance in Spikevax is chemically similar to naturally-occurring mammalian mRNA with the exception that the uridine nucleoside normally present in mammalian mRNA is fully replaced with N-methyl-pseudouridine, a naturally-occurring pyrimidine base present in mammalian transfer RNAs (Rockwood K, Howlett SE. Fifteen years of progress in understanding frailty and health in aging. BMC Med. 2018;16(1):220. Rozenski et al 1999; Karikó et al 2005). This nucleoside is included in elasomeran Drug Substance in place of the normal uridine base to minimise the indiscriminate recognition of the elasomeran mRNA by pathogen-associated molecular pattern receptors (e.g., toll-like receptors) (Desmet and Ishii 2012). The cap structure used in the mRNA is identical to the natural mammalian Cap 1 structure (Kislaya I, Melo A, Barreto M, Henriques C, Aniceto C, Manita C, et al; ISN4COVID-19 Group1. Seroprevalence of Specific SARS-CoV-2 Antibodies during Omicron BA.5 Wave, Portugal, April-June 2022. Emerg Infect Dis. 2023 Feb 2;29(3). Kozak 1991; European Respiratory Virus Surveillance Summary (ERVISS). Available at: https://erviss.org/ Accessed 03 December 2023. [ERVISS 2023] FDA. COVID-19 Vaccines. Available at: https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines#authorized-vaccines Accessed 03 December 2023. [FDA 2023b] FDA. Emergency Use Authorizations for Drugs and Non-Vaccine Biological Products. Available at: https://www.fda.gov/drugs/emergency-preparedness-

drugs/emergency-use-authorizations-drugs-and-non-vaccine-biological-products Accessed 03 December 2023. [FDA2023c]

Fechter and Brownlee 2005).

Structure of mRNA



Abbreviations: mRNA, messenger RNA; PolyA, polyadenylated; UTR, untranslated region.

Summary of mode of action

Spikevax encodes for the prefusion stabilized spike glycoprotein of SARS-CoV-2. After intramuscular (IM; deltoid) injection, cells at the injection site take up the lipid nanoparticle, effectively delivering the mRNA sequence into cells for translation into protein. The mRNA delivery system is based on the principle and observation that cells in vivo can take up mRNA, translate it, and express viral protein antigen(s) in the desired conformation. 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 glycoprotein that is inserted into the cellular membrane of the expressing cell(s). The spike glycoprotein is membrane bound, mimicking the presentation of natural infection.

The expressed spike glycoprotein of SARS-CoV-2 is then recognized by immune cells as a foreign antigen, which elicits both T-cell and B-cell responses. The immune response to the spike glycoprotein results in functional antibody (Ab) and T-cell responses and in the generation of memory immune cell populations.

A modified, variant-matched bivalent COVID-19 mRNA vaccine has been developed that contains equal amounts of two mRNAs that encode for the Spike protein of the ancestral SARS-CoV-2 (Wuhan-Hu-1) and an antigenically divergent variant of concern (Omicron BA.1), each encapsulated into individual lipid nanoparticles, and co-formulated into a single drug product (Spikevax bivalent). After delivery, both mRNAs are delivered to cells in the body where the two distinct spike protomers, each of which represents one of the three components of the spike trimer, are expressed. After expression these spike protomers assemble into the spike trimer and both homotrimers as well heterotrimers (mixed protomers from the Wuhan spike and the Variant spike), form.

The inclusion of both the original and the variant spikes in the vaccine are intended to broaden immunity. Inclusion of the Wuhan spike allows reactivation and boosting of memory immune cell populations, increasing immunity that was previously present. In addition, inclusion of the variant spike, which has novel functional epitopes present primarily on the receptor binding domain (RBD) and the N-terminal domain (NTD), allows new naïve immune populations to be engaged and new memory responses to be elicited. This likely broadens immunity not only to the spike antigens delivered but likely also against a broader diversity of spike proteins. Furthermore, the formation of heterotrimers with spike protomers from both the Wuhan and Variant spikes results in spike trimers that are able to flex more significantly than homotrimers, resulting in more presentation of the receptor binding domain in an "open" or "up" conformation, versus the "closed" conformation seen predominantly in homotrimers. In the open conformation, key sites of neutralization not exposed when the spike is closed are available, providing the immune system with more functional sites with which to engage.

Important information about its composition

Spikevax:

The active substance is mRNA encoding the prefusion stabilized spike glycoprotein of SARS-CoV-2 embedded in lipid nanoparticles (elasomeran)

Spikevax bivalent Original/Omicron BA.1:

<table>
<tr><td></td><td>The active substances are mRNA encoding the prefusion stabilized spike glycoprotein of original SARS-CoV-2 embedded in lipid nanoparticles (elasomeran) and mRNA encoding the prefusion stabilized spike glycoprotein of SARS-CoV-2 Omicron variant (B.1.1.529) embedded in lipid nanoparticles (imelasomeran).
<u>Spikevax bivalent Original/Omicron BA.4-5</u>:
The active substances are mRNA encoding the prefusion stabilised spike glycoprotein of original SARS-CoV-2 embedded in lipid nanoparticles (elasomeran) and mRNA encoding the prefusion stabilised spike glycoprotein of SARS-CoV-2 Omicron lineages BA.4 and BA.5 (Omicron variants B.1.1.529.4 and B.1.1.529.5) embedded in lipid nanoparticles (davesomeran).
<u>Spikevax XBB.1.5:</u>
Andusomeran contains nucleoside-modified messenger RNA (mRNA) encoding the pre-fusion stabilized Spike glycoprotein (S) of the SARS-CoV-2 Omicron variant lineage XBB.1.5.
The other ingredients are SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000 DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate, sucrose, water for injections.</td></tr>
<tr><td>Hyperlink to the Product Information</td><td>Module 1</td></tr>
<tr><td>Indication(s) in the EEA</td><td>Current:
Spikevax is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 6 months of age and older.
Spikevax bivalent Original/Omicron BA.1 is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 6 years of age and older who have previously received at least a primary vaccination course against COVID-19.
Spikevax bivalent Original/Omicron BA.4-5 is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 6 months of age and older.
Spikevax XBB.1.5 is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 6 months of age and older.
Proposed: Not applicable</td></tr>
<tr><td>Dosage in the EEA</td><td>Current:
Spikevax
Spikevax posology for primary series, a third dose in severely immunocompromised and booster doses
<table>
<tr><th>Strength</th><th>Vaccination type</th><th>Age(s)</th><th>Dose</th><th>Recommendations</th></tr>
<tr><td rowspan="2">Spikevax 0.2 mg/L dispersion for injection</td><td rowspan="2">Primary series</td><td>Individuals 12 years of age and older</td><td>2 (two) (0.5 mL each, containing 100 micrograms mRNA)</td><td rowspan="2">It is recommended to administer the second dose 28 days after the first dose</td></tr>
<tr><td>Children 6 years through 11 years of age</td><td>2 (two) doses (0.25 mL each, containing 50 micrograms mRNA, which is half of the primary dose for individuals 12</td></tr>
</table></td></tr>
</table>

				years and older)	
		Third dose in severely immune-compromised individuals	Individuals 12 years of age and older	1 (one) dose of 0.5 mL, containing 100 micrograms mRNA	A third dose may be given at least 28 days after the second dose
			Children 6 years through 11 years of age	1 (one) dose of 0.25 mL containing 50 micrograms mRNA	
		Booster dose	Individuals 12 years of age and older	1 (one) dose of 0.25 mL, containing 50 micrograms mRNA	Spikevax may be used to boost individuals 12 years of age and older who have received a primary series with Spikevax or a primary series comprised of another mRNA vaccine or adenoviral vector vaccine at least 3 months after completion of the primary series.
	Spikevax 0.1 mg/L dispersion for injection and Spikevax 50 micrograms dispersion for injection in pre-filled syringe*	Primary series†	Children 6 years through 11 years of age	2 (two) doses (0.5 mL each, containing 50 micrograms mRNA each)	It is recommended to administer the second dose 28 days after the first dose.
			Children 6 months through 5 years of age	2 (two) doses (0.25 mL each, containing 25 micrograms mRNA, which is half of the primary dose for children 6 years through 11 years of age)*	
		Third dose in severely immuno-compromised individuals‡	Children 6 years through 11 years of age	1 (one) dose of 0.5 mL, containing 50 micrograms mRNA	A third dose may be given at least 28 days after the second dose.
			Children 6 months through 5 years of age	1 (one) dose of 0.25 mL, containing 25 micrograms mRNA*	

	Booster dose	Individuals 12 years of age and older	1 (one) dose of 0.5 mL, containing 50 micrograms mRNA	Spikevax may be used to boost individuals 6 years of age and older who have received a primary series with Spikevax or a primary series comprised of another mRNA vaccine or adenoviral vector vaccine at least 3 months after completion of the primary series.
		Children 6 years through 11 years of age	1 (one) dose of 0.25 mL containing 25 micrograms mRNA*	

*Do not use the pre-filled syringe to deliver a partial volume of 0.25 mL
†For primary series for individuals 12 years of age and older, the 0.2 mg/mL strength vial should be used.
†For the third dose in severely immunocompromised individuals 12 years of age and older, the 0.2 mg/mL strength vial should be used.

Paediatric population

The safety and efficacy of Spikevax in children less than 6 months of age have not yet been established. No data are available.

Elderly

No dose adjustment is required in elderly individuals ≥65 years of age.

Spikevax bivalent Original/Omicron BA.1

Individuals 12 years of age and older

The dose of Spikevax bivalent Original/Omicron BA.1 is 0.5 mL given intramuscularly.

Children 6 years through 11 years of age

The dose of Spikevax bivalent Original/Omicron BA.1 is 0.25 mL given intramuscularly.

There should be an interval of at least 3 months between administration of Spikevax bivalent Original/Omicron BA.1 and the last prior dose of a COVID-19 vaccine.
Spikevax bivalent Original/Omicron BA.1 is only indicated for individuals who have previously received at least a primary vaccination course against COVID-19.

Paediatric population

The safety and efficacy of Spikevax bivalent Original/Omicron BA.1 in children less than 6 months of age have not yet been established. No data are available.

Elderly

No dose adjustment is required in elderly individuals ≥65 years of age.

Spikevax bivalent Original/Omicron BA.4-5

Spikevax bivalent Original/Omicron BA.4-5 posology

Age(s)	**Dose**	**Additional recommendations**

Children 6 months through 4 years of age, without prior vaccination and no known history of SARS-CoV-2 infection	Two doses of 0.25 mL each, given intramuscularly*	Administer the second dose 28 days after the first dose. If a child has received one prior dose of Spikevax, one dose of Spikevax bivalent Original/Omicron BA.4-5 should be administered to complete the two-dose series.
Children 6 months through 4 years of age, with prior vaccination or known history of SARS-CoV-2 infection	One dose of 0.25 mL, given intramuscularly*	Spikevax bivalent Original/Omicron BA.4-5 should be administered at least 3 months after the most recent dose of a COVID 19 vaccine.
Children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	
Individuals 65 years of age and older	One dose of 0.5 mL, given intramuscularly	One additional dose may be administered at least 3 months after the most recent dose of a COVID-19 vaccine.

*Do not use the single dose vial or pre-filled syringe to deliver a partial volume of 0.25 mL.

Spikevax bivalent Original/Omicron BA.4-5 posology for immunocompromised individuals

Age(s)	Dose	Additional recommendations
Immunocompromised children 6 months through 4 years of age, without prior vaccination	Two doses of 0.25 mL, given intramuscularly*	A third dose in severely immunocompromised may be given at least 28 days after the second dose.
Immunocompromised children 6 months through 4 years of age, with prior vaccination	One dose of 0.25 mL, given intramuscularly*	Additional age-appropriate dose(s) may be administered in severely immunocompromised at least 2 months following the most recent dose of a COVID-19 vaccine at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.
Immunocompromised children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Immunocompromised individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	

*Do not use the single-dose vial or pre-filled syringe to deliver a partial volume of 0.25 mL.

Paediatric population

The safety and efficacy of Spikevax bivalent Original/Omicron BA.4-5 in children less than 6 months of age have not yet been established. No data are available.

Elderly

No dose adjustment is required in elderly individuals ≥65 years of age.

Spikevax XBB.1.5 posology

Age(s)	Dose	Additional recommendations
Children 6 months through 4 years of age, without prior vaccination and no known history of SARS CoV-2 infection	Two doses of 0.25 mL each, given intramuscularly*	Administer the second dose 28 days after the first dose. If a child has received one prior dose of any Spikevax vaccine, one dose of Spikevax XBB.1.5 should be administered to complete the two-dose series.
Children 6 months through 4 years of age, with prior vaccination or known history of SARS-CoV-2 infection	One dose of 0.25 mL, given intramuscularly*	Spikevax XBB.1.5 should be administered at least 3 months after the most recent dose of a COVID-19 vaccine.
Children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	
Individuals 65 years of age and older	One dose of 0.5 mL, given intramuscularly	One additional dose may be administered at least 3 months after the most recent dose of a COVID-19 vaccine.

* Do not use the single-dose vial or pre-filled syringe to deliver a partial volume of 0.25 mL.

Spikevax XBB.1.5 posology for immunocompromised individuals

Age(s)	Dose	Additional recommendations
Immunocompromised children 6 months through 4 years of age, without prior vaccination	Two doses of 0.25 mL, given intramuscularly*	A third dose in severely immunocompromised may be given at least 28 days after the second dose.

<table>
<tr>
<td></td>
<td>
<table>
<tr><td>Immunocompromised children 6 months through 4 years of age, with prior vaccination</td><td>One dose of 0.25 mL, given intramuscularly*</td><td rowspan="3">Additional age-appropriate dose(s) may be administered in severely immunocompromised at least 2 months following the most recent dose of a COVID-19 vaccine at the discretion of the healthcare provider, taking into consideration the individual’s clinical circumstances.</td></tr>
<tr><td>Immunocompromised children 5 years through 11 years of age, with or without prior vaccination</td><td>One dose of 0.25 mL, given intramuscularly*</td></tr>
<tr><td>Immunocompromised individuals 12 years of age and older, with or without prior vaccination</td><td>One dose of 0.5 mL, given intramuscularly</td></tr>
</table>
* Do not use the single-dose vial or pre-filled syringe to deliver a partial volume of 0.25 mL.

Paediatric population
The safety and efficacy of Spikevax XBB.1.5 in children less than 6 months of age have not yet been established. No data are available.
Elderly
No dose adjustment is required in elderly individuals ≥65 years of age.

Proposed: Not applicable
</td>
</tr>
<tr>
<td>Pharmaceutical form(s) and strengths</td>
<td>
Current: Dispersion for injection
White to off white dispersion (pH 7.0 - 8.0).
Qualitative and quantitative composition by strength and type of container
<table>
<tr><th>Strength</th><th>Container</th><th>Dose(s)</th><th>Composition per dose</th></tr>
<tr><td rowspan="2">Spikevax 0.2 mg/mL dispersion for injection</td><td rowspan="2">Multidose vial (red flip-off cap)</td><td>Maximum 10 doses of 0.5 mL each</td><td>One dose (0.5 mL) contains 100 micrograms of elasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).</td></tr>
<tr><td>Maximum 20 doses of 0.25 mL each</td><td>One dose (0.25 mL) contains 50 micrograms of elasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).</td></tr>
<tr><td rowspan="2">Spikevax 0.1 mg/mL dispersion for injection</td><td rowspan="2">Multidose vial (blue flip-off cap)</td><td>5 doses of 0.5 mL each</td><td>One dose (0.5 mL) contains 50 micrograms of elasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).</td></tr>
<tr><td>Maximum 10 doses of 0.25 mL each</td><td>One dose (0.25 mL) contains 25 micrograms of elasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).</td></tr>
<tr><td>Spikevax</td><td>Pre-filled syringe</td><td>1 dose of 0.5 mL</td><td>One dose (0.5 mL) contains 50 micrograms of elasomeran, a</td></tr>
</table>
</td>
</tr>
</table>

50 micrograms dispersion for injection in pre-filled syringe		For single-use only. Do not use the pre-filled syringe to deliver a partial volume of 0.25 mL.	COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).

Spikevax bivalent Original/Omicron BA.1 qualitative and quantitative composition

Strength	Container	Dose(s)	Composition per dose
Spikevax bivalent Original/Omicron BA.1 **(50 micrograms/50 micrograms)/mL dispersion for injection**	Multidose 2.5 mL vial (blue flip-off cap)	5 doses of 0.5 mL each or 10 doses of 0.25 mL each	One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of imelasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles). One dose (0.25 mL) contains 12.5 micrograms of elasomeran and 12.5 micrograms of imelasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
	Multidose 5 mL vial (blue flip-off cap)	10 doses of 0.5 mL each or 20 doses of 0.25 mL each	
Spikevax bivalent Original/Omicron BA.1 **25 micrograms/25 micrograms dispersion for injection**	Single-dose 0.5 mL vial (blue flip-off cap)	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of imelasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.5 mL For single-use only.	

Spikevax bivalent Original/Omicron BA.4-5 qualitative and quantitative composition

Strength	Container	Dose(s)	Composition per dose
Spikevax bivalent Original/Omicron BA.4-5 **(50 micrograms/50 micrograms)/mL dispersion for injection**	Multidose 2.5 mL vial (blue flip-off cap)	5 doses of 0.5 mL each or 10 doses of 0.25 mL each	One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of davesomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles). One dose (0.25 mL) contains 12.5 micrograms of elasomeran and 12.5 micrograms of davesomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).

Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection	Single-dose 0.5 mL vial (blue flip-off cap)	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of davesomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of davesomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).

Spikevax XBB.1.5 qualitative and quantitative composition

Strength	**Container**	**Dose(s)**	**Composition per dose**
Spikevax XBB.1.5 0.1mg/mL dispersion for injection	Multidose 2.5 mL vial (blue flip-off cap)	5 doses of 0.5 mL each or 10 doses of 0.25 mL each	One dose (0.5 mL) contains 50 micrograms of andusomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles). One dose (0.25 mL) contains 25 micrograms of andusomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
Spikevax XBB.1.5 50 micrograms dispersion for injection	Single-dose 0.5 mL vial (blue flip-off cap)	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 50 micrograms of andusomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
Spikevax XBB.1.5 50 micrograms dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 50 micrograms of andusomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).

Proposed: Not applicable

Vaccine construct and the formulation	Elasomeran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free in vitro transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (original). Imelasomeran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free in vitro transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (Omicron BA.1). Davesomeran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free in vitro transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (Omicron BA.4-5). The S-proteins of the SARS-CoV-2 Omicron variant lineages BA.4 and BA.5 are identical.

	Andusomeran is a single-stranded, 5'-capped mRNA produced using a cell-free in vitro transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (Omicron XBB.1.5). The other ingredients are SM-102 (heptadecan-9-yl 8-{(2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino}octanoate), Cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), Trometamol, Trometamol hydrochloride, Acetic acid, Sodium acetate trihydrate, Sucrose, and Water for injections.
Is/will the product be subject to additional monitoring in the EU?	Yes.

Part II: Safety Specification

Part II: Module SI – Epidemiology of the Indication and Target Population

Indication: Spikevax is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 6 months of age and older.

Spikevax bivalent Original/Omicron BA.1 is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 6 years of age and older who have previously received at least a primary vaccination course against COVID-19.

Spikevax bivalent Original/Omicron BA.4-5 is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2, in individuals 6 months of age and older.

Spikevax XBB.1.5 is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2, in individuals 6 months of age and older.

Coronaviruses (CoVs) are a large family of viruses that cause illness ranging from the common cold to more severe diseases, such as Middle East respiratory syndrome (MERS-CoV) and severe acute respiratory syndrome (SARS-CoV).

An outbreak of the CoV disease (COVID-19) caused by the 2019 novel CoV (2019-nCoV, later designated SARS-CoV-2) began in Wuhan, Hubei Province, China in December 2019, and has spread globally (WHO 2020a and WHO COVID-19 infection prevention and control living guideline: mask use in community settings, 22 December 20212020b). The World Health Organization (WHO) declared COVID-19 a pandemic on 11 March 2020; however, by that time, there was already widespread community transmission in many locations. As of 30 November 2023, over 772,052,752 confirmed cases and 6,985,278 deaths have been attributed to the COVID-19 pandemic globally (WHO 2023a). Widespread community transmission of SARS-CoV-2 has been reported in all WHO regions (WHO 2020a and WHO COVID-19 infection prevention and control living guideline: mask use in community settings, 22 December 20212020b). WHO has continued to track Variants of Concern (VOC): as well as Variants of Interest (VOI) and Variants Under Monitoring (VUM) under an updated reporting structure that focuses on identifying sub-variants with Omicron lineage. As of 21 November 2023, the currently circulating VOIs are recombinant Omicron sub-variants XBB.1.5, XBB.1.16, EG.5, and BA.2.86 while the VUM are DV.7, and specific XBB sub-variants XBB.1.9.1, XBB.1.9.2, and XBB.2.3 as well as other XBB subvariants (WHO 2023b).

Incidence of COVID-19 in Europe

Following the identification of SARS-CoV-2 and its global spread, large epidemics of COVID-19 occurred in Europe. By mid-March 2020, the WHO European Region had become the epicentre of the pandemic, reporting over 40% of globally confirmed cases. As of 30 November 2023, 32.3% of global mortality from SARS-CoV-2 was from the European Region (WHO 2023a).

During the 28-day period from 23 October to 19 November 2023 countries in the WHO European Region reported 378,602 new confirmed cases of COVID-19 which represented an 18% decline from the previous 28-day period (WHO COVID-19 Epidemiological Update 2023). While reporting of COVID-19 cases was limited to 10 of the 61 countries in the WHO European region, the highest numbers of new cases were reported from the Russian Federation (83.2 new cases per 100,000), Italy (174.7 new cases per 100,000), and Poland (57.6 new cases per 100,000). Recent surveillance data from the European Respiratory Virus Surveillance System (ERVISS) encompassing 29 countries of EU/EEA reported from 30 October 2023 to 27 November 2023 an increase in SARS-COV-2 testing from 2000 to 2660 and increases in test positivity for SARS-CoV-2 infection 14.7% (among 19 countries) to 19.9% (among 18 countries) (ERVISS 2023). Test positivity was highest during this period in Poland (69.1%), Lithuania (52.9%), and Portugal (29.2%). An overall increased trend in SARS-CoV-2 positivity has been observed among individuals 15-64 and 65 years and above starting in July 2023 with recent increases in positivity observed among individuals 5-14 years in October/November 2023.

During the 28-day period from 23 October to 19 November 2023 countries in the WHO European Region reported 1,951 COVID-19 deaths which represented a 49% decline from the previous 28-day period (WHO COVID-19 Epidemiological Update 2023). For COVID-19 deaths, the number of new deaths were reported from Italy (1 new death per 100,000), Sweden (3.6 new deaths per 100,000) and the Russian Federation (<1 new death per 100,000).

Variants of concern (VOC) and Variants of interest (VOI)

Since the outbreak of the COVID-19 caused by the 2019 novel CoV began in Wuhan, in December 2019, the WHO proposed labels for global COVID-19 VOC and VOI (WHO 2022a).

Delta was originally documented in October 2020 in India and Omicron first documented in various countries in November 2021. WHO has continued to track VOC as well as VOI and VUM under an updated reporting structure that focuses on identifying sub-variants with Omicron lineage. From 06 November to 19 November 2023, the estimated distribution of VOCs as reported in ERVISS from 16 countries in the EU/EEA was 51% (43-63%) for XBB.1.5(+F456L), 19% (11%-30%) for BA.2.86, 10% (6-14%) for XBB.1.5, and 1% (0-2%) for BA.2.75 (ERVISS 2023).

Incidence of COVID-19 in the US

As of 25 November 2023, there have been 6, 522, 156 hospitalizations and 1,156,484 deaths due to COVID-19 in the United States as captured by the US CDC (CDC 2023f). Starting in late July/early August 2023, hospitalization rates due to COVID-19 started to increase from the week ending 24 June 2023 being 1.9 hospitalizations per 100,000 to 5.9 hospitalizations per 100,000 in the week ending 25 November 2023 (CDC 2023g). The hospitalization rate from COVID-NET during the week ending 30 September 2023 was 4.6 hospitalizations per 100,000 with individuals 65+ years of age having the highest hospitalization rate (20 cases per 100,000) as compared to individuals 0-17 years of age (0.8 cases per 100,000) (CDC 2023h). However, there was significant differences in hospitalization among children 0-17 years, with infants 0-6 months of age, children 6-12 months, 1-4 years, and 5-17 years having hospitalization rates of 9.4, 5.0, 0.9, 0.3 hospitalizations per 100,000, respectively.

The death rate due to COVID-19 in the US during the month of October 2023 was 1.6 deaths per 100,000. The death rate was higher among older populations with individuals 75+ years of age having a death rate of 17.7 deaths per 100,000 (CDC 2023a).

Nowcast estimates from the US CDC indicated as of 25 Nov 2023, the top three predominant variants was HV.1 (31.7%), EG.5 (13.1%), and BA.2.86 (8.8%). The distribution of variant predominance is consistent across the United States (CDC 2023f).

Risk Factors for severe COVID-19 outcomes

Age

Age has been identified as an independent risk factor for severe COVID-19 disease outcome (Booth 2021). Older adults (especially those ages 50 years and older) are more likely than younger people to be admitted into the hospital or intensive care for COVID-19, or die from SARS-CoV2 infection.

Medical conditions

According to the US CDC (CDC 2023b), many conditions were found to have a conclusive increased risk for at least one severe COVID-19 outcome in at least one published meta-analysis or systematic review or underwent the US CDC systematic review process: asthma, cancer, cerebrovascular disease, chronic kidney disease, chronic lung diseases (bronchiectasis, COPD, interstitial lung disease, pulmonary embolism, and pulmonary hypertension), chronic liver diseases (cirrhosis, non-alcoholic fatty liver disease, alcoholic liver disease, and autoimmune hepatitis), cystic fibrosis, diabetes, heart conditions (such as heart failure, coronary artery disease, or cardiomyopathies), mood disorders including depression, schizophrenia spectrum disorders, dementia, obesity, pregnancy and recent pregnancy, HIV (Human immunodeficiency virus), primary immunodeficiencies, solid organ or blood stem cell transplantation, use of corticosteroids or other immunosuppressive medications, smoking, disabilities including Down syndrome, and tuberculosis. Similar risk factors and risk groups were identified by the European Centre for Disease Prevention and Control (ECDC) (ECDC 2023e).

Main Existing Treatment Options

Global efforts to evaluate novel antivirals and therapeutic strategies to treat severe SARS-CoV-2 infections have intensified and there is an urgent public health need for rapid development of novel prophylactic therapies, including vaccines to prevent the spread of this disease mainly of the new variants.

As of June 2023, eight vaccines have been authorized for COVID prevention in the European Union including: Comirnaty® from BioNTech and Pfizer; Spikevax® from Moderna; Vaxzevria® from Astrazeneca, Jcovden from Janssen, Nuvaxovid® from Novavax, VidPrevtyn Beta from Sanofi Pasteur, COVID-19 Vaccine Valneva from Valneva, and Bimervax from HIPRA Human Health S.L.U. In addition, there are four adapted vaccines authorized for use in the EU, including: Comirnaty Original/Omicron BA.1® from Pfizer; Comirnaty Original/Omicron BA.4-5® from

Pfizer; Comirnaty Omicron XBB.1.5® from Pfizer, Spikevax bivalent Original/Omicron BA.1® from Moderna, Spikevax bivalent Original/Omicron BA.4-5® from Moderna, Spikevax Omicron XBB.1.5® from Moderna; Nuvaxovid® XBB.1.5 from Novavax. The Skycovion vaccine from SK Chemicals GmbH is currently under evaluation (EMA 2023).

In the US, two vaccines were approved (BLA): Comirnaty® from Pfizer (23 August 2021); and Spikevax® from Moderna (31 January 2022). The US FDA approved an sBLA for Comirnaty® Omicron XBB.1.5 from Pfizer and Spikevax® Omicron XBB.1.5 from Moderna for ages 12 years and above and an EUA for individuals 6 months through 11 years of age (FDA 2023b).Other vaccines authorized for emergency use include: Novavax COVID-19 Vaccine Adjuvanted (FDA 2023b).

In addition, the following medicinal products have been authorized in the European Union: Kineret (anakinra), an immunosuppressive medicine; Paxlovid (nirmatrelvir/ritonavir), a protease inhibitor; Regkirona (regdanvimab), a monoclonal antibody medicine; RoActemra (tocilizumab), interleukin-6 inhibitor; Ronapreve (casirivimab/imdevimab), combination of two monoclonal antibodies; Veklury (remdesivir), an antiviral medication; Xevudy (sotrovimab), human neutralizing monoclonal antibody; and Evusheld (tixagevimab/ cilgavimab), combination of two recombinant human IgG1monoclonal antibodies. Additionally, the marketing authorisation for Lagevrio (molnupiravir), a medication that works by introducing errors into the SARS-CoV-2 virus' genetic code is under marketing authorization evaluation by the EMA (EMA 2023).

In the US, a variety of treatments are FDA approved or authorized for Emergency Use (FDA 2023c), such as antiviral drugs - Veklury (remdesivir) for adults and certain paediatric patients with COVID-19, Paxlovid (nirmatrelvir/ritonavir) and Lagevrio (molnupiravir) for patients with mild-to-moderate COVID-19; immune modulators - Olumiant (baricitinib), Actemra (tocilizumab), Kineret (anakinra), and Gohibic (vilobelimab) for certain hospitalized adults with COVID-19; Baricitinib (Olumiant) for emergency use by healthcare providers for the treatment of COVID-19 in hospitalized paediatric patients 2 to less than 18 years of age; and COVID-19 convalescent plasma with high titres of anti-SARS-CoV-2 antibodies in patients with immunosuppressive disease or receiving immunosuppressive treatment.

Natural History of COVID-19 in the Unvaccinated Population

Current evidence suggests that SARS-CoV-2 is primarily transmitted via direct contact or person-to-person via respiratory droplets by coughing or sneezing from an infected individual (whether symptomatic or not). Airborne transmission may be possible during certain medical procedures and in indoor, crowded and poorly ventilated environments (WHO COVID-19 infection prevention and control living guideline: mask use in community settings, 22 December 20212022c). Common symptoms of COVID-19 include fever and cough, and other symptoms can include shortness of breath or difficulty breathing, muscle aches, chills, sore throat, headache, and loss of taste or smell. In comparison to ancestral SARS-CoV-2, Delta and Omicron BA.1 have shorter incubation periods, estimated as approximately 3.7-4 days for Delta and approximately 3-3.4 days for Omicron BA.1. Higher infectious viral loads were detected in patients infected with Delta than in patients infected with Omicron BA.1 or ancestral SARS-CoV-2. Overall patterns of shedding dynamics are conserved between SARS-CoV-2 variants. Infected children appear to shed

SARS-CoV-2 virus with nasopharyngeal viral loads comparable to or higher than those in adults (DeBiasi 2021). The spectrum of illness can range from asymptomatic infection to severe pneumonia with acute respiratory distress syndrome (ARDS) and death. Among 72,314 persons with COVID-19 in China, 81% of cases were reported to be mild (defined as no pneumonia or mild pneumonia), 14% were severe (defined as dyspnea, respiratory frequency ≥ 30 breaths/min, $SpO_2 \leq 93\%$, $PaO_2/FiO_2 < 300$ mmHg, and/or lung infiltrates > 50% within 24 to 48 hours), and 5% were critical (defined as respiratory failure, septic shock, and/or multiple organ dysfunction or failure) (Chowdhury 2020). The abnormalities seen in computed tomography of the chest also vary, but the most commonly observed are bilateral peripheral ground-glass opacities, with areas of consolidation developing later in the clinical course. Imaging may be normal early in infection and can be abnormal in the absence of symptoms. The circulating variants of SARS-CoV-2 evolves rapidly with different transmissibility and virulence. The Omicron variant, like other variants, is made up of several lineages and Sublineages, and share similar systems to previous variants. However, Omicron spreads more easily than earlier variants, including the Delta variant, and tends to cause less severe illness and death in general (CDC 2023c; Wolter 2022).

Common laboratory findings of COVID-19 include leukopenia and lymphopenia. Other laboratory abnormalities have included elevated levels of aminotransferases, C-reactive protein, D-dimer, ferritin, and lactate dehydrogenase. While COVID-19 is primarily a pulmonary disease, emerging data suggest that it also leads to cardiac, dermatologic, hematological, hepatic, neurological, renal, and other complications (Gavriatopoulou 2020). Thromboembolic events also occur in patients with COVID-19, with the highest risk in critically ill patients.

The understanding of immunity against SARS-CoV-2 is still incomplete. Binding antibodies (bAb and neutralizing antibodies (nAb) to SARS-CoV-2 have been shown to develop in most individuals between day 10 and day 21 after infection (Ni 2020; Ruderman RS, Mormol J, Trawick E, Perry MF, Allen EC, Millan D, et al. Association of COVID-19 Vaccination during Early Pregnancy with Risk of Congenital Fetal Anomalies. Jama Pediatr. 2022;176(7):717-9.

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Sáez-Peñataro J, Torres F, Bartra J, Bascuas J, Vilella A, Tortajada M, et al. Tolerability and Reactogenicity Profile of mRNA SARS-Cov-2 Vaccines from a Mass Vaccination Campaign in a Tertiary Hospital: Between-Vaccine and Between-Population Prospective Observational Study (VigilVacCOVID Study). Biodrugs. 2022;36(4):509-20.

Sattui SE, Liew JW, Kennedy K, Sirotich E, Putman M, Moni TT, et al. Early experience of COVID-19 vaccination in adults with systemic rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance Vaccine Survey. Rmd Open. 2021;7(3):e001814.

Seydoux 2020; To 2020). Reviews of the published literature indicate that most patients develop IgG seropositivity and nAb following primary infection with SARS-CoV-2 in > 91% and > 90% of cases, respectively. T-cell responses against the SARS-CoV-2 spike protein have been characterised and correlate well with immunoglobulin (Ig) G and IgA Ab titres in COVID-19 patients, which has important implications for vaccine design and long-term immune response (Botwin GJ, Li D, Figueiredo J, Cheng S, Braun J, McGovern DPB, et al. Adverse Events After

SARS-CoV-2 mRNA Vaccination Among Patients With Inflammatory Bowel Disease. Am J Gastroenterology. 2021;116(8):1746-51.

Braun 2020; Grifoni 2020; Watad A, Marco GD, Mahajna H, Druyan A, Eltity M, Hijazi N, et al. Immune-Mediated Disease Flares or New-Onset Disease in 27 Subjects Following mRNA/DNA SARS-CoV-2 Vaccination. Nato Adv Sci Inst Se. 2021;9(5):435.

Weiskopf 2020). In general, more people were tested positive for infection-induced SARS-CoV-2 antibodies in US and Europe by 2022, with the highest seroprevalence in the paediatric population (Clarke 2022; Castilla 2022; Kislaya 2023). During December 2021 to February 2022, the overall seroprevalence of infection-induced antibodies in US increased from 33.5% to 57.7%, with the highest seroprevalence in February 2022 among children under 12 years old (75.2%), followed by 74.2% in children aged 12-17 years, 63.7% in adults aged 18-49 years, 49.8% in adults aged 50-64 years, and 33.2% in adults aged ≥65 years (CDC 2023d). Similarly, during 26 April to 03 June 2022 the overall seroprevalence of infection-induced antibodies in Navarre, Spain was approximately 59% and decreased with advancing age, with the highest seroprevalence in children aged 5–17 years old (85%) (Castilla 2022). In Portugal, although the overall seroprevalence of infection-introduced antibodies was lower (27.3%) during 27 April to 08 June 2022, a steep increase (12—30%) in N IgG seroprevalence was also observed for all age groups from the last survey in October—December 2021 (Kislaya 2023).

