PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

COMIRNATY®

COVID-19 mRNA vaccine

Suspension for Intramuscular Injection

Single Dose Vial
30 mcg/0.3 mL
10 mcg/0.3 mL

Multiple Dose Vial
30 mcg/0.3 mL (6 doses/vial)
10 mcg/0.3 mL (6 doses/vial)
3 mcg/0.3 mL (3 doses/vial after dilution)

Single Dose Prefilled Syringe
30 mcg/0.3 mL

Active Immunizing Agent

Omicron LP.8.1 variant

ATC Classification J07BN01

COMIRNATY® [COVID-19 mRNA Vaccine] vaccine is indicated for:

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

COMIRNATY® [COVID-19 mRNA Vaccine] vaccine has been issued marketing authorization with Terms and Conditions that need to be met by the Market Authorization Holder to ascertain the continued quality, safety and effectiveness of the vaccine.

Patients should be advised of the nature of the authorization. For further information for COMIRNATY® [COVID-19 mRNA Vaccine] please refer to Health Canada's COVID-19 vaccines and treatments portal.

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Date of Initial Authorization:
September 28, 2023

Date of Revision:

July 13, 2026

Submission Control Number: 304376

RECENT MAJOR LABEL CHANGES

4 Dosage and Administration	09/2024
7 Warnings and Precautions - Cardiovascular	10/2024

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

COMIRNATY (COVID-19 mRNA Vaccine) is indicated for active immunization against coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS- CoV-2) in individuals 6 months of age and older (see 4.2 Recommended Dose and Dosage Adjustment).

1.1 Pediatrics

The safety and efficacy of COMIRNATY in children under 6 months of age have not yet been established (see 8 ADVERSE REACTIONS and 14 CLINICAL TRIALS).

1.2 Geriatrics

Clinical studies of COMIRNATY (Original)[1] and COMIRNATY Original & Omicron BA.4/BA.5 included participants 65 years of age and older (see 8 ADVERSE REACTIONS and 14 CLINICAL TRIALS).

2 CONTRAINDICATIONS

COMIRNATY is contraindicated in individuals who are hypersensitive to the active substance or to any ingredient in the formulation. For a complete listing see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

3 SERIOUS WARNINGS AND PRECAUTIONS

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

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

COMIRNATY is a suspension for intramuscular injection.

The storage, preparation and administration information differ depending on which presentation of the vaccine is considered. **Careful attention should be paid to the vial cap and label border colour and information on the label, and the appropriate corresponding instructions for each presentation must be followed under the subsections below**.

[1] COMIRNATY (Original) refers to the Original monovalent vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu 1 strain (wildtype).

Age Range of Recipient and Strength	Presentation	Vial Cap and Label Colour	Dilution required	Dose Volume
12 years and older 30 mcg per dose	Multiple dose vial[a]: six 0.3 mL doses per vial	Dark gray	No	0.3 mL
	Single dose vial: one 0.3 mL dose per vial	Light gray	No	0.3 mL
	Single dose prefilled syringe: one 0.3 mL dose per syringe	--	No	0.3 mL
5 to 11 years 10 mcg per dose	Multiple dose vial[a]: six 0.3 mL doses per vial	Dark blue	No	0.3 mL
	Single dose vial: one 0.3 mL dose per vial	Light blue	No	0.3 mL
6 months to 4 years 3 mcg per dose	Multiple dose vial: three 0.3 mL doses per vial after dilution	Yellow	Yes	0.3 mL

[a] Low dead-volume syringes and/or needles should be used to extract 6 doses from a multidose vial. If standard syringes and needles are used, there may not be sufficient volume to extract a 6th dose.

4.2 Recommended Dose and Dosage Adjustment

4.2.1 Vaccination Schedule for Individuals 12 Years of Age and Older

COMIRNATY is administered intramuscularly as a single dose of 0.3 mL, regardless of prior COVID-19 vaccination status.

For individuals who have previously been vaccinated with a COVID-19 vaccine, COMIRNATY should be administered at least 3 to 6 months after the most recent dose of a COVID-19 vaccine.

4.2.2 Vaccination Schedule for Individuals Aged 5 Years to 11 Years

COMIRNATY is administered intramuscularly as a single dose of 0.3 mL, regardless of prior COVID-19 vaccination status.

For individuals who have previously been vaccinated with a COVID-19 vaccine, COMIRNATY should be administered at least 6 months after the most recent dose of a COVID-19 vaccine.

4.2.3 Vaccination Schedule for Individuals Aged 6 Months to 4 Years

Without history of completion of a COVID-19 primary course

COMIRNATY is administered intramuscularly as a three-dose course (0.3 mL each). It is recommended to administer the second dose 3 weeks after the first dose, followed by a third dose administered at least 8 weeks after the second dose.

If an infant or child starts a primary vaccination course with COMIRNATY XBB.1.5, they may complete the three-dose course with COMIRNATY.

The interchangeability of COMIRNATY with COVID-19 vaccines from other manufacturers to complete the three-dose course has not been established. Individuals who have received a dose of COMIRNATY

should receive COMIRNATY to complete the three-dose course.

With history of completion of a COVID-19 primary course

COMIRNATY is administered intramuscularly as a single dose of 0.3 mL for infants and children 6 months to 4 years.

For individuals who have previously been vaccinated with a COVID-19 vaccine, COMIRNATY should be administered at least 6 months after the most recent dose of a COVID-19 vaccine.

4.3 Reconstitution

Only the multiple dose vial with yellow cap/label border (for age 6 months to 4 years) is diluted before use. For handling and preparation of other presentations prior to administration, please see 4.4.1 Preparation for Administration.

4.3.1 Vials with Yellow Cap/Label Border (for Age 6 Months to 4 Years)

Verify that the vial has a yellow plastic cap and a label with a yellow border.

COMIRNATY multiple dose vials with yellow cap and yellow label border (for age 6 months to 4 years) are supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.

Thawing Prior to Dilution

- Thaw multiple dose vial(s) before use either by:
  - Allowing vial(s) to thaw in the refrigerator [2°C to 8°C (35°F to 46°F)]. A carton of 10 vials may take up to 2 hours to thaw, and thawed vials can be stored in the refrigerator for up to 10 weeks prior to use within the expiry date printed on the carton. Upon moving vials to 2°C to 8°C storage, update the expiry date on the carton.
  - Allowing vial(s) to sit at room temperature [up to 25°C (77°F)] for 30 minutes.
  - Thawed vials may be stored at room temperature [up to 25°C (77°F)] for up to 12 hours prior to dilution.
- Before dilution, allow the thawed vial to come to room temperature.
- When at room temperature, mix by inverting vaccine vial gently 10 times.
- Do not shake.
- Inspect the liquid in the vial prior to dilution. The liquid is a clear to slightly opalescent suspension and may contain white to off-white opaque amorphous particles.
- Do not use if liquid is discoloured or if other particles are observed.

Dilution

- Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent. This diluent is not packaged with the vaccine and must be sourced separately. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Using aseptic technique, withdraw 1.1 mL of diluent into a transfer syringe (using 21-gauge or narrower needle).
- Cleanse the vaccine vial stopper with a single-use antiseptic swab.

- Add 1.1 mL of 0.9% Sodium Chloride Injection, USP into the vaccine vial.
- Equalize vial pressure before removing the needle from the vial by withdrawing 1.1 mL air into the empty diluent syringe.
- Gently invert the vial 10 times to mix.
- Do not shake.
- Inspect the vaccine in the vial.
- The vaccine will be a clear to slightly opalescent suspension with no particulates visible. Do not use if vaccine is discoloured or contains particulate matter.
- After dilution, record the discard time on vial label. Store between 2°C to 25°C (35°F to 77°F) and use within 12 hours. Discard any unused vaccine 12 hours after dilution.
- Do not freeze or shake the diluted vaccine. If refrigerated, allow the diluted vaccine to come to room temperature prior to use.

4.4 Administration

4.4.1 Preparation for Administration

4.4.1.1 Vials with Gray Cap/Label Border (for 12 Years and Older) and Vials with Blue Cap/Label Border (for Age 5 to 11 Years)

COMIRNATY single dose or multiple dose vials with a gray cap/label border (for 12 years and older) and with a blue cap/label border (for age 5 to 11 years) are supplied as a suspension that does not contain preservative. Frozen vials must be thawed prior to administration. **DO NOT DILUTE prior to use**. Instructions on thawing (if applicable) and dose preparation of the vaccine prior to administration are provided below.

Vial and Dose Verification

- Verify that:
  - the vial has a **gray cap and a label with a gray border** for use in 12 years and older.
  - the vial has a **blue cap and a label with a blue border** for use in age 5 to 11 years.
  - the vial is a single dose vial (containing 1 dose) or a multiple dose vial (containing 6 doses) by checking the label and follow the applicable handling instructions below.

Thawing Prior to Use

Frozen vials:

- Thaw frozen single dose or multiple dose vial(s) before use either by:
  - Allowing vial(s) to thaw in the refrigerator [2°C to 8°C (35°F to 46°F)].
    - Single dose vials: A 10 vial pack of single dose vials may take 2 hours to thaw.
    - Multiple dose vials: A 10 vial pack of multiple dose vials may take 6 hours to thaw.
  - Allowing vial(s) to sit at room temperature [up to 25°C (77°F)] for 30 minutes.
- Thawed vials can be stored in the refrigerator [2°C to 8°C (35°F to 46°F)] for up to 10 weeks prior to use within the expiry date printed on the carton. Upon moving vials to 2°C to 8 °C storage, update the expiry date on the carton.

- Thawed vials may be stored at room temperature [up to 25°C (77°F)] for up to 12 hours prior to use.

Refrigerated only vials (available for 30 mcg/0.3 mL strength only):

- Unopened refrigerated only vials are stored at 2 to 8°C and do not require thawing prior to use.
- Prior to use, the unopened vials can be stored for up to 12 hours at temperatures between 8°C and 25°C and can be handled in room light conditions.

Preparation of Individual 0.3 mL Doses

- Before use, mix by inverting vaccine vial gently 10 times.
- Do not shake.
- Prior to mixing:
    - Gray cap vials: The vaccine is a white to off-white suspension and may contain white to off-white opaque amorphous particles.
    - Blue cap vials: The vaccine is a clear to slightly opalescent suspension and may contain white to off-white opaque amorphous particles.
- After mixing:
    - Gray cap vials: The vaccine should appear as a white to off-white suspension with no visible particles.
    - Blue cap vials: The vaccine should appear as a clear to slightly opalescent suspension with no visible particles.
- Do not use if liquid is discoloured or if particles are observed after mixing.

Single dose vials

- Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw a single 0.3 mL dose.
- Discard vial and any excess volume. Do not pool excess vaccine from multiple vials.

Multiple dose vials

- Multiple dose vials contain 6 doses of 0.3 mL each.
    - Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. In order to ensure consistent withdrawal of 6 doses of 0.3 mL, it is important to adhere to minimizing volume loss during dose extraction.
- Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw a single 0.3 mL dose preferentially using a low dead-volume syringe and/or needle.
- Administer immediately and no later than 12 hours after first puncture.
- After first puncture, record the discard time on the vial label. Store between 2°C to 25°C (35°F to 77°F) and use within 12 hours.
- Each dose must contain 0.3 mL of vaccine.
- If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. Do not pool excess vaccine from multiple vials.
- Discard any unused vaccine 12 hours after first puncture.

4.4.1.2 Vials with Yellow Cap/Label Border (for Age 6 Months to 4 Years)

COMIRNATY multiple dose vials with a yellow cap and yellow label border (for age 6 months to 4 years) MUST BE DILUTED prior to administration. Please see 4.3 Reconstitution for instructions on thawing and dilution.

Preparation of Individual 0.3 mL Doses

- After dilution, multiple dose vials contain 3 doses of 0.3 mL each. Standard syringes and needles can be used.
- Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw a single 0.3 mL dose.
- Administer immediately and no later than 12 hours after dilution.
- Each dose must contain 0.3 mL of vaccine.
- If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. Do not pool excess vaccine from multiple vials.
- Store between 2°C to 25°C (35°F to 77°F). Discard any unused vaccine 12 hours after dilution.

4.4.1.3 Prefilled Syringe (For 12 Years and Older)

- Prior to use, the prefilled syringes can be stored for up to 12 hours at temperatures between 8 °C to 25 °C and can be handled in room light conditions. If prefilled syringe has been frozen, discard.
- Do not shake.
- Remove tip cap by slowly turning the cap counterclockwise while holding the luer lock.
- Attach a needle appropriate for intramuscular injection and administer the entire volume to deliver a 0.3 mL dose.

4.4.2 Administration

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

- In individuals 6 months to less than 12 months of age: administer COMIRNATY in the anterolateral aspect of the thigh.
- In individuals 1 year to 4 years of age: administer COMIRNATY in the anterolateral aspect of the thigh or the deltoid muscle.
- In individuals 5 years of age and older: administer COMIRNATY in the deltoid muscle.

Do not inject the vaccine intravascularly, subcutaneously or intradermally.

Visually inspect each dose in the dosing syringe prior to administration.

- Vials with gray cap/label borders and prefilled syringes: The vaccine will be an off-white suspension.
- Vials with blue cap/label borders and yellow caps/label borders: The vaccine will be a clear to slightly opalescent suspension.

During the visual inspection:

- Verify the final dosing volume of 0.3 mL.
- Confirm there are no particulates and that no discolouration is observed.
- Do not administer if vaccine is discoloured or contains particulate matter.

5 OVERDOSAGE

In the event of suspected overdose, monitoring of vital functions and individualized symptomatic treatment is recommended. Contact your regional poison control centre.

In post-authorization experience, there have been reports of higher than recommended doses of COMIRNATY vaccines. In general, adverse events reported with overdoses have been similar to the known adverse reaction profile of COMIRNATY.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

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

Table 1: Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intramuscular injection	Suspension mRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2 **Single Dose Vial** 30 mcg/0.3 mL 10 mcg/0.3 mL **Multiple Dose Vial** 30 mcg/0.3 mL (6 doses/vial) 10 mcg/0.3 mL (6 doses/vial) 3 mcg/0.3 mL (3 doses/vial after dilution) **Single Dose Prefilled Syringe** 30 mcg/0.3 mL	• ALC-0315 = ((4-hydroxybutyl) azanediyl)bis (hexane-6,1-diyl)bis(2-hexyldecanoate) • ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide • cholesterol • DSPC = 1,2-distearoyl-sn-glycero-3-phosphocholine • sodium chloride[1] • sucrose • tromethamine • tromethamine hydrochloride • water for injection

[1] Present only in the 3 mcg/0.3 mL yellow cap vial following dilution with 0.9% Sodium Chloride Injection USP

COMIRNATY is supplied as a frozen suspension in single dose or multiple dose vials. For the 30 mcg/0.3 mL strength only, COMIRNATY is also supplied as a refrigerated suspension (DO NOT FREEZE) in single dose prefilled syringes and multiple dose vials. Each dose contains nucleoside modified messenger RNA (modRNA) encoding the viral spike (S) protein of SARS-CoV-2 and the non-medicinal ingredients listed in Table 1.

The mRNA encoding spike protein is derived from Omicron variant LP.8.1.

COMIRNATY is supplied in the following presentations (not all may be marketed).

For 12 Years of Age and Older:

- *Single Dose Vial with Light Gray Cap and Light Gray Label Border (DO NOT DILUTE):* 1 dose of 0.3 mL (30 micrograms mRNA/0.3 mL).
- *Multiple Dose Vial with Dark Gray Cap and Dark Gray Label Border (DO NOT DILUTE):* 6 doses of 0.3 mL, (30 micrograms mRNA/0.3 mL)
- *Single Dose Prefilled Syringe:* 1 dose of 0.3 mL (30 micrograms mRNA/0.3 mL)

For Age 5 Years to 11 Years:

- *Single Dose Vial with Light Blue Cap and Light Blue Label Border (DO NOT DILUTE):* 1 dose of 0.3 mL (10 micrograms mRNA/0.3 mL).
- *Multiple Dose Vial with Dark Blue Cap and Dark Blue Label Border (DO NOT DILUTE):* 6 doses of 0.3 mL (10 micrograms mRNA/0.3 mL).

For Age 6 Months to 4 Years:

- *Multiple Dose Vial with Yellow Cap and Yellow Label Border (DILUTE PRIOR TO USE):* 3 doses of 0.3 mL after dilution (3 micrograms mRNA/0.3 mL)

COMIRNATY does not contain preservative.

The vial stoppers are not made with natural rubber latex.

The prefilled syringe tip cap and plunger stopper are not made with natural rubber latex.

COMIRNATY is supplied as:

- Cartons of 10 single dose vials
- Cartons of 10 multiple dose vials
- Cartons of 1 and 10 single dose prefilled syringes

7 WARNINGS AND PRECAUTIONS

General

The administration of COMIRNATY should be postponed in individuals suffering from acute severe febrile illness.

Fainting may occur in association with administration of injectable vaccines. Individuals should be advised to bring symptoms (e.g., dizziness, increases in heart rate, feeling short of breath, tingling sensations or sweating) to the attention of the vaccination provider for evaluation. Procedures should be in place to avoid injury from fainting.