Various studies indicate that most patients mount an immune response following a SARS-CoV-2 infection, but that this immunity may wane over time. More recent studies found that antibody titres peak between 3 to 4 weeks after infection and remain relatively stable up to 4 months after infection (Gudbjartsson 2020). Neutralizing activity also starts to decline after 1 to 3 months from symptom onset, as recently reported in a series of longitudinal studies on convalescent patients (Beaudoin-Bussières 2020; Lambert PH, Ambrosino DM, Andersen SR, Baric RS, Black SB, Chen RT, et al. Consensus summary report for CEPI/BC March 12-13, 2020 meeting: Assessment of risk of disease enhancement with COVID-19 vaccines. Vaccine. 2020;38(31):4783-91.

Lipkind HS, Vazquez-Benitez G, DeSilva M, Vesco KK, Ackerman-Banks C, Zhu J, et al. Receipt of COVID-19 Vaccine During Pregnancy and Preterm or Small-for-Gestational-Age at Birth - Eight Integrated Health Care Organizations, United States, December 15, 2020-July 22, 2021. Morbidity Mortal Wkly Rep. 2022;71(1):26-30.

Long 2020; Perreault 2020; Prévost 2020). The longevity of the Ab response to SARS-CoV-2 is still to be determined, but it is known that Ab levels to other CoVs wane over time (range: 12 to 52 weeks from the onset of symptoms) and homologous reinfections have been documented (Wolter N, Jassat W, Walaza S, Welch R, Moultrie H, Groome M, et al. Early assessment of the clinical severity of the SARS-CoV-2 omicron variant in South Africa: a data linkage study. Lancet. 2022 Jan 29;399(10323):437-446.

Wu 2007; Kellam 2020). Reinfection by SARS-CoV-2 under endemic conditions would likely occur with medians ranged from 16 to 22 months after peak antibody response through natural infection (Townsend 2021; Townsend 2022). Several observational studies report that at least two exposures to S protein, through vaccination and/or infection, provide a degree of protective immunity (Goldberg 2022; Andeweg 2022; Babouee Flury 2022; Hansen 2023; Chin 2022), but the protection against wanes with increasing since the last immunity-conferring event. A systematic review and meta-analysis of 65 studies from 19 different countries showed protection from re-infection from ancestral, alpha, and delta variants declined over time but remained at 78.6% (95% uncertainty interval [UI] 49.8–93.6) at 40 weeks, while protection against re-infection by the omicron BA.1 variant declined more rapidly and was estimated at 36.1% (24.4–51.3) at 40 weeks. On the other hand, protection against severe disease remained high for all variants, with 90.2% (95% UI 69.7–97.5) for ancestral, alpha, and delta variants, and 88.9% (84.7–90.9) for omicron BA.1 at 40 weeks (Team 2022). Most children and adolescents appear to have asymptomatic or non-severe symptomatic SARS-CoV-2 infections (Viner 2020; Forrest 2022). SARS-CoV-2-related death in children and adolescents is rare (Smith 2022). However, COVID-19 can lead to severe outcomes in children and adolescents (Marks 2022; Shi 2022; Preston 2021). For example, coinciding with increased circulation of the Omicron variant in US, COVID-19–associated hospitalisation rates among children and adolescents aged 0–17 years in late December 2021was about four times that of the Delta variant peak, yet the proportions of hospitalised children and adolescents requiring ICU admission (Delta = 27.8%; Omicron = 20.2%) or IMV (Delta = 6.3%; Omicron = 2.3%) were significantly lower during the Omicron period (Marks 2022). Most common chronic conditions associated with hospitalised paediatric patients are diabetes, gastrointestinal, neurological, cardiac, and pulmonary diseases, specifically asthma and obesity, but some of these conditions may not be necessarily causally associated with COVID-19 (Forrest 2022; Bailey 2021).

Multisystem inflammatory syndrome (MIS) is a rare but serious condition associated with COVID-19 in which different body parts become inflamed, including the heart, lungs, kidneys, brain, skin, eyes, or gastrointestinal organs. It can affect people who are younger than 21 years old (MIS-C) and adults 21 years and older (MIS-A) (CDC 2023e). The usual duration between acute infection and onset of MIS-C symptoms is two to 12 weeks (Dufort 2020; Ahmad 2021). In contrast to acute COVID-19 infection in children, MIS-C appears to be a condition of higher severity with 68% of cases having required critical care support (Radia 2021). MIS shares features with other paediatric inflammatory syndromes such as Kawasaki disease, toxic shock syndrome, and macrophage activation syndrome.

Post-acute sequelae of SARS-CoV-2 are characterised by a wide range of persistent symptoms such as fatigue, dyspnoea, chest pain, cognitive impairment, and sleeping disturbances that can last weeks, months or even years after infection (Davis 2023; Soriano 2022). Studies show that around 10-20% of people infected by SARS-CoV-2 may go on to develop symptoms that have been diagnosed as “long COVID” It is estimated that more than 17 million people across the WHO European Region may have experienced some form of post-COVID symptom persistence during the first two years of the pandemic (2020/21) (WHO 2023c). However, the exact numbers of those living with “long COVID” is uncertain, partly because of a lack of consensus of a case definition (Soriano 2022). A systematic review and meta-analysis by ECDC indicate that the risk of post COVID-19 condition may be higher amongst individuals who experience more severe COVID-19 disease (ECDC 2022). Current and future risks to populations for post COVID-19 condition in the context of increased levels of vaccination and hybrid immunity remain unknown.

Part II: Module SII – Nonclinical Part of the Safety Specification

Table 2 summarises the key nonclinical findings and their relevance to safety in humans. In summary, the nonclinical package, which consisted of both studies performed with elasomeran and with mRNA vaccines formulated in the same SM-102 lipid nanoparticle (LNP) vaccine matrix to support elasomeran use in human, shows no important identified or potential risks. A developmental and reproductive study with elasomeran in female Sprague-Dawley rats was completed in December 2020 with no adverse findings.

Table 2: Key Safety Findings From Nonclinical Studies and Relevance to Human Use

Study Type	Important Nonclinical Findings	Relevance to Human Use
Safety pharmacology and toxicology		
Vaccine enhanced disease and specific ERD studies	Several nonclinical studies (e.g., disease pathology, immunoprofiling) in several species have been generated to address the theoretical risk of disease enhancement with elasomeran. In summary, vaccination with elasomeran generated a balanced ratio of IgG1 to IgG2a in mice, indicating a Th2-biased response is not observed. Robust neutralizing antibodies were induced post-vaccination in mice, hamsters, and NHPs following vaccination with elasomeran, with the indication of a Th1 dominant T-cell profile in mouse and NHP models. T-cell response was not measured in hamsters. This strengthens the argument that disease enhancement similar to that observed with previous RSV and measles vaccines is unlikely to be observed. After challenge, viral load and levels of replicating virus were measured in both the nasal passages and lungs of mice, hamsters, and NHPs. In animals vaccinated with higher doses of elasomeran, complete protection was observed. In animals dosed with low levels of elasomeran, some level of protection was evident, with no indications of increased viral load, demonstrating that ERD is not occurring. In addition, lung histopathology analyses after viral challenge in mice, hamsters, and NHPs post-vaccination is also reassuring, as these animals did not have evidence of enhanced disease. See further description below in text.	These nonclinical results show a lack of vaccine-enhanced pulmonary pathology post - challenge with elasomeran in relevant animal species. In addition, the clinical Phase 3 mRNA-1273-P301 study was designed to assess the risk of enhanced disease through continuous unblinded monitoring of cases by the DSMB with prespecified rules for determining harm based on an imbalance in cases unfavourable to elasomeran as defined in the analysis plan. As a result of these assessments, no safety concerns have been identified.
Pharmacokinetics and Drug Metabolism		
Distribution Study	A biodistribution study was performed with mRNA-1647, an mRNA-based vaccine against human cytomegalovirus also formulated in SM-102-containing LNPs. As observed with other IM-delivered vaccines, the highest mRNA concentrations were	The biodistribution of mRNA-based vaccines formulated in LNPs is consistent with administration of IM drug products and distribution via the lymphatics. mRNA does not

Study Type	Important Nonclinical Findings	Relevance to Human Use
	observed at the injection site of the male rat followed by the proximal (popliteal) and distal (axillary) lymph nodes, consistent with distribution via the lymphatic system. These tissues, as well as spleen and eye, had tissue-to-plasma AUC ratios > 1.0. Overall, only a relatively small fraction of the administered mRNA-1647 dose distributed to distant tissues (ie, lung, liver, heart, kidney, axillary distal lymph nodes [bilateral pooled], proximal popliteal and inguinal lymph nodes [bilateral pooled], spleen, brain, stomach, testes, eye, bone marrow femur [bilateral pooled], jejunum [middle region], and injection site muscle), and the mRNA constructs did not persist past 1 to 3 days in tissues other than the injection site, lymph nodes, and spleen where it persisted in general 5 days.	persist past 1 to 3 days in tissues other than the injection site, lymph nodes, and spleen where it persisted in general 5 days.
Repeat-dose toxicity studies		
Evaluation of mRNA vaccines formulated in the same SM-102 LNP vaccine matrix) in rat administered IM at doses ranging from 9 to 150 µg/dose once every 2 weeks for up to 6 weeks.	Clinical observations included generally dose-dependent erythema and edema at the injection site and transient increases in body temperature at 6 hours postdose returning to baseline 24 hours postdose were observed at ≥ 9 µg/dose. These observations resolved or were considered resolving within 72 hrs. There were clinical chemistry and hematology changes consistent with inflammatory responses (ie, increases in white blood cells, neutrophils, eosinophils, and decreased lymphocytes); minimal coagulation changes consisting of a slightly increased activated partial thromboplastin time and an associated increase in fibrinogen were observed. Clinical chemistry results indicated a decrease in albumin, increase in globulin, and a corresponding decrease in albumin/globulin ratio. In general, clinical pathology changes were dose-dependent and transient. Consistent with other indicators of systemic inflammation in response to vaccine administration, transient cytokine increases were observed at ≥ 9 µg/dose at 6 hours postdose including interferon gamma, monocyte chemoattractant protein-1, and macrophage inflammatory protein 1alpha. Increased cytokine/chemokines were generally resolved by the end of the 2-week recovery period. Macroscopic and microscopic changes were observed and included skin thickening at the	Review of the toxicology data found evidence of dose-dependent treatment-related effects at the injection site and systemic inflammatory responses to administration to the LNP. Clinical findings such as increased body temperature, injection site pain, other inflammation related findings In ongoing clinical Phase 1 and 2a studies with elasomeran, evaluation of safety clinical laboratory values of Grade 2 or higher revealed no patterns of concern. In the clinical Phase 3 mRNA-1273-P301 study, solicited local and systemic adverse reactions in the 7 days following administration, increased following the second dose. Solicited local adverse reactions, primarily injection site pain, were common.

Study Type	Important Nonclinical Findings	Relevance to Human Use
	injection site and enlarged lymph nodes. These observations were correlated with microscopic changes that included mixed cell inflammation at the injection site; increased cellularity and mixed cell inflammation in the lymph nodes. Additionally, decreased cellularity in the splenic periarteriolar lymphoid sheath; increased myeloid cellularity in the bone marrow; and hepatocyte vacuolation and Kupffer cell hypertrophy was occasionally observed in the liver. Changes were generally reversing by the end of the 2-week recovery period.	
Other Nonclinical Toxicology Studies		
Evaluation of elasomeran at repeat doses, non-GLP immunogenicity rat study with non-terminal endpoints	Elasomeran-related clinical signs were consistent with previous GLP toxicology studies on other mRNA-based vaccines. At doses ≥30 ug/dose observations included transient dose-dependent injection site edema with or without hindlimb impairment were observed at approximately 24 hours postdose and generally resolved within 7 days after dose administration. Clinical pathology associated with inflammation were observed and included increased neutrophils, eosinophils, and/or globulin. Other mild elasomeran-related changes observed at 30, 60, and/or 100 µg/dose consisted of decreased red cell mass, reticulocytes, and lymphocytes and increased creatinine, triglyceride, cholesterol, and/or glucose. In general, these changes are consistent with the results from the previous GLP rat toxicity studies conducted with other mRNAs formulated in the SM-102 LNP.	
Reproductive/development	A developmental and reproductive toxicity study was performed with elasomeran in female Sprague-Dawley rats in December 2020 with no adverse findings noted. Elasomeran was at the clinical dose of 100 µg/dose. There were no maternal effects on mating and fertility, ovarian/uterine examinations, natural delivery or litter assessments. Further, there were no fetal and/or pup effects on in-life parameters, gross pathology, fetal sex, external or visceral assessments, or skeletal malformations. Non-adverse, common skeletal variations consisting of wavy ribs and increase nodules were observed at 100 µg/dose. The no observed adverse effect level is 100 µg, which on a mg/kg basis, provides a 137-fold safety	The risk for adverse pregnancy outcomes after exposure is unknown in humans, but nonclinical findings do not suggest a specific risk. Pregnancy is an exclusion criterion in the ongoing clinical trials.

Study Type	Important Nonclinical Findings	Relevance to Human Use
	margin to 60-kg woman.	
Genotoxicity	SM-102, the novel lipid used in the elasomeran LNP formulation, was evaluated in as an individual agent in a bacterial reverse mutation (Ames) test and an in vitro micronucleus test in human peripheral blood lymphocytes. The results for SM-102 were negative. In addition, in vivo genotoxicity risk was assessed in a GLP-compliant rat micronucleus test using an mRNA-based vaccine formulated in SM-102-containing LNPs (mRNA-1706), the same formulation as elasomeran. SM-102 induced a minimal, statistically significant increases in MIEs in male rats at both 24 and 48 hours and in female rats at 48 hours only; however, there was no clear dose response, and the increases were generally weak and associated with minimal bone marrow toxicity. A second, non-GLP, in vivo genotoxicity study was conducted using NPI luciferase mRNA in SM-102 containing LNPs. In this study, there was no significant increase in the incidence of micronuclei. The results of these two studies led to an equivocal result. Given the observed increases in body temperature observed in toxicology studies it is likely that drove the slight increases observed in micronuclei formation at high systemic (intravenous) doses. Overall, the genotoxic risk to humans is considered to be low due to minimal systemic exposure following IM administration, limited duration of exposure, and negative in vitro results.	Nonclinical findings suggest that the risk to humans after IM administration is low, due to minimal systemic exposure and negative in vitro results.
Carcinogenicity	No carcinogenicity studies have been performed with elasomeran.	N/A

CMV = cytomegalovirus; DSMB = data safety monitoring board; ERD = enhanced respiratory disease; GLP = Good Laboratory Practice; IgG = immunoglobulin G; IM = intramuscular; LNP = lipid nanoparticle; MIE = micronucleated immature erythrocytes; NHP = nonhuman primate; NPI = nascent peptide imaging; RSV = respiratory syncytial virus; Th = T-helper.

Vaccine-associated Disease Enhancement

There was a theoretical concern over the potential for vaccine associated disease enhancement in recipients of SARS-CoV-2 vaccines. The concern was that a SARS-CoV-2 vaccine could theoretically cause enhanced disease and specifically enhanced respiratory disease (ERD) in vaccines that were subsequently exposed to wild-type SARS-CoV-2. The potential for vaccination against SARS-CoV-2 to be associated with disease enhancement was a theoretical concern, given similar observations with other respiratory viruses in general, and in animal models of some highly pathogenic CoVs. This concern has been triggered by preclinical work on SARS-CoV and MERS-CoV vaccines (

Czub 2005; Davis HE, McCorkell L, Vogel JM, Topol EJ. Long COVID: major findings, mechanisms and recommendations. Nat Rev Microbiol. 2023 Mar;21(3):133-146.

DeBiasi RL, Delaney M. Symptomatic and Asymptomatic Viral Shedding in Pediatric Patients Infected With Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2): Under the Surface. JAMA Pediatr. 2021 Jan 1;175(1):16-18.

Deming 2006; Bolles 2011), the experience with feline infectious peritonitis virus and vaccines in cats (Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV; WHO Clinical Case Definition Working Group on Post-COVID-19 Condition. A clinical case definition of post-COVID-19 condition by a Delphi consensus. Lancet Infect Dis. 2022 Apr;22(4):e102-e107.

Takano 2008; Pedersen 2009; Pedersen 2012), and enhanced disease seen with respiratory syncytial virus, measles (Kharbanda EO, Haapala J, DeSilva M, Vazquez-Benitez G, Vesco KK, Naleway AL, et al. Spontaneous Abortion following COVID-19 Vaccination during Pregnancy. Jama. 2021;326(16):1629-31.

Kim 1969; Polack 2007), and dengue vaccines in humans (Smatti 2018). Importantly, vaccine-associated disease enhancement has not been seen following SARS or MERS vaccines given to humans, albeit the number of people who received these experimental vaccines remains very small.

These events were associated either with macrophage-tropic CoVs susceptible to Ab-dependent enhancement of replication or with vaccine antigens that induced Ab with poor neutralizing activity and Th2-biased responses. The Vaccine Research Center of the NIH and the Sponsor performed nonclinical studies in mice, hamsters, and nonhuman primates (NHPs) to evaluate dose-ranging responses to elasomeran (immunogenicity), high-dose virus SARS-CoV-2 challenge (protection), and to address the theoretical concern of ERD mediated by vaccine-induced Ab responses and/or T helper (Th) 2 directed T-cell responses observed with other vaccines against viral respiratory diseases. These studies demonstrated that elasomeran is immunogenic in all species assessed, showing a dose-dependent response in IgG binding Ab titres and a significant correlation between bAb and nAb activity. In addition, antigen-specific T-cell responses were observed in studies in mice and in the NHP study. Th1-directed CD4+ and CD8+ T-cell responses were measured post boost in animals that were vaccinated with elasomeran. Direct measurement of Th1-directed responses in mice and NHPs, indirect measurement of IgG 2a/c/IgG1 Ab subclasses in mice, and the high levels of nAb in all species lessens concerns regarding disease enhancement associated with administration of elasomeran.

In addition to measurements of the immune response, mice, NHPs, and hamsters were challenged with high-dose SARS-CoV-2 virus. In these studies, dose levels of elasomeran that were predicted to be optimal (fully protective) and suboptimal (subprotective) were included. At higher doses, mice and NHPs were fully protected from viral replication in both lungs and nasal passages. At subprotective dose levels, animals either remained fully protected in the lungs or had reduced viral burden post-challenge versus control animals. There were no observations of increased viral load in vaccinated animals at protective or subprotective dose levels, which further supports that elasomeran does not drive enhanced disease. Lung histopathology assessments were performed to verify reduction of inflammation, immune complex deposition, and immune cell invasion in response to viral challenge in vaccinated animals versus placebo animals. In animals vaccinated with both optimal and suboptimal dose levels, histopathological evaluation of the lungs of mice and NHPs confirms the lack of ERD. This was demonstrated by the presence of minimal inflammation and lack of significant neutrophilic-associated alveolar disease or eosinophil-dominant inflammatory response measured, which have historically been associated with vaccine-associated ERD. In contrast, moderate to severe inflammation was elicited by SARS-CoV-2 infection in phosphate-buffered saline control animal groups, which often involved the small airways and the adjacent alveolar interstitial (Clarke KEN, Jones JM, Deng Y, Nycz E, Lee A, Iachan R, et al. Seroprevalence of Infection-Induced SARS-CoV-2 Antibodies - United States, September 2021-February 2022. MMWR Morb Mortal Wkly Rep. 2022 Apr 29;71(17):606-608.

Corbett 2020). These nonclinical disease pathology and immune profiling studies show immune signatures not predicted to associate with ERD and a lack of vaccine-enhanced viral replication or pulmonary pathology after challenge with SARS-CoV-2 in relevant animal species.

To further address the risk of enhanced disease, peripheral blood mononuclear cells were obtained from study participants in the Phase 1 study and restimulated to assess the cytokine profile post vaccination. The intracellular cytokine profile of the CD4+ and CD8+ T cells reflected a Th1- rather than a Th2-directed response (Jackson 2020). These results were reassuring since the risk of enhanced disease has been previously associated with a Th2-directed immune response. In Study mRNA-1273-P301, prespecified harm rules designed to detect an imbalance in cases of COVID-19 or severe COVID-19 were not met. Most importantly, after a median follow-up of 2 months after the second dose of vaccine, the majority of COVID-19 cases occurred in participants who received placebo rather than elasomeran (Baden 2021), confirming no clinical evidence for vaccine enhanced disease following vaccination with elasomeran.

A conclusion of safety concerns for elasomeran based on nonclinical data is summarised in Table 3.

Table 3: Conclusions on Safety Concerns Based on Nonclinical Data

Safety Concerns
Important identified risks: Not applicable
Important identified risks: Not applicable
Missing information: Not applicable

Part II: Module SIII – Clinical Trial Exposure

Six clinical trials of elasomeran are ongoing and three clinical trials are completed as reported below. Two of the studies were sponsored by DMID of NIAID and include a dose-ranging Phase 1 safety and immunogenicity study 20-0003 (Phase 1 mRNA-1273-P101) and 21-0002 to evaluate safety and immunogenicity of a SARS-CoV-2 variant mRNA1273.351 in naive and previously vaccinated adults. Study 20-0003 is completed. The second completed study is a dose-confirming Phase 2a safety and immunogenicity study (mRNA-1273-P201). The third completed study is the pivotal Phase 3 efficacy, safety, and immunogenicity study mRNA-1273-P301.

The remaining five ongoing studies are a Phase 2/3 safety, reactogenicity, and efficacy study in healthy adolescents ages 12 to < 18 years including an evaluation of the immunogenicity and safety of elasomeran booster and bivalent mRNA-1273.222 vaccine given as 2 primary doses (mRNA-1273-P203); a Phase 2/3, two-part, dose-escalation (open-label), age de-escalation and randomized, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of elasomeran SARS-CoV-2 vaccine in healthy children 6 months to less than 12 years of age including an evaluation of the immunogenicity and safety of elasomeran booster (mRNA-1273-P204); a Phase 3b, open-label, safety and immunogenicity study of SARS-CoV-2 elasomeran vaccine in adult solid organ transplant recipients and healthy controls (mRNA-1273-P304); a Phase 2/3 8-part open-label study to evaluate the immunogenicity and safety of mRNA vaccine boosters for SARS-CoV-2 variants (mRNA-1273-P205); and a Phase 3, open-label, safety and immunogenicity 2-part study of mRNA-1273.214 vaccine in healthy children 6 months to less than 6 years of age (mRNA-1273-P306).

Table 4: Summary of vaccination groups by dose (µg) in the ongoing studies P203 (Part 1A, Part 1B and Part 1C), and P204 (Part 1, Part 2, and Part Booster Dose), and completed studies P301 (Part A), P201 (Part A) and (P101) 20-0003

Study	Dose					
	10 µg	25 µg	50 µg	100 µg	250 µg	Total
20-0003 (Phase 1 P101)	0	35	35	35	15	120
P201 Part A (Phase 2a)	0	0	200	200	0	400
P301 Part A (Phase 3)	0	0	0	15184	0	15184
P203 Parts 1A and 1B (Phase 2/3)	0	0	0	2486	0	2486
P203 Part 1C (Phase 2/3)	0	0	1405	0	0	1405
P204 Part 1 (Phase 2/3)[1]	0	219	535	371	0	1125
P204 Part 2 (Phase 2/3)[1]	0	5024	3007	0	0	8031
P204 Booster Dose (Phase 2/3)[1]	145	1294	0	0	0	1439

Note: Does not include DMID NIAID sponsored phase 1 study 21-0002 a Phase 1 open label study to evaluate safety and immunogenicity of prototypes and modified SARS-CoV-2 vaccines in naïve and previously vaccinated adults and mRNA-1273-P204

[1]Includes children 6 months to < 12 years of age

Source:

Tables 2A-2C in Safety Summary Report Protocol 20-0003: Phase I, Open-Label, Dose-Ranging Study of the Safety and Immunogenicity of 2019-nCoV Vaccine (elasomeran) in Healthy Adults 26 October 2020; mRNA-1273-P201 (Part A) study Table 14.1.6.1 (Data extraction date: 11 June 2021); mRNA-1273-P203 study Table 14.1.6.1.4.2 (Data cutoff date: 31 Jan 2022) and Table 14.1.1.1.5 (Data cutoff date: 15 August 2022); mRNA-1273-P301 (Part A) study Table 14.1.6.2.1 (Data extraction date: 04 May 2021); mRNA-1273-P204 study Part 1 Table 14.1.5.1 and

Part 2 Table 14.1.5.2 (Data cutoff date: 07 September 2022), and Booster Dose Table 14.1.6.5.1 (Data extraction date: 23 May 2022) and Table 14.1.6.1 (Data extraction date: 18 August 2022).

Table 5: Summary of Vaccination groups by dose (µg) in the ongoing open label studies P304, P205 (Part A, Part G, Part F Cohort 2, Part H 2nd Booster, and Part J 3rd Booster), P306 (Part 1 and Part 2), and completed studies P301 (Part B and Part C Booster) and P201 (Part B)

Study	Dose				
	10 µg	25 µg	50 µg	100 µg	Total
P201 Part B	0	0	173	171	344
P301 Part B (Phase 3)	0	0	0	12649	12649
P301 Part C Booster Dose (Phase 3)	0	0	19609	0	19609
P304	0	0	0	214	214
P205 Part A (Phase 2/3)[1]	0	0	300	595	895
P205 Part G (Phase 2/3)[2]	0	0	437	0	437
P205 Part F Cohort 2 (Phase 2/3)[3]	0	0	377	0	377
P205 Part H 2nd booster (Phase 2/3)[4]	0	0	511	0	511
P205 Part J 3rd booster (Phase 2/3)[5]	0	0	101	0	101
P306 Part 1	0	179	0	0	179
P306 Part 2	539	0	0	0	539

Note:
1 Part A includes mRNA-1273.211
2 Part G includes mRNA-1273.214
3 Part F includes Cohort 2 - mRNA-1273
4 Part H includes mRNA-1273.222.
5 Part J includes 50 adults were treated with 50 µg mRNA-1273.815 and 51 adults treated with 50 µg mRNA-1273.213
Source:
mRNA-1273-P201 (Part B) study Table 14.1.1.1 (Data extraction date 23 November 2021); mRNA-1273-P304 study (Data extraction date: 22 November 2022); mRNA-1273-P301 (Part B) study CSR Addendum 3 Table 14.1.1.1.5.5 and Table 14.1.2.1.1.2 (Data extraction date: 07 April 2023); mRNA-1273-P301 (Part C) study CSR Addendum 3 Table 14.1.2.1.3 (Data extraction date: 07 April 2023); mRNA-1273-P205 study Part A Table 14.1.3.1 (Data extraction date: 02 February 2022); mRNA-1273-P205 study Part G/Part F (Cohort 2) Table 14.1.1.1.8 (Data extraction date: 27 April 2022); mRNA-1273-P205 Part H Table 14.1.6.1.9 (Data extraction date: 23 Sept 2022) mRNA-1273-P205 Part J Table 14.1.6.1.10 (Data extraction date: 16 May 2023); mRNA-1273-P306 study Part 1 Table 14.1.3.2.1 (Data extraction date: 05 December 2022) and Part 2 Table 14.1.3.2.2 (Data extraction date: 05 December 2022).

Study 20-0003 (Phase 1)

The open-label dose-finding Phase 1 safety and immunogenicity study (NCT04283461) enrolled 120 healthy adults 18 years of age and older to receive either 25 µg, 50 µg, 100 µg, or 250 µg of elasomeran. Participants received 2 doses of elasomeran given intramuscularly (IM) 28 days apart and were followed up until Day 394. Participants in the trial were offered the option to participate in a substudy in which they would receive a third elasomeran vaccination, administered via an IM injection at a dosage of 100 µg/0.5 mL, given 6 to 12 months after receipt of their second vaccination in the main study. Substudy participants were followed for safety, reactogenicity, and immunogenicity endpoints through 12 months post third vaccination (Substudy Day 366). The study is completed.

Table 6: Participant Exposure by Gender in the Completed 20-0003 Study

Gender	Males	Females	Total
Number of participants	61	59	120

Source: Tables 2A-2C in Safety Summary Report Protocol 20-0003: Phase I, Open-Label, Dose-Ranging Study of the Safety and Immunogenicity of 2019-nCoV Vaccine (elasomeran) in Healthy Adults 26 October 2020.

Table 7: Participant Exposure by Age in the Completed 20-0003 Study

Age (years old)	18-55	56-70	≥ 71	Total
Number of participants	60	30	30	120

Source: Tables 2A-2C in Safety Summary Report Protocol 20-0003: Phase I, Open-Label, Dose-Ranging Study of the Safety and Immunogenicity of 2019-nCoV Vaccine (elasomeran) in Healthy Adults 26 October 2020.

Table 8: Participant Exposure by Race/Ethnic Group in the Completed 20-0003 Study

Race/Ethnicity	Participants (n)
American Indian or Alaska Native	1
Asian	5
Native Hawaiian or Other Pacific Islander	0
Black	3
White	109
Multiracial	1
Unknown	1
Total	120

Source: Tables 2A-2C in Safety Summary Report Protocol 20-0003: Phase I, Open-Label, Dose-Ranging Study of the Safety and Immunogenicity of 2019-nCoV Vaccine (elasomeran) in Healthy Adults 26 October 2020.

Table 9: Summary of Vaccination Groups by Dose, Age Category, and Gender in the Completed 20-0003 Study

Elasomeran dose	25 µg	50 µg	100 µg	250 µg
All participants 18-55 years of age	15 (9 males; 6 females)	15 (9 males, 6 females)	15 (7 males, 8 females)	15 (6 males, 9 females)
All participants 56-70 years of age	10 (3 males, 7 females)	10 (5 males, 5 females)	10 (5 males, 5 females)	0
All participants ≥71 years of age	10 (8 males, 2 females)	10 (6 males, 4 females)	10 (3 males, 7 females)	0

Source: Tables 2A-2C in Safety Summary Report Protocol 20-0003: Phase I, Open-Label, Dose-Ranging Study of the Safety and Immunogenicity of 2019-nCoV Vaccine (elasomeran) in Healthy Adults 26 October 2020.

As of 17 Mar 2021, in study 20-0003 the subjects in Cohorts 1 through 5,7,8 and 10 through 12 have completed Study Milestones Day 209 (±7 days) visit (6 months after second vaccination).

mRNA-1273-P201 (Phase 2a)

The mRNA-1273-P201 is a completed three-part, Phase 2a study: Part A, Part B, and Part C. Part A is a randomized, placebo-controlled dose-confirming Phase 2a safety and immunogenicity study (NCT04405076) that enrolled 600 healthy adults 18 years of age and older in the US. Study participants were randomized 1:1:1 to receive placebo, elasomeran 50 µg, or elasomeran 100 µg. The study is divided into 2 cohorts by age, Cohort 1 with 300 participants (≥ 18 to < 55 years old) and Cohort 2 with 300 participants (≥ 55 years old). Participants received 2 doses of elasomeran or placebo given IM 28 days apart and were followed up until Day 394. Part A, blinded Phase comprised a Participant Decision Clinic Visit (initiation of Part B) or Day 394 (Month 13), whichever was earlier.

Part B was designed to offer participants who received placebo in Part A of this study the option to receive 2 injections of open label elasomeran. Participants who received 1 or 2 doses of 50 µg or 100 µg elasomeran in Part A were offered a single booster dose of elasomeran (50 µg) in Part B.

Part C was a proof-of-concept rollover study of approximately 60 participants who were enrolled in Moderna's Phase 3 mRNA-1273-P301 study, have already been unblinded, and have previously received 2 doses of elasomeran at least 6 months earlier. Upon enrolment into Part C of this study, they received a single IM injection of mRNA-1273.351 (20 µg or 50 µg) or elasomeran/mRNA-1273.351 mixture (50 µg total) at least 6 months after receiving the second vaccination in the mRNA-1273-P301 study.

Table 10: Duration of Exposure in the Completed mRNA-1273-P201 Study (Part A)

Duration of Exposure	Dose		
	Elasomeran 50 µg	**Elasomeran 100 µg**	**Total**
Number of Participants, n (%)	200 (100)	200 (100)	400 (100)
Received First Injection	200 (100)	200 (100)	400 (100)
Received Second Injection	195 (97.5)	198 (99.0)	393 (98.3)
≥ 49 Days Since First Injection	197 (98.5)	200 (100)	397 (99.3)
≥ 56 Days Since First Injection	197 (98.5)	200 (100)	397 (99.3)
≥ 28 Days Since Second Injection	195 (97.5)	198 (99.0)	393 (98.3)
< 28 Days Since Second Injection	0	0	0
≥ 28 and < 56 Days Since Second Injection	2 (1.0)	0	2 (0.5)
≥ 56 Days Since Second Injection	193 (96.5)	198 (99.0)	391 (97.8)
Study Duration from First Injection (Days)			
Mean (Standard Deviation)	242.4 (38.38)	245.1 (28.30)	243.8 (33.7)
Median	245.0	246.0	245.0
Quartile 1, Quartile 3	229.0, 259.5	228.5, 260.0	229.0, 260.0
Minimum, Maximum	30, 346	58, 360	30, 360

Source: mRNA-1273-P201 Table 14.1.6.1 (Data extraction date: 11 June 2021).

Table 11: Age Group and Gender in the Completed mRNA-1273-P201 Study (Part A)

Age Group, N	Dose		
	Elasomeran 50 µg	**Elasomeran 100 µg**	**Total**
Adult, 18 – 64 years	150	157	307
Elderly, 65-74 years	42	37	79
Elderly, 75-84 years	6	5	11
Elderly, 85 + years	2	1	3
Gender			
Male	63	76	139
Female	137	124	261

Source: mRNA-1273-P201 Tables 14.1.6.2.1 and 14.1.6.2.3 (Data extraction date: 11 June 2021).

Table 12: Participant Race in the Completed mRNA-1273-P201 Study (Part A)

Race, N	Dose		
	Elasomeran 50 µg	**Elasomeran 100 µg**	**Total (N)**
White	188	188	376
Black or African American	5	8	13
Asian	2	2	4
American Indian or Alaska Native	2	1	3
Native Hawaiian or Other Pacific Islander	1	0	1
Multiple	1	0	1
Other	1	1	2

Source: mRNA-1273-P201 Table 14.1.6.2.4 and Table 14.1.6.1 (Data extraction date: 11 June 2021).

Table 13: Participant Ethnicity in the Completed mRNA-1273-P201 Study (Part A)

Ethnicity	Dose		
	Elasomeran 50 µg	**Elasomeran 100 µg**	**Total (N)**
Hispanic or Latino	15	16	31
Not Hispanic or Latino	184	184	368
Not Reported	1	0	1

Source: mRNA-1273-P201 Table 14.1.6.2.5 and Table 14.1.6.2.1 (Data extraction date: 11 June 2021).

Table 14: Participants in the Completed mRNA-1273-P201 Open label Study (Part B)

Number of Participants (N)	Elasomeran Dose	
	50 ug (N= 200) n (%)	100 ug (N=200) n (%)
Received First Open-Label Injection	173 (86.5)	171 (8)
Received second Open-Label Injection	0	0

Source: mRNA-1273-P201 (Part B) Table 14.1.1.1 (Data extraction date 23 November 2021).

Table 15: Participant Age Group in the Completed mRNA-1273-P201 Study (Part B)

Age group, N	Elasomeran Booster Dose	
	50 ug (N= 173)	100 ug (N= 171)
Age ≥ 18 years and age < 55 years	80	82
Age ≥ 55 years	93	89

Source: mRNA-1273-P201 (Part B) Table 14.1.1.1 (Data extraction date 23 November 2021).

Table 16: Participant Gender in the Completed mRNA-1273-P201 Study (Part B)

Gender, N	Elasomeran Booster Dose	
	50 ug (N= 173)	100 ug (N= 171)
Male	49	67
Female	124	104

Source: mRNA-1273-P201 Part B Table 14.1.3.7.1 (Data extraction date 23 November 2021).

Table 17: Participant Race in the Completed mRNA-1273-P201 Study (Part B)

Race, n (%)	Elasomeran Booster Dose	
	50 ug (N= 173)	100 ug (N=171)
White	164 (94.8)	164 (95.9)
Black or African American	3 (1.7)	5 (2.9)
Asian	2 (1.2)	1 (0.6)
American Indian or Alaska Native	1 (0.6)	1 (0.6)
Native Hawaiian or Other Pacific Islander	1 (0.6)	0
Multiracial	1 (0.6)	0
Other	1 (0.6)	0

Source: mRNA-1273-P201 Part B Table 14.1.3.7.1 (Extraction Date: 23 November 2021).