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

Acute Allergic Reactions

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

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

COMIRNATY should not be given to those who have experienced anaphylaxis after a prior dose of any COMIRNATY vaccine.

Cardiovascular

Myocarditis and Pericarditis

Very rare cases of myocarditis and/or pericarditis following vaccination with COMIRNATY have been reported during post-authorization use. These cases occurred more commonly after the second dose or first booster dose in adolescent and young adult males. Typically, the onset of symptoms has been within a few days following receipt of COMIRNATY. Based on accumulating data, the reporting rates of myocarditis and pericarditis after COMIRNATY primary series in children ages 5 to 11 years are lower than in ages 12 to 17 years.

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

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

Driving and Operating Machinery

COMIRNATY has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under 8 ADVERSE REACTIONS may temporarily affect the ability to drive or use machines.

Fertility

It is unknown whether this vaccine has an impact on fertility. Animal studies do not indicate direct or indirect harmful effects with respect to female fertility or reproductive toxicity (see 16 NON-CLINICAL TOXICOLOGY).

Hematologic

Individuals receiving anticoagulant therapy or those with a bleeding disorder that would contraindicate intramuscular injection should not be given the vaccine unless the potential benefit clearly outweighs the risk of administration.

Immune

The efficacy and safety of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the vaccine.

7.1 Special Populations

7.1.1 Pregnant Women

No data are available yet regarding the use of COMIRNATY during pregnancy.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/ fetal development, parturition, or post-natal development (see 16 NON-CLINICAL TOXICOLOGY).

7.1.2 Breast-feeding

No data are available yet regarding the use of COMIRNATY during breast-feeding.

It is unknown whether COMIRNATY is excreted in human milk. A risk to the newborns/infants cannot be excluded.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for immunization against COVID-19.

7.1.3 Pediatrics

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

7.1.4 Geriatrics

Clinical studies of COMIRNATY (Original) and COMIRNATY Original & Omicron BA.4/BA.5 included participants 65 years of age and older and their data contribute to the overall assessment of the safety and efficacy of COMIRNATY (See 8 ADVERSE REACTIONS and 14 CLINICAL TRIALS).

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The safety of COMIRNATY is inferred from safety data of the prior COMIRNATY (Original) and COMIRNATY Original & Omicron BA.4/BA.5 vaccines.

Safety data accrued with the COMIRNATY (Original) and COMIRNATY Original & Omicron BA.4/BA.5 formulations are relevant to the subsequent variant updated COMIRNATY vaccines because these vaccines are manufactured using the same process.

8.1.1 COMIRNATY Original & Omicron BA.4/BA.5 (15 mcg/15 mcg)

Participants ≥12 Years of Age – Second Booster (Fourth) Dose

Study 5 was a Phase 2/3 study to evaluate the safety, tolerability, and immunogenicity of the bivalent vaccine COMIRNATY Original & Omicron BA.4/BA.5. Participants 12 years and older received

COMIRNATY Original & Omicron BA.4/BA.5 30 mcg (15/15 mcg) as a second booster dose following a previous primary series and one booster dose of COMIRNATY. Participants were monitored for unsolicited adverse events (AEs) from Dose 1 to 1 month after the last dose, and for serious adverse events (SAEs) 6 months after the last vaccination.

In a substudy from Study 5, 107 participants 12 to 17 years of age, 313 participants 18 to 55 years of age and 306 participants ≥56 years of age who had completed 3 doses of COMIRNATY, received a booster (fourth) dose of COMIRNATY Original & Omicron BA.4/BA.5 (15/15 mcg) 5.4 to 16.9 months after receiving Dose 3. Participants had a median follow-up time of at least 1.5 months.

The overall safety profile for the COMIRNATY Original & Omicron BA.4/BA.5 booster (fourth dose) was similar to that seen after 3 doses of COMIRNATY. The most frequent adverse reactions in participants 12 years of age and older were injection site pain, fatigue, headache, muscle pain, chills and joint pain.

8.1.2 COMIRNATY Original & Omicron BA.4/BA.5 (5 mcg/5 mcg)

Participants 5 to 11 Years of Age – Second Booster (Fourth) Dose

Study 6 evaluated the safety, tolerability, and immunogenicity of the bivalent vaccine COMIRNATY Original & Omicron BA.4/BA.5.

In a subset from Study 6 (Phase 3), 113 participants 5 to 11 years of age who had completed 3 doses of COMIRNATY, received a booster (fourth) dose of COMIRNATY Original & Omicron BA.4/BA.5 (5/5 mcg) 2.6 to 8.5 months after receiving Dose 3. Participants had a median follow-up time of at least 6.3 months.

The overall safety profile for the COMIRNATY Original & Omicron BA.4/BA.5 booster (fourth dose) was similar to that seen after 3 doses of COMIRNATY. The most frequent adverse reactions in participants 5 to 11 years were injection site pain, fatigue, headache and muscle pain.

8.1.3 COMIRNATY Original & Omicron BA.4/BA.5 (1.5 mcg/1.5 mcg)

Study 6 evaluated the safety, tolerability and immunogenicity of COMIRNATY Original & Omicron BA.4/BA.5. The safety of a 3-dose primary series of COMIRNATY Original & Omicron BA.4/BA.5 at 1.5 mcg/1.5 mcg in children 6 months to 4 years of age is inferred primarily from the safety profile of COMIRNATY at 3 mcg administered as a 3-dose primary series in this age bracket. Safety data from study 6 in children 6 months to 4 years of age using the COMIRNATY Original & Omicron BA.4/BA.5 formulation at 1.5 mcg/1.5 mcg administered as a booster (fourth) dose are considered supportive.

Participants 2 to 4 Years of Age – Second Booster (Fourth) Dose

In two groups from Study 6 (Phase 3, Groups 2 and 3), 1,207 participants (Group 2: 218, Group 3: 989) 2 to 4 years of age who had completed 3 doses of COMIRNATY received a booster of COMIRNATY Original & Omicron BA.4/BA.5 (1.5/1.5 mcg) 2.1 to 8.6 months after receiving Dose 3 for Group 2 and 2.8 to 17.5 months after receiving Dose 3 for Group 3. Participants had a median follow-up time of 4.6 months for Group 2 and 6.3 months for Group 3.

The overall safety profile for the COMIRNATY Original & Omicron BA.4/BA.5 booster was similar to that seen after 3 doses of COMIRNATY. The most frequent adverse reactions in participants 2 to 4 years of age were injection site pain and fatigue.

Participants 6 to 23 Months of Age – Second Booster (Fourth) Dose

In two groups from Study 6 (Phase 3, Groups 2 and 3), 160 participants (Group 2: 92, Group 3: 68) 6 to 23 months of age who had completed 3 doses of COMIRNATY received a booster of COMIRNATY Original & Omicron BA.4/BA.5 (1.5/1.5 mcg) 2.1 to 8.6 months after receiving Dose 3 for Group 2 and 3.8 to 12.5 months after receiving Dose 3 for Group 3. Participants had a median follow-up time of 4.4 months for Group 2 and 6.4 months for Group 3.

The overall safety profile for the COMIRNATY Original & Omicron BA.4/BA.5 booster was similar to that seen after 3 doses of COMIRNATY. The most frequent adverse reactions in participants 6 to 23 months of age were irritability, decreased appetite, drowsiness, tenderness at the injection site and fever.

8.1.4 COMIRNATY (Original: 30 mcg)

Study 2 was a Phase 1/2/3, multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection (Phase 1) and efficacy (Phase 2/3) study that enrolled 46,000 participants, 12 years of age or older. All participants 12 to 15 years of age and 16 years of age and older in the reactogenicity subset following the first and second dose, and a subset of 289 participants 18 to 55 years of age who received a booster dose during Phase 3, were monitored for solicited local and systemic reactions and use of antipyretic medication during the 7 days following any dose of vaccination.

The participants were unblinded to offer placebo participants COMIRNATY when they became locally eligible. A total of 25,651 (58.2%) participants (13,031 COMIRNATY; 12,620 placebo) 16 years of age and older were followed up for at least 4 months. A total of 12,006 (54.5%) participants originally randomized to the vaccine group in Study 2 were followed up for at least 6 months after the second dose including the blinded and open-label periods.

Study 4 was a placebo-controlled booster study, with 5,081 participants 16 years of age and older recruited from Study 2 to receive a booster dose of COMIRNATY at least 6 months after the second dose. Overall, participants had a median follow-up time of 2.5 months after the booster dose.

Participants 16 Years of Age and Older

In Study 2 (Phase 2/3), 44,047 participants (22,026 COMIRNATY; 22,021 placebo) were 16 years of age or older, and received 2 doses administered 3 weeks apart. Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection. HIV-positive participants are included in the safety population but are summarized separately in safety analyses.

In Study 2 where 2 doses were administered 3 weeks apart, the most common adverse reactions in the reactogenicity subset (n=4,924) of participants 16 years of age and older after any dose included injection site pain, fatigue, headache, muscle pain, chills, joint pain, fever, injection site swelling and injection site redness.

The safety profile in 545 participants receiving COMIRNATY that were seropositive for SARS-CoV-2 at baseline was similar to that seen in the general population.

In the subset of 289 participants 18 to 55 years of age who received a booster dose of COMIRNATY approximately 6 months (range of 4.8 to 8.0 months) after the second dose, the most commonly reported adverse reactions (≥10%) were pain at the injection site, fatigue, headache, muscle pain, chills and joint pain.

In Study 4, the overall safety profile for the booster dose was similar to that seen after 2 doses.

Adolescents 12 to 15 Years of Age

In Study 2 (Phase 2/3), 2,260 adolescents were 12 to 15 years of age (1,131 COMIRNATY; 1,129 placebo). Of these, 786 COMIRNATY and 773 placebo recipients were followed for ≥4 months after the second dose of COMIRNATY.

The most commonly reported (≥8%) adverse reactions in adolescents 12 to 15 years of age following any dose were pain at the injection site, fatigue, headache, chills, muscle pain, fever, joint pain, injection site swelling and injection site redness.

In a subset from Study 2, 825 adolescents 12 to 15 years of age who completed the COMIRNATY 2-dose course received a booster dose of COMIRNATY approximately 11.2 months (range 6.3 to 20.1 months) after receiving Dose 2. Overall, participants who had a booster dose had a median follow-up time of 9.5 months (range 1.5 to 10.7 months). No new adverse reactions to COMIRNATY were identified.

8.1.5 COMIRNATY (Original: 10 mcg)

Study 3 was a Phase 1/2/3 study comprised of an open-label vaccine dose-finding portion (Phase 1) and a multicenter, multinational, randomized, saline placebo-controlled, observer-blind immunogenicity and efficacy portion (Phase 2/3) that enrolled 4,600 participants 5 to 11 years of age (3,100 COMIRNATY; 1,500 placebo). Participants had at least 3 months follow-up after Dose 2.

In a subset of Study 3 Phase 2/3 participants, 2,408 participants 5 to 11 years of age received a booster dose of COMIRNATY at least 5 months (range 5.3 to 19.4 months) after completing the primary series. The overall safety profile for the booster dose was similar to that seen after the primary series (median follow-up time of 6.4 months).

Participants 5 to 11 Years of Age

In Study 3 Phase 2/3, 95.7% of participants (1,456 COMIRNATY 10 mcg and 715 placebo) were followed for at least 3 months after Dose 2. Adverse event data also included another 2,379 participants (safety expansion group: 1,591 COMIRNATY 10 mcg and 788 placebo), of whom 71.2% had a follow-up period for at least 2 weeks after Dose 2.

Adverse reactions following administration of any dose in the initial enrolment safety population (n = 1,518) of children 5 to 11 years of age included pain at the injection site, fatigue, headache, injection site redness, injection site swelling, muscle pain, chills, fever, joint pain, lymphadenopathy, rash, nausea, malaise and decreased appetite.

The most frequent adverse reactions in participants 5 to 11 years of age following the booster dose (median follow-up time of 6.4 months) were injection site pain, fatigue, headache, myalgia, chills, injection site redness and swelling. The most frequently reported unsolicited adverse event was lymphadenopathy.

8.1.6 COMIRNATY (Original: 3 mcg)

Participants 2 to 4 Years of Age

Study 3 (Phase 2/3) enrolled 3,562 participants 2 to 4 years of age (2,378 COMIRNATY 3 mcg; 1,184 placebo). Of these, 863 COMIRNATY and 405 placebo recipients received a 3-dose primary series and were followed for a median of 2.2 months after the third dose during the blinded, placebo-controlled follow-up period. Adverse reactions following administration of any dose included pain at the injection

site, fatigue, injection site redness, fever, headache, injection site swelling, chills, muscle pain, joint pain and lymphadenopathy.

Participants 6 to 23 Months of Age

Study 3 (Phase 2/3) also enrolled 2,189 participants 6 to 23 months of age (1,460 COMIRNATY 3 mcg; 729 placebo). Of these, 483 COMIRNATY and 237 placebo recipients were followed for a median of 1.7 months after the third dose, during the blinded, placebo-controlled follow-up period. Adverse reactions following administration of any dose included irritability, decreased appetite, tenderness at the injection site, injection site redness, fever, injection site swelling and lymphadenopathy.

8.2 Clinical Trial Adverse Reactions

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

8.2.1 COMIRNATY Original & Omicron BA.4/BA.5 (15 mcg/15 mcg)

Participants 12 Years of Age and Older – Second Booster (Fourth) Dose

Solicited Adverse Reactions

Tables 2 and 3 present the frequency of reported solicited local and systemic reactions within 7 days of a second booster (fourth) dose with COMIRNATY Original & Omicron BA.4/BA.5, in a subset of participants monitored with an electronic diary in Study 5.

Most local reactions were mild or moderate in severity and no Grade 4 local reactions were reported in any group. The median onset for all local reactions was 1 to 3 days, and all events resolved within a median duration of 1 to 3 days after onset.

Table 2: Study 5 - Solicited Local Adverse Reactions Reported for Vaccine Groups Within 7 Days After Second Booster Dose - Participants 12 Years of Age and Older

Local Reaction	COMIRNATY Original & Omicron BA.4/BA.5 (15 mcg/15 mcg)		
	12– 17 years N[a]=107 %	18 – 55 years N[a]=310 %	>55 years N[a]=300 %
Redness[b]			
Any	5.6	6.8	3.7
Severe	0	0	0
Swelling[b]			
Any	7.5	7.4	2.7
Severe	0	0	0
Pain at the injection site[c]			
Any	70.1	76.1	57.1 [+]
Severe	0.9	0	0.3[+]

a. N = number of participants reporting at least 1 yes or no response for the specified reaction after vaccination ([+]N=301).
b. Mild: >2.0 to 5.0 cm; moderate: >5.0 to 10.0 cm; severe: >10.0 cm; Grade 4: necrosis (redness and swelling categories) or exfoliative dermatitis (redness category only).
c. Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity; Grade 4: emergency room visit or hospitalization for severe pain at the injection site.

Most systemic reactions were mild or moderate in severity and no Grade 4 systemic reactions were reported in any group. The median onset for all systemic reactions was 2 to 4 days, and all events resolved within a median duration of 1 to 2 days after onset.

Table 3: Study 5 - Solicited Systemic Adverse Reactions Reported for Vaccine Groups Within 7 Days After Second Booster Dose - Participants 12 Years of Age and Older

Systemic Reaction	COMIRNATY Original & Omicron BA.4/BA.5 (15 mcg/15 mcg)		
	12– 17 years N[a]=107 %	18 – 55 years N[a]=309 %	>55 years N[a]=300 %
Fever			
≥38.0°C	9.3	4.9	4.7
≥38.9°C to 40.0°C	0.9	0	0
Fatigue[b]			
Any	67.3	61.2	38.5[+]
Severe	0	1.9	1.3[+]
Headache[b]			
Any	50.5	46.6	30.7
Severe	0	0.6	0
Chills[b]			
Any	23.4	22.0	12.0
Severe	0	0.6	0.3
Vomiting[c]			
Any	2.8	1.9	2.7
Severe	0	0	0
Diarrhea[d]			
Any	6.5	10.7	9.6[+]
Severe	0	0.3	0[+]
New or worsened muscle pain[b]			
Any	26.2	30.4	18.0
Severe	0	0	0
New or worsened joint pain[b]			
Any	12.1	14.9	12.0
Severe	0.9	0	0
Use of antipyretic or pain medication[e]	33.6	34.0	24.7

a. N = number of participants reporting at least 1 yes or no response for the specified event after vaccination ([+]N=301).
b. Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity; Grade 4: emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
c. Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration; Grade 4: emergency room visit or hospitalization for severe vomiting.
d. Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours; Grade 4: emergency room visit or hospitalization for severe diarrhea.
e. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

Among participants 12 years of age and older, unsolicited adverse events were reported by 6.6% participants who received a second booster dose through 1 month after the booster dose. Lymphadenopathy occurred in 1.0% of participants.

8.2.2 COMIRNATY Original & Omicron BA.4/BA.5 (5 mcg/5 mcg)

Participants 5 to 11 Years of Age – Second Booster (Fourth) Dose

Solicited Adverse Reactions

Tables 4 and 5 present the frequency of reported solicited local and systemic reactions within 7 days of a second booster (fourth) dose with COMIRNATY Original & Omicron BA.4/BA.5.

All local reactions were mild or moderate in severity. The median onset for all local reactions was 1 to 2 days, and all events resolved within a median duration of 2 days after onset.

Table 4: Study 6 - Solicited Local Adverse Reactions Reported Within 7 Days After Second Booster Dose - Participants 5 to 11 Years of Age

Local Reaction	COMIRNATY Original & Omicron BA.4/BA.5 (5 mcg/5 mcg) N[a]=111 %
Redness[b]	
Any	7.2
Severe	0
Swelling[b]	
Any	4.5
Severe	0
Pain at the injection site[c]	
Any	64.0
Severe	0

a. N = number of participants reporting at least 1 yes or no response for the specified reaction after vaccination.
b. Mild: ≥0.5 to 2.0 cm; moderate: >2.0 to 7.0 cm; severe: >7.0 cm; Grade 4: necrosis (redness and swelling categories) or exfoliative dermatitis (redness category only).
c. Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity; Grade 4: emergency room visit or hospitalization for severe pain at the injection site.

Most systemic events were mild or moderate in severity, and no Grade 4 systemic events were reported. The median onset for all systemic events was 2 to 4 days, and all events resolved within a median duration of 1 to 2 days after onset.

Table 5: Study 6 - Solicited Systemic Adverse Reactions Reported Within 7 Days After Second Booster Dose - Participants 5 to 11 Years of Age

Systemic Reaction	COMIRNATY Original & Omicron BA.4/BA.5 (5 mcg/5 mcg) N[a]=111 %
Fever	
≥38.0°C	4.5
≥38.9°C to 40.0°C	1.8
Fatigue[b]	
Any	40.5
Severe	0.9
Headache[b]	
Any	25.2
Severe	0.9
Chills[b]	
Any	9.0
Severe	0
Vomiting[c]	
Any	3.6
Severe	0
Diarrhea[d]	
Any	3.6
Severe	0
New or worsened muscle pain[b]	
Any	13.5
Severe	0
New or worsened joint pain[b]	
Any	9.0
Severe	0
Use of antipyretic or pain medication[e]	23.4

a. N = number of participants reporting at least 1 yes or no response for the specified event after vaccination.
b. Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity; Grade 4: emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
c. Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration; Grade 4: emergency room visit or hospitalization for severe vomiting.
d. Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours; Grade 4: emergency room visit or hospitalization for severe diarrhea.
e. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

Among participants 5 to 11 years of age, unsolicited adverse events were reported in 3.5% participants who received a second booster dose through 1 month after the booster dose. Lymphadenopathy occurred in 0.9% of participants.

8.2.3 COMIRNATY Original & Omicron BA.4/BA.5 (1.5 mcg/1.5 mcg)

Participants 2 to 4 Years of Age – Second Booster (Fourth) Dose

Solicited Adverse Reactions

Tables 6 and 7 present the frequency of solicited local and systemic reactions within 7 days of a booster (fourth) dose with COMIRNATY Original & Omicron BA.4/BA.5.

Most local reactions were mild or moderate in severity. No severe or Grade 4 local reactions were reported. The median onset for all local reactions was 1 to 2 days, and all events resolved within a median duration of 1 day after onset.

Table 6: Study 6 - Solicited Local Adverse Reactions Reported Within 7 Days After Second Booster Dose – Participants 2 to 4 Years of Age (Groups 2 and 3)

Local Reaction	COMIRNATY Original & Omicron BA.4/BA.5 (1.5 mcg/1.5 mcg) N=1194 to 1204[a] %
Redness[b]	
Any	9.5
Severe	0
Swelling[b]	
Any	4.0
Severe	0
Pain at the injection site[c]	
Any	30.3
Severe	0

a. N = number of participants reporting at least 1 yes or no response for the specified reaction after vaccination.
b. Mild: ≥0.5 to 2.0 cm; moderate: >2.0 to 7.0 cm; severe: >7.0 cm; Grade 4: necrosis (redness and swelling categories) or exfoliative dermatitis (redness category only).
c. Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity; Grade 4: emergency room visit or hospitalization for severe pain at the injection site.

Most systemic reactions were mild or moderate in severity. No Grade 4 systemic reactions were reported. The median onset for all systemic reactions was 2 to 6 days, and most events resolved within a median duration of 1 to 2 days after onset.

Table 7: Study 6 - Solicited Systemic Reactions Reported Within 7 Days After Second Booster Dose – Participants 2 to 4 Years of Age

Systemic Reaction	COMIRNATY Original & Omicron BA.4/BA.5 (1.5 mcg/1.5 mcg) N=1193 to 1204[a] %
Fever	
≥38.0°C	5.6
≥38.9°C to 40.0°C	1.4
Fatigue[b]	
Any	29.4
Severe	0.7
Headache[b]	
Any	4.4
Severe	0.1
Chills[b]	
Any	2.8
Severe	0
Vomiting[c]	
Any	4.9
Severe	0
Diarrhea[d]	
Any	6.6
Severe	0.1
New or worsened muscle pain[b]	
Any	2.3
Severe	0
New or worsened joint pain[b]	
Any	0.9
Severe	0
Use of antipyretic or pain medication[e]	12.5

a. N = number of participants reporting at least 1 yes or no response for the specified event after vaccination.
b. Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity; Grade 4: emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe new or worsened muscle pain, or severe new or worsened joint pain.
c. Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration; Grade 4: emergency room visit or hospitalization for hypotensive shock.
d. Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours; Grade 4: emergency room visit or hospitalization for severe diarrhea.
e. Severity was not collected for use of antipyretic or pain medication.

Participants 6 to 23 Months – Second Booster (Fourth) Dose

Solicited Adverse Reactions

Tables 8 and 9 present the frequency of solicited local and systemic reactions within 7 days of a booster (fourth) dose with COMIRNATY Original & Omicron BA.4/BA.5.

No severe or Grade 4 local reactions were reported. The median onset for all local reactions was 1 to 4 days, and all events resolved within a median duration of 1 to 4 days after onset.

Table 8: Study 6 - Solicited Local Adverse Reactions Reported Within 7 Days After Second Booster Dose – Participants 6 to 23 Months of Age

Local Reaction	COMIRNATY Original & Omicron BA.4/BA.5 (1.5 mcg/1.5 mcg) N=154 to 160[a] %
Redness[b]	
Any	6.9
Severe	0
Swelling[b]	
Any	3.8
Severe	0
Tenderness at the injection site[c]	
Any	12.3
Severe	0

a. N = number of participants reporting at least 1 yes or no response for the specified reaction after vaccination.
b. Mild: ≥0.5 to 2.0 cm; moderate: >2.0 to 7.0 cm; severe: >7.0 cm; Grade 4: necrosis (redness and swelling categories) or exfoliative dermatitis (redness category only).
c. Mild: hurts if gently touched; moderate: hurts if gently touched with crying; severe: causes limitation of limb movement; Grade 4: emergency room visit or hospitalization for severe pain (tenderness) at the injection site.

Most systemic reactions were mild or moderate in severity. No Grade 4 systemic reactions were reported. The median onset for all systemic reactions was 2 to 3 days, and all events resolved within a median duration of 1 to 2 days after onset.

Table 9: Study 6 - Solicited Systemic Reactions Reported Within 7 Days After Second Booster Dose – Participants 6 to 23 Months of Age

Systemic Reaction	COMIRNATY Original & Omicron BA.4/BA.5 (1.5 mcg/1.5 mcg) N=153 to 160[a] %
Fever	
≥38.0°C	10.0
≥38.9°C to 40.0°C	2.5
Decreased appetite[b]	
Any	20.3
Severe	0
Drowsiness[c]	
Any	19.0
Severe	0
Irritability[d]	
Any	39.9
Severe	0.7
Use of antipyretic or pain medication[e]	18.1

a. N = number of participants reporting at least 1 yes or no response for the specified event after vaccination.
b. Mild: decreased interest in eating; moderate: decreased oral intake; severe: refusal to feed; Grade 4: emergency room visit or hospitalization for severe decreased appetite (loss of appetite).
c. Mild: increased or prolonged sleeping bouts; moderate: slightly subdued interfering with daily activity; severe: disabling; not interested in usual daily activity; Grade 4: emergency room visit or hospitalization for severe drowsiness (increased sleep).
d. Mild: easily consolable; moderate: requiring increased attention; severe: inconsolable; crying cannot be comforted; Grade 4: emergency room visit or hospitalization for severe irritability (fussiness).
e. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

Overall, AEs were reported by 12.5% and 6.2% participants in the 6 to 23 months of age group and 2 to 4 years of age group, respectively. No AEs leading to withdrawal or death were reported from study vaccination to 1 month after study vaccination.

From study vaccination through 1-month postvaccination, no AEs of anaphylaxis, appendicitis, Bell's palsy, and myo/pericarditis were reported.

8.2.4 COMIRNATY (Original: 30 mcg)

Participants 16 Years of Age and Older – Primary Series (Two Doses)

Solicited Adverse Reactions

Tables 10 through 13 present the frequency and severity of solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 years of age and older (n=9,839) in the safety population who were monitored for reactogenicity with an electronic diary.

Table 10: Study 2 – Solicited Local Reactions Reported Within 7 Days After Each Dose of COMIRNATY– Participants 16 to 55 Years of Age

Local Reaction	Dose 1		Dose 2	
	COMIRNATY‡ N[a]=2,899 %	**Placebo** N[a]=2,908 %	**COMIRNATY‡** N[a]=2,682 %	**Placebo** N[a]=2,684 %
Redness[b]				
Any	5.4	1.0	5.6	0.7
Severe	0.2	0.1	0.4	0.0
Swelling[b]				
Any	6.3	0.6	6.8	0.2
Severe	0.2	0.1	0.3	0.0
Pain at the injection site[c]				
Any	83.7	14.2	78.3	11.6
Severe	1.3	0.1	1.5	0.0

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).
a. - c. See footnote of Table 2.

Table 11: Study 2 – Solicited Systemic Reactions Reported Within 7 Days After Each Dose of COMIRNATY – Participants 16 to 55 Years of Age

Systemic Reaction	Dose 1		Dose 2	
	COMIRNATY‡ N[a]=2,899 %	**Placebo** N[a]=2,908 %	**COMIRNATY‡** N[a]=2,682 %	**Placebo** N[a]=2,684 %
Fever				
≥38.0°C	4.1	0.9	16.4	0.4
>38.9°C	0.3	0.1	1.5	0.1
Fatigue[b]				
Any	49.4	33.0	61.5	22.9
Severe	1.4	0.6	5.3	0.5
Headache[b]				
Any	43.5	33.5	54.0	24.3
Severe	1.1	0.8	3.4	0.7
Chills[b]				
Any	16.5	6.8	37.8	4.2
Severe	0.5	0.1	2.6	0.1
Vomiting[c]				
Any	1.2	1.2	2.2	1.1
Severe	0.0	0.0	0.1	0.0
Diarrhea[d]				
Any	10.7	11.1	10.0	7.6
Severe	0.1	0.0	0.2	0.0
New or worsened muscle pain[b]				
Any	22.9	11.3	39.3	8.8
Severe	0.5	0.1	2.3	0.1
New or worsened joint pain[b]				
Any	11.8	5.8	23.8	5.5
Severe	0.2	0.0	1.0	0.1
Use of antipyretic or pain medication[e]	27.8	13.7	45.2	11.9

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).
a. – e. See footnote of Table 3.

Table 12: Study 2 – Solicited Local Reactions Reported Within 7 Days After Each Dose of COMIRNATY – Participants 56 Years of Age and Older

Local Reaction	Dose 1		Dose 2	
	COMIRNATY‡ N[a]=2,008 %	**Placebo** N[a]=1,989 %	**COMIRNATY‡** N[a]=1,860 %	**Placebo** N[a]=1,833 %
Redness[b]				
Any	5.3	1.0	7.2	0.8
Severe	0.2	0.1	0.5	0.1
Swelling[b]				
Any	7.0	1.2	7.8	0.7
Severe	0.1	0.0	0.2	0.1
Pain at the injection site[c]				
Any	70.1	9.3	66.1	7.8
Severe	0.2	0.0	0.5	0.0

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).
a. – c. See footnote of Table 2.

Table 13: Study 2 – Solicited Systemic Reactions Reported Within 7 Days After Each Dose of COMIRNATY – Participants 56 Years of Age and Older

Systemic Reaction	Dose 1		Dose 2	
	COMIRNATY‡ N[a]=2,008 %	**Placebo** N[a]=1,989 %	**COMIRNATY‡** N[a]=1,860 %	**Placebo** N[a]=1,833 %
Fever				
≥38.0°C	1.3	0.4	11.8	0.2
>38.9°C	0.0	0.1	0.4	0.1
Fatigue[b]				
Any	33.7	22.5	51.0	16.7
Severe	0.1	0.2	3.2	0.1
Grade 4	0.0	0.0	0.1	0.0
Headache[b]				
Any	25.0	18.3	39.4	14.1
Severe	0.1	0.2	0.7	0.3
Chills[b]				
Any	6.5	3.5	23.4	3.1
Severe	0.0	0.1	1.1	0.0
Vomiting[c]				
Any	0.5	0.5	0.7	0.3
Severe	0.0	0.0	0.1	0.0
Diarrhea[d]				
Any	8.4	6.5	8.2	5.6
Severe	0.2	0.1	0.1	0.2
New or worsened muscle pain[b]				
Any	13.6	8.3	28.9	5.4
Severe	0.0	0.2	1.1	0.1
New or worsened joint pain[b]				
Any	8.7	6.2	19.0	3.9
Severe	0.1	0.1	0.5	0.1
Use of antipyretic or pain medication[e]	19.0	11.3	37.0	9.3

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).
a. – e. See footnote of Table 3.

Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection. The safety profile of the participants with stable HIV infection receiving COMIRNATY (n = 100) was similar to that seen in the general population.

Unsolicited Adverse Events

Among participants 16 to 55 years of age who received at least one dose of study vaccine (12,995 COMIRNATY; 13,026 placebo), unsolicited adverse events were reported by 33.8% of participants in the COMIRNATY group and 16.4% of participants in the placebo group. In participants 56 years of age and older (8,931 COMIRNATY; 8,895 placebo), unsolicited adverse events were reported by 28.6% of participants in the COMIRNATY group and 16.1% of participants in the placebo group. Among participants with confirmed stable HIV infection (100 COMIRNATY; 100 placebo), unsolicited adverse

events were reported by 29% of participants in the COMIRNATY group and 15% of participants in the placebo group.

In the safety population (n=21,926) of participants 16 years of age and older from dose 1 to 1 month after dose 2, AEs included nausea (1.2%), malaise (0.6%), lymphadenopathy (0.4%), asthenia (0.3%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%). Adverse reactions were usually mild or moderate in intensity and resolved within a few days after vaccination.

Lymphadenopathy was reported in 0.4% of participants in the vaccine group compared with 0.1% of participants in the placebo group. Bell's palsy (facial paralysis and facial paresis) was reported by four participants in the vaccine group and two in the placebo group. In the four vaccinated participants, events began from 3 to 48 days after their last dose, were mild to moderate in severity, and duration ranged from 3 to 68 days. Currently available information is insufficient to determine a causal relationship with the vaccine.

Serious Adverse Events

In Study 2, among participants 16 to 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY = 12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date were reported by 0.8% of COMIRNATY recipients and 0.9% of placebo recipients. In participants 56 years of age and older (COMIRNATY 8,931; placebo 8,895), serious adverse events were reported by 1.8% of COMIRNATY recipients and 1.7% of placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. Among participants with confirmed stable HIV infection, serious adverse events from Dose 1 up to the participant unblinding date were reported by 2% of COMIRNATY recipients and 2% of placebo recipients.

Pericarditis was reported for one participant in the vaccine group, and no case was reported in the placebo group. Appendicitis was reported in 15 vaccine participants and 12 placebo participants. Currently available information is insufficient to determine a causal relationship with the vaccine.

Participants 16 Years of Age and Older – First Booster Dose (Third Dose)

In a subset from Study 2 (Phase 2/3) participants, 306 adults 18 to 55 years of age who completed the 2-dose series, received a booster (third) dose of COMIRNATY. The overall safety profile for the booster dose was similar to that seen after 2 doses, monitored with an electronic diary up to Day 7 after the booster dose.

In Study 4 a placebo-controlled booster study, participants 16 years of age and older recruited from Study 2 received a booster dose of COMIRNATY (5,081 participants), or placebo (5,044 participants) at least 6 months after the second dose of COMIRNATY. The overall safety profile for the booster dose was similar to that seen after 2 doses.

Solicited Adverse Reactions

Table 14: Study 2 – Solicited Local Reactions Reported Within 7 Days After the Booster Dose of COMIRNATY – Participants 16 Years of Age and Older

Local Reaction	COMIRNATY‡ Original (Wuhan-Hu-1 strain) N[a] = 289 %
Redness[b]	
Any	5.9
Severe	0
Swelling[b]	
Any	8.0
Severe	0.3
Pain at the injection site[c]	
Any	83.0
Severe	0.3

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).
a. – c. See footnote of Table 2.