Table 18: Participant Ethnicity in the Completed mRNA-1273-P201 Study (Part B)

	Elasomeran Booster Dose	
Ethnicity, n (%)	**50 ug (N= 173)**	**100 ug (N=171)**
Hispanic or Latino	10 (5.8)	10 (5.8)
Not Hispanic or Latino	162 (93.6)	161 (94.2)
Not Reported	1 (0.6)	0

Source: mRNA-1273-P201 Part B Table 14.1.3.7.1 (Extraction Date: 23 November 2021).

A total of 60 participants who received 2 primary doses of elasomeran (100 µg) in mRNA-1273-P301 were selected to enter the mRNA-1273 variant booster phase (Part C) of the mRNA-1273-P201 study and assigned to study treatment: 20 participants to the 50 µg mRNA-1273.351 group (Cohort 1), 20 participants to the 50 µg elasomeran/mRNA-1273.351 group (Cohort 2), and 20 participants to the 20 µg mRNA-1273.351 group (Cohort 3) (Table 19 to Table 22).

Table 19: Participants in the Completed mRNA-1273-P201 Open label Study (Part C)

Number of Participants (N)	**mRNA-1273.351 50 µg (Cohort 1) (N=20) n (%)**	**Elasomeran/ mRNA-1273.351 50 µg (Cohort 2) (N=20) n (%)**	**mRNA-1273.351 20 µg (Cohort 3) (N=20) n (%)**
Received booster dose	20 (100)	20 (100)	20 (100)

Source: mRNA-1273-P201 Part C Table 14.1.1.1.2 (Extraction Date: 23 November 2021).

Table 20: Participant Age and Gender in the Completed mRNA-1273-P201 Study (Part C)

Age at Enrollment of mRNA-1273-P301 Study (Years)	**mRNA-1273.351 50 µg (Cohort 1) (N=20)**	**Elasomeran/ mRNA-1273.351 50 µg (Cohort 2) (N=20)**	**mRNA-1273.351 20 µg (Cohort 3) (N=20)**
Mean (SD)	53.9 (12.65)	55.6 (14.78)	47.5 (13.20)
Median	56.5	54.5	50.0
Min, Max	27, 70	28, 79	26, 67
Gender, n (%)			
Male	11 (55.0)	12 (60.0)	5 (25.0)
Female	9 (45.0)	8 (40.0)	15 (75.0)

Abbreviations: max = maximum; min = minimum; SD = standard deviation.
Source: mRNA-1273-P201 Part C Table 14.1.3.12 (Extraction Date: 23 November 2021).

Table 21: Participant Race in the Completed mRNA-1273-P201 Study (Part C)

Race, n (%)	mRNA-1273.351 50 µg (Cohort 1) (N=20)	Elasomeran/ mRNA-1273.351 50 µg (Cohort 2) (N=20)	mRNA-1273.351 20 µg (Cohort 3) (N=20)
White	19 (95.0)	19 (95.0)	20 (100)
Black or African American	0	0	0
Asian	1 (5.0)	0	0
American Indian or Alaska Native	0	1 (5.0)	0
Native Hawaiian or Other Pacific Islander	0	0	0
Multiracial	0	0	0
Other	0	0	0
Not Reported	0	0	0
Unknown	0	0	0

Source: mRNA-1273-P201 Part C Table 14.1.3.12 (Extraction Date: 23 November 2021).

Table 22: Participant Ethnicity in the Completed mRNA-1273-P201 Study (Part C)

Ethnicity, n (%)	mRNA-1273.351 50 µg (Cohort 1) (N=20)	Elasomeran/ mRNA-1273.351 50 µg (Cohort 2) (N=20)	mRNA-1273.351 20 µg (Cohort 3) (N=20)
Hispanic or Latino	0	1 (5.0)	1 (5.0)
Not Hispanic or Latino	20 (100)	19 (95.0)	19 (95.0)
Not Reported	0	0	0
Unknown	0	0	0

Source: mRNA-1273-P201 Part C Table 14.1.3.12 (Extraction Date: 23 November 2021).

mRNA-1273-P203 (Phase 2/3)

Part 1 of Phase 2/3 study (mRNA-1273-P203) is a 3-part (Part A, Part B and Part C) study of the safety, reactogenicity, and efficacy of elasomeran in healthy adolescents ages 12 to < 18 years. Part 1A is a randomized, observer-blind, placebo-controlled study of adolescents randomly assigned 2:1 to receive either 2 injections of 100 µg of elasomeran vaccine or 2 injections of placebo control each given 28 days apart. Part 1B is an open-label observational phase designed to offer participants who received placebo in Part 1A of the study and who meet the EUA eligibility criteria an option to request and receive elasomeran. The study enrolled a total of 2486 participants who received elasomeran vaccine. In Part 1C, all study participants were offered elasomeran as a 50 µg booster and a total of 1346 participants 12 years to < 18 years of age who completed the 100 µg elasomeran primary series received a 50 µg elasomeran booster dose. In Part 1C2, adolescents 12-17 years of age who completed non-Moderna primary COVID-19 vaccination series under EUA (i.e., Pfizer) were enrolled and received a 50 µg elasomeran booster.

Part 2 of mRNA-1273-P203 is an open-label design. The study will evaluate the safety, reactogenicity, and effectiveness of a 50 µg primary series of mRNA-1273 SARS CoV 2 vaccine in healthy adolescents 12 to < 18 years of age. Part 3 (open-label, single-arm design) will evaluate the safety, reactogenicity, and effectiveness of a 2-dose 50 µg primary series of mRNA-1273.222 SARS-CoV-2 vaccine, administered 6 months apart, in approximately 500 healthy adolescents 12 to <18 years of age.

Table 23: Duration of Exposure in Parts 1A and 1B of the Ongoing mRNA-1273-P203 Study (12 Years to < 18 Years)

Duration of Exposure, n (%)	Elasomeran (N=2486)
Received First Injection	2486 (100)
Received Second Injection	2480 (99.8)
≥ 7 Days Since First Injection	2486 (100)
≥ 35 Days Since First Injection	2480 (99.8)
≥ 56 Days Since First Injection	2460 (99.0)
≥ 7 Days Since Second Injection	2474 (99.5)
≥ 28 Days Since Second Injection	2457 (98.8)
≥ 56 Days Since Second Injection	2439 (98.1)
≥ 84 Days Since Second Injection	2420 (97.3)
≥ 112 Days Since Second Injection	2406 (96.8)
≥ 140 Days Since Second Injection	2398 (96.5)
≥ 168 Days Since Second Injection	2378 (95.7)
≥ 196 Days Since Second Injection	2342 (94.2)
≥ 224 Days Since Second Injection	2302(92.6)
≥ 252 Days Since Second Injection	2269 (91.3)
≥ 280 Days Since Second Injection	2197 (88.4)
≥ 308 Days Since Second Injection	1397 (56.2)
≥ 336 Days Since Second Injection	338 (13.6)
≥ 364 Days Since Second Injection	31 (1.2)
Study Duration from First Injection (Days)	
Mean (Standard Deviation)	330.4 (56.85)
Median	342.0
Quartile 1, Quartile 3	326.0, 356.0
Minimum, Maximum	30, 419

Source: mRNA-1273-P203 Table 14.1.6.1.4.2 (31 Jan 2022).

Table 24: Age Group and Gender in Parts 1A and 1B of the Ongoing mRNA-1273-P203 Study (12 Years to < 18 Years)

Characteristic	Elasomeran (N=2486)
Age Group, N	
≥ 12 years and < 16 years	1839
≥ 16 years and < 18 years	647
Gender, N	
Male	1283
Female	1203
Total	**2486**

Source: mRNA-1273-P203 Table 14.1.3.13.1 (31 Jan 2022).

Table 25: Participant Race in Parts 1A and 1B of the Ongoing mRNA-1273-P203 Study (12 Years to < 18 Years)

Characteristic	Elasomeran (N=2486)
Race, N	
White	2084
Black or African American	83
Asian	142
American Indian or Alaska Native	12
Native Hawaiian or Other Pacific Islander	3
Multiple	118
Other	27
Not Reported	11
Unknown	6
Total	**2486**

Source: mRNA-1273-P203 Table 14.1.3.13.1 (31 Jan 2022).

Table 26: Participant Ethnicity in Parts 1A and 1B of the Ongoing mRNA-1273-P203 Study (12 Years to < 18 Years)

Characteristic	Elasomeran (N=2486)
Ethnicity, N	
Hispanic or Latino	280
Not Hispanic or Latino	2186
Not Reported	19
Unknown	1
Total	**2486**

Source: mRNA-1273-P203 Table 14.1.3.13.1 (31 Jan 2022).

Table 27: Duration of Exposure in the Ongoing mRNA-1273-P203 Study (Part 1C, Booster Dose) (12 Years to < 18 Years)

Duration of Exposure, n (%)	Placebo-elasomeran-Booster (N=49)	Elasomeran-Booster (N=1356)	Total (N=1405)
Received Booster	49 (100)	1356 (100)	1405 (100)
< 168 Days Since Primary Series Dose 2 to Booster	16 (32.7)	0	16 (1.1)
≥ 168 and < 196 Days	14 (28.6)	0	14 (1.0)
≥ 196 and < 224 Days	15 (30.6)	0	14 (1.1)
≥ 224 and < 252 Days	3 (6.1)	0	3 (0.2)
≥ 252 and < 280 Days	1 (2.0)	10 (0.7)	11 (0.8)
≥ 280 and < 308 Days	0	529 (39.0)	529 (37.7)
≥ 308 and < 336 Days	0	427 (31.5)	427 (30.4)
≥ 336 and < 364 Days	0	243 (17.9)	243 (17.3)
≥ 364 and < 392 Days	0	115 (8.5)	115 (8.2)
≥ 392 and < 420 Days	0	19 (1.4)	19 (1.4)
≥ 420 and < 448 Days	0	8 (0.6)	8 (0.6)
≥ 448 and < 476 Days	0	0	0
≥ 476 and < 504 Days	0	4 (0.3)	4 (0.3)
> 504 Days	0	1 (<0.1)	1 (<0.1)
Time on Study from Dose 1 of mRNA-1273 (Days)			
Mean (SD)	294.3 (19.77)	550.0 (22.04)	541.1 (51.82)
Median	301.0	546.5	546.0
Q1, Q3	294.0, 307.0	538.0, 561.0	538.0, 561.0
Min, Max	218, 312	347, 615	218, 615
Person-years from Dose 1 of mRNA-1273 [3]	39.5	2041.9	2081.4
Time Since Primary Series Dose 2 to Booster (Days) [1]			
Mean (SD)	182.6 (33.45)	322.5 (30.13)	317.6 (39.68)
Median	185.0	316.0	315.0
Q1, Q3	158.0, 205.0	300.0, 339.0	298.0, 337.0
Min, Max	63, 259	274, 514	63, 514
Follow-Up Time on Study After Booster (Days)			
Mean (SD)	78.1 (33.15)	197.4 (29.81)	193.2 (37.07)
Median	83.0	207.0	204.0
Q1, Q3	54.0, 110.0	187.0, 216.0	183.0, 216.0
Min, Max	1, 155	2, 232	1,232
< 28 Days	3 (6.1)	2 (0.1)	5 (0.4)
≥ 28 Days	46 (93.9)	1354 (99.9)	1400 (99.6)
≥ 28 and < 56 Days	12 (24.5)	8 (0.6)	20 (1.4)
≥ 56 Days	34 (69.4)	1346 (99.3)	1380 (98.2)
≥ 84 Days	22 (44.9)	1336 (98.5)	1358 (96.7)
≥ 112 Days	11 (20.4)	1324 (97.6)	1335 (95.0)
≥ 140 Days	1 (2.0)	1291 (95.2)	1292 (92.0)
≥ 168 Days	0	1204 (88.8)	1204 (85.7)
≥ 196 Days	0	920(67.8)	920 (65.5)
≥ 224 Days	0	109(8.0)	109 (7.8)
Person-years from Booster [2]	10.5	723.7	743.2

Source: mRNA-1273-P203 Table 14.1.6.5.1 (15 August 2022).

Table 28: Age Group and Gender in the Ongoing mRNA-1273-P203 Study (Part 1C, Booster Dose) (12 Years to < 18 Years)

Characteristic	Placebo-elasomeran-Booster (N=49)	Elasomeran-Booster (N=1356)	Total (N=1405)
Age Group, n (%)			
16 to <18 years	10 (20.4)	269 (19.8)	279 (19.9)
12 to <16 years	39 (79.6)	1087 (80.2)	1126 (80.1)
Gender, n (%)			
Female	26 (53.1)	659 (48.6)	685 (48.8)
Male	23 (46.9)	697 (51.4)	720 (51.2)

Source: mRNA-1273-P203 Table 14.1.3.14.1 (15 August 2022).

Table 29: Participant Race in the Ongoing mRNA-1273-P203 Study (Part 1C, Booster Dose) (12 Years to < 18 Years)

Characteristic	Placebo-elasomeran-Booster (N=49)	Elasomeran-Booster (N=1356)	Total (N=1405)
Race, n (%)			
American Indian or Alaska Native	0	7 (0.5)	7 (0.5)
Asian	2 (4.1)	67 (4.9)	69 (4.9)
Black	0	44 (3.2)	44 (3.1)
Native Hawaiian or Other Pacific Islander	0	1 (<0.1)	1 (<0.1)
White	45 (91.8)	1148 (84.7)	1193 (84.9)
Other	0	10 (0.7)	10 (0.7)
Multiracial	2 (4.1)	71 (5.2)	73 (5.2)
Not reported	0	4 (0.3)	4 (0.3)
Unknown	0	4 (0.3)	4 (0.3)

Source: mRNA-1273-P203 Table 14.1.3.14.1 (15 August 2022).

Table 30: Participant Ethnicity in the Ongoing mRNA-1273-P203 Study (Part 1C, Booster Dose) (12 Years to < 18 Years)

Characteristic	Placebo-elasomeran-Booster (N=49)	Elasomeran-Booster (N=1356)	Total (N=1405)
Ethnicity, n (%)			
Hispanic or Latino	15 (30.6)	173 (12.8)	188 (13.4)
Not Hispanic or Latino	34 (69.4)	1172 (86.4)	1206 (85.8)
Not reported	0	11 (0.8)	11 (0.8)

Source: mRNA-1273-P203 Table 14.1.3.14.1 (15 August 2022).

mRNA-1273-P204 study

A Phase 2/3, two-part, dose-escalation (open-label), age de-escalation and randomized, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of elasomeran SARS-CoV 2 vaccine in healthy children 6 months to less than 12 years of age.

The study population was evaluated in 3 discrete age groups (6 years through 11 years, 2 years to < 6 years, and 6 months to < 2 years), assessing up to 3 dosage levels (25, 50, and 100 µg) of elasomeran in the primary series. The study has two parts. Part 1 is the open-label, dose-escalation, age de-escalation phase. Part 2 is the randomized, observer-blind, placebo-controlled expansion phase which evaluated the selected dose of elasomeran.

In total, 751 children 6 years to < 12 years of age were treated in Part 1 (380 elasomeran 50 µg and 371 elasomeran 100 µg) and 4002 children 6 years to < 12 years of age were treated in Part 2 (3007 elasomeran 50 µg and 995 placebo) (Table 31 to Table 38). Participants in Part 1 are distinct from those in Part 2.

Following evidence of enhanced effectiveness of the adult booster dose (BD), study mRNA-1273-P204 was amended to offer a BD (elasomeran, 25 µg) to all children enrolled in the 6 through 11 years age group, which could be administered starting 6 months post-dose 2 of the primary series. A total of 1,294 participants received a 25 µg BD in the Booster Dose Phase of the study.

Table 31: Summary of Study Duration by Dose Level in Part 1 (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Years to < 12 Years)

Duration of Exposure	Elasomeran 50 µg (N=380)	Elasomeran 100 µg (N=371)	Total (N=751)
Received first injection, n (%)	380 (100)	371 (100)	751 (100)
Received second injection, n (%)	379 (99.7)	371 (100)	750 (99.9)
≥ 7 days since first injection, n (%)	380 (100)	371 (100)	751 (100)
≥ 35 days since first injection, n (%)	380 (100)	371 (100)	751 (100)
≥ 56 days since first injection, n (%)	380 (100)	371 (100)	751 (100)
≥ 7 days since second injection, n (%)	379 (99.7)	371 (100)	750 (99.9)
≥ 21 days since second injection, n (%)	379 (99.7)	371 (100)	750 (99.9)
≥ 28 days since second injection, n (%)	379 (99.7)	371 (100)	750 (99.9)
≥ 28 days and <56 days since second injection, n (%)	0	1 (0.3)	1 (0.1)
≥ 56 days since second injection, n (%)	379 (99.7)	370 (99.7)	749 (99.7)
≥ 84 days since second injection, n (%)	379 (99.7)	370 (99.7)	749 (99.7)
≥ 112 days since second injection, n (%)	379 (99.7)	368 (99.2)	747 (99.5)
≥ 140 days since second injection, n (%)	376 (98.9)	368 (99.2)	744 (99.1)
Study duration from dose 1, days			
Median (min, max)	380.0 (149, 531)	364.0 (76, 503)	371.0 (76, 531)
Study duration from dose 2, days			
Median (min, max)	351.0 (0, 500)	334.0 (41, 475)	342.0 (0, 500)

Abbreviations: max = maximum; min = minimum.

Percentages are based on the number of participants in the Part 1 Safety Set,
Source: Study mRNA-1273-P204 Table 14.1.5.1 (07 September 2022)

Table 32: Summary of Blinded and Open-label Phases Study Duration in Part 2 (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Years to < 12 Years)

Duration of Exposure	Elasomeran 50 µg (N=3007)	Placebo (N=995)	Total (N=4002)
Received first injection, n (%)	3007 (100)	995 (100)	4002 (100)
Received second injection, n (%)	2997 (99.7)	972 (97.7)	3969 (99.2)
≥ 7 days since first injection, n (%)	3007 (100)	995 (100)	4002 (100)
≥ 35 days since first injection, n (%)	3004(>99.9)	991 (99.6)	3995 (99.8)
≥ 56 days since first injection, n (%)	2998 (99.7)	985 (99.0)	3983 (99.5)
≥ 7 days since second injection, n (%)	2997 (99.7)	972 (97.7)	3969 (99.2)
≥ 21 days since second injection, n (%)	2995 (99.6)	969 (97.4)	3964 (99.1)
≥ 28 days since second injection, n (%)	2993 (99.5)	967 (97.2)	3960 (99.0)
≥ 28 days and < 56 days since second injection, n (%)	27 (0.9)	134 (13.5)	161 (4.0)
≥ 56 days since second injection, n (%)	2966 (98.6)	833 (83.7)	3799 (94.9)
≥ 84 days since second injection, n (%)	2958 (98.4)	736 (74.0)	3694 (92.3)
≥ 112 days since second injection, n (%)	2956 (98.3)	714 (71.8)	3670 (91.7)
≥ 140 days since second injection, n (%)	2950 (98.1)	709 (71.3)	3659 (91.4)
Study duration from dose 1, days			
Median (min, max)	295.0 (29, 395)	305.0 (14, 395)	299.0 (14, 395)
Study duration from dose 2, days			
Median (min, max)	266.0 (0, 366)	275.0 (0, 366)	268.0 (0, 366)

Abbreviations: max = maximum; min = minimum.
Percentages are based on the number of participants in the Part 2 Safety Set,
Source: Study mRNA-1273-P204 Table 14.1.5.3 (07 September 2022)

Table 33: Participant Age and Gender by Dose Level in Part 1 (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Years to < 12 Years)

Characteristic	Elasomeran 50 µg (N=380)	Elasomeran 100 µg (N=371)	Total (N=751)
Age, years			
Mean (SD)	8.6 (1.66)	8.6 (1.62)	8.6 (1.64)
Median	9.0	9.0	9.0
Min, max	6, 11	6, 11	6, 11
Sex, n (%)			
Male	195 (51.3)	172 (46.4)	367 (48.9)
Female	185 (48.7)	199 (53.6)	384 (51.1)

Abbreviations: max = maximum; min = minimum; SD = standard deviation.
Percentages are based on the number of participants in the Part 1 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.3.1.1 (07 September 2022)

Table 34: Participant Age and Gender in Part 2 (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Years to < 12 Years)

Characteristic	Elasomeran 50 µg (N=3007)	Placebo (N=995)	Total (N=4002)
Age, years			
Mean (SD)	8.5 (1.65)	8.5 (1.64)	8.5 (1.65)
Median	8.0	9.0	9.0
Min, Max	6, 11	6, 11	6, 11
Sex, n (%)			
Male	1554 (51.7)	481 (48.3)	2035 (50.8)
Female	1453 (48.3)	514 (51.7)	1967 (49.2)

Abbreviations: max = maximum; min = minimum; SD = standard deviation.
Percentages are based on the number of participants in the Part 2 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.3.2 (07 September 2022)

Table 35: Participant Race by Dose Level in Part 1 (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Years to < 12 Years)

Characteristic	Elasomeran 50 µg (N=380)	Elasomeran 100 µg (N=371)	Total (N=751)
Race, n (%)			
White	266 (70.0)	284 (76.5)	550 (73.2)
Black	34 (8.9)	13 (3.5)	47 (6.3)
Asian	28 (7.4)	25 (6.7)	53 (7.1)
American Indian or Alaska Native	0	2 (0.5)	2 (0.3)
Native Hawaiian or other Pacific Islander	1 (0.3)	0	1 (0.1)
Multiracial	39 (10.3)	31 (8.4)	70 (9.3)
Other	3 (0.8)	10 (2.7)	13 (1.7)
Not reported	9 (2.4)	4 (1.1)	13 (1.7)
Unknown	0	2 (0.5)	2 (0.3)

Percentages are based on the number of participants in the Part 1 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.3.1.1 (07 September 2022)

Table 36: Participant Race in Part 2 (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Years to < 12 Years)

Characteristic	Elasomeran 50 µg (N=3007)	Placebo (N=995)	Total (N=4002)
Race, n (%)			
White	1958 (65.1)	668 (67.1)	2626 (65.6)
Black	310 (10.3)	93 (9.3)	403 (10.1)
Asian	296 (9.8)	100 (10.1)	396 (9.9)
American Indian or Alaska Native	14 (0.5)	3 (0.3)	17 (0.4)
Native Hawaiian or other Pacific Islander	4 (0.1)	0	4 (< 0.1)
Multiracial	330 (11.0)	98 (9.8)	428 (10.7)
Other	62 (2.1)	22 (2.2)	84 (2.1)

Characteristic	Elasomeran 50 µg (N=3007)	Placebo (N=995)	Total (N=4002)
Not reported	28 (0.8)	10 (1.0)	33 (0.8)
Unknown	10 (0.3)	1 (0.1)	11 (0.3)

Percentages are based on the number of participants in the Part 2 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.3.2 (07 September 2022)

Table 37: Participant Ethnicity by Dose Level in Part 1 (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Years to < 12 Years)

Characteristic	Elasomeran 50 µg (N=380)	Elasomeran 100 µg (N=371)	Total (N=751)
Ethnicity, n (%)			
Hispanic or Latino	72 (18.9)	69 (18.6)	141 (18.8)
Not Hispanic or Latino	304 (80.0)	296 (79.8)	600 (79.9)
Not reported	3 (0.8)	3 (0.8)	6 (0.8)
Unknown	1 (0.3)	3 (0.8)	4 (0.5)

Percentages are based on the number of participants in the Part 1 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.3.1.1 (07 September 2022)

Table 38: Participant Ethnicity in Part 2 (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Years to < 12 Years)

Characteristic	Elasomeran 50 µg (N=3007)	Placebo (N=995)	Total (N=4002)
Ethnicity, n (%)			
Hispanic or Latino	560 (18.6)	181 (18.2)	741 (18.5)
Not Hispanic or Latino	2419 (80.4)	804 (80.8)	3223 (80.5)
Not reported	21 (0.7)	5 (0.5)	26 (0.6)
Unknown	7 (0.2)	5 (0.5)	12 (0.3)

Percentages are based on the number of participants in the Part 2 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.3.2 (07 September 2022)

A total of 1294 children 6 years to < 12 years of age were administered a booster dose (elasomeran 25 µg) in the Booster Dose Phase of the study (Table 39 to Table 42).

Table 39: Summary of Study Duration in Part Booster Dose (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Years to < 12 Years)

Duration of exposure, n (%)	Elasomeran 50 µg Primary Series - Booster (N=1294)
Received First Injection	1294 (100)
Received Second Injection	1294 (100)
< 168 Days Since Primary Series	3 (0.2)

Duration of exposure, n (%)	Elasomeran 50 µg Primary Series - Booster (N=1294)
≥ 168 and < 196 Days	48 (3.7)
≥ 196 and < 224 Days	566 (43.7)
≥ 224 and < 252 Days	480 (37.1)
≥ 252 and < 280 Days	21 (1.6)
≥ 280 and < 308 Days	72 (5.6)
≥ 308 and < 336 Days	66 (5.1)
≥ 336 and < 364 Days	26 (2.0)
≥ 364 Days	12 (0.9)
Time Since First Injection to Second Injection (Days)	
n	1294
Mean (SD)	30.9 (2.62)
Median	30.0
Q1, Q3	29.0, 32.0
Min, Max	27, 47
< 21 Days Since First Injection	0
≥ 21 and ≤ 42 Days Since First Injection	1284 (99.2)
> 42 Days and ≤ 56 Days Since First Injection	10 (0.8)
> 56 Days Since First Injection	0
Received Booster	1294 (100)
Time Since Primary Series Dose 2 to Booster (Days) [1]	
n	1294
Mean (SD)	235.0 (37.63)
Median	225.0
Q1, Q3	213.0, 239.0
Min, Max	124, 378
Follow-Up Time on Study After Booster (Days)	
n	1294
Mean (SD)	29.0 (13.68)
Median	29.0
Q1, Q3	18.0, 40.0
Min, Max	1, 57
< 28 Days	577 (44.6)
≥ 28 Days	717 (55.4)
≥ 28 and < 56 Days	694 (53.6)
≥ 56 Days	23 (1.8)
Person-years from Booster [2]	102.74
Time on Study from Dose 1 of mRNA-1273 (Days)	
n	1294
Mean (SD)	292.9 (35.95)
Median	280.5
Q1, Q3	277.0, 287.0
Min, Max	183, 434
Person-years from Dose 1 of mRNA-1273 [3]	1037.63

Percentages are based on the number of safety subjects in booster dose analysis.

[1] For subjects who received two doses of elasomeran in Primary Series, Time Since Primary Series is calculated as: Date of Booster — Date of Second Dose of elasomeran + 1.
[2] Person-years is defined as the total years from the booster dose date to the earlier date of study discontinuation or data cutoff.
[3] Person-years is defined as the total years from the first dose date of elasomeran to the earlier date of study discontinuation or data cutoff.
Source: Study mRNA-1273-P204 Table 14.1.6.2 (23 May 2022).

Table 40: Participant Age Group and Gender by Dose Level in Part Booster Dose (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Years to < 12 Years)

Characteristic	**Elasomeran 50 µg Primary Series - Booster (N=1294)**
Age group (Years), n%	
≥ 6 and < 9	653 (50.5)
≥ 9 and < 12	641 (49.5)
Age (Years), n (%)	
6	194 (15.0)
7	204 (15.8)
8	255 (19.7)
9	235 (18.2)
10	235 (18.2)
11	171 (13.2)
Age (Years)	
n	1294
Mean (SD)	8.5 (1.62)
Median	8.0
Q1, Q3	7.0, 10.0
Min, Max	6, 11
Gender, n (%)	
Male	672 (51.9)
Female	622 (48.1)

Abbreviations: max = maximum; min = minimum; SD = standard deviation.
Source: mRNA-1273-P204 Table 14.1.3.13.2 (23 May 2022).

Table 41: Participant Race by Dose Level in Part Booster Dose (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Years to < 12 Years)

Characteristic	**Elasomeran 50 µg Primary Series - Booster (N=1294)**
Race, n (%)	
White	850 (65.7)
Black	142 (11.0)
Asian	101 (7.8)
American Indian or Alaska Native	6 (0.5)
Native Hawaiian or Other Pacific Islander	1 (<0.1)
Multiracial	153 (11.8)
Other	24 (1.9)
Not reported	14 (1.1)

Unknown	3 (0.2)

Source: mRNA-1273-P204 Table 14.1.3.13.2 (23 May 2022).

Table 42: Participant Ethnicity by Dose Level in Part Booster Dose (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Years to < 12 Years)

Characteristic	Elasomeran 50 µg Primary Series - Booster (N=1294)
Ethnicity, n (%)	
Hispanic or Latino	202 (15.6)
Not Hispanic or Latino	1079 (83.4)
Not reported	10 (0.8)
Unknown	3 (0.2)

Source: mRNA-1273-P204 Table 14.1.3.13.2 (23 May 2022).

In mRNA-1273-P204, a total of 224 children 2 years to < 6 years of age were treated in Part 1 (69 elasomeran 25 µg and 155 elasomeran 50 µg) and 4038 children 2 years to < 6 years of age were treated in Part 2 (3031 elasomeran 25 µg and 1007 placebo) (Table 43 to Table 50).

Table 43: Summary of Study Duration by Dose Level in Part 1 (Safety Set) in the Ongoing mRNA-1273-P204 Study (2 Years to < 6 Years)

Duration of Exposure	Elasomeran 25 µg (N=69)	Elasomeran 50 µg (N=155)	Total (N=224)
Received first injection, n (%)	69 (100)	155 (100)	224 (100)
Received second injection, n (%)	69 (100)	155 (100)	224 (100)
≥ 7 days since first injection, n (%)	69 (100)	154 (99.4)	223 (99.6)
≥ 35 days since first injection, n (%)	69 (100)	154 (99.4)	223 (99.6)
≥ 56 days since first injection, n (%)	69 (100)	154 (99.4)	223 (99.6)
≥ 7 days since second injection, n (%)	69 (100)	154 (99.4)	223 (99.6)
≥ 21 days since second injection, n (%)	69 (100)	154 (99.4)	223 (99.6)
≥ 28 days since second injection, n (%)	69 (100)	154 (99.4)	223 (99.6)
≥ 28 days and < 56 days since second injection, n (%)	0	0	0
≥ 56 days since second injection, n (%)	69 (100)	154 (99.4)	223 (99.6)
≥ 84 days since second injection, n (%)	69 (100)	154 (99.4)	223 (99.6)
≥ 112 days since second injection, n (%)	69 (100)	154 (99.4)	223 (99.6)
≥ 140 days since second injection, n (%)	69 (100)	152 (98.1)	221 (98.7)
Study duration from dose 1, days			
Median (min, max)	358.0 (264, 436)	380.0 (161, 497)	374.0 (161, 497)
Study duration from dose 2, days			
Median (min, max)	329.0 (236, 407)	349.0 (132, 469)	344.0 (132, 469)

Abbreviations: max = maximum; min = minimum.
Percentages are based on the number of participants in the Part 1 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.5.1 (07 September 2022)

Table 44: Summary of Blinded Study Duration in Part 2 (Safety Set) in the Ongoing mRNA-1273-P204 Study (2 Years to < 6 Years)

Duration of Exposure	Elasomeran 25 µg (N=3031)	Placebo (N=1007)	Total (N=4038)
Received first injection, n (%)	3031 (100)	1007 (100)	4038 (100)
Received second injection, n (%)	3006 (99.2)	984 (97.7)	3990 (98.8)
≥ 7 days since first injection, n (%)	3021 (99.7)	1000 (99.3)	4021 (99.6)
≥ 35 days since first injection, n (%)	2940 (97.0)	980 (97.3)	3920 (97.1)
≥ 56 days since first injection, n (%)	2904 (95.8)	966 (95.9)	3870 (95.8)
≥ 7 days since second injection, n (%)	2917 (96.2)	974 (96.7)	3891 (96.4)
≥ 21 days since second injection, n (%)	2892 (95.4)	966 (95.9)	3858 (95.5)
≥ 28 days since second injection, n (%)	2882 (95.1)	963 (95.6)	3845 (95.2)
≥ 28 days and < 56 days since second injection, n (%)	80 (2.6)	27 (2.7)	107 (2.6)
≥ 56 days since second injection, n (%)	2802 (92.4)	936 (92.9)	3738 (92.6)
≥ 84 days since second injection, n (%)	2734 (90.2)	911 (90.5)	3645 (90.3)
≥ 112 days since second injection, n (%)	2662 (87.8)	882 (87.6)	3544 (87.8)
≥ 140 days since second injection, n (%)	2460 (81.2)	811 (80.5)	3271 (81.0)
Study duration from dose 1, days			
Median (min, max)	217.0 (0, 324)	216.0 (0, 317)	217.0 (0, 324)
Study duration from dose 2, days			
Median (min, max)	186.0 (0, 296)	185.0 (0, 289)	186.0 (0, 296)

Abbreviations: max = maximum; min = minimum.
Percentages are based on the number of participants in the Part 2 Safety Set.
Participants received second injection after unblinding date are excluded. Study duration from second injection is 0 days for participants who received second injection with same unblinding date.
Source: Study mRNA-1273-P204 Table 14.1.5.2 (07 September 2022)

Table 45: Participant Age Group and Gender by Dose Level in Part 1 (Safety Set) in the Ongoing mRNA-1273-P204 Study (2 Years to < 6 Years)

Characteristic	Elasomeran 25 µg (N=69)	Elasomeran 50 µg (N=155)	Total (N=224)
Age group, n (%)			
≥ 2 years and < 4 years	32 (46.4)	66 (42.6)	98 (43.8)
≥ 4 years and < 6 years	37 (53.6)	89 (57.4)	126 (56.3)
≥ 2 years and ≤ 36 months	9 (13.0)	26 (16.8)	35 (15.6)
> 36 months and < 6 years	60 (87.0)	129 (83.2)	189 (84.4)
Sex, n (%)			
Male	36 (52.2)	80 (51.6)	116 (51.8)
Female	33 (47.8)	75 (48.4)	108 (48.2)

Percentages are based on the number of participants in the Part 1 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.3.1.1 (07 September 2022)

Table 46: Participant Age Group and Gender in Part 2 (Safety Set) in the Ongoing mRNA-1273-P204 Study (2 Years to < 6 Years)

Characteristic	Elasomeran 25 µg (N=3031)	Placebo (N=1007)	Total (N=4038)
Age group, n (%)			
< 2 years[a]	18 (0.6)	11 (1.1)	29 (0.7)
≥ 2 years and < 4 years	2065 (68.1)	656 (65.1)	2721 (67.4)
≥ 4 years and < 6 years	948 (31.3)	340 (33.8)	1288 (31.9)
≥ 2 years and ≤ 36 months	996 (32.9)	346 (34.4)	1342 (33.2)
> 36 months and < 6 years	2035 (67.1)	661 (65.6)	2696 (66.8)
Sex, n (%)			
Male	1543 (50.9)	510 (50.6)	2053 (50.8)
Female	1488 (49.1)	497 (49.4)	1985 (49.2)

Abbreviations: IRT = interactive response technology.
Percentages are based on the number of participants in the Part 2 Safety Set.
[a]Some participants < 2 years were included in the ≥ 2 to 6 year subgroup, likely because of coincident enrollment of both age groups, entry errors at the time of randomization and other limitations of the IRT system.
Source: Study mRNA-1273-P204 Table 14.1.3.2 (07 September 2022)

Table 47: Participant Race by Dose Level in Part 1 (Safety Set) in the Ongoing mRNA-1273-P204 Study (2 Years to < 6 Years)

Characteristic	Elasomeran 25 µg (N=69)	Elasomeran 50 µg (N=155)	Total (N=224)
Race, n (%)			
White	49 (71.0)	133 (85.8)	182 (81.3)
Black	3 (4.3)	7 (4.5)	10 (4.5)
Asian	8 (11.6)	3 (1.9)	11 (4.9)
American Indian or Alaska Native	0	0	0
Native Hawaiian or other Pacific Islander	0	0	0
Multiracial	3 (4.3)	10 (6.5)	13 (5.8)
Other	6 (8.7)	2 (1.3)	8 (3.6)
Not reported	0	0	0
Unknown	0	0	0

Percentages are based on the number of participants in the Part 1 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.3.1.1 (07 September 2022)

Table 48: Participant Race in Part 2 (Safety Set) in the Ongoing mRNA-1273-P204 Study (2 Years to < 6 Years)

Characteristic	Elasomeran 25 µg (N=3031)	Placebo (N=1007)	Total (N=4038)
Race, n (%)			
White	2299 (75.8)	792 (78.6)	3091 (76.5)
Black	142 (4.7)	38 (3.8)	180 (4.5)

Characteristic	Elasomeran 25 µg (N=3031)	Placebo (N=1007)	Total (N=4038)
Asian	191 (6.3)	51 (5.1)	242 (6.0)
American Indian or Alaska Native	11 (0.4)	3 (0.3)	14 (0.3)
Native Hawaiian or other Pacific Islander	5 (0.2)	3 (0.3)	8 (0.2)
Multiracial	323 (10.7)	100 (9.9)	423 (10.5)
Other	43 (1.4)	16 (1.6)	59 (1.5)
Not reported	13 (0.4)	4 (0.4)	17 (0.4)
Unknown	4 (0.1)	0	4 (0.1)

Percentages are based on the number of participants in the Part 2 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.3.2 (07 September 2022)

Table 49: Participant Ethnicity by Dose Level in Part 1 (Safety Set) in the Ongoing mRNA-1273-P204 Study (2 Years to < 6 Years)

Characteristic	Elasomeran 25 µg (N=69)	Elasomeran 50 µg (N=155)	Total (N=224)
Ethnicity, n (%)			
Hispanic or Latino	18 (26.1)	23 (14.8)	41 (18.3)
Not Hispanic or Latino	51 (73.9)	129 (83.2)	180 (80.4)
Not reported	0	3 (1.9)	3 (1.3)
Unknown	0	0	0

Percentages are based on the number of participants in the Part 1 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.3.1.1 (07 September 2022)

Table 50: Participant Ethnicity in Part 2 (Safety Set) in the Ongoing mRNA-1273-P204 Study (2 Years to < 6 Years)

Characteristic	Elasomeran 25 µg (N=3031)	Placebo (N=1007)	Total (N=4038)
Ethnicity, n (%)			
Hispanic or Latino	429 (14.2)	142 (14.1)	571 (14.1)
Not Hispanic or Latino	2584 (85.3)	856 (85.0)	3440 (85.2)
Not reported	13 (0.4)	8 (0.8)	21 (0.5)
Unknown	5 (0.2)	1 (0.1)	6 (0.1)

Percentages are based on the number of participants in the Part 2 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.3.2 (07 September 2022)

A total of 150 children 6 months to < 2 years of age were treated in Part 1 (elasomeran 25 µg) and 2660 children 6 months to < 2 years of age were treated in Part 2 (1993 elasomeran 25 µg and 667 placebo) (Table 51 to Table 58).

Table 51: Summary of Study Duration by Dose Level in Part 1 (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Months to < 2 Years)

Duration of Exposure	Elasomeran 25 µg (N=150)
Received first injection, n (%)	150 (100)
Received second injection, n (%)	150 (100)
≥ 7 days since first injection, n (%)	150 (100)
≥ 35 days since first injection, n (%)	150 (100)
≥ 56 days since first injection, n (%)	150 (100)
≥ 7 days since second injection, n (%)	150 (100)
≥ 21 days since second injection, n (%)	150 (100)
≥ 28 days since second injection, n (%)	150 (100)
≥ 28 days and < 56 days since second injection, n (%)	0
≥ 56 days since second injection, n (%)	150 (100)
≥ 84 days since second injection, n (%)	150 (100)
≥ 112 days since second injection, n (%)	149 (99.3)
≥ 140 days since second injection, n (%)	149 (99.3)
Study duration from dose 1, days	
Median (min, max)	361.5 (134, 469)
Study duration from dose 2, days	
Median (min, max)	330.5 (101, 437)

Abbreviations : max = maximum; min = minimum.
Percentages are based on the number of participants in the Part 1 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.5.1 (07 September 2022)

Table 52: Summary of Blinded and Open-label Phases Study Duration in Part 2 (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Months to < 2 Years)

Duration of Exposure	Elasomeran 25 µg (N=1993)	Placebo (N=667)	Total (N=2660)
Received first injection, n (%)	1993 (100)	667 (100)	2660 (100)
Received second injection, n (%)	1979 (99.3)	649 (97.3)	2628 (98.8)
≥ 7 days since first injection, n (%)	1991 (99.9)	666 (99.9)	2657 (99.9)
≥ 35 days since first injection, n (%)	1968 (98.7)	654 (98.1)	2622 (98.6)
≥ 56 days since first injection, n (%)	1936 (97.1)	639 (95.8)	2575 (96.8)
≥ 7 days since second injection, n (%)	1953 (98.0)	647 (97.0)	2600 (97.7)
≥ 21 days since second injection, n (%)	1936 (97.1)	641 (96.1)	2577 (96.9)
≥ 28 days since second injection, n (%)	1924 (96.5)	636 (95.4)	2560 (96.2)
≥ 28 days and < 56 days since second injection, n (%)	62 (3.1)	20 (3.0)	82 (3.1)
≥ 56 days since second injection, n (%)	1862 (93.4)	616 (92.4)	2478 (93.2)
≥ 84 days since second injection, n (%)	1738 (87.2)	570 (85.5)	2308 (86.8)
≥ 112 days since second injection, n (%)	1632 (81.9)	531 (79.6)	2163 (81.3)

Duration of Exposure	Elasomeran 25 µg (N=1993)	Placebo (N=667)	Total (N=2660)
≥140 days since second injection, n (%)	1494 (75.0)	478 (71.7)	1972 (74.1)
Study duration from dose 1, days			
Median (min, max)	213.0 (2, 322)	211.0 (2, 324)	212.0 (2, 324)
Study duration from dose 2, days			
Median (min, max)	183.0 (1, 294)	183.0 (2, 296)	183.0 (1, 296)

Abbreviations: max = maximum; min = minimum.
Percentages are based on the number of participants in the Part 2 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.5.2 (07 September 2022)

Table 53: Participant Age Group and Gender by Dose Level in Part 1 (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Months to < 2 Years)

Characteristic	Elasomeran 25 µg (N=150)
Age group, n (%)	
≥ 6 months and < 1 year	37 (24.7)
≥ 1 year and < 2 years	113 (75.3)
Sex, n (%)	
Male	83 (55.3)
Female	67 (44.7)

Percentages are based on the number of participants in the Part 1 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.3.1.1 (07 September 2022)

Table 54: Participant Age Group and Gender in Part 2 (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Months to < 2 Years)

Characteristic	Elasomeran 25 µg (N=1993)	Placebo (N=667)	Total (N=2660)
Age group, n (%)			
≥ 6 months and < 1 year	449 (22.5)	140 (21.0)	589 (22.1)
≥ 1 year and < 2 years	1535 (77.0)	525 (78.7)	2060 (77.4)
≥ 2 years[a]	9 (0.5)	2 (0.3)	11 (0.4)
Sex, n (%)			
Male	1013 (50.8)	327 (49.0)	1340 (50.4)
Female	980 (49.2)	340 (51.0)	1320 (49.6)

Abbreviations: IRT = interactive response technology.
Percentages are based on the number of participants in the Part 2 Safety Set.
[a]Due to parallel enrollment of age groups, entry errors at the time of randomization and other limitations of the IRT system, some participants who were ≥ 2 years old were included in the 6 months to < 2-years-old subgroup.
Source: Study mRNA-1273-P204 Table 14.1.3.2 (07 September 2022)

Table 55: Participant Race by Dose Level in Part 1 (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Months to < 2 Years)

Characteristic	Elasomeran 25 µg (N=150)
Race, n (%)	
White	124 (82.7)
Black	3 (2.0)
Asian	7 (4.7)
American Indian or Alaska Native	1 (0.7)
Native Hawaiian or other Pacific Islander	0
Multiracial	11 (7.3)
Other	3 (2.0)
Not reported	0
Unknown	1 (0.7)

Percentages are based on the number of participants in the Part 1 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.3.1.1 (07 September 2022)

Table 56: Participant Race in Part 2 (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Months to < 2 Years)

Characteristic	Elasomeran 25 µg (N=1993)	Placebo (N=667)	Total (N=2660)
Race, n (%)			
White	1567 (78.6)	525 (78.7)	2092 (78.6)
Black	62 (3.1)	18 (2.7)	80 (3.0)
Asian	94 (4.7)	38 (5.7)	132 (5.0)
American Indian or Alaska Native	7 (0.4)	0	7 (0.3)
Native Hawaiian or other Pacific Islander	0	0	0
Multiracial	215 (10.8)	76 (11.4)	291 (10.9)
Other	33 (1.7)	7 (1.0)	40 (1.5)
Not reported	10 (0.5)	2 (0.3)	12 (0.5)
Unknown	5 (0.3)	1 (0.1)	6 (0.2)

Percentages are based on the number of participants in the Part 2 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.3.2 (07 September 2022)

Table 57: Participant Ethnicity by Dose Level in Part 1 (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Months to < 2 Years)

Characteristic	Elasomeran 25 µg (N=150)
Ethnicity, n (%)	
Hispanic or Latino	15 (10.0)
Not Hispanic or Latino	133 (88.7)
Not reported	1 (0.7)
Unknown	1 (0.7)

Percentages are based on the number of participants in the Part 1 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.3.1.1 (07 September 2022)

Table 58: Participant Ethnicity in Part 2 (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Months to < 2 Years)

Characteristic	Elasomeran 25 µg (N=1993)	Placebo (N=667)	Total (N=2669)
Ethnicity, n (%)			
Hispanic or Latino	256 (12.8)	94 (14.1)	350 (13.2)
Not Hispanic or Latino	1718 (86.2)	566 (84.9)	2284 (85.9)
Not reported	17 (0.9)	6 (0.9)	23 (0.9)
Unknown	2 (0.1)	1 (0.1)	3 (0.1)

Percentages are based on the number of participants in the Part 2 Safety Set.
Source: Study mRNA-1273-P204 Table 14.1.3.2 (07 September 2022)

A total of 145 children including 114 infants/toddlers 6 months to < 2 years of age and 31 children 2 to < 6 years of age were treated in Part 1 (elasomeran 25 µg) and received a BD (elasomeran 10 µg) in the Booster Dose Phase of the study (Table 59 to Table 62).

Table 59: Summary of Study Duration in Part Booster Dose (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Months to < 6 Years)

	Elasomeran 25 µg Primary Series - Booster 10 µg		
Duration of exposure, n (%)	**6 Months to < 2 Years (N=114)**	**2 Years to < 6 Years (N=31)**	**Total (N=145)**
Received First Injection	114 (100)	31 (100)	145 (100)
Received Second Injection	114 (100)	31 (100)	145 (100)
Time Since First Injection to Second Injection (Days)			
n	114	31	145
Mean (SD)	31.1 (2.60)	30.5 (2.23)	31.0 (2.53)
Median	30.0	30.0	30.0
Q1, Q3	29.0, 33.0	29.0, 30.0	29.0, 33.0
Min, Max	29, 42	29, 35	29, 42
< 21 Days Since First Injection	0	0	0
≥ 21 and ≤ 42 Days Since First Injection	114 (100)	31 (100)	145 (100)
> 42 Days and ≤ 56 Days Since First Injection	0	0	0
> 56 Days Since First Injection	0	0	0
Received Booster	114 (100)	31 (100)	145 (100)
Time Since Primary Series Dose 2 to Booster (Days) [1]			
n	114	31	145
Mean (SD)	323.3 (30.73)	287.1 (31.15)	315.5 (34.14)
Median	316.5	278.0	307.0
Q1, Q3	299.0, 349.0	270.0, 305.0	289.0, 342.0
Min, Max	267, 392	237, 375	237, 392
< 168 Days Since Primary Series	0	0	0

≥ 168 and < 196 Days	0	0	0
≥ 196 and < 224 Days	0	0	0
≥ 224 and < 252 Days	0	2 (6.5)	2 (1.4)
≥ 252 and < 280 Days	4 (3.5)	15 (48.4)	19 (13.1)
≥ 280 and < 308 Days	46 (40.4)	7 (22.6)	53 (36.6)
≥ 308 and < 336 Days	20 (17.5)	4 (12.9)	24 (16.6)
≥ 336 and < 364 Days	28 (24.6)	2 (6.5)	30 (20.7)
≥ 364 and < 392 Days	15 (13.2)	1 (3.2)	16 (11.0)
≥ 392 Days	1 (0.9)	0	1 (0.7)
Follow-Up Time on Study After Booster (Days)			
n	114	31	145
Mean (SD)	88.5 (30.37)	96.9 (31.76)	90.3 (30.76)
Median	94.0	107.0	99.0
Q1, Q3	64.0, 114.0	72.0, 114.0	67.0, 114.0
Min, Max	29, 137	11, 144	11, 144
< 28 Days	0	1 (3.2)	1 (0.7)
≥ 28 Days	114 (100)	30 (96.8)	144 (99.3)
≥ 28 and < 56 Days	20 (17.5)	3 (9.7)	23 (15.9)
≥ 56 Days	94 (82.5)	27 (87.1)	121 (83.4)
≥ 84 Days	64 (56.1)	23 (74.2)	87 (60.0)
≥ 112 Days	38 (33.3)	12 (38.7)	50 (34.5)
≥ 140 Days	0	1 (3.2)	1 (0.7)
Person-years from Booster [2]	27.62	8.22	35.85
Time on Study from Dose 1 of elasomeran (Days)			
n	114	31	145
Mean (SD)	440.9 (6.75)	412.5 (4.23)	434.8 (13.26)
Median	441.0	414.0	438.0
Q1, Q3	436.0, 444.0	413.0, 415.0	435.0, 443.0
Min, Max	404, 456	402, 416	402, 456
Person-years from Dose 1 of elasomeran [3]	137.60	35.01	172.61

Percentages are based on the number of safety subjects in booster dose analysis.
[1] For subjects who received two doses of elasomeran in Primary Series, Time Since Primary Series is calculated as: Date of Booster — Date of Second Dose of elasomeran + 1.
[2] Person-years is defined as the total years from the booster dose date to the earlier date of study discontinuation or data cutoff.
[3] Person-years is defined as the total years from the first dose date of elasomeran to the earlier date of study discontinuation or data cutoff.
Source: Study mRNA-1273-P204 Table 14.1.6.1 (18 August 2022).

Table 60: Participant Age Group and Gender by Dose Level in Part Booster Dose (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Months to < 6 Years)

	Elasomeran 25 µg Primary Series - Booster 10 µg		
Characteristic	**6 Months to < 2 Years (N=114)**	**2 Years to < 6 Years (N=31)**	**Total (N=145)**
Age (Years), n (%)			
< 1	28 (24.6)	0	28 (19.3)
1	86 (75.4)	0	86 (59.3)
2	0	8 (25.8)	8 (5.5)

3	0	8 (25.8)	8 (5.5)
4	0	14 (45.2)	14 (9.7)
5	0	1 (3.2)	1 (0.7)
Age (Years)			
n	114	31	145
Mean (SD)	0.94 (0.125)	3.26 (0.893)	1.43 (1.044)
Median	1.00	3.00	1.00
Q1, Q3	1.00, 1.00	2.00, 4.00	1.00, 1.00
Min, Max	0.5, 1.0	2.0, 5.0	0.5, 5.0
Age (Months) [1]			
n	114		
Mean (SD)	15.2 (4.92)		
Median	14.0		
Q1, Q3	11.0, 20.0		
Min, Max	6, 23		
Gender, n (%)			
Male	63 (55.3)	17 (54.8)	80 (55.2)
Female	51 (44.7)	14 (45.2)	65 (44.8)

Abbreviations: max = maximum; min = minimum; SD = standard deviation.
[1] Age in months is summarised for ≥ 6 months and < 2 years group only.
Source: mRNA-1273-P204 Table 14.1.3.13.1 (18 August 2022).

Table 61: Participant Race by Dose Level in Part Booster Dose (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Months to < 6 Years)

	Elasomeran 25 µg Primary Series - Booster 10 µg		
Characteristic	**6 Months to < 2 Years (N=114)**	**2 Years to < 6 Years (N=31)**	**Total (N=145)**
Race, n (%)			
White	92 (80.7)	24 (77.4)	116 (80.0)
Black	3 (2.6)	1 (3.2)	4 (2.8)
Asian	6 (5.3)	3 (9.7)	9 (6.2)
American Indian or Alaska Native	1 (0.9)	0	1 (0.7)
Native Hawaiian or Other Pacific Islander	0	0	0
Multiracial	9 (7.9)	2 (6.5)	11 (7.6)
Other	3 (2.6)	1 (3.2)	4 (2.8)
Not reported	0	0	0
Unknown	0	0	0

Source: mRNA-1273-P204 Table 14.1.3.13.1 (18 August 2022).

Table 62: Participant Ethnicity by Dose Level in Part Booster Dose (Safety Set) in the Ongoing mRNA-1273-P204 Study (6 Months to < 6 Years)

	Elasomeran 25 µg Primary Series - Booster 10 µg		
Characteristic	**6 Months to < 2 Years (N=114)**	**2 Years to < 6 Years (N=31)**	**Total (N=145)**
Ethnicity, n (%)			
Hispanic or Latino	11 (9.6)	4 (12.9)	15 (10.3)
Not Hispanic or Latino	102 (89.5)	27 (87.1)	129 (89.0)
Not reported	1 (0.9)	0	1 (0.7)
Unknown	0	0	0

Source: mRNA-1273-P204 Table 14.1.3.13.1 (18 August 2022).

mRNA-1273-P304 study

This is a Phase 3b, open-label study to evaluate the safety, reactogenicity, and immunogenicity of elasomeran SARS-CoV-2 vaccine in SOT recipients and Healthy controls. Approximately 240 participants (220 adult kidney or liver transplant recipients and 20 healthy controls) who are least 18 years of age will be enrolled. All SOT recipients and healthy participants will receive 2 doses of 100 µg of elasomeran 28 days apart. The SOT recipients will be offered the opportunity to receive a third dose of elasomeran at Day 85. In Part B, a 100 µg BD will be administered to participants at least 4 months from the last dose of a completed primary COVID-19 vaccination series. Study Endpoints included Safety and Reactogenicity and adverse events for 12 months after the last dose. Immunogenicity endpoints included neutralizing and binding antibody.

Table 63: Participants exposure by Age in mRNA-1273-P304 study

Age range	Participants (N)
≥18 and <65 years	184
≥65 and <75 years	43
≥75 and <85 years	7
Total	**214**

Data extraction date: 22 November 2022.

Table 64: Participant exposure by Gender in mRNA-1273-P304 study

Gender	Participants (N)
Male	114
Female	100
Total	**214**

Data from ongoing trial as of 17 Dec 2021.

Table 65: Participant exposure by Racial group in mRNA-1273-P304 study

Race	Participants (N)
White	149
Black	36
Asian	11
American Indian or Alaska Native	1
Native Hawaiian or Other Pacific Islander	0
Other	7
Multiple	3
Not reported	6
Unknown	1
Total	**214**

Data extraction date: 22 November 2022.

Table 66: Participant exposure by Ethnicity in mRNA-1273-P304 study

Ethnicity	Participants (N)
Hispanic or Latino	20
Not Hispanic or Latino	192
Not reported	2
Total	**214**

Data extraction date: 22 November 2022.

mRNA-1273-P301 (Phase 3)

The Phase 3 study (mRNA-1273-P301) is a completed pivotal three parts study. Part A was a randomized, stratified, observer-blind, placebo-controlled study to evaluate safety, efficacy, and immunogenicity of elasomeran in adults ≥ 18 years of age conducted in the US. This study enrolled 30,418 participants with no known history of SARS-CoV-2 infection, but whose location or circumstances put them at appreciable risk of acquiring SARS-CoV-2 infection. Participants were randomly assigned to receive two injections of either 100 µg of elasomeran vaccine or a placebo control given 28 days apart in a 1:1 ratio. The study enrolled adults at increased risk of complications from COVID-19 based on pre-existing medical co-morbidities. The study enrolled participants with underlying medical conditions at increased risk of severe COVID -19 such as chronic lung disease, significant cardiac disease, severe obesity diabetes, liver disease, and HIV infection. The Part B Open-Label Observational Phase of the study was prompted by the authorization of a COVID-19 vaccine under EUA. Transitioning the study to Part B permitted all ongoing study participants to be informed of the availability and eligibility criteria of any COVID-19 vaccine made available under an EUA and the option to offer all ongoing study participants who request unblinding, an opportunity to schedule a Participation Decision Visit to know their original treatment assignment (placebo vs. elasomeran vaccine). The Part B Open-Label Observation Phase also provided the opportunity for EUA-eligible study participants who previously received placebo to actively request to receive 2 doses of elasomeran vaccine.

Participants enrolled in Part B who had received at least one dose of elasomeran in the study were eligible to proceed to Part C, the booster dose phase of the study. Initiation of Part C was prompted by the need to proactively prepare for vaccination strategies to induce broader protection against SARS-CoV-2 due to the emergence of VOCs. Part C provided data on the safety, effectiveness and immunogenicity of a 50 µg booster dose of elasomeran.

Table 67: Duration of Exposure in the Completed mRNA-1273-P301 Study (Part A)

Duration of Exposure	**Elasomeran (N=15184)**
Received First Injection	15184 (100)
Received Second Injection	14731 (97.0)
≥ 49 Days Since First Injection	15039 (99.0)
≥ 56 Days Since First Injection	15023 (98.9)
≥ 2 Months Since First Injection	14995 (98.8)
< 28 Days Since Second Injection	24 (0.2)
≥ 28 and < 56 Days Since Second Injection	51 (0.3)
≥ 28 Days Since Second Injection	14707 (96.9)
≥ 56 Days Since Second Injection	14656 (96.5)
≥ 2 Months Since Second Injection	14645 (96.5)
≥ 3 Months Since Second Injection	14595 (96.1)
≥ 4 Months Since Second Injection	14485 (95.4)
≥ 5 Months Since Second Injection	12861 (84.7)
≥ 6 Months Since Second Injection	7499 (49.4)
Study Duration from First Injection (Days)	
Mean (Standard Deviation)	206.0 (31.02)
Median	213.0
Quartile 1, Quartile 3	197.0, 226.0
Minimum, Maximum	1, 243
Study Duration from Second Injection (Days)	
Mean (Standard Deviation)	173.7 (38.95)
Median	183.0
Quartile 1, Quartile 3	166.0, 194.0
Minimum, Maximum	0, 218

Table 68: Age Group and Gender in the Completed mRNA-1273-P301 Study (Part A)

Age Group	**Elasomeran (N=15184)**
Adults, 18-64 years	11415
Elderly, 65-74 years	3112
Elderly, 75-84 years	616

Age Group	**Elasomeran (N=15184)**
Elderly 85 + years	41
Gender	
Male	7918
Female	7266

Source: mRNA-1273-P301 Part A Tables 14.1.6.2.2 and 14.1.6.2.4 (Data extraction date: 04 May 2021).

Table 69: Participant Race in the Completed mRNA-1273-P301 Study (Part A)

Race	**Elasomeran (N=15184)**
White	12034
Black or African American	1567
Asian	656
American Indian or Alaska Native	113
Native Hawaiian or Other Pacific Islander	36
Multiple	320
Other / Not reported / Unknown	458
Total	15184

Source: mRNA-1273-P301 Part A Table 14.1.6.2.5 and Table 14.1.6.2.1 (Data extraction date: 04 May 2021).

Table 70: Participant Ethnicity in the Completed mRNA-1273-P301 Study (Part A)

Ethnicity	**Elasomeran (N=15184)**
Hispanic or Latino	3122
Not Hispanic or Latino	11920
Not Reported / Unknown	142
Total	15184

Source: mRNA-1273-P301 Part A Table 14.1.6.2.6 and Table 14.1.6.2.1 (Data extraction date: 04 May 2021).

Table 71: Comorbidities in the Completed mRNA-1273-P301 Study (Part A)

Age and Risk Group: ≥ 18 and < 65 Years	**Elasomeran (N=15184)**
Number of Participants at Risk (N)	2320
Chronic lung disease	473
Significant cardiac disease	321
Severe obesity	896
Diabetes	919
Liver disease	84
HIV infection	77

Age and Risk Group: > 65 Years	
Number of Participants at Risk (N)	1128
Chronic lung disease	239
Significant cardiac disease	441
Severe obesity	174
Diabetes	541
Liver disease	20
HIV infection	17

Source: mRNA-1273-P301 Part A Table 14.1.6.2.8 (Data extraction date: 04 May 2021).

Table 72: Risk Factors in the Completed mRNA-1273-P301 Phase 3 Study (Part A)

Age and Risk Group: ≥ 18 and < 65 Years	**Elasomeran (N=15184)**
At least one risk factor (N)	2320
One risk factor	1925
Two risk factors	351
Three risk factors	34
Four risk factors	9
Five risk factors	1
Six risk factors	0
Age and Risk Group: > 65 Years	
At least one risk factor (N)	1128
One risk factor	866
Two risk factors	223
Three risk factors	36
Four risk factors	3
Five risk factors	0
Six risk factors	0

Source: mRNA-1273-P301 Part A Table 14.1.6.2.9 (Data extraction date: 04 May 2021).

Table 73: Participants by Age group in the Completed mRNA-1273-P301 Phase 3 Study (Part B)

	≥ 18 and <65 Years				**≥ 65 Years**			
	Placebo (N=2156)	Placebo-elasomeran (N=9256)	Elasomeran (N=11414)	Total (N=22826)	Placebo (N=357)	Placebo-elasomeran (N=3393)	Elasomeran (N=3770)	Total (N=7520)
Age Subgroup at Screening, n (%)								
≥ 18 and <65 Years	2156 (100)	9256 (100)	11414 (100)	22826 (100)	0	0	0	0

	≥ 18 and <65 Years				≥ 65 Years			
	Placebo (N=2156)	Placebo-elasomeran (N=9256)	Elasomeran (N=11414)	Total (N=22826)	Placebo (N=357)	Placebo-elasomeran (N=3393)	Elasomeran (N=3770)	Total (N=7520)
≥ 65 and <70 Years	0	0	0	0	196 (54.9)	1620 (47.7)	1906 (50.6)	3722 (49.5)
≥ 70 and <75 Years	0	0	0	0	101 (28.3)	1092 (32.2)	1206 (32.0)	2399 (31.9)
≥ 75 and <80 Years	0	0	0	0	37 (10.4)	470 (13.9)	467 (12.4)	974 (13.0)
≥ 80 Years	0	0	0	0	23 (6.4)	211 (6.2)	191 (5.1)	425 (5.7)
Age Subgroup at Screening, n (%)								
≥ 18 and <65 Years	2156 (100)	9256 (100)	11414 (100)	22826 (100)	0	0	0	0
≥ 65 and <75 Years	0	0	0	0	297 (83,2)	2712 (79.9)	3112 (82.5)	6121 (81.4)
≥ 75 and <85 Years	0	0	0	0	53 (14.8)	639 (18.8)	617 (16.4)	1309 (17.4)
≥ 85 Years	0	0	0	0	7 (2.0)	42 (1.2)	41 (1.1)	90 (1.2)

Source: mRNA-1273-P301 Part B Table 14.1.3.2.2.2 (Data extraction date: 07 Apr 2023).

Table 74: Participants Risk Factors / Comorbidities in the Completed mRNA-1273-P301 Phase 3 Study (Part B)

	≥ 18 and <65 Years				≥ 65 Years			
	Placebo (N=2156)	Placebo-elasomeran (N=9256)	Elasomeran (N=11414)	Total (N=22826)	Placebo (N=357)	Placebo-elasomeran (N=3393)	Elasomeran (N=3770)	Total (N=7520)
Age and Health Risk for Severe COVID-19, n (%)*								
≥ 18 and <65 Years and Not at Risk	1797 (83.3)	7082 (76.5)	8889 (77.9)	17768 (77.8)	0	2 (<0.1)	0	2 (<0.1)
≥ 18 and <65 Years and at Risk	359 (16.7)	2173 (23.5)	2524 (22.1)	5056 (22.2)	0	3 (<0.1)	6 (0.2)	9 (0.1)
≥ 65 Years	0	1 (<0.1)	1 (<0.1)	2 (<0.1)	357 (100)	3388 (99.9)	3764 (99.8)	7509 (99.9)
Risk Factor for Severe COVID-19 at Screening, n (%)**								
Chronic Lung Disease	69 (3.2)	435 (4.7)	473 (4.1)	977 (4.3)	22 (6.2)	223 (6.6)	239 (6.3)	484 (6.4)
Significant Cardiac Disease	26 (1.2)	266 (2.9)	321 (2.8)	613 (2.7)	41 (11.5)	409 (12.1)	441 (11.7)	891 (11.8)

	≥ 18 and <65 Years				≥ 65 Years			
	Placebo (N=2156)	Placebo-elasomeran (N=9256)	Elasomeran (N=11414)	Total (N=22826)	Placebo (N=357)	Placebo-elasomeran (N=3393)	Elasomeran (N=3770)	Total (N=7520)
Severe Obesity	119 (5.5)	786 (8.5)	896 (7.9)	1801 (7.9)	14 (3.9)	139 (4.1)	174 (4.6)	327 (4.3)
Diabetes	132 (6.1)	780 (8.4)	919 (8.1)	1831 (8.0)	45 (12.6)	499 (14.7)	541 (14.4)	1085 (14.4)
Liver Disease	10 (0.5)	60 (0.6)	84 (0.7)	154 (0.7)	3 (0.8)	23 (0.7)	20 (0.5)	46 (0.6)
HIV Infection	8 (0.4)	67 (0.7)	77 (0.7)	152 (0.7)	2 (0.6)	14 (0.4)	17 (0.5)	33 (0.4)

Source: mRNA-1273-P301 Part B Table 14.1.3.2.2.2 (Data extraction date: 07 Apr 2023).
* Based on stratification factor from IRT, subjects who are < 65 years old are categorized as at risk for severe COVID-19 illness if they have at least 1 of the risk factors specified in the study protocol at Screening.
** Subjects could be under one or more categories and are counted once at each category.

Table 75: Participants Gender in the Completed mRNA-1273-P301 Study (Part B)

	≥ 18 and <65 Years				≥ 65 Years			
	Placebo (N=2156)	Placebo-elasomeran (N=9256)	Elasomeran (N=11414)	Total (N=22826)	Placebo (N=357)	Placebo-elasomeran (N=3393)	Elasomeran (N=3770)	Total (N=7520)
Sex, n (%)								
Male	1157 (53.7)	4799 (51.8)	5840 (51.2)	11796 (51.7)	236 (66.1)	1864 (54.9)	2078 (55.1)	4178 (55.6)
Female	999 (46.3)	4457 (48.2)	5574 (48.8)	11030 (48.3)	121 (33.9)	1529 (45.1)	1692 (44.9)	3342 (44.4)

Source: mRNA-1273-P301 Part B Table 14.1.3.2.2.2 (Data extraction date: 07 Apr 2023).

Table 76: Participant Race in the Completed mRNA-1273-P301 Study (Part B)

	≥ 18 and <65 Years				≥ 65 Years			
	Placebo (N=2156)	Placebo-elasomeran (N=9256)	Elasomeran (N=11414)	Total (N=22826)	Placebo (N=357)	Placebo-elasomeran (N=3393)	Elasomeran (N=3770)	Total (N=7520)
Race, n (%)								
White	1600 (74.2)	7057 (76.2)	8654 (75.8)	17311 (75.8)	310 (86.8)	3032 (89.4)	3381 (89.7)	6723 (89.4)
Black or African American	241 (11.2)	1075 (11.6)	1344 (11.8)	2660 (11.7)	10 (2.8)	204 (6.0)	222 (5.9)	436 (5.8)
Asian	195 (9.0)	467 (5.0)	589 (5.2)	1251 (5.5)	18 (5.0)	59 (1.7)	67 (1.8)	144 (1.9)
American Indian or	19 (0.9)	76 (0.8)	92 (0.8)	187 (0.8)	2 (0.6)	24 (0.7)	21 (0.6)	47 (0.6)

	≥ 18 and <65 Years				≥ 65 Years			
	Placebo (N=2156)	Placebo-elasomeran (N=9256)	Elasomeran (N=11414)	Total (N=22826)	Placebo (N=357)	Placebo-elasomeran (N=3393)	Elasomeran (N=3770)	Total (N=7520)
Alaska Native								
Native Hawaiian or Other Pacific Islander	10 (0.5)	19 (0.2)	33 (0.3)	62 (0.3)	0	3 (<0.1)	3 (<0.1)	6 (<0.1)
Multiracial	33 (1.5)	250 (2.7)	288 (2.5)	571 (2.5)	8 (2.2)	27 (0.8)	32 (0.8)	67 (0.9)
Other	44 (2.0)	218 (2.4)	276 (2.4)	538 (2.4)	5 (1.4)	27 (0.8)	23 (0.6)	55 (0.7)
Not Reported	9 (0.4)	51 (0.6)	84 (0.7)	144 (0.6)	2 (0.6)	12 (0.4)	13 (0.3)	27 (0.4)
Unknown	5 (0.2)	43 (0.5)	54 (0.5)	102 (0.4)	2 (0.6)	5 (0.1)	8 (0.2)	15 (0.2)

Source: mRNA-1273-P301 Part B Table 14.1.3.2.2.2 (Data extraction date: 07 Apr 2023).

Table 77: Participant Ethnicity in the Completed mRNA-1273-P301 Study (Part B)

	≥ 18 and <65 Years				≥ 65 Years			
	Placebo (N=2156)	Placebo-elasomeran (N=9256)	Elasomeran (N=11414)	Total (N=22826)	Placebo (N=357)	Placebo-elasomeran (N=3393)	Elasomeran (N=3770)	Total (N=7520)
Ethnicity, n (%)								
Hispanic or Latino	551 (25.6)	2222 (24.0)	2768 (24.3)	5541 (24.3)	59 (16.5)	275 (8.1)	354 (9.4)	688 (9.1)
Not Hispanic or Latino	1583 (73.4)	6961 (75.2)	8548 (74.9)	17092 (74.9)	295 (82.6)	3080 (90.8)	3372 (89.4)	6747 (89.7)
Not Reported	14 (0.6)	43 (0.5)	72 (0.6)	129 (0.6)	1 (0.3)	25 (0.7)	33 (0.9)	59 (0.8)
Unknown	8 (0.4)	30 (0.3)	26 (0.2)	64 (0.3)	2 (0.6)	13 (0.4)	11 (0.3)	26 (0.3)

Source: mRNA-1273-P301 Part B Table 14.1.3.2.2.2 (Data extraction date: 07 Apr 2023).

Table 78: Participants Age group in the Completed mRNA-1273-P301 Phase 3 Study (Part C)

	≥ 18 and <65 Years			≥ 65 Years		
	Placebo-elasomeran (N=7176)	**Elasomeran (N=7027)**	**Total (N=14212)**	**Placebo-elasomeran (N=2776)**	**Elasomeran (N=2620)**	**Total (N=5397)**
≥ 18 and <65 Years	7176 (100)	7027 (100)	14212 (100)	0	0	0

	≥ 18 and <65 Years			≥ 65 Years		
	Placebo-elasomeran (N=7176)	**Elasomeran (N=7027)**	**Total (N=14212)**	**Placebo-elasomeran (N=2776)**	**Elasomeran (N=2620)**	**Total (N=5397)**
≥ 65 and <70 Years	0	0	0	1346 (48.5)	1313 (50.1)	2659 (49.3)
≥ 70 and <75 Years	0	0	0	877 (31.6)	843 (32.2)	1721 (31.9)
≥ 75 and <80 Years	0	0	0	383 (13.8)	331 (12.6)	714 (13.2)
≥ 80 Years	0	0	0	170 (6.1)	133 (5.1)	303 (5.6)
Age Subgroup at Screening, n (%)						
≥ 18 and <65 Years	7176 (100)	7027 (100)	14212 (100)	0	0	0
≥ 65 and <75 Years	0	0	0	2223 (80.1)	2156 (82.3)	4380 (81.2)
≥ 75 and <85 Years	0	0	0	521 (18.8)	440 (16.8)	961 (17.8)
≥ 85 Years	0	0	0	32 (1.2)	24 (0.9)	56 (1.0)

Source: mRNA-1273-P301 Part C Table 14.1.3.6.2.1 (Data extraction date: 07 Apr 2023).