In participants who received a booster dose the mean duration of pain at the injection site after the booster dose was 2.6 days (range 1 to 8 days), for redness 2.2 days (range 1 to 15 days), and for swelling 2.2 days (range 1 to 8 days). No Grade 4 solicited systemic reactions were reported.

Table 15: Study 2 – Solicited Systemic Reactions Reported Within 7 Days After the Booster Dose of COMIRNATY – Participants 16 Years of Age and Older

Systemic Reaction	COMIRNATY‡ Original (Wuhan-Hu-1 strain) N[a] = 289 %
Fever	
≥38.0℃	8.7
>38.9℃ to 40.0℃	0.3
Fatigue[b]	
Any	63.7
Severe	4.5
Headache[b]	
Any	48.4
Severe	1.0
Chills[b]	
Any	29.1
Severe	1.0
Vomiting[c]	
Any	1.7
Severe	0
Diarrhea[d]	
Any	8.7
Severe	0
New or worsened muscle pain[b]	
Any	39.1
Severe	1.4
New or worsened joint pain[b]	

Table 15: Study 2 – Solicited Systemic Reactions Reported Within 7 Days After the Booster Dose of COMIRNATY – Participants 16 Years of Age and Older

Systemic Reaction	COMIRNATY‡ Original (Wuhan-Hu-1 strain) N[a] = 289 %
Any	25.3
Severe	0.3
Use of antipyretic or pain medication[e]	46.7

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).
a. – e. See footnote of Table 3.

Unsolicited Adverse Events

In participants 16 to 87 years of age (N = 5,055), unsolicited adverse events reported following the booster dose of COMIRNATY, through 1 month after the booster dose, included headache (5%), fever (4.8%), lymphadenopathy (2.8%), decreased appetite (0.2%), malaise (0.7%), nausea (0.9%), and pain in extremity (1.1%).

Serious Adverse Events

Serious adverse events were reported by 0.3% of COMIRNATY recipients and 0.5% by placebo recipients. A 17-year-old male in Study 2 was diagnosed with myocarditis three days after receiving the booster dose (Dose 3). The participant was treated and recovered.

Coadministration of COMIRNATY with Seasonal Influenza Vaccine

In Study 8 (C4591030), a Phase 3 study, participants 18 to 64 years of age who received COMIRNATY coadministered with standard dose unadjuvanted seasonal inactivated influenza vaccine (SIIV), quadrivalent followed 1 month later by placebo (n=564) were compared with participants who received SIIV quadrivalent with placebo followed 1 month later by COMIRNATY alone (n=564).

Reactogenicity events were reported more frequently by participants who received COMIRNATY coadministered with SIIV quadrivalent, compared with participants who received COMIRNATY or SIIV quadrivalent alone, but overall the reactogenicity events were mostly mild to moderate in severity. The most common adverse reactions reported in the coadministration group and after COMIRNATY alone were injection site pain (86.2% and 84.4%, respectively), fatigue (64.0% and 50.8%, respectively) and headache (47.2% and 37.8%, respectively).

Adolescents 12 to 15 Years of Age – Primary Series (Two Doses)

Solicited Adverse Reactions

Table 16 and Table 17 present the frequency and severity of solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in adolescents 12 to 15 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 16: Study 2 – Solicited Local Reactions Reported Within 7 Days After Each Dose of COMIRNATY – Adolescents 12 to 15 Years of Age

Local Reaction	COMIRNATY‡ Dose 1 N[a]=1,127 %	Placebo Dose 1 N[a]=1,127 %	COMIRNATY‡ Dose 2 N[a]=1,097 %	Placebo Dose 2 N[a]=1,078 %
Redness[b]				
Any	5.8	1.1	5.0	0.9
Severe	0.1	0.0	0.0	0.0
Swelling[b]				
Any	6.9	1.0	4.9	0.6
Severe	0.0	0.0	0.0	0.0
Pain at the injection site[c]				
Any	86.2	23.3	78.9	17.9
Severe	1.0	0.0	0.6	0.0

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).
a. – c. See footnote of Table 2.

Table 17: Study 2 – Solicited Systemic Reactions Reported Within 7 Days After Each Dose of COMIRNATY – Adolescents 12 to 15 Years of Age

Systemic Reaction	COMIRNATY‡ Dose 1 N[a]=1,127 %	Placebo Dose 1 N[a]=1,127 %	COMIRNATY‡ Dose 2 N[a]=1,097 %	Placebo Dose 2 N[a]=1,078 %
Fever				
≥38.0°C	10.1	1.1	19.6	0.6
>38.9°C	1.0	0.2	2.3	0.1
Fatigue[b]				
Any	60.1	40.6	66.2	24.5
Severe	1.3	0.7	2.4	0.4
Headache[b]				
Any	55.3	35.1	64.5	24.4
Severe	1.0	0.8	2.0	0.1
Chills[b]				
Any	27.6	9.7	41.5	6.8
Severe	0.4	0.2	1.8	0.0
Vomiting[c]				
Any	2.8	0.9	2.6	1.1
Severe	0.1	0.0	0.0	0.0
Diarrhea[d]				
Any	8.0	7.3	5.9	4.0
Severe	0.0	0.0	0.0	0.0
New or worsened muscle pain[b]				
Any	24.1	13.1	32.4	8.3
Severe	0.2	0.0	0.5	0.2
New or worsened joint pain[b]				
Any	9.7	6.8	15.8	4.7
Severe	0.1	0.0	0.4	0.0
Use of antipyretic or pain medication[e]	36.6	9.8	50.8	8.8

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).
a. – e. See footnote of Table 3.

Unsolicited Adverse Events

Unsolicited adverse events reported following any dose, through 1 month after Dose 2, in adolescents 12 to 15 years of age (1,131 COMIRNATY group vs. 1,129 placebo group), were reported by 8.4% of participants in the COMIRNATY group and 10.0% of participants in the placebo group. Non-serious adverse events from Dose 1 through up to 30 days after Dose 2 were reported by 5.8% of COMIRNATY recipients and by 5.8% of placebo recipients. Adverse reactions not captured by solicited local and systemic reactions were lymphadenopathy (0.8% vs. 0.2%), and nausea (0.4% vs. 0.1%).

Serious Adverse Events

Serious adverse events from Dose 1 up to the participant unblinding date were reported by 0.9% of COMIRNATY recipients and 0.2% of placebo recipients. One (1) 16-year-old male was diagnosed with myopericarditis 3 days after his second dose. The participant was treated and recovered.

8.2.5 COMIRNATY (Original: 10 mcg)

Children 5 to 11 Years of Age – Primary Series (Two Doses)

Solicited Adverse Reactions

Table 18 and Table 19 present the frequency and severity of solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in children 5 to 11 years of age. Reactions were monitored with an electronic diary.

Table 18: Study 3 – Solicited Local Reactions Reported Within 7 Days After Each Dose – Children 5 to 11 Years of Age

Local Reaction	COMIRNATY‡ Dose 1 N[a]=1,511 %	Placebo Dose 1 N[a]=748 %	COMIRNATY‡ Dose 2 N[a]=1,501 %	Placebo Dose 2 N[a]=740 %
Redness[b]				
Any (≥0.5 cm)	14.7	5.7+	18.5	5.4+
Severe	0.0	0.0	0.2	0.0
Swelling[b]				
Any (≥0.5 cm)	10.5	2.7+	15.3	2.7+
Severe	0.1	0.0	0.0	0.0
Pain at the injection site[c]				
Any	74.1	31.3	71.0	29.5
Severe	0.3	0.0	0.3	0.0

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).

a. – c. See footnote of Table 4.

+ N used in the calculation of percentages for redness and swelling were 749 after Dose 1 and 741 after Dose 2 in the placebo group, due to an e-diary error.

Table 19: Study 3 – Solicited Systemic Reactions Reported Within 7 Days After Each Dose – Children 5 to 11 Years to of Age

Systemic Reaction	COMIRNATY‡ Dose 1 N[a]=1,511 %	Placebo Dose 1 N[a]=748 %	COMIRNATY‡ Dose 2 N[a]=1,501 %	Placebo Dose 2 N[a]=740 %
Fever				
≥38.0°C	2.5	1.3+	6.5	1.2+
>38.9°C	0.2	0.1	0.6	0.1
Fatigue[b]				
Any	33.6	31.3	39.4	24.3
Severe	0.3	0.1	0.7	0.1
Headache[b]				
Any	22.4	24.1	28.0	18.6
Severe	0.1	0.5	0.2	0.0
Chills[b]				
Any	4.6	4.7	9.8	4.3
Severe	0.0	0.0	0.1	0.1
Vomiting[c]				
Any	2.2	1.5	1.9	0.8
Severe	0.0	0.0	0.0	0.0
Diarrhea[d]				
Any	5.9	4.1	5.3	4.7
Severe	0.0	0.0	0.0	0.0
New or worsened muscle pain[b]				
Any	9.1	6.8	11.7	7.4
Severe	0.1	0.0	0.1	0.0
New or worsened joint pain[b]				
Any	3.3	5.5	5.2	3.6
Severe	0.0	0.0	0.0	0.0
Use of antipyretic or pain medication[e]	14.4	8.3+	19.7	8.1+

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).

a. - e. See footnote of Table 5.

+N used in the calculation of percentages for fever and use of antipyretic or pain medication were 749 after Dose 1 and 741 after Dose 2 in the placebo group, due to an e-diary error.

Unsolicited Adverse Events

Serious adverse events from Dose 1 through up to 30 days after Dose 2 in the initial enrolment group were reported by 1 participant (0.1%) in each group after receiving the vaccine or placebo. No serious adverse events were reported that were considered related to vaccination.

Non-serious adverse events from Dose 1 through up to 30 days after Dose 2 in the initial enrolment group were reported by 10.9% of COMIRNATY 10 mcg recipients and by 9.1% of placebo recipients. Lymphadenopathy was reported in 0.9% of participants in the COMIRNATY 10 mcg group vs. 0.1% in the placebo group. All cases were considered to be mild, with a median onset of 3 days after Dose 1, and 2 days after Dose 2 in the vaccine group. The median duration was 3.5 days (range 1 to 14 days) in the vaccine group. Skin and subcutaneous tissue disorders (including skin rash, dermatitis, eczema and urticaria) were reported in 1.1% of participants in the vaccine group and 0.7% of participants in the placebo group. Most of the events began from 3-11 days after the second dose and were characterized

as mild and self-limited. There were no reports of myocarditis/pericarditis or anaphylaxis from dose 1 through up to 6 months post-dose 2.

Children 5 to 11 Years of Age – First Booster Dose (Third Dose)

Solicited Adverse Reactions

Table 20 and Table 21 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of a booster dose of COMIRNATY for Phase 2/3 participants 5 to 11 years of age. Reactogenicity was monitored with an electronic diary and during unscheduled clinical assessments.

In participants who received a booster dose, the mean duration of pain at the injection site after the booster dose was 2.3 days (range 1 to 9 days), for redness 2.1 days (range 1 to 12 days), and for swelling 2.1 days (range 1 to 9 days).

Table 20: Study 3 – Solicited Local Reactions Reported Within 7 Days After the Booster Dose – Children 5 to 11 Years of Age

Local Reaction	COMIRNATY Original (Wuhan-Hu-1 strain) N[a]=2,265 %
Redness[b]	
Any	15.6
Severe	0.1
Swelling[b]	
Any	12.6
Severe	0
Pain at the injection site[c]	
Any	69.2
Severe	0.3

a. – c. See footnote of Table 4.

Table 21: Study 3 – Solicited Systemic Reactions Reported Within 7 Days After the Booster Dose of COMIRNATY– Children 5 to 11 Years of Age

Systemic Reaction	COMIRNATY‡ Booster N[a]=2,265 %
Fever	
≥38.0°C	6.8
>38.9°C	0.9
Fatigue [b]	
Any	39.6
Severe	1.3
Headache[b]	
Any	26.9
Severe	0.4
Chills[b]	
Any	10.2
Severe	0.1
Vomiting[c]	
Any	2.7
Severe	0.0
Diarrhea[d]	
Any	4.6
Severe	0.0
New or worsened muscle pain[b]	
Any	15.5
Severe	0.1
New or worsened joint pain[b]	
Any	5.7
Severe	0.0
Use of antipyretic or pain medication[e]	27.9

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).
a. – e. See footnote of Table 5.

Unsolicited Adverse Events

Unsolicited adverse events reported in 2,408 participants 5 to 11 years of age through up to 1 month after the booster dose that were not captured by solicited local and systemic reactions included abdominal pain (0.1%), arthralgia (0.1%), axillary pain (0.2%), dizziness (0.1%), lymphadenopathy (1.9%) pain in extremity (0.2%), and rash (0.2%).

Serious Adverse Events

No serious adverse events were reported after the booster dose of COMIRNATY.

8.2.6 COMIRNATY (Original: 3 mcg)

Children 2 to 4 Years of Age – Primary Series (Three Doses)

Solicited Adverse Reactions

Table 22 and Table 23 present the frequency of solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in children 2 to 4 years of age who were monitored for reactogenicity with an electronic diary.

Table 22: Study 3 – Solicited Local Reactions Reported Within 7 Days After Each Dose – Children 2 to 4 Years of Age

Local Reaction	COMIRNATY† Dose 1 Na=2,305 to 2,327 %	Placebo Dose 1 Na=1,159 to 1,164 %	COMIRNATY† Dose 2 Na=2,082 to 2,094 %	Placebo Dose 2 Na=1,037 to 1,038 %	COMIRNATY† Dose 3 Na=793 to 799 %	Placebo Dose 3 Na=375 to 376 %
Redness[b]						
Any	9.0	8.4	11.2	5.4	10.4	4.8
Severe	0.0	0.1	0.0	0	0	0
Swelling[b]						
Any	3.9	3.1	5.6	2.0	3.1	1.6
Severe	0	0	0	0	0	0
Pain at the injection site[c]						
Any	30.3	20.6	30.5	20.3	28.0	12.8
Severe	0	0.1	0	0.1	0	0

† COMIRNATY 3 mcg. (vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain [Original]).
a. – c. See Table 6.

Table 23: Study 3 – Solicited Systemic Reactions Reported Within 7 Days After Each Dose – Children 2 to 4 Years of Age

Systemic Reaction	COMIRNATY† Dose 1 Na=2,304 to 2,327 %	Placebo Dose 1 Na=1,159 to 1,164 %	COMIRNATY† Dose 2 Na=2,082 to 2,094 %	Placebo Dose 2 Na=1,037 to 1,038 %	COMIRNATY† Dose 3 Na=793 to 799 %	Placebo Dose 3 Na=375 to 376 %
Fever						
≥38.0°C	5.5	5.7	5.2	5.8	5.1	5.6
>38.9°C	1.0	1.0	1.2	1.0	0.9	1.6
Fatigue[b]						
Any	30.6	31.9	26.1	24.3	25.5	24.3
Severe	0.4	0.8	0.4	0.4	0.3	0.3
Headache[b]						
Any	5.1	4.8	4.6	4.1	4.5	4.0
Severe	0	0.1	0	0.1	0	0
Chills[b]						
Any	2.8	2.9	3.2	2.8	2.8	2.7
Severe	0.1	0.1	0	0	0.1	0

Table 23: Study 3 – Solicited Systemic Reactions Reported Within 7 Days After Each Dose – Children 2 to 4 Years of Age

Systemic Reaction	COMIRNATY† Dose 1 N[a]=2,304 to 2,327 %	Placebo Dose 1 N[a]=1,159 to 1,164 %	COMIRNATY† Dose 2 N[a]=2,082 to 2,094 %	Placebo Dose 2 N[a]=1,037 to 1,038 %	COMIRNATY† Dose 3 N[a]=793 to 799 %	Placebo Dose 3 N[a]=375 to 376 %
Vomiting[c]						
Any	3.5	2.9	3.4	3.4	2.0	4.3
Severe	0	0	0	0	0	0
Diarrhea[d]						
Any	8.6	8.3	6.8	8.0	4.9	5.6
Severe	0	0	0.1	0.1	0	0
New or worsened muscle pain[b]						
Any	2.6	2.3	2.6	2.6	1.9	1.6
Severe	0.0	0.1	0	0	0	0
New or worsened joint pain[b]						
Any	1.2	1.8	1.2	1.2	1.1	1.1
Severe	0.0	0	0	0	0.1	0
Use of antipyretic or pain medication[e]						
Any	11.6	10.4	10.6	8.9	9.3	8.2

† COMIRNATY 3 mcg (vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain [Original]).
a. – e. See Table 7.

Unsolicited Adverse Events

In participants 2 to 4 years of age (863 COMIRNATY; 405 placebo), 80.1% of participants had at least 1 month of follow-up after Dose 3.

Serious adverse events from Dose 1 through 1 month after Dose 3, with an overall median of 2.2 months follow-up after Dose 3, were reported by 0.5% of COMIRNATY recipients and by 0.9% of placebo recipients. One serious adverse event of fever (maximum temperature 40.3°C) on Day 3 after Dose 2 in a 4-year-old was considered possibly related to vaccination.

Non-serious adverse events from Dose 1 through up to 1 month after Dose 3 were reported by 19.0% of COMIRNATY recipients and by 17.9 % of placebo recipients.

From Dose 1 through 1 month after Dose 3, lymphadenopathy was reported in 1 (0.04%) of COMIRNATY recipients vs. 0 (0.0%) of placebo recipients. Other unsolicited AEs included abdominal pain (COMIRNATY: 0.1%; placebo: 0.1%), chills (COMIRNATY: 0.2%; placebo: 0%), febrile convulsion (COMIRNATY: 0.1%; placebo: 0.1%), rash (COMIRNATY: 0.3%; placebo: 0.1%) and urticaria (COMIRNATY: 0.3%; placebo: 0.3%).

Children 6 to 23 Months of Age – Primary Series (Three Doses)

Solicited Adverse Reactions

Table 24 and Table 25 present the frequency of solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in children 6 to 23 months of age who were monitored for reactogenicity with an electronic diary.

Table 24: Study 3 – Solicited Local Reactions Reported Within 7 Days After Each Dose – Children 6 to 23 Months of Age

Local Reaction	COMIRNATY† Dose 1 N[a]=1,425 to 1,439 %	Placebo Dose 1 N[a]=706 to 712 %	COMIRNATY† Dose 2 N[a]=1,314 to 1,323 %	Placebo Dose 2 N[a]=664 to 666 %	COMIRNATY† Dose 3 N[a]=455 to 459 %	Placebo Dose 3 N[a]= 222 %
Redness[b]						
Any (≥0.5 cm)	10.7	7.6	9.9	6.3	7.2	5.0
Severe	0	0	0	0	0.2	0
Swelling[b]						
Any (≥0.5 cm)	3.8	2.5	4.1	1.5	3.3	2.3
Severe	0	0	0	0	0	0
Tenderness at the injection site[c]						
Any	17.2	12.6	15.4	9.3	14.7	9.9
Severe	0.1	0	0.1	0	0	0

† COMIRNATY 3 mcg. (vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain [Original]).
a. – c. See footnote of Table 8.

Table 25: Study 3 – Solicited Systemic Reactions Reported Within 7 Days After Each Dose – Children 6 to 23 Months of Age

Systemic Reaction	COMIRNATY† Dose 1 N[a]=1,425 to 1,439 %	Placebo Dose 1 N[a]=706 to 712 %	COMIRNATY† Dose 2 N[a]=1,314 to 1,323 %	Placebo Dose 2 N[a]=664 to 666 %	COMIRNATY† Dose 3 N[a]=455 to 459 %	Placebo Dose 3 N[a]= 222 %
Fever						
≥38.0°C	7.2	7.4	7.6	6.5	6.1	5.9
>38.9°C to 40.0°C	1.6	1.4	2.0	1.2	1.5	0.9
Decreased appetite[b]						
Any	22.7	21.2	22.5	19.4	19.6	13.1
Severe	0.2	0.3	0.5	0.2	0.9	0
Drowsiness[c]						
Any	27.8	30.0	24.1	21.4	21.5	12.2
Severe	0.2	0.4	0.3	0.2	0.4	0.5
Irritability[d]						
Any	51.0	48.2	46.9	41.4	42.0	36.9
Severe	0.7	0.3	0.6	0.9	0.4	0
Use of antipyretic or pain medication[e]						
Any	23.1	20.9	20.9	18.6	18.3	17.1

† COMIRNATY 3 mcg (vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain [Original]).
a. – e. See footnote of Table 9.

Unsolicited Adverse Events

In participants 6 to 23 months of age (483 COMIRNATY; 237 placebo), 86.8% of participants had at least 1 month of follow-up after Dose 3.

Serious adverse events from Dose 1 through 1 month after Dose 3, with an overall median of 1.7 months follow-up after Dose 3, were reported by 1.7% of COMIRNATY recipients and by 2.4% of placebo recipients. No serious adverse events were reported that were considered related to vaccination.

Non-serious adverse events from Dose 1 through up to 1 month after Dose 3 were reported by 29.0 % of COMIRNATY recipients and by 26.3% of placebo recipients.

From Dose 1 through 1 month after Dose 3, lymphadenopathy was reported in 1 (0.1%) of COMIRNATY recipients vs. 0 (0%) of placebo recipients.

Other unsolicited AEs included febrile convulsion (COMIRNATY: 0.3%; placebo: 0%), irritability (COMIRNATY: 1.4%; placebo: 0.8%), somnolence (COMIRNATY: 0.3%; placebo: 0.1%), rash (COMIRNATY: 1.2%; placebo: 1.1%) and urticaria (COMIRNATY: 0.6%; placebo: 0.4%).

8.5 Post-Market Adverse Reactions

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

Cardiac disorders: myocarditis and/or pericarditis (see 7 WARNING AND PRECAUTIONS)

Immune system disorders: severe allergic reactions, including anaphylaxis

Musculoskeletal and connective tissue disorders: arthralgia, myalgia, pain in extremity (arm)

Nervous system disorders: Facial paralysis / Bell's Palsy, hypoesthesia, paresthesia, dizziness

Skin and subcutaneous tissue disorders and other hypersensitivity reactions: skin rash, pruritus, urticaria, angioedema, erythema multiforme

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to product exposure. They are included because: a) they represent reactions that are known to occur following immunizations generally; b) they are potentially serious; or c) on the basis of their frequency of reporting.

9 DRUG INTERACTIONS

Adults 18 to 64 Years of Age

COMIRNATY may be administered concomitantly with seasonal inactivated influenza vaccine. The effectiveness of the coadministration is inferred from a study which evaluated non-inferiority of immune response to coadministration of COMIRNATY (original) with an unadjuvanted seasonal inactivated influenza vaccine as compared with either vaccine alone. (see 14.2.3.3 Coadministration of COMIRNATY with Influenza Vaccine).

Different injectable vaccines should be given at different sites.

Do not mix COMIRNATY with other vaccines/products in the same syringe.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

The nucleoside-modified messenger RNA in COMIRNATY encodes for the viral spike (S) protein of SARS-CoV-2 Omicron variant lineage LP.8.1. The mRNA is formulated in lipid nanoparticles, which enable delivery of the RNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits both neutralizing antibody and cellular immune responses to the spike (S) antigen, which may contribute to protection against COVID-19 disease.

11 STORAGE, STABILITY AND DISPOSAL

Regardless of presentation, during storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Regardless of storage condition, the vaccine should not be used after the expiration date printed on the vials, prefilled syringes and cartons.

Do not refreeze thawed vials.

Storage Prior to Use

Confirm the storage conditions stated on the packaging of frozen storage and refrigerated only vials.

Refrigerated only vials have printed “EXP” at 2 to 8°C.

Frozen Single Dose or Multiple Dose Vials

Cartons of frozen COMIRNATY single dose or multiple dose vials may arrive frozen at ultra-cold conditions in thermal containers with dry ice.

Once received, frozen single dose or multiple dose vials may be immediately transferred to the refrigerator at 2°C to 8°C (35°F to 46°F), thawed and stored for a single period of up to 10 weeks within the shelf-life. The 10-week refrigerated expiry date should be recorded on the carton at the time of transfer. Thaw times for 10-vial packs are noted below:

Vial Cap and Vial Label Colour	Time That May Be Required for a 10-Vial Pack to Thaw (at 2°C to 8°C)
Dark Gray Dark Blue	6 hours
Light Gray Light Blue Yellow	2 hours

Alternatively, frozen single dose or multiple dose vials may be stored in an ultra-low temperature freezer at -90°C to -60°C (-130°F to -76°F). Do not store vials at -25°C to -15°C (-13°F to 5°F). Once vials are thawed they should not be refrozen.

Cartons of frozen COMIRNATY single dose or multiple dose vials may also arrive at 2°C to 8°C (35°F to 46°F). If received at 2°C to 8°C, they should be stored at 2°C to 8°C. Check that the carton has been updated to reflect the 10-week refrigerated expiry date.

Refrigerated Only Multiple Dose Vials

COMIRNATY refrigerated only multiple dose vials (available for the 30 mcg/0.3 mL strength only) should be received at 2°C to 8°C (35°F to 46°F) and stored at 2°C to 8°C (35°F to 46°F) until the expiration date printed on the carton and vial labels. DO NOT FREEZE.

Prefilled Syringes

COMIRNATY prefilled syringes may be stored at 2°C to 8°C (35°F to 46°F) until the expiration date printed on the carton and syringe labels. DO NOT FREEZE.

Storage During Use

Frozen Single Dose or Multiple Dose Vials

If not previously thawed at 2°C to 8°C (35°F to 46°F), allow single dose or multiple dose vials to thaw at room temperature [up to 25°C (77°F)] for 30 minutes.

Thawed single dose or multiple dose vials may be stored at room temperature up to 25°C (77°F) for a total of 12 hours prior to the first puncture.

DO NOT DILUTE PRIOR TO USE.

After first puncture, the single dose or multiple dose vial should be stored at 2°C to 25°C (35°F to 77°F). Vials should be discarded 12 hours after first puncture.

Thawed single dose or multiple dose vials can be handled in room light conditions.

Refrigerated Only Multiple Dose Vials

Vials may be stored at room temperature up to 25°C (77°F) for a total of 12 hours prior to the first puncture and can be handled in room light conditions.

DO NOT DILUTE PRIOR TO USE.

After first puncture, vials should be stored at 2°C to 25°C (35°F to 77°F). Vials should be discarded 12 hours after first puncture.

Prefilled Syringes

After removing the tip cap and attaching an appropriate needle, the prefilled syringes should be used immediately. If it cannot be used immediately, it must be used within 4 hours.

Transportation

Frozen Single Dose or Multiple Dose Vials

If local redistribution is needed, full cartons containing unpunctured single dose or multiple dose vials may be transported at -90°C to -60°C (-130°F to -76°F); full cartons or individual unpunctured single dose or multiple dose vials may also be transported at 2°C to 8°C (35°F to 46°F).

Refrigerated Only Multiple Dose Vials and Prefilled Syringes

Refrigerated only multiple dose vials and prefilled syringes may be transported at 2°C to 8°C (35°F to 46°F) and should never be frozen.

12 SPECIAL HANDLING INSTRUCTIONS

COMIRNATY should be prepared by a healthcare professional using aseptic technique to ensure the sterility of the prepared suspension. COMIRNATY single dose and multiple dose vials do not contain preservative.

Frozen COMIRNATY single dose and multiple dose vials contain a frozen suspension that must be thawed and may require dilution prior to administration.

Refrigerated only COMIRNATY multiple dose vials (available for the 30 mcg/0.3 mL strength only) should not be frozen.

Careful attention should be paid to the vial cap colour and label border and information on the label, and the appropriate corresponding instructions must be followed. For important information on handling and preparation for administration, please refer to 11 STORAGE, STABILITY AND DISPOSAL and 4 DOSAGE AND ADMINISTRATION.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance:

Proper name: COVID-19 mRNA Vaccine

Medicinal ingredient name:

mRNA encoding SARS-CoV-2 spike protein, 5' [$m_2^{7,3'\text{-O}}$Gppp($m_1^{2'\text{-O}}$)ApG] cap, 110-nucleotide 3' poly(A) tail with a 10-nucleotide linker sequence

Product Characteristics:

COMIRNATY (COVID-19 mRNA Vaccine) contains highly purified single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA template encoding the viral spike (S) protein of the SARS-CoV-2 Omicron variant LP.8.1.

This vaccine is a white to off-white suspension.

For 12 Years and Older: **DO NOT DILUTE** (Single Dose Vials with Light Gray Cap/Label Border)
One single dose vial contains 1 dose of 0.3 mL. One dose (0.3 mL) contains 30 micrograms of COVID-19 mRNA, embedded in lipid nanoparticles.

For 12 Years and Older: **DO NOT DILUTE** (Multiple Dose Vials with Dark Gray Cap/Label Border)
One multiple dose vial (2.25 mL) contains 6 doses of 0.3 mL. One dose (0.3 mL) contains 30 micrograms of COVID-19 mRNA, embedded in lipid nanoparticles.

For Age 5 Years to 11 Years: **DO NOT DILUTE** (Single Dose Vials with Light Blue Cap/Label Border)
One single dose vial contains 1 dose of 0.3 mL. One dose (0.3 mL) contains 10 micrograms of COVID-19 mRNA, embedded in lipid nanoparticles.

For Age 5 Years to 11 Years: **DO NOT DILUTE** (Multiple Dose Vials with Dark Blue Cap/Label Border)
One multiple dose vial (2.25 mL) contains 6 doses of 0.3 mL. One dose (0.3 mL) contains 10 micrograms of COVID-19 mRNA, embedded in lipid nanoparticles.

For Age 6 Months to 4 Years: **DILUTE PRIOR TO USE** (Multiple Dose Vials with Yellow Cap/Label Border)
One multiple dose vial (0.48 mL) contains 3 doses of 0.3 mL **after dilution**. One dose (0.3 mL) contains 3 micrograms of COVID-19 mRNA Vaccine, embedded in lipid nanoparticles.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

The safety and effectiveness of COMIRNATY for individuals 6 months of age and older are inferred from studies which evaluated the primary series and booster vaccination with COMIRNATY (Original) and supported by studies which evaluated a booster dose of COMIRNATY Original & Omicron BA.4/BA.5.

14.1.1 COMIRNATY Original & Omicron BA.4/BA.5 (15/15 mcg)

Relative vaccine immunogenicity in participants greater than 12 years of age – after second booster (fourth) dose

Study 5 (C4591044) was a Phase 2/3 study to evaluate the safety, tolerability, and immunogenicity of the bivalent vaccine COMIRNATY Original & Omicron BA.4/BA.5 (15/15 mcg). A subset of 107 participants 12 to 17 years of age, 313 participants 18 to 55 years of age and 306 participants 56 years of age and older previously vaccinated with a 2-dose primary series and 1 booster dose of COMIRNATY (original vaccine), received a second booster dose with COMIRNATY Original & Omicron BA.4/BA.5. Participants received a second booster dose 11.1 months (median time; range 5.4 to 16.9 months) after receiving the first booster dose and had a median follow up time of 1.5 months. The median age was 48.0 years, 42.7% were male, 57.3% were female, 80.6% were White, 11.4% were Hispanic/Latino, 5.9% were Asian, and 11.4% were Black or African American.

14.1.2 COMIRNATY Original & Omicron BA.4/BA.5 (1.5/1.5 mcg)

Relative vaccine Immunogenicity in children 6 months to 4 years of age – after second booster (fourth) dose

Study 6 (C4591048) is a Phase 1/2/3 master study investigating the safety, tolerability, and immunogenicity of COMIRNATY Original & Omicron BA.4/BA.5 (1.5/1.5 mcg) bivalent vaccine. In Study 6, a subset of 60 participants 6 months to 4 years of age received a booster dose (fourth dose) of COMIRNATY Original & Omicron BA.4/BA.5 after receiving 3 prior doses of COMIRNATY (3 mcg), with their last dose 60 to 240 days prior to enrollment. The evaluable immunogenicity population (with or without evidence of infection up to 1month post-Dose 4) included 58 participants 6 months to 4 years of age (23 were 6 to 23 months of age and 35 were 2 to 4 years of age). A total of 50.0% of participants were male. Most participants were White (58.6%), with 5.2% Black or African American participants, 15.5% Asian participants, and 20.7% multiracial participants. There were 25.9% Hispanic/Latino participants. Median age at the fourth dose was 19.0 months for the 6 to 23 months of age group and 2.0 years for the 2 to 4 years of age group. Overall, 8.6% of participants reported comorbidities. A total of 27.6% of participants had evidence of prior SARS-CoV-2 infection at the time of Dose 4 ("baseline positive").

14.1.3 COMIRNATY (Original: 30 mcg)

The safety and efficacy of COMIRNATY were evaluated in Study 2 (C4591001), a multicenter, multinational, Phase 1/2/3, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 to 15 years of age, 16 to 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56 year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with pre-existing stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV).

In the Phase 2/3 portion of Study 2, 44,000 participants 12 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. The efficacy analyses included participants that received their second vaccination within 19 to 42 days after their first vaccination. The majority

(93.1%) of vaccine recipients received the second dose 19 days to 23 days after Dose 1. Participants were followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

The population for the analysis of the primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 COMIRNATY; 18,379 placebo) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. Table 26 presents the specific demographic characteristics in the studied population.