Note that there were 10 participants who received placebo in Part A and did not receive the elasomeran primary series prior to receiving the booster dose. These participants are accounted for in the total but are not included among the elasomeran and placebo-elasomeran groups.

Table 79: Participants Risk Factors / Comorbidities in the Completed mRNA-1273-P301 Phase 3 Study (Part C)

	≥ 18 and <65 Years			≥ 65 Years		
	Placebo-elasomeran (N=7176)	**Elasomeran (N=7027)**	**Total (N=14212)**	**Placebo-elasomeran (N= 2776)**	**Elasomeran (N=2620)**	**Total (N=5397)**
Age and Health Risk for Severe COVID-19, n (%)*						
≥ 18 and <65 Years and Not at Risk	5418 (75.5)	5375 (76.5)	10796 (76.0)	1 (<0.1)	0	1 (<0.1)
≥ 18 and <65 Years and at Risk	1757 (24.5)	1652 (23.5)	3415 (24.0)	2 (<0.1)	4 (0.2)	6 (0.1)
≥ 65 Years	1 (<0.1)	0	1 (<0.1)	2773 (99.9)	2616 (99.8)	5390 (99.9)
Risk Factor for Severe COVID-19 at Screening, n (%)**						
Chronic Lung Disease	351 (4.9)	321 (4.6)	672 (4.7)	179 (6.4)	168 (6.4)	347 (6.4)
Significant Cardiac Disease	211 (2.9)	206 (2.9)	417 (2.9)	322 (11.6)	307 (11.7)	629 (11.7)
Severe Obesity	643 (9.0)	584 (8.3)	1229 (8.6)	115 (4.1)	119 (4.5)	234 (4.3)
Diabetes	635 (8.8)	603 (8.6)	1240 (8.7)	391 (14.1)	396 (15.1)	788 (14.6)
Liver Disease	50 (0.7)	61 (0.9)	111 (0.8)	18 (0.6)	12 (0.5)	30 (0.6)
HIV Infection	54 (0.8)	58 (0.8)	113 (0.8)	12 (0.4)	13 (0.5)	25 (0.5)

	≥ 18 and <65 Years			≥ 65 Years		
	Placebo-elasomeran (N=7176)	**Elasomeran (N=7027)**	**Total (N=14212)**	**Placebo-elasomeran (N= 2776)**	**Elasomeran (N=2620)**	**Total (N=5397)**

Source: mRNA-1273-P301 Part C Table 14.1.3.6.2.1 (Data extraction date: 07 Apr 2023).
* Based on stratification factor from IRT, subjects who are < 65 years old are categorized as at risk for severe COVID-19 illness if they have at least 1 of the risk factors specified in the study protocol at Screening.
** Subjects could be under one or more categories, and are counted once at each category.
Note that there were 10 participants who received placebo in Part A and did not receive the elasomeran primary series prior to receiving the booster dose. These participants are accounted for in the total, but are not included among the elasomeran and placebo-elasomeran groups.

Table 80: Participants Gender in the Completed mRNA-1273-P301 Study (Part C)

	≥ 18 and <65 Years			≥ 65 Years		
	Placebo-elasomeran (N=7176)	**Elasomeran (N=7027)**	**Total (N=14212)**	**Placebo-elasomeran (N=2776)**	**Elasomeran (N=2620)**	**Total (N=5397)**
Sex, n (%)						
Male	3736 (52.1)	3611 (51.4)	7353 (51.7)	1505 (54.2)	1409 (53.8)	2915 (54.0)
Female	3440 (47.9)	3416 (48.6)	6859 (48.3)	1271 (45.8)	1211 (46.2)	2482 (46.0)

Source: mRNA-1273-P301 Part C Table 14.1.3.6.2.1 (Data extraction date: 07 Apr 2023).
Note that there were 10 participants who received placebo in Part A and did not receive the elasomeran primary series prior to receiving the booster dose. These participants are accounted for in the total but are not included among the elasomeran and placebo-elasomeran groups.

Table 81: Participant Race in the Completed mRNA-1273-P301 Study (Part C)

	≥ 18 and <65 Years			≥ 65 Years		
	Placebo-elasomeran (N=7176)	**Elasomeran (N=7027)**	**Total (N=14212)**	**Placebo-elasomeran (N=2776)**	**Elasomeran (N=2620)**	**Total (N=5397)**
Race, n (%)						
White	5451 (76.0)	5212 (74.2)	10669 (75.1)	2478 (89.3)	2333 (89.0)	4812 (89.2)
Black or African American	857 (11.9)	880 (12.5)	1740 (12.2)	174 (6.3)	168 (6.4)	342 (6.3)
Asian	362 (5.0)	366 (5.2)	728 (5.1)	44 (1.6)	40 (1.5)	84 (1.6)
American Indian or Alaska Native	59 (0.8)	58 (0.8)	117 (0.8)	19 (0.7)	16 (0.6)	35 (0.6)
Native Hawaiian or Other Pacific Islander	11 (0.2)	24 (0.3)	35 (0.2)	2 (<0.1)	3 (0.1)	5 (<0.1)
Multiracial	196 (2.7)	191 (2.7)	387 (2.7)	25 (0.9)	27 (1.0)	52 (1.0)
Other	161 (2.2)	193 (2.7)	354 (2.5)	22 (0.8)	19 (0.7)	41 (0.8)
Not Reported	42 (0.6)	61 (0.9)	103 (0.7)	8 (0.3)	11 (0.4)	19 (0.4)
Unknown	37 (0.5)	42 (0.6)	79 (0.6)	4 (0.1)	3 (0.1)	7 (0.1)

Source: mRNA-1273-P301 Part C Table 14.1.3.6.2.1 (Data extraction date: 07 Apr 2023).

Note that there were 10 participants who received placebo in Part A and did not receive the elasomeran primary series prior to receiving the booster dose. These participants are accounted for in the total, but are not included among the elasomeran and placebo-elasomeran groups.

Table 82: Participant Ethnicity in the Completed mRNA-1273-P301 Study (Part C)

	≥ 18 and <65 Years			≥ 65 Years		
	Placebo-elasomeran (N=7176)	**Elasomeran (N=7027)**	**Total (N=14212)**	**Placebo-elasomeran (N=2776)**	**Elasomeran (N=2620)**	**Total (N=5397)**
Ethnicity, n (%)						
Hispanic or Latino	1716 (23.9)	1751 (24.9)	3471 (24.4)	232 (8.4)	251 (9.6)	484 (9.0)
Not Hispanic or Latino	5399 (75.2)	5216 (74.2)	10620 (74.7)	2514 (90.6)	2337 (89.2)	4851 (89.9)
Not Reported	34 (0.5)	45 (0.6)	79 (0.6)	20 (0.7)	25 (1.0)	45 (0.8)
Unknown	27 (0.4)	15 (0.2)	42 (0.3)	10 (0.4)	7 (0.3)	17 (0.3)

Source: mRNA-1273-P301 Part C Table 14.1.3.6.2.1 (Data extraction date: 07 Apr 2023).

Note that there were 10 participants who received placebo in Part A and did not receive the elasomeran primary series prior to receiving the booster dose. These participants are accounted for in the total but are not included among the elasomeran and placebo-elasomeran groups.

mRNA-1273-P205 study

Study mRNA-1273-P205 is an ongoing, open-label, Phase 2/3 study that is evaluating the immunogenicity, safety, and reactogenicity of mRNA vaccine boosters for SARS-CoV-2 variants including mRNA-1273.211, mRNA-1273 (Spikevax), mRNA-1273.617.2, mRNA-1273.213, mRNA-1273.529, mRNA-1273.214 (Spikevax bivalent Original/Omicron BA.1), mRNA-1273-222 (Spikevax bivalent Original/Omicron BA.4-5), mRNA-1273.815 and mRNA-1273.231.

The study consists of 9 parts: A, (1, 2), B, C, D, E, F, G, H, and J covering the following vaccines and doses:

Part A.1: 50 µg mRNA-1273.211 and 100 µg mRNA-1273.211

Part A.2: Second booster dose 50 µg mRNA-1273.214: Participants who received mRNA-1273.211 50 µg as a first booster dose in Part A.

Part B: 100 µg mRNA-1273

Part C: 50 µg mRNA-1273.617.2 and 100 µg mRNA-1273.617.2

Part D: 50 µg mRNA-1273.213 and 100 µg mRNA-1273.213

Part E: 100 µg mRNA-1273.213

Part F - Cohort 1- 50 µg mRNA-1273.529: Participants who previously received 100 µg mRNA 1273 primary series and have not received a mRNA-1273 booster dose previously.

Part F - Cohort 2, Second booster dose 50 µg mRNA-1273.529 or 50 µg mRNA-1273 dose: Participants who previously received 100 µg mRNA-1273 primary series and a booster dose of 50 µg mRNA-1273

Part G – Second booster dose 50 µg mRNA-1273.214: Participants who received 100 µg mRNA-1273 primary series and a booster dose of 50 µg mRNA-1273

Part H - Second booster dose 50 µg mRNA-1273.222: Participants who received 100 µg mRNA-1273 primary series and a booster dose of 50 µg mRNA-1273

Part J - Third booster dose 50 µg mRNA-1273.815 and 50 µg mRNA-1273.231: Participants who previously received a primary series of mRNA vaccine, a first booster dose of a monovalent mRNA vaccine, and a second booster dose of a bivalent mRNA vaccine against SARS-CoV-2.

In total, 895 adults were treated with mRNA-1273.211 in Part A of the study including 300 adults treated with 50 µg mRNA-1273.211 and 595 adults treated with 100 µg mRNA-1273.211 up to 2 February 2022 (Table 83 to Table 86).

A further 437 adults were treated with Spikevax bivalent (50 µg elasomeran/imelasomeran) in Part G of the study and 377 adults were treated with Spikevax (50 µg elasomeran) in Part F (Cohort 2), up to 27 April 2022 (Table 87 to Table 90). In Part H 511 adults were treated with 50 µg mRNA-1273.222 up to 23 Sep 2022. In Part J, 50 adults were treated with 50 µg mRNA-1273.815 and 51 adults were treated with 50 µg mRNA-1273.213 up to 16 May 2023.

Table 83: Duration of Exposure in the Ongoing mRNA-1273-P205 Study (Part A)

	mRNA-1273.211 50 µg (N=300)	mRNA-1273.211 100 µg (N=595)	Total mRNA-1273.211 (N=895)
Number of Subjects, n (%)			
Received Injection	300 (100)	595 (100)	895 (100)
≥ 28 Days Since Injection	299 (99.7)	593 (99.7)	892 (99.7)
≥ 2 Months Since Injection	299 (99.7)	586 (98.5)	885 (98.9)
≥ 3 Months Since Injection	299 (99.7)	586 (98.5)	885 (98.9)
≥ 4 Months Since Injection	299 (99.7)	585 (98.3)	884 (98.8)
≥ 6 Months Since Injection	297 (99.0)	583 (98.0)	880 (98.3)
≥ 8 Months Since Injection	290 (96.7)	0	290 (32.4)
≥ 10 Months Since Injection	0	0	0
Study Duration from Injection (Days)			
Mean (SD)	243.7 (16.11)	208.1 (22.47)	220.0 (26.55)
Median	245.0	210.0	216.0
Q1, Q3	245.0, 246.0	206.0, 216.0	209.0, 245.0
Min, Max	13, 251	16, 218	13, 251

Abbreviations: max = maximum; min = minimum.
1 Month= 30.4375 Days
Percentages are based on the number of subjects in the Safety Set.
This interim analysis includes Part A subjects (mRNA-1273.211) immunogenicity data up to Day 181 visit. The data cutoff date for safety and SARS-CoV-2 infection is 02Feb2022.
Source: Study P205 Table 14.1.6.1

Table 84: Age Group and Gender in the Ongoing mRNA-1273-P205 Study (Part A)

	mRNA-1273.211 50 µg (N=300)	mRNA-1273.211 100 µg (N=595)	Total mRNA-1273.211 (N=895)
Age group, n (%)			
≥ 18 years and < 65 years	238 (79.3)	449 (75.5)	687 (76.8)
≥ 65 years	62 (20.7)	146 (24.5)	208 (23.2)
Gender, n (%)			
Male	133 (44.3)	264 (44.4)	397 (44.4)
Female	167 (55.7)	331 (55.6)	498 (55.6)

Percentages are based on the number of subjects in the Safety Set.
This interim analysis includes Part A subjects (mRNA-1273.211) immunogenicity data up to Day 181 visit. The data cutoff date for safety and SARS-CoV-2 infection is 02Feb2022.
Source: Study P205 Table 14.1.3.1

Table 85: Participant Race in the Ongoing mRNA-1273-P205 Study (Part A)

	mRNA-1273.211 50 µg (N=300)	mRNA-1273.211 100 µg (N=595)	Total mRNA-1273.211 (N=895)
Race, n (%)			
White	257 (85.7)	520 (87.4)	777 (86.8)
Black or African American	19 (6.3)	34 (5.7)	53 (5.9)
Asian	9 (3.0)	18 (3.0)	27 (3.0)
American Indian or Alaska Native	1 (0.3)	5 (0.8)	6 (0.7)
Native Hawaiian or Other Pacific Islander	0	1 (0.2)	1 (0.1)
Multiracial	7 (2.3)	7 (1.2)	14 (1.6)
Other	4 (1.3)	6 (1.0)	10 (1.1)
Not Reported	3 (1.0)	3 (0.5)	6 (0.7)
Unknown	0	1 (0.2)	1 (0.1)

Percentages are based on the number of subjects in the Safety Set.
This interim analysis includes Part A subjects (mRNA-1273.211) immunogenicity data up to Day 181 visit. The data cutoff date for safety and SARS-CoV-2 infection is 02Feb2022.
Source: Study P205 Table 14.1.3.1

Table 86: Participant Ethnicity in the Ongoing mRNA-1273-P205 Study (Part A)

	mRNA-1273.211 50 µg (N=300)	mRNA-1273.211 100 µg (N=595)	Total mRNA-1273.211 (N=895)
Ethnicity, n (%)			
Hispanic or Latino	38 (12.7)	52 (8.7)	90 (10.1)
Not Hispanic or Latino	262 (87.3)	539 (90.6)	801 (89.5)
Not Reported	0	4 (0.7)	4 (0.4)
Unknown	0	0	0

Percentages are based on the number of subjects in the Safety Set.
This interim analysis includes Part A subjects (mRNA-1273.211) immunogenicity data up to Day 181 visit. The data cutoff date for safety and SARS-CoV-2 infection is 02Feb2022.
Source: Study P205 Table 14.1.3.1

Table 87: Duration of Exposure in the Ongoing mRNA-1273-P205 Study (Part G/ Part F Cohort 2)

	Part G Elasomeran/Imelasomeran 50 µg (N=437)	Part F Cohort 2 Elasomeran 50 µg (N=377)
Number of subjects, n (%)		
Received Injection	437 (100)	377 (100)
≥ 28 Days Since Injection	436 (99.8)	377 (100)
≥ 56 Days Since Injection	0	285 (75.6)
≥ 2 Months Since Injection	0	114 (30.2)
≥ 3 Months Since Injection	0	0
Follow up Time from Injection (Days)		
Mean (SD)	43.1 (4.13)	57.9 (4.08)
Median	43.0	57.0
Q1, Q3	41.0, 45.0	56.0, 62.0
Min, Max	22, 51	51, 66

Abbreviations: max = maximum; min = minimum.
1 Month= 30.4375 Days
Percentages are based on the number of subjects in the Safety Set.
This interim analysis includes Part F Cohort 2 (elasomeran) and Part G subjects (elasomeran/imelasomeran) immunogenicity data up to Day 29 visit. The data cutoff date for safety and SARS-CoV-2 infection is 27Apr2022.
Source: Study P205 Table 14.1.6.1.8

Table 88: Age Group and Gender in the Ongoing mRNA-1273-P205 Study (Part G/ Part F Cohort 2)

	Part G Elasomeran/Imelasomeran 50 µg (N=437)	Part F Cohort 2 Elasomeran 50 µg (N=377)
Age group, n (%)		
≥ 18 years and < 65 years	263 (60.2)	227 (60.2)
≥ 65 years	174 (39.8)	150 (39.8)
Gender, n (%)		
Male	179 (41.0)	186 (49.3)
Female	258 (59.0)	191 (50.7)

Percentages are based on the number of subjects in the Safety Set.
This interim analysis includes Part F Cohort 2 (elasomeran) and Part G subjects (elasomeran/imelasomeran) immunogenicity data up to Day 29 visit. The data cutoff date for safety and SARS-CoV-2 infection is 27Apr2022.
Source: Study P205 Table 14.1.3.1.8

Table 89: Participant Race in the Ongoing mRNA-1273-P205 Study (Part G/Part F Cohort 2)

	Part G Elasomeran/Imelasomeran 50 µg (N=437)	Part F Cohort 2 Elasomeran 50 µg (N=377)
Race, n (%)		
White	381 (87.2)	322 (85.4)
Black or African American	31 (7.1)	29 (7.7)
Asian	14 (3.2)	16 (4.2)
American Indian or Alaska Native	0	1 (0.3)

Native Hawaiian or Other Pacific Islander	0	1 (0.3)
Multiracial	7 (1.6)	2 (0.5)
Other	3 (0.7)	2 (0.5)
Not Reported	1 (0.2)	3 (0.8)
Unknown	0	1 (0.3)

Percentages are based on the number of subjects in the Safety Set.
This interim analysis includes Part F Cohort 2 (elasomeran) and Part G subjects (elasomeran/imelasomeran) immunogenicity data up to Day 29 visit. The data cutoff date for safety and SARS-CoV-2 infection is 27Apr2022.
Source: Study P205 Table 14.1.3.1.8

Table 90: Participant Ethnicity in the Ongoing mRNA-1273-P205 Study (Part G/ Part F Cohort 2)

	Part G Elasomeran/Imelasomeran 50 µg (N=437)	Part F Cohort 2 Elasomeran 50 µg (N=377)
Ethnicity, n (%)		
Hispanic or Latino	46 (10.5)	37 (9.8)
Not Hispanic or Latino	390 (89.2)	340 (90.2)
Not Reported	1 (0.2)	0
Unknown	0	0

Percentages are based on the number of subjects in the Safety Set.
This interim analysis includes Part F Cohort 2 (elasomeran) and Part G subjects (elasomeran/imelasomeran) immunogenicity data up to Day 29 visit. The data cutoff date for safety and SARS-CoV-2 infection is 27Apr2022.
Source: Study P205 Table 14.1.3.1.8

Table 91: Duration of Exposure in the Ongoing mRNA-1273-P205 Study (Part H)

	Part H Davesomeran 50 µg (N=511)
Number of subjects, n (%)	
Received Injection	511(100)
≥ 28 Days Since Injection	509 (99.6)
≥ 56 Days Since Injection	0
Follow up Time from Injection (Days)	
Mean (SD)	36.9 (4.26)
Median	37.0
Q1, Q3	33.0, 39.0
Min, Max	5, 45

Abbreviations: max = maximum; min = minimum.
1 Month= 30.4375 Days
Percentages are based on the number of subjects in the Safety Set.
This interim analysis includes Part H immunogenicity data up to Day 29 visit. The data cutoff date for safety and SARS-CoV-2 infection is 23 Sep 2022.
Source: Study P205 Table 14.1.6.1.9

Table 92: Age Group and Gender in the Ongoing mRNA-1273-P205 Study (Part H)

	Part H Davesomeran 50 µg (N=511)
Age group, n (%)	
≥ 18 years and < 65 years	406 (79.5)
≥ 65 years	105 (20.5)
Gender, n (%)	
Male	195 (38.2)
Female	316 (61.8)

Percentages are based on the number of subjects in the Safety Set.
This interim analysis includes Part H immunogenicity data up to Day 29 visit. The data cutoff date for safety and SARS-CoV-2 infection is 23 Sep 2022.
Source: Study P205 Table 14.1.3.1.9

Table 93: Participant Race in the Ongoing mRNA-1273-P205 Study (Part H)

	Part H Davesomeran 50 µg (N=511)
Race, n (%)	
White	426 (83.4)
Black or African American	56 (11.0)
Asian	11 (2.2)
American Indian or Alaska Native	1 (0.2)
Native Hawaiian or Other Pacific Islander	0
Multiracial	8 (1.6)
Other	6 (1.2)
Not Reported	2 (0.4)
Unknown	1 (0.2)

Percentages are based on the number of subjects in the Safety Set.
This interim analysis includes Part H immunogenicity data up to Day 29 visit. The data cutoff date for safety and SARS-CoV-2 infection is 23 Sep 2022.
Source: Study P205 Table 14.1.3.1.9

Table 94: Participant Ethnicity in the Ongoing mRNA-1273-P205 Study (Part H)

	Part H Davesomeran 50 µg (N=511)
Ethnicity, n (%)	
Hispanic or Latino	58 (11.4)
Not Hispanic or Latino	448 (87.7)
Not Reported	4 (0.8)
Unknown	1 (0.2)

Percentages are based on the number of subjects in the Safety Set.
This interim analysis includes Part H immunogenicity data up to Day 29 visit. The data cutoff date for safety and SARS-CoV-2 infection is 23 Sep 2022.
Source: Study P205 Table 14.1.3.1.9

Table 95: Duration of Exposure in the Ongoing mRNA-1273-P205 Study (Part J)

	Part J Andusomeran 1273.231 50 µg (N=51)	Part J Andusomeran 1273.815 50 µg (N=50)
Number of subjects, n (%)		
Received Injection	51 (100)	50 (100)
≥ 14 Days Since Injection	51 (100)	50 (100)
Follow up Time from Injection (Days)		
Mean (SD)	20.5 (0.61)	20.5 (0.61)
Median	20.0	20.0
Q1, Q3	20.0, 21.0	20.0, 21.0
Min, Max	20, 22	20, 22

Abbreviations: max = maximum; min = minimum.
1 Month= 30.4375 Days
Percentages are based on the number of subjects in the Safety Set.
This interim analysis includes Part J immunogenicity data up to Day 15 visit. The data cutoff date for safety and SARS-CoV-2 infection is 16 May 2022.
Source: Study P205 Table 14.1.6.1.10

Table 96: Age Group and Gender in the Ongoing mRNA-1273-P205 Study (Part J)

	Part J Andusomeran 1273.231 50 µg (N=51)	Part J Andusomeran 1273.815 50 µg (N=50)
Age group, n (%)		
≥ 18 years and < 65 years	44 (86.3)	39 (78.0)
≥ 65 years	7 (13.7)	11 (22.0)
Gender, n (%)		
Male	20 (39.2)	20 (40.0)
Female	31 (60.8)	30 (60.0)

Percentages are based on the number of subjects in the Safety Set.
This interim analysis includes Part J immunogenicity data up to Day 15 visit. The data cutoff date for safety and SARS-CoV-2 infection is 16 May 2022.
Source: Study P205 Table 14.1.3.1.10

Table 97: Participant Race in the Ongoing mRNA-1273-P205 Study (Part J)

	Part J Andusomeran 1273.231 50 µg (N=51)	Part J Andusomeran 1273.815 50 µg (N=50)
Race, n (%)		
White	41 (80.4)	45 (90.0)
Black or African American	4 (7.8)	4 (8.0)
Asian	3 (5.9)	1 (2.0)
American Indian or Alaska Native	0	0
Native Hawaiian or Other Pacific Islander	0	0
Multiracial	2 (3.9)	0
Other	1 (2.0)	0
Not Reported	0	0
Unknown	0	0

Percentages are based on the number of subjects in the Safety Set.

This interim analysis includes Part J immunogenicity data up to Day 15 visit. The data cutoff date for safety and SARS-CoV-2 infection is 16 May 2022.
Source: Study P205 Table 14.1.3.1.10

Table 98: Participant Ethnicity in the Ongoing mRNA-1273-P205 Study (Part J)

	Part J Andusomeran 1273.231 50 µg (N=51)	Part J Andusomeran 1273.815 50 µg (N=50)
Ethnicity, n (%)		
Hispanic or Latino	6 (11.8)	9 (18.0)
Not Hispanic or Latino	44 (86.3)	40 (80.0)
Not Reported	1 (2.0)	1 (2.0)
Unknown	0	0

Percentages are based on the number of subjects in the Safety Set.
This interim analysis includes Part J immunogenicity data up to Day 15 visit. The data cutoff date for safety and SARS-CoV-2 infection is 16 May 2022.
Source: Study P205 Table 14.1.3.1.10

mRNA-1273-P306 study

Study mRNA-1273-P306 is an ongoing open-label, Phase 3 study to evaluate the safety and immunogenicity of the mRNA-1273.214 vaccine (Spikevax bivalent Original/Omicron BA.1), for SARS-CoV-2 variants of concern in participants aged 6 months to < 6 years. The study consists of 2 parts:

Part 1 enrolled participants aged 6 months to <6 years who have not been previously vaccinated against SARS-CoV-2. Participants receive 2 doses of the mRNA-1273.214 vaccine (Spikevax bivalent Original/Omicron BA.1) and will be followed for approximately 12 months after the second dose for safety and additional immunogenicity follow-up. Participants who have not been previously vaccinated against SARS-CoV-2, will receive 2 IM injections of 25 µg mRNA-1273.214 on Day 1 and Day 29.

Part 2 enrolled participants aged 6 months to <6 years who have previously been vaccinated with a mRNA-1273 (Spikevax) primary series in Study mRNA-1273-P204. Participants received a single booster dose of the mRNA-1273.214 vaccine (Spikevax bivalent Original/Omicron BA.1), at least 4 months after completion of the mRNA-1273 (Spikevax) primary series and will be followed for approximately 6 months after the booster dose for safety and immunogenicity. Participants who have previously been vaccinated with a mRNA-1273 primary series, will receive a single IM booster dose (BD) of 10 µg mRNA-1273.214 at least 4 months after the last dose on BD Day 1.

Table 99: Duration of Exposure in the Ongoing mRNA-1273-P306 Study (Part 1)

Duration of exposure	mRNA-1273.214 25 µg ≥6 months and <2 years (N=48)	mRNA-1273.214 25 µg ≥2 years and <6 years (N=131)	Total mRNA-1273.214 25 µg (N=179)
Number of subjects, n (%)			
Received first injection	48 (100)	131 (100)	179 (100)

Duration of exposure	mRNA-1273.214 25 µg ≥6 months and <2 years (N=48)	mRNA-1273.214 25 µg ≥2 years and <6 years (N=131)	Total mRNA-1273.214 25 µg (N=179)
Received second injection	36 (75.0)	106 (80.9)	142 (79.3)
≥ 7 days since first injection	47 (97.9)	123 (93.9)	170 (95.0)
≥ 35 days since first injection	38 (79.2)	108 (82.4)	146 (81.6)
≥ 56 days since first injection	30 (62.5)	86 (65.6)	116 (64.8)
≥ 7 days since second injection	33 (68.8)	100 (76.3)	133 (74.3)
≥ 21 days since second injection	28 (58.3)	88 (67.2)	116 (64.8)
≥ 28 days since second injection	28 (58.3)	80 (61.1)	108 (60.3)
≥ 28 days and < 56 days since second injection	6 (12.5)	18 (13.7)	24 (13.4)
≥ 56 days since second injection	22 (45.8)	62 (47.3)	84 (46.9)
≥ 84 days since second injection	9 (18.8)	33 (25.2)	42 (23.5)
≥ 112 days since second injection	2 (4.2)	14 (10.7)	16 (8.9)
≥ 140 days since second injection	0	0	0
Study duration from first injection (days)			
n	48	131	179
Mean (SD)	76.8 (39.72)	83.4 (45.68)	81.6 (44.15)
Median	75.5	85.0	85.0
Q1, Q3	41.5, 107.5	46.0, 118.0	43.0, 113.0
Min, Max	6, 165	1, 168	1, 168
Person-years from first injection [1]	10.09	29.91	40.00
Study duration from second injection (days) [2]			
n	48	131	179
Mean (SD)	45.3 (40.54)	52.7 (42.50)	50.7 (42.00)
Median	41.0	49.0	49.0
Q1, Q3	0.5, 78.5	13.0, 85.0	6.0, 82.0
Min, Max	0, 137	0, 138	0, 138
Study duration from second injection in participants who received second injection (days)			
n	36	106	142
Mean (SD)	60.3 (35.66)	65.2 (37.65)	64.0 (37.09)
Median	67.0	72.0	68.0
Q1, Q3	31.0, 85.5	34.0, 97.0	34.0, 90.0
Min, Max	1, 137	1, 138	1, 138

Abbreviations: max = maximum; min = minimum; Q1 = quartile 1; Q3 = quartile 3; SD = standard deviation.
Percentages are based on the number of subjects in Safety Set.
[1] Person-years is defined as the total years from the first dose date to the earlier date of study discontinuation or data cut-off.
[2] Study duration from second injection is 0 day for subjects who did not receive second injection.
Source: Study mRNA-1273-P306 Table 14.1.5.1 (05 December 2022).

Table 100: Participant Age Group and Gender in the Ongoing mRNA-1273-P306 Study (Part 1)

Characteristic	mRNA-1273.214 25 µg ≥6 months and <2 years (N=48)	mRNA-1273.214 25 µg ≥2 years and <6 years (N=131)	Total mRNA-1273.214 25 µg (N=179)
Age (years), n (%)			
<1	21 (43.8)	0	21 (11.7)
1	27 (56.3)	0	27 (15.1)
2	0	41 (31.3)	41 (22.9)
3	0	46 (35.1)	46 (25.7)
4	0	23 (17.6)	23 (12.8)
5	0	21 (16.0)	21 (11.7)
Age (years)			
n	48	131	179
Mean (SD)	0.82 (0.227)	3.18 (1.051)	2.55 (1.387)
Median	1.00	3.00	3.00
Q1, Q3	0.50, 1.00	2.00, 4.00	1.00, 3.00
Min, Max	0.5, 1.0	2.0, 5.0	0.5, 5.0
Age (months) [1]			
n	48		
Mean (SD)	13.2 (6.20)		
Median	13.5		
Q1, Q3	6.0, 18.5		
Min, Max	6, 23		
Gender, n (%)			
Male	22 (45.8)	76 (58.0)	98 (54.7)
Female	26 (54.2)	55 (42.0)	81 (45.3)

Abbreviations: max = maximum; min = minimum; Q1 = quartile 1; Q3 = quartile 3; SD = standard deviation.
Percentages are based on the number of subjects in Safety Set.
[1] Age in months is summarised for ≥6 months and <2 years group only.
Source: Study mRNA-1273-P306 Table 14.1.3.2.1 (05 December 2022).

Table 101: Participant Race in the Ongoing mRNA-1273-P306 Study (Part 1)

Characteristic	mRNA-1273.214 25 µg ≥6 months and <2 years (N=48)	mRNA-1273.214 25 µg ≥2 years and <6 years (N=131)	Total mRNA-1273.214 25 µg (N=179)
Race, n (%)			
White	31 (64.6)	86 (65.6)	117 (65.4)
Black	11 (22.9)	35 (26.7)	46 (25.7)
Asian	4 (8.3)	1 (0.8)	5 (2.8)
American Indian or Alaska Native	0	1 (0.8)	1 (0.6)
Native Hawaiian or Other Pacific Islander	0	0	0
Multiracial	1 (2.1)	7 (5.3)	8 (4.5)
Other	1 (2.1)	1 (0.8)	2 (1.1)

Characteristic	mRNA-1273.214 25 µg ≥6 months and <2 years (N=48)	mRNA-1273.214 25 µg ≥2 years and <6 years (N=131)	Total mRNA-1273.214 25 µg (N=179)
Unknown	0	0	0
Not reported	0	0	0

Percentages are based on the number of subjects in Safety Set.
Source: Study mRNA-1273-P306 Table 14.1.3.2.1 (05 December 2022).

Table 102: Participant Ethnicity in the Ongoing mRNA-1273-P306 Study (Part 1)

Characteristic	mRNA-1273.214 25 µg ≥6 months and <2 years (N=48)	mRNA-1273.214 25 µg ≥2 years and <6 years (N=131)	Total mRNA-1273.214 25 µg (N=179)
Ethnicity, n (%)			
Hispanic or Latino	4 (8.3)	17 (13.0)	21 (11.7)
Not Hispanic or Latino	44 (91.7)	114 (87.0)	158 (88.3)
Not reported	0	0	0
Unknown	0	0	0

Percentages are based on the number of subjects in Safety Set.
Source: Study mRNA-1273-P306 Table 14.1.3.2.1 (05 December 2022).

Table 103: Duration of Exposure in the Ongoing mRNA-1273-P306 Study (Part 2)

Duration of exposure	mRNA-1273.214 10 µg ≥6 months and <2 years (N=114)	mRNA-1273.214 10 µg ≥2 years and <6 years (N=425)	Total mRNA-1273.214 10 µg (N=539)
Number of subjects, n (%)			
Received booster injection	114 (100)	425 (100)	539 (100)
≥ 7 days since booster injection	114 (100)	425 (100)	539 (100)
≥ 21 days since booster injection	114 (100)	425 (100)	539 (100)
≥ 28 days since booster injection	113 (99.1)	425 (100)	538 (99.8)
≥ 28 days and < 56 days since booster injection	0	5 (1.2)	5 (0.9)
≥ 56 days since booster injection	113 (99.1)	420 (98.8)	533 (98.9)
≥ 84 days since booster injection	109 (95.6)	417 (98.1)	526 (97.6)
≥ 112 days since booster injection	72 (63.2)	294 (69.2)	366 (67.9)
≥ 140 days since booster injection	14 (12.3)	37 (8.7)	51 (9.5)
Study duration from booster injection (days)			
Mean (SD)	117.6 (19.68)	118.9 (16.82)	118.6 (17.45)
Median	114.5	117.0	117.0
Q1, Q3	110.0, 127.0	109.0, 130.0	109.0, 130.0
Min, Max	25, 166	34, 167	25, 167
Person-years from booster injection [1]	36.71	138.33	175.04

Abbreviations: max = maximum; min = minimum; Q1 = quartile 1; Q3 = quartile 3; SD = standard deviation.
Percentages are based on the number of subjects in Safety Set.

[1] Person-years is defined as the total years from the booster dose date to the earlier date of study discontinuation or data cutoff.
Source: Study mRNA-1273-P306 Table 14.1.5.2 (05 December 2022).

Table 104: Participant Age Group and Gender in the Ongoing mRNA-1273-P306 Study (Part 2)

Characteristic	mRNA-1273.214 10 µg ≥6 months and <2 years (N=114)	mRNA-1273.214 10 µg ≥2 years and <6 years (N=425)	Total mRNA-1273.214 10 µg (N=539)
Age (years), n (%)			
<1	2 (1.8)	0	2 (0.4)
1	112 (98.2)	0	112 (20.8)
2	0	138 (32.5)	138 (25.6)
3	0	113 (26.6)	113 (21.0)
4	0	125 (29.4)	125 (23.2)
5	0	49 (11.5)	49 (9.1)
Age (years)			
n	114	425	539
Mean (SD)	1.00 (0.013)	3.20 (1.021)	2.73 (1.277)
Median	1.00	3.00	3.00
Q1, Q3	1.00, 1.00	2.00, 4.00	2.00, 4.00
Min, Max	0.9, 1.0	2.0, 5.0	0.9, 5.0
Age (months) [1]			
n	114		
Mean (SD)	19.1 (3.04)		
Median	20.0		
Q1, Q3	17.0, 22.0		
Min, Max	11, 23		
Gender, n (%)			
Male	52 (45.6)	224 (52.7)	276 (51.2)
Female	62 (54.4)	201 (47.3)	263 (48.8)

Abbreviations: max = maximum; min = minimum; Q1 = quartile 1; Q3 = quartile 3; SD = standard deviation.
Percentages are based on the number of subjects in Safety Set.
[1] Age in months is summarised for ≥6 months and <2 years group only.
Source: Study mRNA-1273-P306 Table 14.1.3.2.2 (05 December 2022).