Table 26: Demographics (Population for the Primary Efficacy Endpoint)[a]

	COMIRNATY[‡] N=18,242 %	**Placebo N=18,379 %**
Sex		
Male	51.1	50.2
Female	48.9	49.8
Age (years)		
Mean (SD)	50.6 (15.70)	50.4 (15.81)
Median	52.0	52.0
Min, max	(12, 89)	(12, 91)
Age group		
12 to 15 years	0.3	0.2
16 to 64 years	77.9	77.8
65 to 74 years	17.4	17.6
≥75 years	4.4	4.4
Race		
White	82.8	83.3
Black or African American	8.9	8.8
American Indian or Alaska Native	0.6	0.6
Asian	4.5	4.4
Native Hawaiian or other Pacific Islander	0.3	0.2
Other[b]	2.9	2.8
Ethnicity		
Hispanic or Latino	26.8	26.4
Not Hispanic or Latino	72.7	73.0
Not reported	0.6	0.6
Comorbidities[c]		
Yes	46.2	46.0
No	53.8	54.0

[‡] Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).

a. All eligible randomized participants who receive all vaccination(s) and had no evidence of SARS-CoV-2 infection prior to 7 days after Dose 2.

b. Includes multiracial and not reported.

c. Number of participants who had 1 or more comorbidities that increase the risk of severe COVID-19 disease: Chronic lung disease (e.g., emphysema and chronic bronchitis, idiopathic pulmonary fibrosis, and cystic fibrosis) or moderate to severe asthma; Significant cardiac disease (e.g., heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and pulmonary hypertension); Obesity (body mass index ≥30 kg/m^2); Diabetes (Type 1, Type 2, or gestational); Liver disease; Human Immunodeficiency Virus (HIV) infection (not included in the efficacy evaluation)

To assess boostability, a subset of Study 2 participants were enrolled in selected sites, and 306 participants aged 18 to 55 years were re-randomized to receive a booster dose approximately 6 months after completion of the two-dose regimen (median interval between dose 2 and booster dose –

6.8 months; range 4.8 to 8.0 months). The median age was 42 years (range 19 to 55 years of age), 45.8% were male and 54.2% were female, 81.4% were White, 27.8% were Hispanic/Latino, 9.2% were Black or African American, 5.2% were Asian, and 0.7% were American Indian/Alaska Native.

In Study 4 (C4591031), a placebo-controlled booster study, 5,081 participants 16 years of age and older were recruited from Study 2 to receive a booster dose of COMIRNATY at least 6 months after the second dose. Among the participants, the median age was 53.0 years (range 16 to 87 years of age), including 1,175 booster dose recipients (23.1%) who were ≥65 years of age, 49.1% were male and 50.9% were female, 79.0% were White, 14.9% were Hispanic/Latino, 9.2% were Black or African American, 5.5% were Asian, and 1.7% were American Indian/Alaska Native.

14.1.4 COMIRNATY (Original: 10 mcg)

Participants 5 to 11 Years of Age

Study 3 (C4591007) was a Phase 1/2/3 study comprised of an open-label vaccine dose finding portion (Phase 1) and a multicentre, multinational, randomized, saline placebo-controlled, observer-blind immunogenicity and efficacy portion (Phase 2/3) that has enrolled participants 6 months to 11 years of age.

Demographic characteristics in Study 3 were generally similar with regard to age, gender, race, and ethnicity among participants 5 to 11 years of age who received COMIRNATY 10 mcg and those who received placebo. Among the 1,518 participants (initial enrolment group) 5 to 11 years of age who received at least 1 dose of COMIRNATY (10 mcg), 52.6% were male and 47.4% were female, 79.3% were White, 5.9% were Black or African American, 21.0% were Hispanic/Latino, 5.9% were Asian, and 0.8% were American Indian/Alaska Native.

A descriptive efficacy analysis of Study 3 has been performed in 1,968 children 5 to 11 years of age without evidence of infection prior to 7 days after Dose 2.

Table 27 presents the specific demographic characteristics in participants who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose.

Table 27: Demographics Characteristics – Participants Without Evidence of Infection Prior to 7 Days After Dose 2 – Phase 2/3 – 5 to 11 Years of Age

	COMIRNATY‡ 10 mcg N[a]=1,305 %	**Placebo N[a]=663 %**
Sex		
Male	52.0	51.7
Female	48.0	48.3
Age at Vaccination (years)		
Mean (SD)	8.2 (1.93)	8.1 (1.98)
Median	8.0	8.0
Min, max	(5, 11)	(5, 11)
Race		
White	78.0	77.5
Black or African American	5.8	7.2
American Indian or Alaska Native	<1.0	<1.0
Asian	6.6	6.9
Native Hawaiian or other Pacific Islander	<1.0	<1.0
Other[b]	8.4	7.8
Ethnicity		

Table 27: Demographics Characteristics – Participants Without Evidence of Infection Prior to 7 Days After Dose 2 – Phase 2/3 – 5 to 11 Years of Age

	COMIRNATY‡ 10 mcg N[a]=1,305 %	Placebo N[a]=663 %
Hispanic or Latino	18.6	19.6
Not Hispanic or Latino	81.1	80.4
Not reported	<1.0	<1.0
Comorbidities[c]		
Yes	20.1	20.1
No	79.9	79.9

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).

a. N = number of participants in the specified group from the evaluable efficacy population with no evidence of SARS CoV-2 infection prior to 7 days after Dose 2. This value is the denominator for the percentage calculations. Evaluable efficacy population included all eligible randomized participants who received all vaccination(s) as randomized within the predefined window, had no other important protocol deviations as determined by the clinician.

b. Includes multiracial and not reported.

c. Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as participants who had at least 1 of the prespecified comorbidities based on MMWR 69(32);1081-1088 and/or obesity (BMI ≥95th percentile).

In Study 3 (Phase 2/3), the 2,408 participants in the 5 to 11 years booster dose subset had a median age of 8.0 years (range 5 to 11 years), 50.5% were male and 49.5% were female, 76.3% were White, 5.9% were Black or African American, 16.9% were Hispanic/Latino, 8.2% were Asian, and 0.5% were American Indian/Alaska Native.

14.1.5 COMIRNATY (Original: 3 mcg)

Participants 2 to 4 Years of Age: The evaluable immunogenicity population without prior evidence of SARS-CoV-2 infection up to 1 month after Dose 3 of COMIRNATY was comprised of 143 participants 2 to 4 years of age. Most participants in this analysis population were White (69.2%), with 5.6% Black or African American participants, 11.2% Asian participants, and 11.9% multiracial participants. There were 11.2% Hispanic/Latino participants. The median age was 3.0 years and 44.1% of participants were male. There were 6.3% of participants reported as obese. In the evaluable immunogenicity population (regardless of evidence of prior infection), 11 of 204 participants (5.4%) were baseline positive for prior SARS-CoV-2 infection.

Participants 6 to 23 Months of Age: The evaluable immunogenicity population without prior evidence of SARS-CoV-2 infection up to 1 month after Dose 3 of COMIRNATY was comprised of 82 participants 6 to 23 months of age. Most participants in this analysis population were White (72.0%), with 1.2% Black or African American participants, 13.4% Asian participants, and 12.2% multiracial participants. There were 15.9% Hispanic/Latino participants. The median age was 16.0 months and 62.2% of participants were male. In the evaluable immunogenicity population (regardless of evidence of prior infection), 6 of 132 participants (4.5%) were baseline positive for prior SARS-CoV-2 infection.

14.2 Study Results

14.2.1 COMIRNATY Original & Omicron BA.4/BA.5 (15/15mcg)

14.2.1.1 Immunogenicity in Participants 12 Years of Age and Older – Second Booster (Fourth) Dose

In Study 5, 105 participants 12 to 17 years of age, 297 participants 18 to 55 years of age, and 286 participants 56 years of age and older who had previously received a 2-dose primary series and 1 booster dose with COMIRNATY (original vaccine) received a second booster (fourth) dose of COMIRNATY Original & Omicron BA.4/BA.5 (15/15 mcg) bivalent vaccine. In participants 12 to 17 years of age, 18 to 55 years of age, and 56 years of age and older, 75.2%, 71.7% and 61.5% were positive for SARS-CoV-2 at baseline, respectively.

Analyses of 50% neutralizing antibody titers (NT50) against Omicron BA.4/BA.5 and against reference strain among participants 56 years of age and older who received a second booster dose of COMIRNATY Original & Omicron BA.4/5 in Study 5 were compared with a subset of participants from Study 4 (C4591031) who received a second booster dose of COMIRNATY. Superiority of COMIRNATY Original & Omicron BA.4/BA.5 to COMIRNATY was demonstrated based on geometric mean ratio (GMR), noninferiority based on difference in seroresponse rates with respect to anti-Omicron BA.4/BA.5 response, and noninferiority of anti-reference strain immune response based on GMR (Table 28 and Table 29).

In Study 5, analyses of NT50 against Omicron BA.4/BA.5 among participants 18 to 55 years of age were compared with participants 56 years of age and older who received a second booster dose of COMIRNATY Original & Omicron BA.4/BA.5. Noninferiority of anti-Omicron BA.4/BA.5 response among participants 18 to 55 years of age compared with participants 56 years of age and older for both GMR and difference in seroresponse rates (Table 28 and Table 29).

The study also assessed the level of NT50 of the anti-Omicron BA.4/BA.5 SARS-COV-2 strains pre-vaccination and 1 month after vaccination in participants who received a second booster dose (Table 30).

Table 28: Geometric Mean Ratios – COMIRNATY Original & Omicron BA.4/BA.5 (Study 5) and COMIRNATY (Study 4) – Participants With or Without Evidence of Infection – 18 Years of Age and Older

SARS-CoV-2 Neutralization Assay	COMIRNATY Original & Omicron BA.4/BA.5 Study 5				COMIRNATY‡ Subset of Study 4		Age Group Comparison	Vaccine Group Comparison
	18 to 55 Years of Age		≥ 56 Years of Age		≥ 56 Years of Age		18 to 55 Years vs. ≥ 56 Years	COMIRNATY Original & Omicron BA.4/BA.5 vs. COMIRNATY (≥ 56 Years)
	n[a]	GMT[b] (95% CI[b])	n[a]	GMT[b] (95% CI[b])	n[a]	GMT[b] (95% CI[b])	GMR[b] (95% CI[b])	GMR[b] (95% CI[b])
Omicron BA.4/BA.5 – NT50 (titer)[c]	297	4455.9 (3851.7, 5154.8)	284	4158.1 (3554.8, 4863.8)	282	938.9 (802.3, 1098.8)	0.98 (0.83, 1.16)[d]	2.91 (2.45, 3.44)[e]
Reference Strain – NT50 (titer)[c]	-	-	286	16250.1 (14499.2, 18212.4)	289	10415.5 (9366.7, 11581.8)	-	1.38 (1.22, 1.56)[f]

Abbreviations: CI = confidence interval; GMR = geometric mean ratio; GMT = geometric mean titer; LLOQ = lower limit of quantitation; NAAT = nucleic acid amplification test; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).

a. n = Number of participants with valid assay results for the specified assay, 1 month after vaccination.
b. GMTs, GMRs and 2-sided 95% CIs were calculated using logarithm transformed titers and the corresponding CIs (based on the Student t distribution).
c. Reference (original) USA-WA1/2020 strain and Omicron B.1.1.529 subvariant BA.4/BA.5.
d. Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67.
e. Superiority is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 1.
f. Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67 and the point estimate of the GMR is ≥ 0.8.

Table 29: Percentage Difference in Seroresponse Rates – COMIRNATY Original & Omicron BA.4/BA.5 (Study 5) and COMIRNATY (Study 4) – Participants With or Without Evidence of Infection – 18 Years of Age and Older

SARS-CoV-2 Neutralization Assay	COMIRNATY Original & Omicron BA.4/BA.5 Study 5				COMIRNATY‡ Subset of Study 4		Age Group Comparison	Vaccine Group Comparison
	18 to 55 Years of Age		≥ 56 Years of Age		≥ 56 Years of Age		18 to 55 Years vs. ≥ 56 Years (Study 5)	COMIRNATY Original & Omicron BA.4/BA.5 vs.COMIRNATY (≥ 56 Years)
	n[a]	% (95% CI[b])	n[a]	% (95% CI[b])	n[a]	% (95% CI[b])	% Difference (95% CI[c])	% Difference (95% CI[c])
Omicron BA.4/BA.5 – NT50 (titer)	294	61.2 (55.4, 66.8)	282	66.7 (60.8, 72.1)	273	46.5 (40.5, 52.6)	-3.03 (-9.68, 3.63)[d]	26.77 (19.59, 33.95)[e]

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).

a. and abbreviations: See footnote of Table 28. Note: Seroresponse is defined as achieving a ≥ 4-fold rise from baseline.
b. Exact 2-sided CI, based on the Clopper and Pearson method.
c. 2-sided CI based on the Miettinen and Nurminen method stratified by baseline neutralizing titer category (< median, ≥ median) for the difference in proportions.
d. Noninferiority is declared if the lower bound of the 2-sided 95% CI for the difference in percentages of participants with seroresponse is > -10%.
e. Noninferiority is declared if the lower bound of the 2-sided 95% CI for the difference in percentages of participants with seroresponse is > -5%.

Table 30: Geometric Mean Titers by Baseline SARS-CoV-2 Status – COMIRNATY Original & Omicron BA.4/BA.5 (Study 5) – Prior to and 1 Month After Second Booster – Participants 12 Years of Age and Older

SARS-CoV-2 Neutralization Assay	Baseline SARS-CoV-2 Status	Sampling Time Point	COMIRNATY Original & Omicron BA.4/BA.5					
			12 to 17 Years of Age		18 to 55 Years of Age		≥ 56 Years of Age	
			n[a]	GMT[b] (95% CI[b])	n[a]	GMT[b] (95% CI[b])	n[a]	GMT[b] (95% CI[b])
Omicron BA.4/BA.5 – NT50 (titer)[c]	All	Pre-vaccination	104	1105.8 (835.1, 1464.3)	294	569.6 (471.4, 688.2)	284	458.2 (365.2, 574.8)
		1 Month	105	8212.8 (6807.3, 9908.7)	297	4455.9 (3851.7, 5154.8)	284	4158.1 (3554.8, 4863.8)
	Positive[d]	Pre-vaccination	78	1791.1 (1379.6, 2325.3)	210	1181.4 (1005.3, 1388.3)	174	1291.7 (1027.5, 1623.8)
		1 Month	79	9892.5 (8114.6, 12059.8)	213	6031.6 (5203.9, 6991.0)	176	6688.9 (5664.4, 7898.8)
	Negative[e]	Pre-vaccination	26	260.2 (157.1, 430.9)	84	91.9 (71.5, 118.1)	110	88.9 (69.8, 113.4)
		1 Month	26	4666.1 (3096.1, 7032.2)	84	2067.7 (1530.2, 2793.9)	108	1916.2 (1489.5, 2465.1)
Reference Strain – NT50 (titer)[c]	All	Pre-vaccination	105	6863.3 (5587.8, 8430.1)	296	4017.3 (3430.7, 4704.1)	284	3690.6 (3082.2, 4419.0)
		1 Month	105	23641.3 (20473.1, 27299.8)	296	16323.3 (14686.5, 18142.6)	286	16250.1 (14499.2, 18212.4)
	Positive[d]	Pre-vaccination	79	8685.4 (7062.7, 10680.9)	213	7068.6 (6251.9, 7992.0)	174	8082.1 (6843.6, 9544.8)
		1 Month	79	25991.8 (22377.5, 30189.8)	212	19076.6 (17056.5, 21336.0)	176	21273.3 (18604.2, 24325.3)
	Negative[e]	Pre-vaccination	26	3356.2 (2106.9, 5346.2)	83	942.3 (705.6, 1258.3)	110	1068.0 (835.9, 1364.6)
		1 Month	26	17725.2 (12376.4, 25385.7)	84	11014.6 (8793.9, 13796.0)	110	10560.6 (8827.1, 12634.5)

a. – c. and abbreviations: See footnote of Table 28.

d. Positive N-binding antibody result at baseline, positive NAAT result at baseline, or medical history of COVID-19.

e. Negative N-binding antibody result at baseline, negative NAAT result at baseline, and no medical history of COVID-19.

14.2.2 COMIRNATY Original & Omicron BA.4/BA.5 (1.5/1.5 mcg)

14.2.2.1 Immunogenicity in Participants 6 Months to 4 Years of Age – Second Booster (Fourth Dose)

In Study 6, a subset of 310 participants 6 months to 4 years of age (Group 2) received a booster (fourth dose) of COMIRNATY Original & Omicron BA.4/BA.5 (1.5/1.5 mcg) after receiving three doses of COMIRNATY 3 mcg. Data from a subset of participants 6 months to 4 years of age in Study 3 who received three doses of COMIRNATY 3 mcg are included as a reference.

Analyses of NT50 against Omicron BA.4/BA.5 and against reference strain among participants 6 months to 4 years of age who received COMIRNATY Original & Omicron BA.4/BA.5 as a booster dose in Study 6 compared to a subset of participants from Study 3 who received 3 doses of COMIRNATY demonstrated superiority of anti-Omicron BA.4/BA.5 response based on GMR and noninferiority based on difference

in seroresponse rates, and noninferiority of anti-reference strain immune response based on GMR and difference in seroresponse rates (Table 31 and Table 32).