Table 105: Participant Race in the Ongoing mRNA-1273-P306 Study (Part 2)

Characteristic	mRNA-1273.214 10 µg ≥6 months and <2 years (N=114)	mRNA-1273.214 10 µg ≥2 years and <6 years (N=425)	Total mRNA-1273.214 10 µg (N=539)
Race, n (%)			
White	91 (79.8)	346 (81.4)	437 (81.1)
Black	1 (0.9)	16 (3.8)	17 (3.2)
Asian	6 (5.3)	20 (4.7)	26 (4.8)
American Indian or Alaska Native	0	0	0

Characteristic	**mRNA-1273.214 10 µg ≥6 months and <2 years (N=114)**	**mRNA-1273.214 10 µg ≥2 years and <6 years (N=425)**	**Total mRNA-1273.214 10 µg (N=539)**
Native Hawaiian or Other Pacific Islander	0	2 (0.5)	2 (0.4)
Multiracial	15 (13.2)	37 (8.7)	52 (9.6)
Other	0	0	0
Unknown	0	1 (0.2)	1 (0.2)
Not Reported	1 (0.9)	3 (0.7)	4 (0.7)

Percentages are based on the number of subjects in Safety Set.
Source: Study mRNA-1273-P306 Table 14.1.3.2.2 (05 December 2022).

Table 106: Participant Ethnicity in the Ongoing mRNA-1273-P306 Study (Part 2)

Characteristic	**mRNA-1273.214 10 µg ≥6 months and <2 years (N=114)**	**mRNA-1273.214 10 µg ≥2 years and <6 years (N=425)**	**Total mRNA-1273.214 10 µg (N=539)**
Ethnicity, n (%)			
Hispanic or Latino	7 (6.1)	52 (12.2)	59 (10.9)
Not Hispanic or Latino	105 (92.1)	371 (87.3)	476 (88.3)
Not reported	1 (0.9)	1 (0.2)	2 (0.4)
Unknown	1 (0.9)	1 (0.2)	2 (0.4)

Percentages are based on the number of subjects in Safety Set.
Source: Study mRNA-1273-P306 Table 14.1.3.2.2 (05 December 2022).

Part II: Module SIV – Populations Not Studied in Clinical Trials

SIV.1 Exclusion Criteria in Pivotal Clinical Studies Within the Development Program

Participants were excluded from the studies according to the general criteria listed below. Detailed descriptions of all exclusion criteria are provided in the individual protocols.

Table 107: Important Exclusion Criteria in Pivotal Studies Across the Development Program

Criterion	**Reason for Exclusion**	**Included as Missing information (Yes/No)**	**Rationale (if not included as missing)**
Paediatric participants.	Clinical development programs generally investigate first the benefit-risk in adults. In adults, the risk of symptomatic and severe COVID-19 disease is higher.	No	A paediatric investigation plan was agreed upon by the Agency. Respective studies are ongoing in paediatric patient groups ages 6 months to < 12 years and 12 years to < 18 years.
Pregnant/Lactating women.	Clinical development generally first demonstrates safety and efficacy in non-pregnant and lactating women.	Yes	Not applicable.

Criterion	**Reason for Exclusion**	**Included as Missing information (Yes/No)**	**Rationale (if not included as missing)**
Acutely ill/febrile (temperature >38°C/100.4°F) prior to screening visit.	Allowance of these conditions would confound assessment of safety and these febrile participants might already be infected with SARS-CoV-2.	No	It is common medical practice to not administer vaccines in febrile participants. Febrile participants with minor illnesses could be enrolled at the discretion of the investigator. This is managed with the product prescribing information.
Known or suspected allergy or history of anaphylaxis, urticaria, or other significant adverse reaction to the vaccine or its excipients.	Participants with medical history significant for allergic reactions following the vaccine or its excipients are at increased risk for hypersensitivity reactions when receiving another vaccine.	No	It is common medical practice to not administer a new vaccine in participants who have history of significant allergic reactions to the vaccine or its excipients.
Bleeding disorder considered a contraindication to intramuscular injection or phlebotomy.	Participants have a potential risk of hematoma due to the puncture of the deep tissues. Allowance of these conditions would confound assessment of safety.	No	It is common medical practice to not administer a product by the intramuscular route in participants with coagulopathy or bleeding disorders although the use of a needle with proper gauge can decreased the risk.
Known history of SARS-CoV-2 infection Of note, in Phase 3 mRNA-1273-P301 study seropositive participants are not excluded from enrolment, although they are excluded from the Per-Protocol cohort.	Allowance of this condition would confound assessment of safety and efficacy.	No	Baseline SARS-CoV-2 status was negative for most participants in Study mRNA-1273-P301. Testing occurred on the day of vaccination with Dose 1, and results were available subsequently. In the Safety Set, 347 participants in the elasomeran group had positive baseline SARS-CoV-2 status (Source Table 14.1.3.2.2).
Has received or plans to receive a non-study vaccine within 28 days prior to or after any dose of IP (except for seasonal influenza vaccine which is not permitted within 14 days before or	Allowance of this condition would confound assessment of safety and efficacy.	Yes*	Not applicable.

Criterion	Reason for Exclusion	Included as Missing information (Yes/No)	Rationale (if not included as missing)
after any dose of vaccine).			
Immunosuppressive or immunodeficient state, asplenia, recurrent severe infections (HIV positive participants with CD4+ T-cell count ≥350 cells/mm^3 and an undetectable HIV viral load within the past year [low level variations from 50-500 viral copies which do not lead to changes in antiretroviral therapy are permitted).	Allowance of these conditions would confound assessment of efficacy.	Yes*	Participants with stable HIV infection were enrolled in Study mRNA-1273-P301 (n=176). The small number of participants precludes complete assessment of risk.
Has received systemic immunosuppressants or immune-modifying drugs for > 14 days in total within 6 months prior to Screening (for corticosteroids ≥ 20 mg/day of prednisone equivalent).	Allowance of these conditions would confound assessment of efficacy.	Yes*	Not applicable.
Has received systemic immunoglobulins or blood products within 3 months prior to the day of screening.	Allowance of these conditions would confound assessment of efficacy.	Yes*	Not applicable.
Has donated ≥ 450 mL of blood products within 28 days prior to Screening.	Allowance of these conditions would confound assessment of safety.	No	It is common practice to not give blood prior to entry in a clinical trial. There is no suspected biological reason to expect the safety or efficacy of elasomeran in these participants would be different from the rest of the

Criterion	Reason for Exclusion	Included as Missing information (Yes/No)	Rationale (if not included as missing)
			population receiving elasomeran.

* No longer safety concerns in the RMP.

SIV.2 Limitations to Detect Adverse Reactions in Clinical Trial Development Program

Rare Adverse Drug Reactions

The vaccine exposed population of the Phase 3 mRNA-1273-P301 study allowed the detection of rare events with a frequency of 1/10,000 persons or 0.01%. Most rare AEs of special interest (AESIs) for post-marketing safety surveillance have incidence rates lower than the 2/10,000 persons or 0.02%.

Adverse Drug Reactions of Long Latency

The current vaccination regimen for the elasomeran vaccine consists of two doses administered 28 days apart. There is no prolonged exposure to elasomeran. The delivered mRNA does not enter the cellular nucleus or interact with the genome, is nonreplicating, and is expressed transiently, with a rapid degradation of the mRNA as demonstrated in the nonclinical biodistribution study; thus, no long-term sequalae due to vaccine exposure are expected.

In both the elasomeran injection group and the placebo group in the Phase 3 mRNA-1273-P301 study, the median follow-up time after randomization for the entire period up to the data cut-off for database lock (including Part A and Part B) was 212 days (range: 1 to 243 days). The median duration of follow-up from randomization to the PDV/unblinding (i.e., Part A) before the data cut-off date was 148 days (range: 30 to 241 days). For participants who received both injections, the median duration of follow-up after the second injection to the data cut-off for database lock (including Part A and Part B) was 183 days (range: 1 to 218 days), or approximately 6 months. Therefore, with additional follow up time there has been more opportunity to observe potential adverse drug reactions (ADRs) that might occur with more prolonged latency.

SIV.3 Limitations in Respect to Populations Typically Under-Represented in Clinical Trial Development Program

Table 108: Exposure of Special Populations Included or Not in Clinical Trial Development Program

Type of Special Population	Exposure
Paediatric participants	Studies are ongoing in paediatric patient groups ages 6 months to < 12 years and 12 years to < 18 years. Clinical trial data from Study mRNA-1273-P203 that includes 12 years to ≤ 18 years participants are presented in this RMP. On 23 Jul 2021, EMA (CHMP) has recommended granting an extension of indication for the COVID-19 vaccine Spikevax (previously COVID-19 Vaccine Moderna) to include use in children aged 12 to 17 years. In ongoing Study

Type of Special Population	Exposure
	mRNA-1273-P204, 751 children 6 to < 12 years of age have been exposed to elasomeran (380 elasomeran 50 µg and 371 elasomeran 100 µg) in Part 1 (Table 14.1.5.1) and 4002 children 6 to < 12 years of age (3007 elasomeran 50 µg and 995 placebo) in Part 2 (Table 14.1.5.2 (Data extraction date: 10 November 2021)). A total of 1294 children 6 to < 12 years of age were administered a booster dose (elasomeran 25 µg) in the Booster Dose Phase of the study (Table 14.1.6.2 (Data extraction 23 May 2022)). On 02 March 2022, EMA (CHMP) recommended granting an extension of indication for the COVID-19 vaccine Spikevax to include use in children aged 6 to 11 years. In Study mRNA-1273-P204, a total of 224 children 2 to < 6 years of age were exposed to elasomeran (69 elasomeran 25 µg and 155 elasomeran 50 µg) in Part 1 (Table 14.1.5.1) and 4038 children 2 to < 6 years of age were treated in Part 2 (3031 elasomeran 25 µg and 1007 placebo) (Table 14.1.5.2 (Data extraction date: 21 February 2022)). Furthermore, 150 children 6 months to < 2 years of age were exposed to elasomeran 25 µg in Part 1 (Table 14.1.5.1) and 2350 children 6 months to < 2 years of age were treated in Part 2 (1761 elasomeran 25 µg and 589 placebo) (Table 14.1.5.2 (Data extraction date: 21 February 2022)). A total of 145 children including 114 infants/toddlers 6 months to < 2 years of age and 31 children 2 to < 6 years of age treated in Part 1 (elasomeran 25 µg) were administered a booster dose (elasomeran 10 µg) in the Booster Dose Phase of the study (Table 14.1.6.1 (Data extraction date: 18 August 2022)). Cumulatively, as of 17 December 2022, a total of 10,080 cases (1,224 serious and 37 fatal cases) with 21,597 events 2,920 serious events) reported in children <18 years of age. Of these total cases, 8,153 cases were medically confirmed. When gender was known more cases were reported in females (51.7%; 5,213 cases) compared to males (42.8%; 4,315), with small proportion of cases (5.5%; 552 cases) having no gender reported. The mean age was 13.8 years (SD: 4.6) and median age was 16.0 years (min: -1.0/max: 17.0). Majority of these cases were received from regulatory authorities (73.5%; 7,404 cases), with highest number of cases reported in United States (50.0%; 5,041 cases), EEA (22.6%; 2,282 cases), Asia (11.4%;1,153 cases) followed by Latin America (7.0%; 708 cases) and Australia (5.7%; 570 cases). Use of Spikevax monovalent and Spikevax bivalent vaccines in paediatric population is approved (see Part I).
Pregnant women	Pregnant women were excluded from the clinical trials, although a small number of pregnancies were reported in the elasomeran clinical program. In completed study mRNA-1273-P301 Part A and Part B (primary series) there were 135 pregnancies reported in 130 participants, including 12 pregnancies in 12 participants associated with Dose 1 of elasomeran, 112 pregnancies in 107 participants associated with Dose 2 of elasomeran, and 11 pregnancies in 11 participants associated with placebo as of 12 June 2023 (mRNA-1273-P301 CSR Addendum 3, Table 26). Of these 135 pregnancies, the outcome was known for 116 pregnancies and included 78 live birth term, 7 live birth pre-term, 20 spontaneous abortion/miscarriage, 1 ectopic pregnancy, 1 stillbirth, and 9 elective terminations. The outcome was pending/lost to follow-up for 19 pregnancies. In Part C, the booster phase of mRNA-1273-P301, there were 51 pregnancies reported as of 12 June 2023 (mRNA-1273-P301 CSR

Type of Special Population	Exposure
	Addendum 3, Table 27). The outcome was known for 43 of these pregnancies and included 30 live birth term, 3 live birth pre-term, 7 spontaneous abortion/miscarriage, 1 ectopic pregnancy, and 1 elective termination. The outcome was pending/lost to follow-up for 8 pregnancies. A developmental and reproductive study with elasomeran in female Sprague-Dawley rats was completed in December 2020 with no adverse findings. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development. Cumulatively up to 17 December 2022, Moderna has received 5,131 pregnancy cases with 16,817 events (pregnancy and non-pregnancy specific), of which 5,467 events were serious, after receipt of Spikevax. Of the 5,131 pregnancy cases, 2,463 cases were medically confirmed, 1,817 (35.4%) cases were serious, and 32 had fatal outcomes. There are 53 reports classified as stillbirth but there is insufficient evidence to support a causal relationship between Spikevax and stillbirth. Cumulatively, there have been 140 reports of congenital anomalies. Upon medical review, 64 pregnancy reports (some contain parent-child duplicates) occurred in fetuses and neonates and the other 76 reports of congenital anomalies occurred in non-pregnancy cases. Review of the congenital anomalies indicates that the anomalies are varied in type, aetiology, and critical gestational age at exposure; indicating that the anomalies have occurred as part of the background incidence rather than as a result of vaccine exposure. Published literature has not identified any evidence of an increased risk of pregnancy, foetal or neonatal complications related to Spikevax maternal immunisation. Furthermore, published literature supports the favourable benefit/risk profile of maternal Spikevax immunisation as there is transfer of maternal antibodies to the foetus and early evidence that infants benefit from passive protection from SARS-CoV-2 infection and severe disease following maternal COVID-19 vaccination. Use of Spikevax in pregnancy is now embedded in clinical practice and included in relevant health guidelines and the SmPC states that Spikevax can be used during pregnancy.
Breastfeeding women	Lactating women were excluded from clinical trials. There have been no reports of women taking elasomeran while breastfeeding in the elasomeran clinical program. Cumulatively up to 17 December 2022, Moderna has received 2,036 lactation cases (6,922 events) of which 527 were serious cases (2,026 serious events); no cases reported a fatal outcome. There were 508 cases medically confirmed. These cases and cases from the literature of changes in milk production, infant irritability, decreased feeding, sleepiness/sleep disturbance, vomiting, diarrhoea, and pyrexia are consistent with the safety profile of Spikevax or what is expected in the general population (ACOG 2007; UpToDate 2021). No safety concerns related to Spikevax vaccination during lactation have been identified. Vaccination can induce cytokines which can be passed via breast milk but vaccination while breast-feeding has not been linked to adverse events in infants (Sachs 2013). In fact, women with fever and illness are encouraged to continue breast-feeding given the positive impact of the transfer of antibodies, which has also been reported for COVID-19

Type of Special Population	Exposure
	vaccines, as well as to support infant nutritional needs (UpToDate 2021). Use of Spikevax while breast-feeding is now embedded in clinical practice and included in relevant health guidelines and the SmPC states that Spikevax can be used during breast-feeding.
Participants with relevant comorbidities[#]	
Participants with hepatic impairment[1]	In the clinical trial mRNA-1273-P301 (Part A), 104 (0.7%) participants with hepatic disease have been exposed to elasomeran (Table 14.1.6.2.8). While in mRNA-1273-P301 (Part B), 83 (0.7%) in placebo+elasomeran vaccine group and 104 (0.7%) in mRNA vaccine group participants with hepatic disease have been exposed (Table 14.1.3.2.2.2 (Data extraction date: 04 May 2021)). In Part C, the booster phase of mRNA-1273-P301, a total of 141 (0.7%) participants with hepatic disease received the 50 µg booster dose elasomeran, including 73 (0.8%) participants in the elasomeran primary series group and 68 (0.7%) participants in the placebo-elasomeran primary series group (mRNA-1273-P301 Part C CSR, Table 14.1.3.6.2 (Data extraction 07 April 2023)).
Participants with renal impairment	A Phase 3b open-label safety and immunogenicity study (elasomeran - Study mRNA-1273-P304) in target population of approximately 220 adult solid organ transplant recipients is ongoing. Cumulatively, as of 17 December 2022, a total of 54,153 cases (246,375 events) were reported in frail individuals, which represents 8.2% of all cases reported in all populations (658,759 cases). Of these 54,153 cases, 1496 individuals had a medical history of chronic kidney disease. Use of Spikevax in frail individuals with unstable health conditions and co-morbidities has become fully integrated into standard clinical practice, such as inclusion into treatment protocols or clinical guidelines.
Participants with cardiovascular impairment[2]	In the Study mRNA-1273-P301 (Part A), 762 (5.0%) participants with significant cardiac diseases have been exposed to elasomeran (Table 14.1.6.2.8). While in mRNA-1273-P301 (Part B), 675 (5.3%) in placebo+elasomeran vaccine group and 762 (5.0%) in mRNA vaccine group participants with significant cardiac diseases have been exposed (Table 14.1.3.2.2.2 (Data extraction date: 04 May 2021)). In Part C, the booster phase of mRNA-1273-P301, a total of 1046 (5.3%) participants with significant cardiac disease received the 50 µg booster dose elasomeran, including 513 (5.3%) participants in the elasomeran primary series group and 533 (5.4%) participants in the placebo-elasomeran primary series group (mRNA-1273-P301 Part C CSR, Table 14.1.3.6.2 (Data extraction 07 April 2023)). Cumulatively, as of 17 December 2022, a total of 54,153 cases (246,375 events) were reported in frail individuals, which represents 8.2% of all cases reported in all populations (658,759 cases). Of these 54,153 cases, 2214 individuals had a medical history of coronary artery disease and 4011 individuals a medical history of atrial fibrillation. Use of Spikevax in frail individuals with unstable health conditions and co-morbidities has become fully integrated into standard clinical practice, such as inclusion into treatment protocols or clinical guidelines.
Immunocompromised participants	In the clinical development program, participants with immunosuppression were generally excluded. In Study mRNA-1273-

Type of Special Population	Exposure
	P301 (Part A), participants with HIV who did not meet the exclusion criteria were enrolled. A total of 94 (0.6%) participants with HIV were exposed to elasomeran (Table 14.1.6.2.8). While in mRNA-1273-P301 (Part B), 81 (0.6%) in placebo+ elasomeran vaccine group and 94 (0.6%) in mRNA vaccine group participants with HIV were exposed (Table 14.1.3.2.2.2 (Data extraction date: 04 May 2021)). In Part C, the booster phase of mRNA-1273-P301, a total of 138 (0.7%) participants with HIV received the 50 µg booster dose elasomeran, including 71 (0.7%) participants in the elasomeran primary series group and 66 (0.7%) participants in the placebo-elasomeran primary series group (mRNA-1273-P301 Part C CSR, Table 14.1.3.6.2 (Data extraction 07 April 2023)). A Phase 3b open-label safety and immunogenicity study (elasomeran - Study mRNA-1273-P304) in target population of approximately 220 adult solid organ transplant recipients is ongoing. Cumulatively, as of 17 December 2022, there were 7,559 cases (31,444 events) in immunocompromised individuals, of which 2,936 were serious cases (11,514 serious events); there were 199 cases reporting a fatal outcome; 3,829 cases were medically confirmed. There was a higher number of cases reported cumulatively in females (4,785; 63.3%) when compared to males (2,567;34.0%), with 207 cases (2.7%) missing gender information. Among the reported cases, the median age was 60.0 years with a range of 0.3 year to 101.0 years (571 cases had missing age information). Cumulatively, most of the events reported a resolved/ resolving outcome (13,482; 42.9%), with 8,482 events (30.2%) reported as not resolved. Review of the safety information has not identified any patterns/trends or specific safety concerns in the immunocompromised population. Serious events and fatal reports are heavily confounded by underlying medical conditions. The general pattern of commonly reported adverse events in those with a medical history of immunosuppression/immune compromise or taking immunosuppressive concomitant medications is comparable to the general population. In general, public health and professional groups recommend COVID-19 vaccination for immunocompromised patients. These recommendations highlight the likely potential benefits of COVID-19 vaccines in this population with the potential risk of more severe COVID-19 infections, sequelae, and impact on underlying immune-mediated diseases (Botwin 2021; Briggs 2021; Izmirly 2022; Tang 2021). Use of Spikevax in immunocompromised individuals is now embedded in clinical practice and included in relevant health guidelines and in the SmPC.
Participants with a disease severity different from inclusion criteria in clinical trials	Not applicable.
Population with relevant different ethnic origin	While most participants enrolled in clinical trials were White, participants from other races or ethnicities were also enrolled. In the Phase 3 mRNA-1273-P301 study (Part A), 12034 (79.3%) participants were White, 1567 (10.3%) were Black or African American; 3122 (20.6%) were Hispanic or Latino, and 656 (4.3%) were Asian (mRNA-1273-P301 study Table 14.1.6.2.5 and Table 14.1.6.2.6). In the Phase 2/3 Study mRNA-1273-P203, 2084 (83.8%) participants were White,

Type of Special Population	Exposure
	83 (3.3%) were Black, 142 (5.7%) were Asian, 118 (4.7%) were multiracial and 280 (11.3%) were Hispanic or Latino (study mRNA-1273-P203 Table 14.1.3.13.1). Spikevax has been administered extensively worldwide in populations of different ethnic origin (>800 million individuals vaccinated with at least one dose). No safety concerns related to ethnic origin have been identified.
Subpopulations carrying relevant genetic polymorphisms	Not applicable.
Others	
1. Participants ≥ 75 years of age	In the Phase 3 mRNA-1273-P301 study (Part A), a total of 616 (4.1%) participants were 75 to 84 years of age and 41 (0.3%) were ≥ 85 years of age (Table 14.1.6.2.4). In study P201 (Part A), a total of 11 (2.75) participants were 75 to 84 years of age and 3 (0.8%) were ≥ 85 years of age. Cumulatively, as of 17 December 2022, a total of 54,153 cases (246,375 events) were reported in frail individuals, which represents 8.2% of all cases reported in all populations (658,759 cases). Of these, 37,792 cases (69.8%) were medically confirmed, 19,708 (36.4%) were serious, and 2,457 cases (4.5%) had a fatal outcome. The median age of frail individuals was 61.0 years (range: less than 1 year – 121.0 years); 1,161 reports were missing age information. A total of 52,174 cases were reported in individuals ≥75 years of age (7.9% of the total number of cases reported), including 33,373 cases in females (5.1%), 17,824 cases in males (2.7%), and 977 cases where the gender was not specified (0.1%). Use of Spikevax in frail individuals with unstable health conditions and co-morbidities has become fully integrated into standard clinical practice, such as inclusion into treatment protocols or clinical guidelines.
2. Diabetes (Type 1, Type 2)	In the Phase 3 mRNA-1273-P301 study (Part A), 1460 (9.6%) participants with diabetes have been exposed to elasomeran (Table 14.1.6.2.8). While in mRNA-1273-P301 (Part B), 1279 (10.1%) in placebo+elasomeran vaccine group and 1460 (9.6%) in mRNA vaccine group participants with diabetes have been exposed (Table 14.1.3.2.2.2 (Data extraction date: 04 May 2021)). In Part C, the booster phase of mRNA-1273-P301, a total of 2028 (10.3%) participants with diabetes received the 50 µg booster dose elasomeran, including 999 (10.4%) participants in the elasomeran primary series group and 1026 (10.3%) participants in the placebo-elasomeran primary series group (mRNA-1273-P301 Part C CSR, Table 14.1.3.6.2 (Data extraction 07 April 2023)). Cumulatively, as of 17 December 2022, a total of 54,153 cases (246,375 events) were reported in frail individuals, which represents 8.2% of all cases reported in all populations (658,759 cases). Of these 54,153 cases, 10,819 individuals had a medical history of diabetes mellitus and 5274 individuals a medical history of Type 2 diabetes mellitus. Use of Spikevax in frail individuals with unstable health conditions and co-morbidities has become fully integrated into standard clinical practice, such as inclusion into treatment protocols or clinical guidelines.

Type of Special Population	Exposure
3. Chronic lung disease[3]	In the Phase 3 mRNA-1273-P301 study (Part A), 712 (4.7%) participants with chronic lung disease have been exposed to elasomeran (Table 14.1.6.2.8). While in mRNA-1273-P301 (Part B), 658 (5.2%) in placebo+elasomeran vaccine group and 712 (4.7%) in mRNA vaccine group participants with chronic lung disease have been exposed (Table 14.1.3.2.2.2 (Data extraction date: 04 May 2021)). In Part C, the booster phase of mRNA-1273-P301, a total of 1019 (5.2%) participants with chronic lung disease received the 50 µg booster dose elasomeran, including 489 (5.1%) participants in the elasomeran primary series group and 530 (5.3%) participants in the placebo-elasomeran primary series group (mRNA-1273-P301 Part C CSR, Table 14.1.3.6.2 (Data extraction 07 April 2023)). Cumulatively, as of 17 December 2022, a total of 54,153 cases (246,375 events) were reported in frail individuals, which represents 8.2% of all cases reported in all populations (658,759 cases). Of these 54,153 cases, 17,470 individuals had a medical history of asthma and 4188 individuals had a medical history of COPD. Use of Spikevax in frail individuals with unstable health conditions and co-morbidities has become fully integrated into standard clinical practice, such as inclusion into treatment protocols or clinical guidelines.
4. Severe obesity (BMI > 40 kg/m^2)	In the Phase 3 mRNA-1273-P301 study (Part A), 1070 (7.1%) participants with severe obesity have been exposed to elasomeran (Table 14.1.6.2.8). While in mRNA-1273-P301 (Part B), 925 (7.3%) in placebo+elasomeran vaccine group and 1070 (7.1%) in mRNA vaccine group participants with severe obesity have been exposed (Table 14.1.3.2.2.2 (Data extraction date: 04 May 2021)). In Part C, the booster phase of mRNA-1273-P301, a total of 1463 (7.5%) participants with severe obesity received the 50 µg booster dose elasomeran, including 703 (7.3%) participants in the elasomeran primary series group and 758 (7.6%) participants in the placebo-elasomeran primary series group (mRNA-1273-P301 Part C CSR, Table 14.1.3.6.2 (Data extraction 07 April 2023)). Cumulatively, as of 17 December 2022, a total of 54,153 cases (246,375 events) were reported in frail individuals, which represents 8.2% of all cases reported in all populations (658,759 cases). Of these 54,153 cases, 2411 individuals had a medical history of obesity. Use of Spikevax in frail individuals with unstable health conditions and co-morbidities has become fully integrated into standard clinical practice, such as inclusion into treatment protocols or clinical guidelines.
5. HIV infection	In the Phase 3 mRNA-1273-P301 study (Part A), participants with HIV who did not meet the exclusion criteria have been enrolled. A total of 94 (0.6%) participants with HIV have been exposed to elasomeran (Table 14.1.6.2.8). While in mRNA-1273-P301 (Part B), 81 (0.6%) in placebo+elasomeran vaccine group and 94 (0.6%) in mRNA vaccine group participants with HIV have been exposed (Table 14.1.3.2.2.2 (Data extraction date: 04 May 2021)). In Part C, the booster phase of mRNA-1273-P301, a total of 138 (0.7%) participants with HIV received the 50 µg booster dose elasomeran, including 71 (0.7%) participants in the elasomeran primary series group and 66 (0.7%) participants in the placebo-elasomeran primary series group (mRNA-

Type of Special Population	Exposure
	1273-P301 Part C CSR, Table 14.1.3.6.2 (Data extraction 07 April 2023)). Cumulatively, as of 17 December 2022, there were 7,559 cases (31,444 events) in immunocompromised individuals, of which 2,936 were serious cases (11,514 serious events); there were 199 cases reporting a fatal outcome; 3,829 cases were medically confirmed. Use of Spikevax in immunocompromised individuals is now embedded in clinical practice and included in relevant health guidelines and in the SmPC.

[#] In the Phase 3 mRNA-1273-P301 study, comorbidities are defined as follows:
[1]Hepatic disease including cirrhosis;
[2]Significant cardiac disease such as heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and pulmonary hypertension;
[3]Chronic lung disease such as emphysema and chronic bronchitis, idiopathic pulmonary fibrosis and cystic fibrosis, or moderate to severe asthma.

Part II: Module SV – Post-Authorisation Experience

SV.1.1. Method Used to Calculate Exposure

Moderna supply chain data are used to define the number of doses Spikevax distributed by country; however, administration data is estimated as 55% of the total doses distributed.

SV.1.2. Exposure

Cumulatively, as of 17 October 2023, a total of 1,318,183,956 doses of Spikevax (Original) had been delivered to 91 countries and an estimated total of 774,433,074 doses had been administered. North America, Europe, and Asia accounted for approximately 89% of Spikevax doses distributed and approximately 84% of Spikevax doses administered.

Cumulatively, as of 17 October 2023, 129,007,543 booster doses of Spikevax Bivalent .214 (Spikevax bivalent Original/Omicron BA.1) had been delivered to 42 countries and an estimated total of 70,954,149 doses had been administered. North America, Europe, and Asia accounted for approximately 96% of doses distributed and administered. A total of 245,752,934 booster doses of Bivalent .222 (Spikevax bivalent Original/Omicron BA.4-5) had been delivered to 43 countries and an estimated total of 135,164,114 doses had been administered. North America, Europe, and Asia accounted for approximately 93% of all doses delivered and administered.

Cumulatively as of 17 October 2023, 52,586,870 doses of Spikevax XBB.1.5 had been delivered to 9 countries and an estimated 28,922,779 doses had been administered. North America, Europe, and Asia accounted for approximately all (>99%) of the doses delivered and administered.

As of 17 October 2023, low- and middle-income countries (The World Bank 2022) are estimated to account for approximately 13% of all doses distributed and administered globally.

Extrapolating from the proportion of US vaccine recipients to estimate global use, it is estimated that 421,024,776 individuals received a first dose, 324,176,332 received a second dose, 198,511,205 received a third dose, and 81,787,327 received a fourth dose, with third and fourth doses including both original Spikevax (Original) and Spikevax bivalent booster dose formulations. Because of variation in the timing of use of Spikevax bivalent boosters and limited available global data, extrapolation from the US to estimate the use of bivalent boosters was not deemed appropriate.

Part II: Module SVI – Additional EU Requirements for the Safety Specification

Not relevant for COVID-19 vaccines.

Part II: Module SVII – Identified and Potential Risks

SVII.1 Identification of Safety Concerns in the Initial RMP Submission

Important identified risks	Anaphylaxis
Important potential risks	Vaccine-associated enhanced disease (VAED) including vaccine-associated enhanced respiratory disease (VAERD)
Missing information	Use in pregnancy and while breast-feeding Long-term safety Use in immunocompromised subjects Interaction with other vaccines Use in frail subjects with unstable health conditions and co-morbidities (e.g. chronic obstructive pulmonary disease (COPD), diabetes, chronic neurological disease, cardiovascular disorders) Use in subjects with autoimmune or inflammatory disorders

SVII.1.1 Risks Not Considered Important for Inclusion in the List of Safety Concerns in the RMP

Not applicable

SVII.1.2 Risks Considered Important for Inclusion in the List of Safety Concerns in the RMP

Not applicable

SVII.2 New Safety Concerns and Reclassification With a Submission of an Updated RMP

Not applicable

SVII.3 Details of Important Identified Risks, Important Potential Risks, and Missing Information

Table 109: Presentation of Important Identified Risks

Important Identified Risk	**Myocarditis**
Potential mechanisms	Myocarditis is an under-diagnosed cardiac disease resulting from any one of a broad range of infectious, immune, and toxic causes. Most cases of myocarditis are caused by infectious agents, toxic substances, drugs or autoimmune disorders. Hence, it is increasingly recognized that myocarditis is an inflammatory condition of the myocardium triggered by various factors rather than a distinct cardiovascular disease. Infectious causes include viruses, bacteria, Chlamydia, rickettsia, fungi, and protozoa. Noninfectious

	triggers have been identified such as toxins, auto immunes disease and hypersensitive reactions. Numerous medications like antipsychotics (e.g., clozapine), antibiotics (penicillin, ampicillin, sulfonamides, tetracyclines), and antiphlogistic (e.g., mesalamine) can induce hypersensitivity eosinophilic myocarditis. Myocarditis has been reported following many different vaccines including flu vaccine, however the smallpox vaccine has the strongest association. During the influenza epidemic of the winter 1998-1999 there were several reports of patients who had preceding flu-like symptoms and fever and developed cardiac involvement between 4 and 7 days after the onset of influenza symptoms (Onitsuka 2001). Evaluation of the post-authorization safety data suggest a very rare risk of myocarditis following COVID-19 vaccination, the mechanisms involved in such vaccine-related myocarditis are not clear based on the data currently available.
Evidence source(s) and strength of evidence	Data to evaluate the safety concern were derived from clinical trials and the post-authorisation safety.
Characterization of risk	In Study mRNA-1273-P301 (Part A), there were 15,184 participants exposed to the elasomeran vaccine, and 15,166 participants in the placebo arm. There were no reported TEAEs of Myocarditis follow-up period after vaccination. No cases have been reported in Part B of the study (CSR mRNA-1273-P301 addendum 1 (Safety from open label phase [Part B]). In Part C, the booster phase of mRNA-1273-P301, of the 19,609 participants who received the 50 µg booster dose elasomeran, there was one confirmed case of myocarditis in a male in his 40s' on Day 1 after the booster dose; the serious adverse event (SAE) was considered related to study vaccine by the Investigator and Sponsor and adjudicated positively as a probable case of acute myocarditis by the independent Cardiac Event Adjudication Committee (CEAC). However, the case was confounded by a documented rhinovirus/Enterovirus infection 6 weeks earlier and was attributed as due to the post-viral etiology (mRNA-1273-P301 Final CSR, Section 7.3.2.3.2.4.1 (Data extraction 07 April 2023)). Two other cases of suspected myocarditis were reported during the study and both were adjudicated by the CEAC as not meeting the definition of acute myocarditis. Using post authorization safety data, an evaluation of all the cases identified as cases of Myocarditis, utilizing the WHO-UMC causality assessment and the newly developed DRAFT Myocarditis Brighton Collaboration case definition (30 May 2021) was conducted. A total of 77 cases were identified. Analysis of the 77 cases that reported events of myocarditis using the WHO-UMC standardized case causality assessment revealed that there were 20 reports (8% of the Myocarditis cases) classified as "Possible" events, 11 reports were classified as "Conditional", 17 reports were classified as "Unlikely", and 29 were classified as "Unassessable". Of the "Possible" 20 cases, there were 18 males and 2 females. Their ages were between 18 and 52 years of age. The reported TTO was between 0 days and 10 days (Median= 3 days). The 20 reports that were classified as "Possible" according to the WHO-UMC causality assessment, were evaluated according to the Myocarditis Brighton Collaboration case definition. Out of the 20 possible reports, there were 2 classified as Level 1 (Definitive case); 12 classified as Level 2 (Probable case); and 6 were classified as Level 4 (a reported event of myocarditis with insufficient evidence to meet level 1,2 or 3 of the case definition).

	As of DLP of this RMP, there were 362 cases of Myocarditis reported. The corresponding reporting rate of myocarditis was 3.45 per 100,000 person – years based on a 21-day risk window following each dose of vaccine administered.
Risk factors and risk groups	Approximately 1% to 5% of patients that test positive for acute viral infection(s) may exhibit a form of myocarditis. The annual prevalence of myocarditis has been reported from 10.2 to 105.6 per 100,000 worldwide, and its annual occurrence is estimated at about 1.8 million cases. Most studies of acute myocarditis report a greater prevalence and severity in male patients, speculated to be caused by a protective effect of natural hormonal influences on immune responses in women when compared with men (Gavriatopoulou M, Korompoki E, Fotiou D, Ntanasis-Stathopoulos I, Psaltopoulou T, Kastritis E, et al. Organ-specific manifestations of COVID-19 infection. Clin Exp Med. 2020 Nov;20(4):493-506. Giannoccaro MP, Vacchiano V, Leone M, Camilli F, Zenesini C, Panzera I, et al. Difference in safety and humoral response to mRNA SARS-CoV-2 vaccines in patients with autoimmune neurological disorders: the ANCOVAX study. J Neurol. 2022;269(8):4000-12. Goldberg Y, Mandel M, Bar-On YM, Bodenheimer O, Freedman LS, Ash N, Alroy-Preis S, Huppert A, Milo R. Protection and Waning of Natural and Hybrid Immunity to SARS-CoV-2. N Engl J Med. 2022 Jun 9;386(23):2201-2212. Golpour 2021). Patients are usually between the ages of 20 and 50. Acute myocarditis and hyperthyroidism are also common diseases that often present in young, otherwise healthy patients. The spontaneous reports included in the global safety database included 4 cases that reported previous COVID-19 infection (5.9%) with these reports in the 18 to 39 years of age group. There were 5 reports of previous Myocarditis/ Pericarditis medical history (5.9%), 14 reports of cardiovascular conditions (16.5%), 5 with Thyroid conditions (5.9%), and 12 (14.1%) had previous medical histories of allergy-type conditions including history of anaphylaxis.
Preventability	Myocarditis presents with a spectrum of symptoms ranging from mild dyspnea or chest pain that spontaneously resolves without treatment to cardiogenic shock and sudden death. The major long-term consequence is dilated cardiomyopathy (DCM) with chronic heart failure. Common viral infections are the most frequent cause of myocarditis, but other pathogens, hypersensitivity reactions, and systemic and autoimmune diseases have also been implicated (Berman. Institute of Bioethics & Center for Immunization Research, Johns Hopkins University. Covid-19 Maternal Immunization Tracker (COMIT). 2022; Available from: www.comitglobal.org, Accessed: 17 Dec 2022. Blauwet 2009). Very rare cases of myocarditis and pericarditis have been observed following vaccination with Spikevax. These cases have primarily occurred within 14 days following vaccination, more often after the second

	vaccination, and more often in younger men. Available data suggest that the course of myocarditis and pericarditis following vaccination is not different from myocarditis or pericarditis in general. Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination. Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition. For patients presenting with myocarditis or pericarditis after the 1st dose CDC recommends deferring the 2nd dose of mRNA COVID-19 vaccine until more information is known. However, if heart has recovered, it could consider proceeding with 2nd dose (Townsend JP, Hassler HB, Wang Z, Miura S, Singh J, Kumar S, et al. The durability of immunity against reinfection by SARS-CoV-2: a comparative evolutionary study. Lancet Microbe. 2021 Dec;2(12):e666-e675. Townsend JP, Hassler HB, Sah P, Galvani AP, Dornburg A. The durability of natural infection and vaccine-induced immunity against future infection by SARS-CoV-2. Proc Natl Acad Sci U S A. 2022 Aug 2;119(31):e2204336119. Trostle ME, Limaye MA, Avtushka MsV, Lighter JL, Penfield CA, Roman AS. COVID-19 vaccination in pregnancy: early experience from a single institution. Am J Obstetrics Gynecol Mfm. 2021;3(6):100464. UpToDate 2021. Spencer J. Common Problems of Breastfeeding and Weaning. Updated: 18 Oct 2021. Available at: https://www.uptodate.com/contents/common-problems-of-breastfeeding-and-weaning. Accessed: 17 December 2022. UpToDate 2022. Kellams A. Breastfeeding: Parental Education and Support. Updated: 05 Apr 2022. Available at: https://www.uptodate.com/contents/breastfeeding-parental-education-and-support. Accessed: 17 December 2022. Vijenthira A, Gong IY, Fox TA, Booth S, Cook G, Fattizzo B, et al. Outcomes of patients with hematologic malignancies and COVID-19: a systematic review and meta-analysis of 3377 patients. Blood. 2020;136(25):2881-92. Viner RM, Ward JL, Hudson LD, Ashe M, Patel SV, Hargreaves D, et al. Systematic review of reviews of symptoms and signs of COVID-19 in children and adolescents. Arch Dis Child. 2020 Dec 17:archdischild-2020-320972. Wallace 2021).

	Current SmPC and PIL adequately covers the information on this risk awareness to the health care professionals, caregivers and vaccinees.
Impact on the benefit-risk balance of the product	Based on the analysis of all the safety data, there have been very rare reports of myocarditis occurring after vaccination with Moderna COVID-19 Vaccine. Causal association between Spikevax and myocarditis is considered of at least a reasonable possibility. The majority of the cases have been reported in young males, and shortly after the second dose of the vaccine. These are typically mild cases and individuals tend to recover within a short time following standard treatment and rest. Healthcare professionals should be alert to the signs and symptoms of myocarditis. The benefits (prevention of COVID-19 disease and associated hospitalizations, ICU admissions, and deaths) outweighed the risks (expected myocarditis cases after vaccination) in all populations for which vaccination has been recommended (Forrest CB, Burrows EK, Mejias A, Razzaghi H, Christakis D, Jhaveri R, et al. Severity of Acute COVID-19 in Children <18 Years Old March 2020 to December 2021. Pediatrics. 2022 Apr 1;149(4):e2021055765. Gargano 2021).
Public health impact	Myocarditis associated with vaccines typically occur at a low incidence, which results in a low public health impact. Although the potential clinical consequences of the occurrence of myocarditis is serious, this is a risk known to healthcare professionals and can be managed with early diagnosis with supportive treatment. Most observed cases have been of mild severity, and spontaneously resolved.

Important identified risk	**Pericarditis**
Potential mechanisms	Acute pericarditis is an inflammatory process involving the pericardium that results in a clinical syndrome characterized by chest pain, pericardial friction rub, changes in the electrocardiogram (ECG) and occasionally, a pericardial effusion. Generally, the diagnosis requires 2 of these 4 features. Epidemiologic data on the incidence of acute pericarditis are lacking, likely because this condition is frequently inapparent clinically, despite its presence in numerous disorders (Imazio 2015). However, it appears to be the most common form of pericardial disease and a relatively common cause of chest pain. It is diagnosed in approximately 0.1% of patients hospitalized for chest pain and in 5% of patients admitted to the emergency department for chest pain unrelated to acute myocardial infarction (MI). Although acute pericarditis occurs in all age groups and in men and women, it presents most often in men 20 to 50 years of age. The most common form of acute pericarditis is idiopathic, which accounts for about 90% of cases. Other common causes include infection, renal failure, myocardial infarction (MI), post-cardiac injury syndrome, malignancy, radiation, and trauma. Acute pericarditis is more common in men than in women. However, although this condition is more common in adults than in children, adolescents are more commonly affected than young adults.
Evidence source(s) and strength of evidence	Data to evaluate the safety concern were derived from the clinical trials and post-authorisation safety data.
Characterization of risk	In study mRNA-1273-P301 (Part A), in the safety set, there were 15,184 participants exposed to the elasomeran vaccine, and 15,166 participants in the placebo arm. There were four TEAE of "Pericarditis" in P301: Two TEAEs in the Placebo arm, and two in the Vaccine arm of the safety set in

Important identified risk	Pericarditis
	the overall stage after any injection. The 2 events in the placebo arm were reported in the >18 to <65 years of age. The events in the vaccination arm were reported in a male in his 60s' and a female in her 50s'. In Part B, one case of acute pericarditis (verbatim: "acute infective pericarditis") was reported in a male in his 60s' in the placebo group; the event occurred 24 days after a COVID-19 diagnosis. In addition, one case of pericardial effusion was reported as an SAE (resolving) in a 20s' years old male in the placebo–elasomeran group. No participant in the elasomeran group experienced pericarditis (CSR mRNA-1273-P301 addendum 1 (Safety from open label phase [Part B]). In Part C, the booster phase of mRNA-1273-P301, of the 19,609 participants who received the 50 µg booster dose elasomeran, there was one non-serious case of CEAC-confirmed acute pericarditis in a male in his 60s' reported on Day 64 after the booster dose and 10 days following a viral infection (mRNA-1273-P301 Part C CSR, Section 7.3.2.3.2.4.1 (Data extraction 07 April 2023)). The pericarditis was considered unrelated to study vaccine by both Investigator and Sponsor, and more likely related to a viral upper respiratory infection 10 days prior. Two additional cases of pericarditis were reported at 10 and 11 months after the study booster injection but both cases were considered unrelated to booster injection by the Investigator and Sponsor due to the long latency and in one case, the presence of an alternative explanation (a concurrent COVID-19 infection). The CEAC adjudicated these cases as acute pericarditis in one case and as undecided in the other case, as there was not enough information to determine the final category. A review of the spontaneous reports from the company's global safety identified 68 case reports with the PTs of Pericarditis. All of the aforementioned reports were considered serious reports. As a difference with the Myocarditis reports, most of the Pericarditis reports (64.7%) involved persons >50 years of age. There was not an important difference between the reported genders, with 51% Males, and 47% females. There was not an important difference in the TTO for the pericarditis cases with 16% reporting a TTO less than 1 day, 18 % for each 2 to 3 days and 4 to 7 days. The majority of the reports reported a TTO of more than 8 days following last vaccination. Occurrence following dose 1 was very similar (37% of reports) to the one seeing following dose 2 (41%). Dose number was not reported in 22% of the cases. Evaluation of all the 68 cases identified as cases of Pericarditis, utilizing the WHO-UMC causality assessment, there were 18 reports that were classified as "Possible" according to the WHO-UMC causality assessment. Of these "Possible" 18 cases, there were 9 males and 9 females. Their ages were between 28 and 82 years of age (Median= 51.5). 8 reports were after the 1st dose, 9 after the 2nd dose of the elasomeran vaccine, and 1 did not provided dose information. The reported TTO was between 1 days and 23 days (Mean 11.3 days). The rest of the 68 cases that reported Pericarditis, 11 cases (16.2%) were classified as "Conditional"; 21 cases (30.8%) were classified as "Unassessable/ Unclassifiable"; and 18 (26.5%) were classified as "Unlikely". The post-marketing reporting rate for pericarditis (without myocarditis) was 2.16 per 100,000 person-years based on a 21-day risk window following each dose of vaccine administered.
Risk factors and risk groups	Acute pericarditis occurs when the bilayer pericardial sac becomes inflamed. In most cases, the cause of pericarditis is idiopathic or is assumed to be due to a viral infection for which the antecedent virus is not identified.

Important identified risk	**Pericarditis**
	There are several less common infectious and non-infectious causes of pericarditis, but most patients with acute pericarditis present with a history suggestive of recent or concurrent viral illness. Most cases resolve with no long-term sequelae. While pericardial effusions might develop as a result of pericarditis, they are usually minor and rarely result in cardiac tamponade (Sharif 2013). Acute pericarditis is more common in men than in women. However, although this condition is more common in adults than in children, adolescents are more commonly affected than young adults. A prospective clinical cohort study in Italy identified an incidence of 27.7 cases per 100,000 person-years (Imazio 2008). Another study, a retrospective analysis of Finnish registry data capturing admissions to 29 hospitals over a span of 9.5 years identified an age standardized incidence of 3.32 per 100,000 person-years, with higher rates in men ages 16-65 (Kytö 2014). Pericarditis is the most common pericardial disorder. Congenital pericardial disorders are rare.
Preventability	Pericarditis may be caused by many disorders (e.g., infection, myocardial infarction, trauma, tumors, metabolic disorders) but is often idiopathic. Symptoms include chest pain or tightness, often worsened by deep breathing. Cardiac output may be greatly reduced if cardiac tamponade or constrictive pericarditis develops. Diagnosis is based on symptoms, a friction rub, electrocardiographic changes, and evidence of pericardial fluid accumulation on x-ray or echocardiogram (Hoit 2020). Pericarditis may result in one of two serious complications: cardiac tamponade and chronic constrictive pericarditis. Cardiac tamponade is considered a medical emergency and, if left untreated, can quickly become fatal. Very rare cases of myocarditis and pericarditis have been observed following vaccination with Spikevax. These cases have primarily occurred within 14 days following vaccination, more often after the second vaccination, and more often in younger men. Available data suggest that the course of myocarditis and pericarditis following vaccination is not different from myocarditis or pericarditis in general. Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination. Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition. CDC recommends deferring the 2nd dose of mRNA COVID-19 vaccine until more information is known. However, if heart has recovered, could consider proceeding with 2nd dose (Townsend JP, Hassler HB, Wang Z, Miura S, Singh J, Kumar S, et al. The durability of immunity against reinfection by SARS-CoV-2: a comparative evolutionary study. Lancet Microbe. 2021 Dec;2(12):e666-e675. Townsend JP, Hassler HB, Sah P, Galvani AP, Dornburg A. The durability of natural infection and vaccine-induced

Important identified risk	Pericarditis
	immunity against future infection by SARS-CoV-2. Proc Natl Acad Sci U S A. 2022 Aug 2;119(31):e2204336119. Trostle ME, Limaye MA, Avtushka MsV, Lighter JL, Penfield CA, Roman AS. COVID-19 vaccination in pregnancy: early experience from a single institution. Am J Obstetrics Gynecol Mfm. 2021;3(6):100464. UpToDate 2021. Spencer J. Common Problems of Breastfeeding and Weaning. Updated: 18 Oct 2021. Available at: https://www.uptodate.com/contents/common-problems-of-breastfeeding-and-weaning. Accessed: 17 December 2022. UpToDate 2022. Kellams A. Breastfeeding: Parental Education and Support. Updated: 05 Apr 2022. Available at: https://www.uptodate.com/contents/breastfeeding-parental-education-and-support. Accessed: 17 December 2022. Vijenthira A, Gong IY, Fox TA, Booth S, Cook G, Fattizzo B, et al. Outcomes of patients with hematologic malignancies and COVID-19: a systematic review and meta-analysis of 3377 patients. Blood. 2020;136(25):2881-92. Viner RM, Ward JL, Hudson LD, Ashe M, Patel SV, Hargreaves D, et al. Systematic review of reviews of symptoms and signs of COVID-19 in children and adolescents. Arch Dis Child. 2020 Dec 17:archdischild-2020-320972. Wallace 2021).
Impact on the benefit-risk balance of the product	Based on the analysis of all the safety data, it shows that there have been very rare reports of pericarditis occurring after vaccination with Moderna COVID-19 Vaccine. Although causality cannot be established at this time, the majority of the cases have been reported in young males, and shortly after the second dose of the vaccine. These are typically mild cases and individuals tend to recover within a short time following standard treatment and rest. Healthcare professionals should be alert to the signs and symptoms of pericarditis. The benefits (prevention of COVID-19 disease and associated hospitalizations, ICU admissions, and deaths) outweighed the risks (expected myocarditis cases after vaccination) in all populations for which vaccination has been recommended.
Public health impact	Pericarditis associated with vaccines typically occur at a low incidence, which results in a low public health impact. Although the potential clinical consequences of the occurrence of pericarditis are serious, this is a risk known to healthcare professionals.

Table 110: Presentation of Missing Information

Missing Information	Use in Pregnancy and While Breast-Feeding
Evidence source	As pregnancy was an exclusion criterion for the mRNA clinical trials,

	there is limited data from the use of elasomeran in pregnant women from the clinical trials. A developmental and reproductive study with elasomeran in female Sprague-Dawley rats was completed in December 2020 with no adverse findings. In post authorization, preliminary analysis of the v-Safe pregnancy registry conducted by the US CDC did not identify safety signals (Shi DS, Whitaker M, Marks KJ, Anglin O, Milucky J, Patel K, et al; COVID-NET Surveillance Team. Hospitalizations of Children Aged 5-11 Years with Laboratory-Confirmed COVID-19 - COVID-NET, 14 States, March 2020-February 2022. MMWR Morb Mortal Wkly Rep. 2022 Apr 22;71(16):574-581. Shimabukuro 2021).
Anticipated risk/consequence of the missing information	Targeted populations of the indication will include women of childbearing potential, thus, the use of elasomeran in pregnant and breastfeeding women may happen. Pregnancy outcome data will be collected in enhanced pharmacovigilance. An observational cohort pregnancy study will inform on the risk of adverse outcome in women who were exposed to elasomeran during pregnancy.
Missing Information	**Long-Term Safety**
Evidence source	Per protocols, the clinical development program had a safety follow up period of 12 months in the completed Phase 1 study 20-0003, Phase 2a Study mRNA-1273-P201 and, 24 months in the completed Phase 3 study mRNA-1273-P301. In the Phase 3 Study mRNA-1273-P301 the safety follow-up was based on a median duration of follow-up after the second injection to the data cut-off for database lock (including Part A and Part B) was 183◦days (range: 1 to 218 days), or approximately 6 months. The follow up time was through Day 209 for the Phase 1 study DMID 20-0003 and through at least 180 days (6 months) after the most recent injection (Day 209) for the 555/600 (92.5%) participants who had not discontinued from the study before Day 209 in the Phase 2a Study mRNA-1273-P201. Long-term safety continues to be characterised in Phase 2/3 study mRNA-1273-P203, Phase 2/3 study mRNA-1273-P204, Phase 2/3 study mRNA-1273-P205, post-authorisation active surveillance safety study mRNA-1273-P904, and open-label, Phase 3 study mRNA-1273-P306.
Anticipated risk/consequence of the missing information	The long-term safety profile remains to be characterised. The long-term safety profile is to be characterised through continued trial follow-up, active surveillance for safety, a European post-authorisation safety study, and routine pharmacovigilance.

Part II: Module SVIII – Summary of the Safety Concerns

Table 111: Summary of Safety Concerns

Summary of Safety Concerns	
Important identified risks	Myocarditis Pericarditis
Important potential risks	None
Missing information	Use in pregnancy and while breast-feeding

Summary of Safety Concerns	
	Long-term safety

Part III: Pharmacovigilance Plan (Including Post-Authorisation Safety Studies)

III.1 Routine Pharmacovigilance Activities

The MAH has an established signal management process including signal detection, validation and evaluation of spontaneous reports from all sources. During signal detection data sources are screened for new safety information related to Spikevax. Following initial review of the available data, a determination is made on the basis of the nature and the quality of the new information whether further investigation is warranted, at which point those topics referred for further investigation are considered "validated signals". Potential signal detection data sources include safety data from MAH-sponsored clinical trials and clinical as well as non-interventional studies, spontaneous AE reports, published literature, and communications from external sources, including regulatory agencies, and (if applicable) business partners. Moderna's PV system relies primarily on AEs contained in its global PV database (Argus platform) that captures suspected AE reports and in addition, signal from regulatory databases (eg Eudravigilance, VAERS). Routine PV also includes a periodic review of the literature that involves targeted keyword searches in widely recognised databases (i.e., MEDLINE, EMBASE). Moderna performs monthly aggregate quantitative signal detection review of the global safety database in order to identify possible adverse reactions. Moderna also conducts monthly safety reports that are shared with some regulatory agencies as per their request.

Routine Pharmacovigilance Activities Beyond Adverse Reactions Reporting and Signal Detection:

Specific adverse reaction follow-up questionnaires for Spikevax

None.

Signal Detection

The Moderna signal management process for Spikevax includes signal detection, validation, prioritization, evaluation, and recommendation for actions as well as documentation and tracking of signals. It follows the principles of the Good Pharmacovigilance Practices Module IX for Signal Management (refer to https://www.ema.europa.eu/en/human-regulatory/post-authorisation/pharmacovigilance/good-pharmacovigilance-practices).

Moderna signal detection strategy for Spikevax is described in the product safety strategy form. It describes the data sources, type and frequency of the signal detection analyses summarised in Table 112.

As available, standard case definitions from the Brighton Collaboration will be used to classify AESIs by level of diagnostic certainty.

Table 112: Spikevax Signal Data Sources and Frequency of Evaluations

Data Source	Frequency of Safety Evaluations
Company global safety database	Ongoing monitoring of Individual Cases Safety Reports (ICSRs) from all sources, safety concerns, and Adverse Events (AE) of Special Interest. Weekly aggregated review of ICSRs for trend analyses. Review of disproportionate reporting of preferred terms (PT) during a time

Data Source	Frequency of Safety Evaluations
	interval as compared to all data prior to the RP for Spikevax. Review of endpoints of interest (ie, case counts, demographics, country of origin, time to onset, seriousness, batch numbers, fatalities, AE from the product surveillance list of safety topics and based on MedDRA system organ class and high-level term, and identification of potential clusters of ICSRs.
Literature	Weekly literature review. Any literature abstract or article signal detection run will be reviewed.
EudraVigilance	Continuous monitoring. Biweekly critical review of the EudraVigilance data analysis system using available reports (i.e, Electronic Reaction Monitoring Reports [e-RMRs] and active substance groupings, ICSR line listings and ICSR forms).
VAERS	Frequency of review will depend on public availability of redacted VAERS extracts. Current estimates based on public communication as well as processing time indicate this frequency will range between every two to four weeks. Generation of disproportionality scores using Empirical Bayesian Geometrical Mean and its 90% confidence intervals after new uploads of Vaccine Adverse Event Reporting System extracts in Empirica Signal.
Health Authorities websites	Ongoing review of data published on the Safety Web Portals of selected major regulatory agencies to identify required actions regarding the product and similar products.

Product surveillance to identify safety signals will occur for any reported AEs including reactogenicity. Safety surveillance prioritization is for the safety concerns of the RMP, AESIs, or those AEs that may be serious or known to be often medicine related.

If any cluster of events is detected which points towards an unexpected event/syndrome, Moderna will perform appropriate signal evaluation and will provide this information to the appropriate regulatory agencies.

Table 113: Product Surveillance List of Spikevax Signalling Strategy By Category

Category	Safety Topics (Updates may be Needed if New Adverse Events Emerge)
Safety concerns	Myocarditis Pericarditis Use in pregnancy and while breast-feeding Long-term safety
Adverse events of special interest (AESI)	List of AESI (AESIs will be updated at least quarterly and as new information arises): Brighton Collaboration (Safety Platform for Emergency vACcines) ACCESS protocol US Centers for Disease Control and Prevention (preliminary list of AESI for VAERS surveillance) Medicines and Healthcare products Regulatory Agency (unpublished guideline).
Standard safety topics	Off-label Use

Category	Safety Topics (Updates may be Needed if New Adverse Events Emerge)
	Overdose Vaccination Administration Errors Product Quality Issues Drug-Drug Interactions Death Paediatric Use Geriatric Use Designated Medical Events (EMA/326038/2020)

As support to signal detection, observed rates of AEs will be compared with the expected rates which will be available from the scientific literature or other sources including those reported by the EMA-funded COVID-19 vaccine monitoring ACCESS program (DiPiazza AT, Leist SR, Abiona OM, Moliva JI, Werner A, Minai M, et al. COVID-19 vaccine mRNA-1273 elicits a protective immune profile in mice that is not associated with vaccine-enhanced disease upon SARS-CoV-2 challenge. Immunity. 2021;54(8):1869-1882.e6.

Dodd 2020).

During the evaluation of validated signals, Moderna has access to large US population of de-identified patient level information in healthcare claims databases to conduct additional Observed to Expected (O/E) analyses in defined cohorts as well as to potentially launch inferential epidemiologic studies to evaluate these safety signals in a rapid manner.

Reporting to EMA

Valid ICSRs that fulfil the local regulatory requirements for submission to the EudraVigilance database will be submitted within the 15- or 90-day time frame. This includes any COVID-19 cases requiring hospitalisation, vaccination administration errors, and MIS that may have been reported to occur in vaccinees.

Potential Medication Errors

Large scale mass vaccination may potentially introduce the risk of medication errors related to storage, handling, dosing, and administration errors associated with a multidose vial, and confusion with other COVID-19 vaccines. These potential medication errors are mitigated through the information in the SmPC.

Traceability

The SmPC includes instructions for healthcare professionals to record the name and batch number of the administered vaccine to improve traceability.

The vaccine carton labelling also contains a scannable 2D barcode that provides the batch/lot number and expiry date. In addition, Moderna also provides stickers (two stickers per dose, containing printed batch/lot information, product identification, and 2D bar code that encodes a unique identifier [serial number]) either in cartons or to be shipped along with each shipment, in the countries where this is required.

III.2 Additional Pharmacovigilance Activities

In addition to actions targeted at identified and potential risks described in the safety specifications, the MAH intends to address general safety through continued clinical trial follow-up, a European Post Authorisation Safety Study, an observational study of Spikevax using routinely collected health data in 5 European countries, which monitors safety of Spikevax in pregnancy, a US Post Authorization safety study, and an observational study to assess maternal and infant outcomes following exposure to Spikevax during pregnancy, collecting data in the US.

The immunogenicity and safety of mRNA vaccine boosters for SARS-CoV-2 variants, including Spikevax bivalent Original/Omicron BA.1 and Spikevax bivalent Original/Omicron BA.4-5, are being evaluated in an open-label Phase 2/3 study. Some other study protocols will be updated to include these bivalent vaccines as well as any new variant vaccine, when feasible.

Study key detailed information is provided in text below and milestones in Table 114:.

Table 114: Additional Pharmacovigilance Activities

Study Number *Country(ies)*	**Study Title** **Study Type** *Study Status*	**Rationale and Study Objectives**	**Study Design**	**Study Population(s)**	**Milestones**
mRNA-1273-P203 *US* *Part 3 – US and Ex-US*	A Phase 2/3, Randomized, Observer-Blind, Placebo-Controlled Study to Evaluate the Safety, Reactogenicity, and Effectiveness of mRNA-1273 SARS-CoV-2 Vaccine in Healthy Adolescents 12 to < 18 years of age Interventional *Ongoing*	Evaluate the safety, reactogenicity, and effectiveness of Spikevax Assess safety and immunogenicity of mRNA-1273.222.	Randomized, observer-blind, placebo-controlled study	Healthy adolescents 12 to < 18 years of age	LPLV: 09 Jun 2025 Interim long-term safety CSR for Part A & B: 31 Oct 2022 Final CSR: 15 Jul 2025
mRNA-1273-P204 *US, Canada*	Phase 2/3, two-part, open-label, dose-escalation, age de-escalation and subsequent randomized, observer-blind, placebo-controlled	Safety, tolerability, reactogenicity, and effectiveness of up to 3 doses of elasomeran administered as 2 doses 28 days apart in healthy children 6 months to less	Two-part, open-label, dose-escalation, age de-escalation and subsequent randomized,	The study population includes healthy children of 3 age groups (6 years to < 12 years, 2 years to < 6 years, and 6 months to < 2 years)	Study start: 15 Mar 2021 Final CSR: 31 Dec 2024

Study Number *Country(ies)*	**Study Title** **Study Type** *Study Status*	**Rationale and Study Objectives**	**Study Design**	**Study Population(s)**	**Milestones**
	expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of mRNA-1273 in healthy children 6 months to less than 12 years of age Interventional *Ongoing*	than 12 years of age	observer-blind, placebo-controlled expansion study	No participants in Part 1 participate in Part 2 of the study	
Study mRNA-1273-P304 *US*	A Phase 3b, Open-Label, Safety and Immunogenicity Study of SARS-CoV-2 mRNA-1273 Vaccine in Adult Solid Organ Transplant Recipients and Healthy Controls. Interventional *Ongoing*	Safety and reactogenicity and adverse events for 12 months after receiving 2 or 3 doses of elasomeran. Immunogenicity: neutralizing and binding antibody titres as surrogate endpoints expected to predict clinical benefit.	Open label single treatment arm study in solid organ transplant recipients and healthy controls	Approximately 240 adult (≥18 years of age) male and female participants (220 kidney or liver transplant recipients, and 20 healthy adults) will be enrolled	Protocol submission: 05 Feb 2021 Interim Report: 31 Mar 2023 Final CSR: 31 May 2024
mRNA-1273-P904 *Denmark, Norway, Italy, Spain, United Kingdom*	Post-Authorization Active Surveillance Safety Study Using Secondary Data to Monitor Real-World Safety of the mRNA-1273 Vaccine in the EU. Non-interventional Study protocol will be adapted to stratify the result by Spikevax and	The overarching research question of this study: Is the occurrence of each adverse event of special interest (AESI) among persons vaccinated with Spikevax in Europe higher than the occurrence of that AESI that would have been expected in the same population in the absence of Spikevax? Primary objective: - To assess whether	Secondary database analysis of observational data to estimate incidence rates of safety events of interest and other clinically significant events in cohorts of COVID-19 vaccine recipients in the EU.	Pediatric, adolescent, and adult individuals within the catchment area of participating data partners from the VAC4EU network	Feasibility assessment: 31 Jan 2021 Protocol submission: 30 Jun 2021 Interim updates: 30 Sep 2021, 31 Mar 2022, 30 Sep 2022, 31 Mar 2023 Final study report: 30 Sep 2024

Study Number *Country(ies)*	**Study Title Study Type** *Study Status*	**Rationale and Study Objectives**	**Study Design**	**Study Population(s)**	**Milestones**
	Spikevax bivalents (both Original/ Omicron BA.1 and BA.4-5), and to report on the progress and eventual updates in the submissions of the interim results *Ongoing*	vaccination with Spikevax (by dose number where feasible and for any dose) is associated with increased rates of the AESI compared with the expected rates overall and stratified by country, sex, and age group. Secondary objective: - To assess whether vaccination with Spikevax is associated with increased rates of the AESI compared with the expected rates in subpopulations of interest: women of childbearing age, patients who are immunocompromised, patients previously diagnosed with COVID-19 infection, patients with unstable health conditions and comorbidities, and patients with autoimmune or inflammatory disorders			
mRNA-1273-P905 *Denmark, Norway, Italy, Spain, United Kingdom*	Monitoring safety of COVID-19 Vaccine Moderna in pregnancy: an observational study using routinely	The overarching research question is: is there a greater risk or prevalence of pregnancy complications, adverse pregnancy outcomes, or adverse neonatal	Secondary database analysis comparing birth prevalence of study outcomes for pregnancies	The study population will encompass all pregnancies, identifiable in the databases, ending in a live or still birth; a spontaneous	Feasibility assessment: 31 Jan 2021 Protocol submission: 30 Jun 2021 Interim updates:

Study Number *Country(ies)*	**Study Title Study Type** *Study Status*	**Rationale and Study Objectives**	**Study Design**	**Study Population(s)**	**Milestones**
	collected health data in five European countries. Non-interventional Study protocol will be adapted to stratify the result by Spikevax and Spikevax bivalents (both Original/ Omicron BA.1 and BA.4-5), and to report on the progress and eventual updates in the submissions of the interim results Ongoing	outcomes following pregnancies exposed to Spikevax compared with pregnancies unexposed to Spikevax? Primary objectives: - To determine whether exposure to the Moderna COVID-19 vaccine during pregnancy is associated with an increased risk of: a. Pregnancy complications b. Adverse pregnancy outcomes c. Major congenital malformations in the offspring (overall and organ-specific if feasible) d. Adverse neonatal outcomes Secondary objectives: - To describe utilization of COVID-19 Vaccine Moderna in pregnancy	with and without COVID-19 Vaccine Moderna exposure.	abortion; or an induced abortion, or an ectopic pregnancy, as identifiable in the participating databases	31 Mar 2022, 30 Sep 2022, 31 Mar 2023 Final study report: 30 Sep 2024
mRNA-1273-P901 *US*	Real-world study of the effectiveness of the Moderna COVID-19 Vaccine Non-interventional *Ongoing*	Evaluate the vaccine effectiveness (VE) of Moderna COVID-19 vaccine in preventing COVID-19 diagnosis (symptomatic and asymptomatic) and severe COVID-19	Prospective cohort study using electronic healthcare data from the Kaiser Permanente Southern California Integrated	Individuals ≥6 months of age	Protocol submission: 01 Mar 2021 Interim updates: 14 Sept 2021; 14 Dec 2021; 14 Mar 2022; 30 Jun 2022; 31 Jul 2022; 14 Dec 2022;

Study Number *Country(ies)*	Study Title Study Type *Study Status*	Rationale and Study Objectives	Study Design	Study Population(s)	Milestones
		disease (hospitalizations and mortality) in a large integrated healthcare system in the United States Primary Objectives 1. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection 2. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing severe COVID-19 disease Secondary Objectives 1. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-COV-2 infection by age and by sex 2. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection by race/ethnicity groups 3. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection in individuals with	healthcare system		30 Jun 2023; 20 Dec 2023 Final study report: 14 Apr 2025

Study Number *Country(ies)*	**Study Title** **Study Type** *Study Status*	**Rationale and Study Objectives**	**Study Design**	**Study Population(s)**	**Milestones**
		chronic diseases (e.g., chronic kidney disease, lung disease including chronic obstructive pulmonary disease [COPD] and asthma, diabetes) 4. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection in individuals who are immunocompromised (e.g., HIV, cancer, transplant, immunosuppressive medications) 5. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection in individuals with autoimmune conditions (e.g., rheumatoid arthritis, inflammatory bowel disease, psoriasis, psoriatic arthritis, multiple sclerosis, systemic lupus erythematosus) 6. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection in frail individuals 7. To evaluate the effectiveness of 2			

Study Number *Country(ies)*	**Study Title Study Type** *Study Status*	**Rationale and Study Objectives**	**Study Design**	**Study Population(s)**	**Milestones**
		doses of Moderna COVID-19 vaccine administered during pregnancy in preventing SARS-CoV-2 infection in pregnant women 8. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection among individuals with a history of SARS-CoV-2 infection 9. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection when given concomitantly with another vaccine 10. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing asymptomatic SARS-CoV-2 infection 11. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing symptomatic SARS-CoV-2 infection 12. To evaluate the durability of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2			

Study Number *Country(ies)*	**Study Title** **Study Type** *Study Status*	**Rationale and Study Objectives**	**Study Design**	**Study Population(s)**	**Milestones**
		infection 13. To evaluate the durability of 2 doses of Moderna COVID-19 vaccine in preventing severe COVID-19 disease 14. To evaluate the effectiveness of 1 dose of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection 15. To evaluate the effectiveness of 1 dose of Moderna COVID-19 vaccine in preventing severe COVID-19 disease. 16. To assess the effectiveness of two doses of Moderna COVID-19 vaccine against SARS-CoV-2 variants (test-negative design) 17. To assess the effectiveness of one dose of Moderna COVID-19 vaccine against SARS-CoV-2 variants (test-negative design) 18. To assess the effectiveness of a booster dose of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection and severe COVID-19 disease in non-immunocompromised individuals			

Study Number *Country(ies)*	**Study Title Study Type** *Study Status*	**Rationale and Study Objectives**	**Study Design**	**Study Population(s)**	**Milestones**
		19. To assess the effectiveness of a booster dose of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection and severe COVID-19 disease in immunocompromised individuals			
mRNA-1273-P910 *Denmark, Norway, Spain, United Kingdom*	Clinical course, outcomes and risk factors of myocarditis and pericarditis following administration of Moderna vaccines targeting SARS-CoV-2 *Ongoing*	Describe the clinical course, outcomes and risk factors for myocarditis and pericarditis associated with Moderna vaccination targeting SARS-CoV-2.	Observational cohort study	Spikevax recipients and individuals diagnosed with myocarditis of all ages	Protocol submission: 26 Apr 2022 Interim report: 30 Aug 2022 31 Jan 2023 30 Jun 2023 31 Jan 2024* 30 Jun 2024 31 Jan 2025* Final study report: 30 Jun 2025
mRNA-1273-P911 *US*	Long-term outcomes of myocarditis following administration of SPIKEVAX (COVID-19 vaccine mRNA) *Ongoing*	The overarching goal of this study is to characterize long-term outcomes of myocarditis temporally associated with administration of elasomeran (SPIKEVAX) and Moderna COVID 19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5).	Observational cohort study	Individuals diagnosed with myocarditis of all ages	Protocol submission: 30 Apr 2022 Interim report: 31 Oct 2022 31 Oct 2023 31 Oct 2024 31 Oct 2025 31 Oct 2026 31 Oct 2027 Final study report: 31 Oct 2028
mRNA-1273-P205 *US*	A Phase 2/3 Study to Evaluate the Immunogenicity and	To evaluate the immunogenicity, safety, and reactogenicity of mRNA vaccine boosters for	Open-label Phase 2/3 study consisting of 9 parts: A (1, 2), B, C, D,	Men and nonpregnant women, at least 18 years of age who previously received 2 doses of	Study Start: 28 May 2021

Study Number ***Country(ies)***	**Study Title** **Study Type** ***Study Status***	**Rationale and Study Objectives**	**Study Design**	**Study Population(s)**	**Milestones**
	Safety of mRNA Vaccine Boosters for SARS-CoV-2 Variants Initial development *Ongoing*	SARS-CoV-2 variants including mRNA-1273.211, Spikevax, mRNA-1273.617.2, mRNA-1273.213, mRNA-1273.529, mRNA-1273.214 (Spikevax bivalent Original/Omicron BA.1), and mRNA-1273.222 (Spikevax bivalent Original/Omicron BA.4-5).	E, F, G, H, and J.	Spikevax (with other criteria depending on the Part of the study)	Protocol Submission: 30 Jun 2022 Interim report: 30 Jun 2022 LSLV: 07 Nov 2023 Final CSR: 07 Nov 2024
mRNA-1273-P919 *US*	An observational study to assess maternal and infant outcomes following exposure to Spikevax during pregnancy Non-interventional *Ongoing*	This observational post-marketing safety study will evaluate the risk of adverse pregnancy outcomes, birth outcomes, infant outcomes, or early life infections following maternal exposure to Spikevax during pregnancy.	Observational cohort study	An administrative claims data source in the US will be selected that includes capture of longitudinal data on diagnoses, procedures, medications, and vaccines used across all applicable healthcare settings (inpatient, emergency, and outpatient care). Mothers and infants will be linked via a common identifier and date of birth event. Mothers will be included in the study if they have adequate database enrollment to capture all pregnancy and pre-pregnancy baseline data with no prenatal exposure to major teratogenic infections or medications.	Protocol submission: 28 Oct 2022 Study completion: 30 Sep 2023 Final study report: 31 Mar 2024

Study Number ***Country(ies)***	**Study Title** **Study Type** ***Study Status***	**Rationale and Study Objectives**	**Study Design**	**Study Population(s)**	**Milestones**
mRNA-1273-P920 US	Post-marketing safety of Moderna elasomeran/davesomeran and andusomeran vaccines in the United States *Ongoing*	The overarching aim of this study is to characterize the safety of elasomeran/davesomeran and andusomeran booster vaccines as used in routine clinical practice.	Observational cohort study with signal refinement through self-controlled risk interval analyses.	Pediatric, adolescent and adult individuals enrolled in health plans contributing data to HealthVerity.	Protocol submission: 01 Nov 2022 Interim report: 15 Sep 2023 Final study report: 15 Sep 2024
mRNA-1273-P306 US	An Open-Label, Phase 3 Study to Evaluate the Safety and Immunogenicity of the mRNA-1273.214 Vaccine for SARS-CoV-2 Variants of Concern in Participants Aged 6 Months to < 6 Years *Ongoing*	Evaluate the safety and reactogenicity of 25 µg of the mRNA-1273.214 vaccine administered as a 2-dose primary series 28 days apart in participants aged 6 months to < 6 years Evaluate the safety and reactogenicity of 10 µg of the mRNA-1273.214 vaccine administered as a single booster dose (BD) at least 4 months post-Dose 2 in participants aged 6 months to < 6 years, who have previously received mRNA-1273 as a primary series	Two parts open label double treatment arm study for SARS-CoV-2 Variants of Concern in Participants Aged 6 Months to < 6 Years	Individuals 6 Months to < 6 Years that are unvaccinated against SARS-CoV-2	Protocol submission: 27 May 2022 Study completion: 31 May 2024 Final study report: 31 Jan 2025

* According to MEA/H/C/005791/MEA/065.3 (CHMP Conclusion 12/10/2023) the interim reports scheduled for these dates are deemed not reportable and hence submission to EMA is waived.