Table 31: Substudy B Group 2 – Geometric Mean Ratios (1 Month After Dose 4 Study 6/ 1 Month After Dose 3 Study 3) - Participants With or Without Evidence of Infection - 6 Months to 4 Years of Age - Evaluable Immunogenicity Population

SARS-CoV-2 Neutralization Assay[f]	COMIRNATY Original & Omicron BA.4/BA.5 (3 mcg) Study 6		COMIRNATY[‡] (3 mcg) Subset of Study 3		COMIRNATY Original & Omicron BA.4/BA.5 (3 mcg) vs. COMIRNATY (3 mcg)
	n[a]	GMT[b] (95% CI[b])	n[a]	GMT[b] (95% CI[b])	GMR[c] (95% CI[c])
Omicron BA.4/BA.5 – NT50 (titer)	224	2228.4 (1841.8, 2696.2)	239	791.0 (680.9, 919.0)	1.95 (1.65, 2.31)[d]
Reference strain – NT50 (titer)	224	7489.6 (6631.7, 8458.5)	238	6529.9 (5864.5, 7270.8)	0.91 (0.79, 1.04)[e]

[‡] Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).

a. and abbreviations: See footnote of Table 28.

b. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

c. GMRs and 2-sided CIs were calculated by exponentiating the mean difference of the logarithms of the titers (COMIRNATY Original & Omicron BA.4/BA.5 [3 mcg] – COMIRNATY [3 mcg]) and the corresponding CI using a linear regression model with baseline log-transformed neutralizing titers, postbaseline infection status, age group and vaccine group as covariates).

d. Superiority is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 1.

e. Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67 and the point estimate of the GMR is ≥0.8.

f. Reference (original) USA-WA1/2020 strain and Omicron B.1.1.529 subvariant BA.4/BA.5.

Table 32: Substudy B Group 2 – Percentage Difference in Seroresponse Rates (1 Month After Dose 4 Study 6/1 Month After Dose 3 Study 3) - Participants With or Without Evidence of Infection - 6 Months to 4 Years of Age - Evaluable Immunogenicity Population

	COMIRNATY Original & Omicron BA.4/BA.5 (3 mcg) Study 6		COMIRNATY‡ (3 mcg) Subset of Study 3		Difference
SARS-CoV-2 Neutralization Assay[g]	N[a]	% (95% CI[b])	N[a]	% (95% CI[b])	%[c] (95% CI[d])
Omicron BA.4/BA.5 – NT50 (titer)	223	66.8 (60.2, 73.0)	238	50.4 (43.9, 56.9)	19.99 (11.61, 28.36)[e]
Reference strain – NT50 (titer)	223	49.3 (42.6, 56.1)	238	59.2 (52.7, 65.5)	-0.15 (-7.79, 7.48)[f]

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).

a. and abbreviations: See footnote of Table 28.

b. Exact 2-sided CI based on the Clopper and Pearson method.

c. Adjusted difference in proportions, based on the Miettinen and Nurminen method stratified by baseline neutralizing titer category (<median, ≥median), expressed as a percentage COMIRNATY Original & Omicron BA.4/BA.5 [3 mcg] – COMIRNATY [3 mcg]. The median of baseline neutralizing titers was calculated based on the pooled data in 2 comparator groups.

d. 2-sided CI based on the Miettinen and Nurminen method for the difference in proportions stratified by baseline neutralizing titer category (<median, ≥median), expressed as a percentage.

e. Noninferiority is declared if the lower bound of the 2-sided 95% CI for the difference in percentages of participants with seroresponse is >-5%.

f. Noninferiority is declared if the lower bound of the 2-sided 95% CI for the difference in percentages of participants with seroresponse is >-10%.

g. Reference (original) USA-WA1/2020 strain and Omicron B.1.1.529 subvariant BA.4/BA.5.

14.2.3 COMIRNATY (Original: 30 mcg)

14.2.3.1 Efficacy and Immunogenicity in Participants 16 Years of Age and Older

14.2.3.1.1 Efficacy in Participants 16 Years of Age and Older – Primary Series (Two Doses)

Primary Vaccine Efficacy Analysis

At the time of the primary efficacy analysis, participants had been followed for symptomatic COVID19 for at least 2,214 person-years in the COMIRNATY group and at least 2,222 person-years in the placebo group.

There were no meaningful clinical differences in overall vaccine efficacy in participants who were at risk of severe COVID-19 including those with 1 or more comorbidities that increase the risk of severe COVID-19 [e.g., asthma, body mass index (BMI) ≥30 kg/m^2, chronic pulmonary disease, diabetes mellitus, hypertension]. The primary endpoint was defined as any symptomatic COVID-19 case confirmed by Reverse Transcription-Polymerase Chain Reaction (RT-PCR). The population for the analysis of the primary efficacy endpoint included participants who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose (first primary efficacy endpoint), as well as participants with and without evidence of prior infections with SARS-CoV-2 through 7 days after the second dose (second primary efficacy endpoint). The pre-specified success criterion for vaccine efficacy was met. The vaccine efficacy information is presented in Table 33.

Table 33: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Participants Without and/or With Evidence of Infection Prior to 7 Days After Dose 2 (Study 2) – By Age Subgroups

Participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY‡** N[a]=18,198 Cases[b] (Surveillance Time)[c]	**Placebo** N[a]=18,325 Cases[b] (Surveillance Time)[c]	**Vaccine Efficacy %** (95% CI)
All participants[d]	8 (2.2)	162 (2.2)	95.0 (90.3, 97.6)[e]
16 to 64 years	7 (1.7)	143 (1.7)	95.1 (89.6, 98.1)[f]
65 years and older	1 (0.5)	19 (0.5)	94.7 (66.7, 99.9)[f]
Participants with or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY‡** N[a]=19,965 Cases[b] (Surveillance Time)[c]	**Placebo** N[a]=20,172 Cases[b] (Surveillance Time)[c]	**Vaccine Efficacy %** **(95% CI)**
All participants[d]	9 (2.3)	169 (2.3)	94.6 (89.9, 97.3)[e]
16 to 64 years	8 (1.8)	150 (1.8)	94.6 (89.1, 97.7)[f]
65 years and older	1 (0.5)	19 (0.5)	94.7 (66.8, 99.9)[f]

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).

* Participants had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and NAAT [nasal swab] negative at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2.

Abbreviations: See footnote of Table 28.

a. N = number of participants in the specified group.

b. Number of confirmed cases with at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

c. Total surveillance time in 1000 person-years is from 7 days after Dose 2 to the end of the surveillance period.

d. No confirmed cases were identified in adolescents 12 to 15 years of age.

e. Confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

f. Two-sided confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Six Months Follow-up of Vaccine Efficacy

Efficacy analyses in Study 2 were performed with additional confirmed COVID-19 cases accrued during the blinded placebo-controlled 6 months of follow-up after Dose 2. There were 77 confirmed COVID-19 cases identified in the COMIRNATY and 850 in the placebo groups, respectively. In this analysis, compared with placebo, the vaccine efficacy of COMIRNATY in participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2 was 91.3% (95% CI: 89.0% to 93.2%). In participants 65 years of age and older without evidence of prior infection vaccine efficacy was 94.5% (95% CI: 88.3% to 97.8%). The vaccine efficacy of COMIRNATY in participants with or without evidence of prior infection was 91.1% (95% CI: 88.8% to 93.0%) with 81 COVID-19 cases in the COMIRNATY group compared with 873 cases in the placebo group.

Vaccine Efficacy Against Severe COVID-19

Secondary efficacy analyses in Study 2 supported benefit of COMIRNATY in preventing severe COVID-19. During the blinded placebo-controlled 6 months follow-up after Dose 2, the vaccine efficacy against severe COVID 19 in participants with or without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2 was 95.3% (95% CI: 70.9%, 99.9%) with 1 and 21 cases in the vaccine and placebo groups, respectively. The COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the COMIRNATY and placebo groups.

14.2.3.1.2 Efficacy and Immunogenicity in Participants 16 Years of Age and Older – First Booster Dose (Third Dose)

Immunogenicity in Participants 18 to 55 Years of Age – After Booster Dose

Noninferiority of immune responses 1 month after a COMIRNATY booster dose compared with 1 month after completion of the primary 2-dose series was assessed, in a subset of participants in Study 2, by evaluating NT50 against the reference strain. Immunogenicity was evaluated in subjects who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after the booster vaccination. The analysis demonstrated noninferior immune responses 1 month after a booster dose compared with 1 month after Dose 2 in individuals 18 to 55 years of age (Table 34).

Table 34: Geometric Mean Titers and Seroresponse Rates - Comparison of Booster Dose With Primary Series (Study 2) – Participants Without Evidence of Infection up to 1 Month After Booster Dose* – Participants 18 to 55 Years of Age

Assay	n[a]	COMIRNATY[‡] Sampling Time Point		Booster dose vs. Primary series (97.5% CI)	Met noninferiority objective
		1 month after booster dose (95% CI)	1 month after Dose 2 (95% CI)		
Geometric mean 50% neutralizing titer[b]	210	2,476.4[b] (2,210.1, 2774.9)	753.7[b] (658.2, 863.1)	3.29[b] (2.76, 3.91)	Yes[d]
Seroresponse rate (%) for 50% neutralizing titer[c]	198	99.5% (97.2%, 100.0%)	98.0% (94.4%, 99.4%)	1.5%[e] (-0.7%, 3.7%[f])	Yes[g]

[‡] Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).

* Participants had no evidence (up to 1 month after receipt of a booster dose of COMIRNATY) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative and NAAT [nasal swab] negative) and had a negative NAAT (nasal swab) at any unscheduled visit up to 1 month after the booster dose.

a. - b. and abbreviations: See footnote of Table 28.

c. Number of participants with seroresponse defined as achieving a ≥4-fold rise from baseline (before Dose 1). Exact 2-sided CI are based on the Clopper and Pearson method.

d. Noninferiority is declared if the lower bound of the 2-sided 97.5% CI for the GMR is >0.67 and the point estimate of the GMR is ≥0.80.

e. Difference in proportions, expressed as a percentage (1 month after booster dose – 1 month after Dose 2).

f. Adjusted Wald 2-sided CI for the difference in proportions, expressed as a percentage.

g. Noninferiority is declared if the lower bound of the 2-sided 97.5% CI for the percentage difference is >-10%.

Relative Vaccine Efficacy in Participants 16 Years of Age and Older – After Booster Dose

An interim efficacy analysis of Study 4, a placebo-controlled booster study was performed in approximately 10,000 participants 16 years of age and older who were recruited from Study 2 and evaluated confirmed COVID-19 cases accrued from at least 7 days after booster vaccination up to a data cut-off date of 5 October 2021, which represents a median of 2.5 months post-booster follow-up. Vaccine efficacy of the COMIRNATY booster dose after the primary series relative to the placebo booster group who only received the primary series dose was assessed. The relative vaccine efficacy information for participants 16 years of age and older is presented in Table 35.

Table 35: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Booster Dose – Participants Without and/or With Evidence of Infection Prior to 7 Days After Booster Dose (Study 4) – 16 Years of Age and Older

Participants without evidence of prior SARS-CoV-2 infection*			
	COMIRNATY‡ N[a]=4,695 Cases[b] (Surveillance Time)[c]	**Placebo** N[a]=4,671 Cases[b] (Surveillance Time)[c]	**Vaccine Efficacy[d]** **%** (95% CI[e])
First COVID-19 occurrence from 7 days after booster	6 (0.8)	123 (0.8)	95.3 (89.5, 98.3)
Participants with or without evidence of prior SARS-CoV-2 infection			
	COMIRNATY‡ N[a]=4,993 Cases[b] (Surveillance Time)[c]	**Placebo** N[a]=4,952 Cases (n1[b]) (Surveillance Time)[c]	**Vaccine Efficacy[d]** **%** (95% CI[e])
First COVID-19 occurrence from 7 days after booster	7 (0.8)	124 (0.8)	94.6 (88.5, 97.9)

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).

* Participants had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and NAAT [nasal swab] negative at Visit 1), and had negative NAAT (nasal swab) at any unscheduled visit, prior to 7 days after booster dose.

a.- c. and abbreviations: See footnote of Table 33.

d. Relative vaccine efficacy of the COMIRNATY booster group relative to the placebo group (non-booster).

e. Two-sided confidence interval (CI) for relative vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

14.2.3.2 Efficacy and Immunogenicity in Adolescents 12 to 15 Years of Age

14.2.3.2.1 Efficacy and Immunogenicity in Adolescents 12 to 15 Years of Age – Primary Series (Two Doses)

Efficacy

The vaccine efficacy in participants 12 to 15 years of age was evaluated on a subgroup analysis of Study 2 during the blinded placebo-controlled follow-up period of 6 months (Table 36).

Table 36: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Participants Without and/or With Evidence of Infection Prior to 7 Days After Dose 2 (Study 2) – Adolescents 12 to 15 Years of Age

Adolescents 12 to 15 years of age without evidence of prior SARS-CoV-2 infection*			
	COMIRNATY‡ N[a]=1,005 Cases[b] (Surveillance Time)[c]	**Placebo** N[a]=978 Cases[b] (Surveillance Time)[c]	**Vaccine Efficacy %** **(95% CI[d])**
Adolescents 12 to 15 Years of Age	0 0.154 (1,001)	16 0.147 (972)	100.0 (75.3, 100.0)
Adolescents 12 to 15 years of age with or without* evidence of prior SARS-CoV-2 infection			
	COMIRNATY‡ N[a]=1,119 Cases[b] (Surveillance Time)[c]	**Placebo** N[a]=1,110 Cases[b] (Surveillance Time)[c]	**Vaccine Efficacy %** **(95% CI[d])**
Adolescents 12 to 15 Years of Age	0 0.170 (1,109)	18 0.163 (1094)	100.0 (78.1, 100.0)

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).

* Participants had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and NAAT [nasal swab] negative at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2.

a.- c. and abbreviations: See footnote of Table 33.

d. Confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

Efficacy analysis of Study 2 was performed in 2,260 adolescents 12 to 15 years of age evaluating confirmed COVID-19 cases up to 6 months of follow-up after Dose 2.

COVID-19 cases, reported from at least 7 days after Dose 2 through a median of 4.4 (range 0-10.8) months of follow-up, were 0 in the COMIRNATY and 28 in the placebo groups. In this analysis, compared with placebo, the estimated VE against confirmed COVID-19 was 100% (95% CI: 86.8%, 100%) for individuals without evidence of prior SARS-CoV-2 infection before and during vaccination regimen. The estimated VE against confirmed COVID-19 was 100% (95% CI: 87.5%, 100%) for those with or without evidence of prior SARS-CoV-2 infection before and during vaccination regimen, with 0 COVID-19 cases in the COMIRNATY group compared with 30 cases in the placebo group.

Among participants without and with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen, VE against COVID-19 occurring at least 7 days after Dose 2 was evaluated for demographic and risk subgroups, and the estimated VE was 100.0% for all subgroups.

Immunogenicity – After Two Doses

In Study 2, an analysis of SARS-CoV-2 50% neutralizing titers (NT50), 1 month after Dose 2 in a randomly selected subset of participants without evidence of past SARS-CoV-2 infection, demonstrated non-inferior immune responses (within 1.5-fold) comparing adolescents 12 to 15 years of age with participants 16 to 25 years of age (Table 37).

Table 37: Geometric Mean Ratio – Comparison of Adolescents 12 to 15 Years of Age With Participants 16 to 25 Years of Age (Study 2) – Participants Without Evidence of Infection up to 1 Month After Dose 2

		COMIRNATY‡		12 to 15 Years vs. 16 to 25 Years	
		12 to 15 Years n[a]=190	16 to 25 Years n[a]=170		
SARS-CoV-2 Neutralization Assay	**Sampling Time Point**	**GMT[b]** (95% CI[b])	**GMT[b]** (95% CI[b])	**GMR[b]** (95% C[b])	**Met Noninferiority Objective[c]**
NT50 (titer)	1 month after Dose 2	1,239.5 (1,095.5, 1,402.5)	705.1 (621.4, 800.2)	1.76 (1.47, 2.10)	Yes

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).

Note: Participants had no evidence (up to 1 month after receipt of the last dose) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and NAAT [nasal swab] negative at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit up to 1 month after Dose 2.

a. – b. and abbreviations: See footnote of Table 28.

c. Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67.

14.2.3.3 Coadministration of COMIRNATY with Influenza Vaccine

In Study 8 (C4591030), a Phase 3, multicenter, randomized, observer-blind study, 1,134 participants 18 to 64 years of age who had received 3 doses of COMIRNATY at least 3 months prior were randomized in a 1:1 ratio to receive either COMIRNATY coadministered with a standard dose unadjuvanted seasonal inactivated influenza vaccine (SIIV), quadrivalent followed 1 month later by placebo (Group 1, n=568) or SIIV quadrivalent with placebo followed 1 month later with COMIRNATY (Group 2, n=566).

Following administration of COMIRNATY concomitantly with SIIV, the criteria for non-inferiority of the immune responses were met as lower limits of 2-sided 95% confidence interval on the group geometric mean titer ratios were above the predefined noninferiority criterion of 0.67 for both full-length S-binding immunoglobulin G (IgG) and all 4 influenza strain-specific haemagglutinin inhibition antibodies.