III.3 Summary Table of Additional Pharmacovigilance Activities

Table 115: Ongoing and Planned Additional Pharmacovigilance Activities

Study Number, Title, and Categories Status	Summary of Objectives	Safety Concerns Addressed	Milestones	Due Dates
Category 2 – Imposed mandatory additional pharmacovigilance activities which are Specific Obligations in the context of a conditional marketing authorisation under exceptional circumstances				
None				
Category 3 – Required pharmacovigilance activities				
Study mRNA-1273-P203 A Phase 2/3, Randomized, Observer-Blind, Placebo-Controlled Study to Evaluate the Safety, Reactogenicity, and Effectiveness of mRNA-1273 SARS-CoV-2 Vaccine in Healthy Adolescents 12 to < 18 years of age Study Status: Ongoing	Evaluate the safety, reactogenicity, and effectiveness of Spikevax. Assess safety and immunogenicity of mRNA-1273.222	Myocarditis Pericarditis Long-term safety	Interim long-term safety CSR for Part A & B	31 Oct 2022
			Final CSR	15 Jul 2025
Study mRNA-1273-P204 Phase 2/3, two-part, open-label, dose-escalation, age de-escalation and subsequent randomized, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of mRNA-1273 in healthy children 6 months to less than 12 years of age Study status: Ongoing	Safety, tolerability, reactogenicity, and effectiveness of up to 3 doses of elasomeran administered as 2 doses 28 days apart in healthy children 6 months to less than 12 years of age	Myocarditis Pericarditis Vaccine-associated enhanced disease (VAED) including vaccine-associated enhanced respiratory disease (VAERD)* Long-term safety	Study start	15 Mar 2021
			Final CSR	31 Dec 2024
Study mRNA-1273-P205	Evaluate the immunogenicity, safety, and reactogenicity of mRNA vaccine boosters for	Long-term safety	Study start	28 May 2021
			Interim report:	30 Jun 2022

Study Number, Title, and Categories Status	Summary of Objectives	Safety Concerns Addressed	Milestones	Due Dates
Phase 2/3 Study to Evaluate the Immunogenicity and Safety of mRNA Vaccine Boosters for SARS-CoV-2 Variants Study status: Ongoing	SARS CoV-2 variants including mRNA-1273.211, Spikevax, mRNA-1273.617.2, mRNA-1273.213, mRNA-1273.529, mRNA-1273.214 (Spikevax bivalent Original/Omicron BA.1), and mRNA-1273.222 (Spikevax bivalent Original/Omicron BA.4-5).		Final CSR	07 Nov 2024
Study mRNA-1273-P304 A Phase 3b, Open-Label, Safety and Immunogenicity Study of SARS-CoV-2 mRNA-1273 Vaccine in Adult Solid Organ Transplant Recipients and Healthy Controls Study status: Ongoing	Safety and reactogenicity and adverse events for 12 months after receiving 2 or 3 doses of elasomeran. Immunogenicity: neutralizing and binding antibody titres as surrogate endpoints expected to predict clinical benefit.	Myocarditis Pericarditis Use in immunocompromised subjects* AESI	Protocol submission	05 Feb 2021
			Interim report	31 Mar 2023
			Final CSR	31 May 2024
Study mRNA-1273-P904 Post-Authorization Active Surveillance Safety Study Using Secondary Data to Monitor Real-World Safety of the mRNA-1273 Vaccine in the EU Study status: Ongoing	The overarching research question of this study: Is the occurrence of each adverse event of special interest (AESI) among persons vaccinated with Spikevax in Europe higher than the occurrence of that AESI that would have been expected in the same population in the absence of Spikevax? Primary objective: - To assess whether vaccination with Spikevax (by dose number where feasible and for any dose) is associated with increased rates of the AESI compared with the expected rates overall and stratified by country, sex, and age group. Secondary objective: - To assess whether vaccination with Spikevax is associated with increased rates	Myocarditis Pericarditis Vaccine-associated enhanced disease (VAED) including vaccine-associated enhanced respiratory disease (VAERD)* Long-term safety Use in frail subjects with unstable health conditions and co-morbidities (e.g., chronic obstructive pulmonary disease (COPD), diabetes, chronic	Protocol submission	30 Jun 2021
			Interim Updates	30 Sep 2021 31 Mar 2022 30 Sep 2022 31 Mar 2023
			Final study report	30 Sep 2024

Study Number, Title, and Categories Status	Summary of Objectives	Safety Concerns Addressed	Milestones	Due Dates
	of the AESI compared with the expected rates in subpopulations of interest: women of childbearing age, patients who are immunocompromised, patients previously diagnosed with COVID-19 infection, patients with unstable health conditions and comorbidities, and patients with autoimmune or inflammatory disorders	neurological disease, cardiovascular disorders)* Use in subjects with autoimmune or inflammatory disorders*		
Study mRNA-1273-P905 Monitoring safety of COVID-19 Vaccine Moderna in pregnancy: an observational study using routinely collected health data in five European countries Study status: Ongoing	The overarching research question is: is there a greater risk or prevalence of pregnancy complications, adverse pregnancy outcomes, or adverse neonatal outcomes following pregnancies exposed to Spikevax compared with pregnancies unexposed to Spikevax? Primary objectives: - To determine whether exposure to the Moderna COVID-19 vaccine during pregnancy is associated with an increased risk of: a. Pregnancy complications b. Adverse pregnancy outcomes c. Major congenital malformations in the offspring (overall and organ-specific if feasible) d. Adverse neonatal outcomes Secondary objectives: - To describe utilization of COVID-19 Vaccine Moderna in pregnancy	Use in pregnancy	Protocol submission	30 Jun 2021
			Interim updates	31 Mar 2022 30 Sep 2022 31 Mar 2023
			Final study report	30 Sep 2024
Study mRNA-1273-P901 Real-world study of the effectiveness of the Moderna COVID-19 Vaccine Study Status: Ongoing	Evaluate the vaccine effectiveness (VE) of Moderna COVID-19 vaccine in preventing COVID-19 diagnosis (symptomatic and asymptomatic) and severe COVID-19 disease	Use in immunocompromised subjects* Interaction with other vaccines, as possible*	Protocol submission	01 Mar 2021
			Interim updates	14 Sept 2021; 14 Dec 2021; 14 Mar 2022; 30 Jun 2022; 31 Jul 2022;

Study Number, Title, and Categories Status	Summary of Objectives	Safety Concerns Addressed	Milestones	Due Dates
	(hospitalizations and mortality) in a large integrated healthcare system in the United States Primary Objectives 1. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection2. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing severe COVID-19 disease Secondary Objectives 1. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection by age and by sex 2. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection by race/ethnicity groups 3. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection in individuals with chronic diseases (e.g., chronic kidney disease, lung disease including chronic obstructive pulmonary disease [COPD] and asthma, diabetes) 4. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection in individuals who are immunocompromised (e.g., HIV, cancer, transplant, immunosuppressive medications) 5. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection in individuals with	Use in frail subjects with unstable health conditions and co-morbidities (e.g., chronic obstructive pulmonary disease (COPD), diabetes, cardiovascular disorders)* Use in subjects with autoimmune or inflammatory disorders*		14 Dec 2022; 30 Jun 2023; 20 Dec 2023
			Final study report	14 Apr 2025

Study Number, Title, and Categories Status	Summary of Objectives	Safety Concerns Addressed	Milestones	Due Dates
	autoimmune conditions (e.g., rheumatoid arthritis, inflammatory bowel disease, psoriasis, psoriatic arthritis, multiple sclerosis, systemic lupus erythematosus) 6. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection in frail individuals 7. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine administered during pregnancy in preventing SARS-CoV-2 infection in pregnant women 8. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection among individuals with a history of SARS-CoV-2 infection 9. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection when given concomitantly with another vaccine 10. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing asymptomatic SARS-CoV-2 infection 11. To evaluate the effectiveness of 2 doses of Moderna COVID-19 vaccine in preventing symptomatic SARS-CoV-2 infection 12. To evaluate the durability of 2 doses of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection 13. To evaluate the durability of 2 doses of Moderna COVID-19 vaccine in			

Study Number, Title, and Categories Status	Summary of Objectives	Safety Concerns Addressed	Milestones	Due Dates
	preventing severe COVID-19 disease 14. To evaluate the effectiveness of 1 dose of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection 15. To evaluate the effectiveness of 1 dose of Moderna COVID-19 vaccine in preventing severe COVID-19 disease. 16. To assess the effectiveness of two doses of Moderna COVID-19 vaccine against SARS-CoV-2 variants (test-negative design) 17. To assess the effectiveness of one dose of Moderna COVID-19 vaccine against SARS-CoV-2 variants (test-negative design) 18. To assess the effectiveness of a booster dose of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection and severe COVID-19 disease in non-immunocompromised individuals 19. To assess the effectiveness of a booster dose of Moderna COVID-19 vaccine in preventing SARS-CoV-2 infection and severe COVID-19 disease in immunocompromised individuals			
mRNA-1273-P910 Clinical course, outcomes and risk factors of myocarditis and pericarditis following administration of Moderna vaccines targeting SARS-CoV-2 Study status: Ongoing	Describe the clinical course, outcomes and risk factors for myocarditis and pericarditis associated with Moderna vaccination targeting SARS-CoV-2.	Myocarditis, Pericarditis	Protocol submission	26 Apr 2022
			Interim report	30 Aug 2022 31 Jan 2023 30 Jun 2023 31 Jan 2024‡ 30 Jun 2024 31 Jan 2025‡
			Final study report	30 Jun 2025

Study Number, Title, and Categories Status	**Summary of Objectives**	**Safety Concerns Addressed**	**Milestones**	**Due Dates**
mRNA-1273-P911 Long-term outcomes of myocarditis following administration of SPIKEVAX (COVID-19 vaccine mRNA) Study status: Ongoing	The overarching goal of this study is to characterize long-term outcomes of myocarditis temporally associated with administration of elasomeran (SPIKEVAX) and Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5).	Myocarditis	Protocol submission	30 Apr 2022
			Interim report	31 Oct 2022 31 Oct 2023 31 Oct 2024 31 Oct 2025 31 Oct 2026 31 Oct 2027
			Final study report	31 Oct 2028
mRNA-1273-P919 An observational study to assess maternal and infant outcomes following exposure to Spikevax during pregnancy Study status: Ongoing	This observational post-marketing safety study will evaluate the risk of adverse pregnancy outcomes, birth outcomes, infant outcomes, or early life infections following maternal exposure to Spikevax during pregnancy.	Use in pregnancy	Protocol submission	28 Oct 2022
			Study completion	30 Sep 2023
			Final study report	31 Mar 2024
mRNA-1273-P920 Post-marketing safety of Moderna elasomeran/davesomeran and andusomeran vaccines in the United States Study status: Ongoing	The overarching aim of this study is to characterize the safety of elasomeran/davesomeran and andusomeran booster vaccines as used in routine clinical practice.	Anaphylaxis* Myocarditis Pericarditis Use in immunocompromised subjects* AESI and emerging validated safety signals	Protocol submission	01 Nov 2022
			Interim report	15 Sep 2023
			Final study report	15 Sep 2024
mRNA-1273-P306 An Open-Label, Phase 3 Study to Evaluate the Safety and Immunogenicity of the mRNA-1273.214 Vaccine for SARS-CoV-2 Variants of Concern in Participants Aged 6 Months to < 6 Years Study status: Ongoing	Evaluate the safety and reactogenicity of 25 µg of the mRNA-1273.214 vaccine administered as a 2-dose primary series 28 days apart in participants aged 6 months to < 6 years Evaluate the safety and reactogenicity of 10 µg of the mRNA-1273.214 vaccine administered as a single booster dose (BD) at least 4 months post-Dose 2 in participants aged 6 months to < 6 years, who have	Anaphylaxis* Myocarditis Pericarditis Long-term safety	Protocol submission	27 May 2022
			Study completion:	31 May 2024
			Final study report:	31 Jan 2025

Study Number, Title, and Categories Status	Summary of Objectives	Safety Concerns Addressed	Milestones	Due Dates
	previously received mRNA-1273 as a primary series			

* No longer safety concerns in the RMP.
‡ According to MEA/H/C/005791/MEA/065.3 (CHMP Conclusion 12/10/2023) the interim reports scheduled for these dates are deemed not reportable and hence submission to EMA is waived.

Part IV: Plans for Post-Authorisation Efficacy Studies

Not applicable

Part V: Risk Minimisation Measures (Including Evaluation of the Effectiveness of Risk Minimisation Activities)

Risk Minimisation Plan

V.1 Routine Risk Minimisation Measures

Table 116: Description of Routine Risk Minimisation Measures by Safety Concern

Safety Concern	Routine Risk Minimisation Activities
Myocarditis	<u>Routine risk communication:</u> SmPC 4.4 Special Warnings and Precautions for Use and 4.8 Undesirable Effects PL 2. What you need to know before you are given Spikevax; 4 Possible side effects <u>Routine risk minimisation activities recommending specific clinical measures to address the risk:</u> Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination. Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition. (SmPC Section 4.4). Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur. (PL Section 2). <u>Other routine risk minimisation measures beyond the Product Information:</u> None.
Pericarditis	<u>Routine risk communication:</u> SmPC 4.4 Special Warnings and Precautions for Use and 4.8 Undesirable Effects PL 2. What you need to know before you are given Spikevax; 4 Possible side effects <u>Routine risk minimisation activities recommending specific clinical measures to address the risk:</u> Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees should be instructed to seek immediate medical attention if they

Safety Concern	Routine Risk Minimisation Activities
	develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination. (SmPC Section 4.4). Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur. (PL Section 2). <u>Other routine risk minimisation measures beyond the Product Information:</u> None.
Use in pregnancy and while breast-feeding	<u>Routine risk communication:</u> SmPC, Section 4.6 Fertility, pregnancy and lactation and 5.3 Preclinical safety data; PL: 2. What you need to know before you are given Spikevax? <u>Routine risk minimisation activities recommending specific clinical measures to address the risk</u>: None. <u>Other routine risk minimisation measures beyond the Product Information:</u> None.
Long-term safety	<u>Routine risk communication:</u> None. <u>Routine risk minimisation activities recommending specific clinical measures to address the risk:</u> None. <u>Other routine risk minimisation measures beyond the Product Information:</u> None.

V.2 Additional Risk Minimisation Measures

Routine risk minimisation activities as described in Part V.1 are sufficient to manage the safety of Spikevax.

V.3 Summary of Risk Minimisation Measures

Table 117: Summary Table of Pharmacovigilance Activities and Risk Minimisation Activities by Safety Concern

Safety Concern	Risk Minimisation Measures	Pharmacovigilance Activities
Myocarditis	Routine risk minimisation measures: SmPC Sections 4.4 Special Warnings and Precautions for Use 4.8 Undesirable effects PL Section 2 and 4 Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination. Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition. (SmPC section 4.4). Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur. (PL Section 2). Additional risk minimisation measures: None	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None. Additional pharmacovigilance activities (final CSR due date): Study mRNA-1273-P904 (final CSR: 30 Sep 2024) Study mRNA-1273-P204 (final CSR: 31 Dec 2024) Study mRNA-1273-P304 (final CSR: 31 May 2024) Study mRNA-1273-P203 (final CSR: 31 Jul 2024) Study mRNA-1273-P306 (final CSR: 31 Jan 2025) Study mRNA-1273-P910 (final CSR: 28 Feb 2025) Study mRNA-1273-P911 (final CSR: 31 Oct 2028) Study mRNA-1273-P920 (final CSR: 15 Sep 2024)
Pericarditis	Routine risk minimisation measures: SmPC Sections 4.4 Special Warnings and Precautions for Use; 4.8 Undesirable effects; PL Section 2 and 4. Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination. Healthcare	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None. Additional pharmacovigilance activities (final CSR due date): Study mRNA-1273-P904 (final CSR: 30 Sep 2024) Study mRNA-1273-P204 (final CSR: 31 Dec 2024) Study mRNA-1273-P304 (final CSR: 31 May 2024) Study mRNA-1273-P203 (final CSR: 31 Jul 2024) Study mRNA-1273-P306 (final

Safety Concern	Risk Minimisation Measures	Pharmacovigilance Activities
	professionals should consult guidance and/or specialists to diagnose and treat this condition. (SmPC section 4.4). Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur. (PL Section 2). Additional risk minimisation measures: None	CSR: 31 Jan 2025) Study mRNA-1273-P920 (final CSR: 15 Sep 2024) Study mRNA-1273-P910 (final CSR: 28 Feb 2025)
Use in pregnancy and while breast-feeding	Routine risk minimisation measures: SmPC Sections 4.6 Fertility, pregnancy and lactation; 5.3 Preclinical safety data; PL Section 2. Additional risk minimisation measures: None.	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None. Additional pharmacovigilance activities (final CSR due date): Study mRNA-1273-P905 (final CSR: 30 Sep 2024) Study mRNA-1273-P919 (final CSR: 31 Mar 2024)
Long-term safety	Routine risk minimisation measures: None. Additional risk minimisation measures: None.	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None. Additional pharmacovigilance activities (final CSR due date): Study mRNA-1273-P904 (final CSR: 30 Sep 2024) Study mRNA-1273-P204 (final CSR: 31 Dec 2024) Study mRNA-1273-P203 (final CSR: 31 Jul 2024) Study mRNA-1273-P205 (final CSR: 07 Nov 2024) Study mRNA-1273-P306 (final CSR: 31 Jan 2025)

Part VI: Summary of the Risk Management Plan

Summary of risk management plan for Spikevax (Elasomeran), Spikevax bivalent Original/Omicron BA.1 (Elasomeran/Imelasomeran), Spikevax bivalent Original/Omicron BA.4-5 (Elasomeran/Davesomeran), and Spikevax XBB.1.5 (Andusomeran)

This is a summary of the risk management plan (RMP) for Spikevax, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5, and Spikevax XBB.1.5. The RMP details important risks of Spikevax, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5, and Spikevax XBB.1.5, how these risks can be minimised, and how more information will be obtained about Spikevax's, Spikevax bivalent Original/Omicron BA.1's, Spikevax bivalent Original/Omicron BA.4-5, and Spikevax XBB.1.5's risks and uncertainties (missing information).

Spikevax's, Spikevax bivalent Original/Omicron BA.1's, Spikevax bivalent Original/Omicron BA.4-5 and Spikevax XBB.1.5's summaries of product characteristics (SmPCs) and their package leaflets give essential information to healthcare professionals and patients on how Spikevax, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5 and Spikevax XBB.1.5 should be used.

This summary of the RMP for Spikevax, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5 and Spikevax XBB.1.5 should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of the Spikevax's, Spikevax bivalent Original/Omicron BA.1's, Spikevax bivalent Original/Omicron BA.4-5's and Spikevax XBB.1.5's RMP.

I The Medicine and What it is Used for

Spikevax is authorised for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 6 months of age and older. Spikevax bivalent Original/Omicron BA.1 is authorised for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 6 years of age and older who have previously received at least a primary vaccination course against COVID-19. Spikevax bivalent Original/Omicron BA.4-5 is authorised for active immunisation to prevent COVID-19 caused by SARS-CoV-2, in individuals 6 months of age and older. Spikevax XBB.1.5 is authorised for active immunisation to prevent COVID-19 caused by SARS-CoV-2, in individuals 6 months of age and older.

The active substance in Spikevax is mRNA encoding the SARS-CoV-2 Spike protein embedded in lipid nanoparticles (elasomeran) and it is given by intramuscular route. The active substances in Spikevax bivalent Original/Omicron BA.1 are mRNA encoding the original SARS-CoV-2 Spike protein embedded in lipid nanoparticles (elasomeran) and mRNA encoding the SARS-CoV-2 Spike protein of the Omicron variant embedded in lipid nanoparticles (imelasomeran) and it is given by intramuscular route. The active substances in Spikevax bivalent Original/Omicron BA.4-5 are mRNA encoding the original SARS-CoV-2 Spike protein embedded in lipid nanoparticles (elasomeran) and mRNA encoding the SARS-CoV-2 Spike protein of the Omicron variant embedded in lipid nanoparticles (davesomeran) and it is given by intramuscular route. The active substances in Spikevax XBB.1.5 are nucleoside-modified messenger RNA (mRNA) encoding the pre-fusion stabilized Spike glycoprotein (S) of the SARS-CoV-2 Omicron variant lineage XBB.1.5 and it is given by intramuscular route.

Further information about the evaluation of Spikevax, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5, and Spikevax XBB.1.5 benefits can be found in the Spikevax EPAR, including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine's webpage: www.ema.europa.eu/en/medicines/human/EPAR/spikevax

II Risks Associated With the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Spikevax, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5, and Spikevax XBB.1.5, together with measures to minimise such risks and the proposed studies for learning more about Spikevax, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5 and Spikevax XBB.1.5's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;

Important advice on the medicine's packaging;

The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;

The medicine's legal status — the way a medicine is supplied to the patient (e.g., with or without prescription) can help to minimise its risks.

Together, these measures constitute routine risk minimisation measures.

In addition to these measures, information about Adverse Reactions (ARs) is collected continuously and regularly analysed, including Periodic Safety Update Report (PSUR) assessment, so that immediate action can be taken, as necessary. These measures constitute routine pharmacovigilance activities. If important information that may affect the safe use of Spikevax, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5 and Spikevax XBB.1.5 is not yet available, it is listed under "missing information" below.

In the case of Spikevax, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5 and Spikevax XBB.1.5, these measures are supplemented with additional pharmacovigilance activities mentioned under the relevant important risks below.

II.A List of Important Risks and Missing Information

Important risks of Spikevax, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5 and Spikevax XBB.1.5 are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Spikevax, Spikevax bivalent

Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5 and Spikevax XBB.1.5. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g., on the long-term use of the medicine).

Table 118: List of Important Risks and Missing Information

List of Important Risks and Missing Information	
Important identified risks	Myocarditis Pericarditis
Important potential risks	None
Missing information	Use in pregnancy and while breast-feeding Long-term safety

II.B Summary of Important Risks

Table 119: Important Identified Risk: Myocarditis

Important Identified Risk: Myocarditis	
Evidence for linking the risk to the medicine	Data to evaluate the safety concern were derived from clinical trials and the post-authorisation safety.
Risk factors and risk groups	Approximately 1% to 5% of patients that test positive for acute viral infection(s) may exhibit a form of myocarditis. The annual prevalence of myocarditis has been reported from 10.2 to 105.6 per 100,000 worldwide, and its annual occurrence is estimated at about 1.8 million cases. Most studies of acute myocarditis report a greater prevalence and severity in male patients, speculated to be caused by a protective effect of natural hormonal influences on immune responses in women when compared with men. Patients are usually between the ages of 20 and 50. Acute myocarditis and hyperthyroidism are also common diseases that often present in young, otherwise healthy patients. The spontaneous reports included in the global safety database included 4 cases that reported previous COVID-19 infection (5.9%) with these reports in the 18 to 39 years of age group. There were 5 reports of previous Myocarditis/ Pericarditis medical history (5.9%), 14 reports of cardiovascular conditions (16.5%), 5 with Thyroid conditions (5.9%), and 12 (14.1%) had previous medical histories of allergy-type conditions including history of anaphylaxis.
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC 4.4 Special Warnings and Precautions for Use and 4.8 Undesirable Effects PL 2. What you need to know before you are given Spikevax; 4 Possible side effects Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination. Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition. (SmPC Section 4.4).

Important Identified Risk: Myocarditis	
	Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur. (PL Section 2). Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study mRNA-1273-P904 Study mRNA-1273-P204 Study mRNA-1273-P910 Study mRNA-1273-P911 Study mRNA-1273-P304 Study mRNA-1273-P203 Study mRNA-1273-P306 Study mRNA-1273-P920 See Section II.C of this summary for an overview of the post-authorisation development plan.

Table 120: Important Identified Risk: Pericarditis

Important Identified Risk: Pericarditis	
Evidence for linking the risk to the medicine	Data to evaluate the safety concern were derived from the clinical trials and post-authorisation safety data.
Risk factors and risk groups	In most cases, the cause of pericarditis is idiopathic or is assumed to be due to a viral infection. There are several less common infectious and non-infectious causes of pericarditis, but most patients with acute pericarditis present with a history suggestive of recent or concurrent viral illness. Most cases resolve with no long-term sequelae. While pericardial effusions might develop as a result of pericarditis, they are usually minor and rarely result in cardiac tamponade. Acute pericarditis is more common in men than in women. However, although this condition is more common in adults than in children, adolescents are more commonly affected than young adults. A prospective clinical cohort study in Italy identified an incidence of 27.7 cases per 100,000 person-years. Another study, a retrospective analysis of Finnish registry data capturing admissions to 29 hospitals over a span of 9.5 years identified an age standardized incidence of 3.32 per 100,000 person-years, with higher rates in men ages 16-65. Pericarditis is the most common pericardial disorder. Congenital pericardial disorders are rare.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.4 Special Warnings and Precautions for Use and 4.8 Undesirable Effects PL 2. What you need to know before you are given Spikevax; 4 Possible side effects Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such

Important Identified Risk: Pericarditis	
	as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination. (SmPC Section 4.4). Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur. (PL Section 2). <u>Additional risk minimisation measures:</u> None.
Additional pharmacovigilance activities	<u>Additional pharmacovigilance activities</u>: Study mRNA-1273-P904 Study mRNA-1273-P204 Study mRNA-1273-P304 Study mRNA-1273-P203 Study mRNA-1273-P910 Study mRNA-1273-P306 Study mRNA-1273-P920 See Section II.C of this summary for an overview of the post-authorisation development plan.

Table 121: Missing information: Use in Pregnancy and While Breast-Feeding

Risk minimisation measures	<u>Routine risk minimisation measures</u>: SmPC Sections 4.6 Fertility, pregnancy and lactation 5.3 Preclinical safety data PL Section 2 <u>Additional risk minimisation measures</u>: None
Additional pharmacovigilance activities	<u>Additional pharmacovigilance activities</u>: Study mRNA-1273-P905 Study mRNA-1273-P919 See section II.C of this summary for an overview of the post-authorisation development plan.

Table 122: Missing information: Long-Term Safety

Risk minimisation measures	<u>Routine risk minimisation measures</u>: None <u>Additional risk minimisation measures</u>: None
Additional pharmacovigilance activities	<u>Additional pharmacovigilance activities</u>: Study mRNA-1273-P904 Study mRNA-1273-P204 Study mRNA-1273-P203 Study mRNA-1273-P205 Study mRNA-1273-P306

	See section II.C of this summary for an overview of the post-authorisation development plan.

II.C Post-Authorisation Development Plan

II.C.1 Studies Which are Conditions of the Marketing Authorisation

There are no studies which are conditions of the marketing authorisation or specific obligations of Spikevax, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5 or Spikevax XBB.1.5.

II.C.2 Other Studies in Post-Authorisation Development Plan

The following studies are considered ongoing and/or planned additional pharmacovigilance activities:

Study Title and Number	Purpose of the Study
A Phase 2/3, Randomized, Observer-Blind, Placebo-Controlled Study to Evaluate the Safety, Reactogenicity, and Effectiveness of mRNA-1273 SARS-CoV-2 Vaccine in Healthy Adolescents 12 to < 18 years of age (mRNA-1273-P203)	Evaluate the safety, reactogenicity, and effectiveness of Spikevax. Assess safety and immunogenicity of mRNA-1273.222.
Phase 2/3, two-part, open-label, dose-escalation, age de-escalation and subsequent randomized, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of mRNA-1273 in healthy children 6 months to less than 12 years of age (mRNA-1273-P204)	Safety, tolerability, reactogenicity, and effectiveness of up to 3 doses of elasomeran administered as 2 doses 28 days apart in healthy children 6 months to less than 12 years of age
Phase 2/3 Study to Evaluate the Immunogenicity and Safety of mRNA Vaccine Boosters for SARS-CoV-2 Variants (mRNA-1273-P205)	Evaluate the immunogenicity, safety, and reactogenicity of mRNA vaccine boosters for SARS CoV-2 variants including mRNA-1273.211, Spikevax, mRNA-1273.617.2, mRNA-1273.213, mRNA-1273.529, mRNA-1273.214 (Spikevax bivalent Original/Omicron BA.1), mRNA-1273.222 (Spikevax bivalent Original/Omicron BA.4-5), mRNA-1273.815 and mRNA-1273.231.
A Phase 3b, Open-Label, Safety and Immunogenicity Study of SARS-CoV-2 mRNA-1273 Vaccine in Adult Solid Organ Transplant Recipients and Healthy Controls (mRNA-1273-P304)	Safety and reactogenicity and adverse events for 12 months after receiving 2 or 3 doses of SARS-CoV-2 elasomeran vaccine. Immunogenicity: neutralizing and binding antibody titres as surrogate endpoints expected to predict clinical benefit.
Post-Authorization Active Surveillance Safety Study Using Secondary Data to Monitor Real-World Safety of the mRNA-1273 Vaccine in the EU (mRNA-1273-P904)	The overarching research question of this study: Is the occurrence of each adverse event of special interest (AESI) among persons vaccinated with Spikevax in Europe higher than the occurrence of that AESI that would have been expected in the same population in the absence of Spikevax?
Monitoring safety of COVID-19 Vaccine Moderna in pregnancy: an observational study using routinely	The overarching research question is: is there a greater risk or prevalence of pregnancy complications, adverse pregnancy outcomes, or adverse neonatal outcomes

Study Title and Number	Purpose of the Study
collected health data in five European countries (mRNA-1273-P905)	following pregnancies exposed to Spikevax compared with pregnancies unexposed to Spikevax?
Real-world study of the effectiveness of the Moderna COVID-19 vaccine (mRNA-1273-P901)	Evaluate the vaccine effectiveness (VE) of Moderna COVID-19 vaccine in preventing COVID-19 diagnosis (symptomatic and asymptomatic) and severe COVID-19 disease (hospitalizations and mortality) in a large integrated healthcare system in the United States.
Clinical course, outcomes and risk factors of myocarditis and pericarditis following administration of Moderna vaccines targeting SARS-CoV-2 (mRNA-1273-P910)	Describe the clinical course, outcomes and risk factors for myocarditis and pericarditis associated with Moderna vaccination targeting SARS-CoV-2.
Long-term outcomes of myocarditis following administration of SPIKEVAX (COVID-19 vaccine mRNA) (mRNA-1273-P911)	The overarching goal of this study is to characterize long-term outcomes of myocarditis temporally associated with administration of elasomeran (SPIKEVAX) and Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5).
An observational study to assess maternal and infant outcomes following exposure to Spikevax during pregnancy (mRNA-1273-P919)	This observational post-marketing safety study will evaluate the risk of adverse pregnancy outcomes, birth outcomes, infant outcomes, or early life infections following maternal exposure to Spikevax during pregnancy
Post-marketing safety of Moderna elasomeran/davesomeran and andusomeran vaccines in the United States (mRNA-1273-P920)	The overarching aim of this study is to characterize the safety of elasomeran/davesomeran and andusomeran booster vaccines as used in routine clinical practice.
An Open-Label, Phase 3 Study to Evaluate the Safety and Immunogenicity of the mRNA-1273.214 Vaccine for SARS-CoV-2 Variants of Concern in Participants Aged 6 Months to < 6 Years (mRNA-1273-P306)	Evaluate the safety and reactogenicity of 25 µg of the mRNA-1273.214 vaccine administered as 2-dose primary series 28 days apart in participants aged 6 months to < 6 years. Evaluate the safety and reactogenicity of 10 µg of the mRNA-1273.214 vaccine administered as a single booster dose (BD) at least 4 months post-Dose 2 in participants aged 6 months to < 6 years, who have previously received mRNA-1273 as a primary series

Part VII: Annexes

Annex 4 – Specific Adverse Drug Reaction Follow-Up Forms

Not applicable.

Annex 6 – Details of Proposed Additional Risk Minimisation Activities

Not applicable.

Annex 7 – Other Supporting Data (Including Referenced Material)

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