14.2.4 COMIRNATY (Original: 10 mcg)

14.2.4.1 Efficacy and Immunogenicity in Children 5 to 11 Years of Age

14.2.4.1.1 Efficacy and Immunogenicity in Children 5 to 11 Years of Age – Primary Series (Two Doses)

Immunogenicity

In Study 3, an analysis of SARS-CoV-2 50% neutralizing titers (NT50) 1 month after Dose 2 in a randomly selected subset of participants demonstrated effectiveness by immunobridging of immune responses. Children 5 to 11 years of age in the Phase 2/3 part of Study 3 were compared with participants 16 to 25 years of age in the Phase 2/3 part of Study 2 who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after Dose 2. The study met the prespecified immunobridging criteria for both the geometric mean ratio (GMR) and the seroresponse difference with seroresponse defined as achieving at least 4-fold rise in SARS-CoV-2 NT50 from baseline (before Dose 1). The ratio of the SARS-CoV-2 NT50 in children 5 to 11 years of age to that of young adults 16 to 25 years of age was 1.04 (2-sided 95% CI: 0.93, 1.18), meeting the 1.5-fold noninferiority criterion (the lower bound of the 2-sided 95% CI for the geometric mean ratio [GMR] >0.67). Results are presented in Table 38.

Table 38: Geometric Mean Ratio And Difference in Seroresponse Rates – Comparison of Children 5 to 11 Years of Age (Study 3) With Participants 16 to 25 Years of Age (Study 2) – Participants Without Evidence of Infection up to 1 Month After Dose 2

Geometric Mean Titers (NT50)					
SARS-CoV-2 neutralization Assay		**COMIRNATY‡**		**5 to 11 Years vs. 16 to 25 Years**	
		10 mcg/Dose 5 to 11 Years N[a]=264	30 mcg/Dose 16 to 25 Years N[a]=253		
	Time Point	**GMT[b]** (95% CI[b])	**GMT[b]** (95% CI[b])	**GMR[b]** (95% CI[b])	**Met Immunobridging Objective[c]**
NT50 (titer)	1 month after Dose 2	1,197.6 (1,106.1, 1,296.6)	1,146.5 (1,045.5, 1,257.2)	1.04 (0.93, 1.18)	Yes
Seroresponse Rate					
	Time Point	**%** (95% CI[d])	**%** (95% CI[d])	**% Difference[e]** (95% CI[f])	**Met Immunobridging Objective[g]**
NT50 (titer)	1 month after Dose 2	99.2 (97.3, 99.9)	99.2 (97.2, 99.9)	0.0 (-2.0, 2.2)	Yes

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).

Note: Participants had no evidence (up to 1 month post-Dose 2 blood sample collection) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and 1 month after Dose 2, NAAT [nasal swab] negative at Visits 1 and 2, and negative NAAT (nasal swab) at any unscheduled visit up to 1 month after Dose 2) and had no medical history of COVID-19.

a.- b. and abbreviations: See footnote of Table 28.

c. Immunobridging is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67 and the point estimate of the GMR is ≥0.8.

d. Exact 2-sided CI based on the Clopper and Pearson method.

e. Seroresponse is defined as achieving a ≥4-fold rise from baseline (before Dose 1). Percentage difference in response rates between 5 to 11 years of age and 16 to 25 years of age.

f. 2-Sided CI, based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

g. Immunobridging is declared if the lower bound of the 2-sided 95% CI for the difference in proportions is greater than - 10.0%.

Among participants without prior evidence of SARS-CoV-2 infection up to 1 month after Dose 2, 99.2% of children 5 to 11 years of age and 99.2% of participants 16 to 25 years of age had a seroresponse from before vaccination to 1 month after Dose 2. The difference in proportions of participants who had seroresponse between children and young adults was 0.0% (2-sided 95% CI: -2.0%, 2.2%), meeting the - 10% noninferiority criterion (the lower bound of the 2-sided 95% CI for the difference in seroresponse rate>-10%). Results are presented in Table 37.

Efficacy

An exploratory efficacy analysis in participants 5 to 11 years of age without evidence of SARS-CoV-2 infection prior to Dose 2 was determined at least 7 days after Dose 2. The observed vaccine efficacy against confirmed COVID-19 was 90.7% (95% CI: 67.7%, 98.3%), with 3 COVID-19 cases in the vaccine group compared with 16 in the placebo group.

No severe COVID-19 or multisystem inflammatory syndrome in children (MIS-C) were reported in children 5 to 11 years of age, as of the data cut-off date (October 8, 2021).

14.2.4.2 Immunogenicity in Children 5 to 11 Years of Age – After Booster Dose

Immunogenicity of the COMIRNATY (10 mcg) booster dose administered 7 to 9 months after the second primary series dose was evaluated in a subset of 67 evaluable study participants with no evidence of prior SARS-CoV-2 infection up to 1 month after the booster dose in Study 3. Results were compared with 96 subjects in the same age group following 2 doses of COMIRNATY.

Vaccine effectiveness of a booster dose of COMIRNATY was inferred based on a descriptive analysis of NT50 against the reference strain of SARS-CoV-2 (USA_WA1/2020). The GMT at 1 month after the booster dose was increased compared with before the booster dose and after dose 2. See Table 39.

Table 39: Geometric Mean Ratio – Comparison of Dose 3 With Dose 2 – Participants Without Evidence of Infection (Study 3) – 5 to 11 Years of Age

Post-Dose 2 N = 96 **GMT (95% CI)**	**Pre-Booster** N = 67 **GMT (95% CI)**	**Post-Booster** N = 67 **GMT (95% CI)**	**GMR*** **Post-Booster/Post-Dose 2** **(95% CI)**
1,253.9 (1,116.0, 1,408.9)	270.1 (229.1, 320.6)	2,720.9 (2,280.1, 3,247.0)	2.17 (1.76, 2.68)

* GMR and confidence interval based on post-hoc descriptive analysis.

14.2.5 COMIRNATY (Original: 3 mcg)

14.2.5.1 Immunogenicity in Children 6 Months to 4 Years of Age

14.2.5.1.1 Immunogenicity in Children 6 Months to 4 Years of Age – Primary Series (Three Doses)

Effectiveness in individuals 6 months to 4 years of age is based on the immunobridging of this age group with individuals 16 to 25 years of age.

Immunogenicity in Children 2 to 4 Years of Age

Immunogenicity analyses were performed in a subset of 143 participants 2 to 4 years of age without evidence of infection up to 1 month after Dose 3 from Study 3. SARS-CoV-2 50% neutralizing antibody titers (NT50) against the reference strain (USA_WA1/2020), were compared with a randomly selected subset of 170 participants 16 to 25 years of age without evidence of infection up to 1 month after the 2-dose primary series from Study 2 (Phase 2/3). The primary immunobridging analyses compared the geometric mean titers (based on the GMR) and the seroresponse rates (defined as achieving at least 4-fold rise in NT50 from before Dose 1). The immunobridging criteria were met for both the GMR and the seroresponse difference (Table 40).

Table 40: Geometric Mean Ratio And Difference in Seroresponse Rates – Immunobridging Subset – Participants 2 To 4 Years of Age (Study 3) Compared With Participants 16 To 25 Years of Age (Study 2) – Participants Without Evidence of SARS-CoV-2 Infection

Geometric Mean Titers (GMT)			
SARS-CoV-2 neutralization Assay	**COMIRNATY‡**		
	3 mcg/Dose 2 to 4 Years (1 Month after Dose 3) n[a]=143	**30 mcg/Dose** 16 to 25 Years (1 Month after Dose 2) n[a]=170	**GMR** (95%CI) (2 to 4 Years / 16 to 25 Years)[b,d]
	GMT[b] (95% CI[b])	**GMT[b]** (95% CI[b])	
NT50 (titer)[c]	1,535.2 (1,388.2, 1,697.8)	1,180.0 (1,066.6, 1305.4)	1.30 (1.13, 1.50)
Seroresponse Rate			
	n=141	n =170	**% Difference in Seroresponse Rates[e] (95% CI)[f]**
	% (95% CI)	**%** (95% CI)	
NT50 (titer)[c]	100.0 (97.4, 100.0)	98.8 (95.8, 99.9)	1.2 (-1.5, 4.2)

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).

a. – c. and abbreviations: See footnote of Table 28.

Note: Participants had no evidence [up to 1 month after Dose 2 (Study 2) or 1 month after Dose 3 (Study 3)] of past SARS-CoV-2 infection.

d. Immunobridging is declared if the lower bound of the 2-sided 95% CI for the GMR ratio is greater than 0.67 and the point estimate of the GMR is ≥ 0.8. Exact 2-sided CI based on the Clopper and Pearson method.
e. Difference in percentages (2 to 4 years minus 16 to 25 years); with 2-sided CI based on the Miettinen and Nurminen method.
f. Immunobridging is declared if the lower bound of the 2-sided 95% CI for the difference in proportions is greater than -10.0% provided that the immunobridging criteria based on GMR were met.

Immunogenicity in Children 6 to 23 Months of Age

Immunogenicity analyses were performed in a subset of 82 participants 6 to 23 months of age without evidence of infection up to 1 month after Dose 3 from Study 3 (Phase 2/3). SARS-CoV-2 50% neutralizing antibody titers (NT50) against the reference strain (USA_WA1/2020), were compared with a randomly selected subset of 170 participants 16 to 25 years of age without evidence of infection up to 1 month after the 2-dose primary series from Study 2 (Phase 2/3). The primary immunobridging analyses compared the geometric mean titers based on the GMR and the seroresponse rates (defined as achieving at least 4-fold rise in NT50 from before Dose 1. The immunobridging criteria were met for both the GMR and the seroresponse difference (Table 41).

Table 41: Geometric Mean Ratio And Difference in Seroresponse Rates – Immunobridging Subset – Participants 6 to 23 Months of Age (Study 3) Compared With Participants 16 To 25 Years of Age (Study 2) – Participants Without Evidence of SARS-CoV-2 Infection

Geometric Mean Titers (NT50)			
SARS-CoV-2 neutralization Assay	**COMIRNATY‡**		
	3 mcg/Dose 6 to 23 Months (1 Month After Dose 3) n[a]=82	**30 mcg/Dose** 16 to 25 Years (1 Month After Dose 2) n[a]=170	**GMR** (95%CI) (6 to 23 Months / 16 to 25 Years)[b,d]
	GMT[b] **(95% CI[b])**	**GMT[b]** **(95% CI[b])**	
NT50 (titer)[c]	1,406.5 (1,211.3, 1,633.1)	1,180.0 (1,066.6, 1,305.4)	1.19 (1.00, 1.42)
Seroresponse Rate			
	% (95% CI)	**%** (95% CI)	**% Difference in Seroresponse Rates[e]** (95% CI)[f]
NT50 (titer)[c]	100.0 (95.5, 100.0)	98.8 (95.8, 99.9)	1.2 (-3.4, 4.2)

‡ Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).
a. – f: See footnote of Table 39.

15 MICROBIOLOGY

No microbiological information is required for this product.

16 NON-CLINICAL TOXICOLOGY

Non-clinical data reveal no special hazard for humans based on conventional studies of repeat dose toxicity.

General Toxicology:

In a repeat-dose toxicity study, rats were administered three once weekly doses of 30 mcg/animal (0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) and other ingredients included in a single human dose) of COMIRNATY by intramuscular injection. Vaccine administration resulted in transient erythema and edema at the site of injection, as well as increased cellularity in draining and inguinal lymph nodes, spleen, and bone marrow, along with transiently increased body temperature, increased white blood counts, and decreased reticulocyte counts coupled with decreased red blood cell mass. Clinical chemistry changes (e.g., increased acute phase protein levels) indicated an acute phase response. These changes are consistent with an expected immunostimulatory response following intramuscular administration of a vaccine. Transient periportal hepatocyte vacuolation was also observed without evidence of liver injury. Full or partial recovery from all findings was observed following a 3-week recovery period.

Carcinogenicity:

Carcinogenic potential was not assessed, as carcinogenicity studies were not considered relevant to this vaccine.

Genotoxicity:

Genotoxic potential was not assessed, as genotoxicity studies were not considered relevant to this vaccine.

Reproductive and Developmental Toxicology:

In a reproductive and developmental toxicity study, 30 mcg/animal (0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) and other ingredients included in a single human dose) of COMIRNATY was administered to female rats by the intramuscular route on four occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

COMIRNATY®

COVID-19 mRNA Vaccine, Suspension for Intramuscular Injection

This leaflet is a summary and will not tell you everything about this vaccine. Talk to your/your child's healthcare professional about your/your child's medical condition and treatment and ask if there is any new information about **COMIRNATY**.

What is COMIRNATY used for?

COMIRNATY is a vaccine used to provide protection against COVID-19 disease caused by the SARS-CoV-2 virus.

COMIRNATY can be given to people 6 months of age and older.

How does COMIRNATY work?

The vaccine causes our body to produce protection (such as antibodies) that prevent the COVID-19 virus from entering our cells to make us sick. The vaccine uses a new method (messenger RNA - mRNA, the genetic code for a piece of the virus) to help our bodies make protection against the virus. The vaccine is given by injection with a needle in the upper arm.

You cannot get COVID-19 from the vaccine.

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

What are the ingredients in COMIRNATY?

Medicinal ingredient: mRNA encoding SARS-CoV-2 spike protein

The mRNA encoding spike protein is derived from Omicron variant LP.8.1.

Non-medicinal ingredients:

- ALC-0315 = ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)
- ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide
- cholesterol
- DSPC = 1,2-distearoyl-sn-glycero-3-phosphocholine
- sodium chloride*
- sucrose
- tromethamine
- tromethamine hydrochloride
- water for injection

* present only in the vial with yellow cap/label border (for age 6 months to 4 years) following dilution with 0.9% Sodium Chloride Injection USP.

COMIRNATY comes in the following dosage forms:

Suspension for intramuscular injection, provided as follows (not all presentations may be available):

For 12 Years of Age and Older:

- ***Single Dose Vial with Light Gray Cap and Light Gray Label Border (DO NOT DILUTE):*** 1 dose of 0.3 mL (30 micrograms mRNA/0.3 mL).
- ***Multiple Dose Vial with Dark Gray Cap and Dark Gray Label Border (DO NOT DILUTE):*** 6 doses of 0.3 mL (30 micrograms mRNA/0.3 mL).
- ***Single Dose Prefilled Syringe:*** 1 dose of 0.3 mL (30 micrograms mRNA/0.3 mL).

For Age 5 Years to 11 Years:

- ***Single Dose Vial with Light Blue Cap and Light Blue Label Border (DO NOT DILUTE):*** 1 dose of 0.3 mL (10 micrograms mRNA/0.3 mL).
- ***Multiple Dose Vial with Dark Blue Cap and Dark Blue Label Border (DO NOT DILUTE):*** 6 doses of 0.3 mL (10 micrograms mRNA/0.3 mL).

For Age 6 Months to 4 Years:

- ***Multiple Dose Vial with Yellow Cap and Yellow Label Border (DILUTE PRIOR TO USE):*** 3 doses of 0.3 mL after dilution (3 micrograms mRNA/0.3 mL).

You/your child should not receive COMIRNATY if:

- you/your child are allergic to any of the ingredients in this vaccine (see **What are the ingredients in COMIRNATY?**).
- you/your child had a severe allergic reaction after a previous dose of any COMIRNATY vaccine.
- you/your child have any symptoms that could be due to COVID-19. Talk with your/your child's healthcare professional about your/your child's symptoms and getting a COVID-19 test. Your/your child's healthcare professional will advise you when you/your child are able to receive the vaccine.

To help avoid side effects and ensure proper use, talk to your/your child's healthcare professional before you/your child receive COMIRNATY. Talk about any health conditions or problems you/your child may have, including if you/your child:

- have had any problems following a previous dose of any COMIRNATY vaccine, such as an allergic reaction or breathing problems
- have any allergies
- have a weakened immune system due to a medical condition or are on a medicine that affects the immune system
- have previously had episodes of myocarditis (inflammation of the heart muscle) and/or pericarditis (inflammation of the outer lining of the heart)
- have a history of febrile convulsions
- are feeling nervous about the vaccination process or have ever fainted in association with an injection
- have a bleeding problem, bruise easily or use a blood thinning medication
- are pregnant, think you may be pregnant or plan to become pregnant
- are breast-feeding

Other warnings you should know about:

As with any vaccine, COMIRNATY may not fully protect all those who receive it.

Some of the effects of vaccination mentioned under "***What are possible side effects from using COMIRNATY?"*** may temporarily affect your ability to drive or use machines. Wait until these effects have worn off before you drive or use machines.

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

COMIRNATY may be given at the same time as a flu vaccine in adults 18 to 64 years of age.

Tell your healthcare professional if you/your child have recently received any other vaccine.

How COMIRNATY is given:

Usual dose:

For 12 Years of Age and Older

COMIRNATY is given as an injection of 0.3 mL, preferably into a muscle of the upper arm.

You will receive 1 injection, regardless whether you have received a COVID-19 vaccine before.

If you were previously vaccinated with a COVID-19 vaccine, you should not receive a dose of COMIRNATY until at least 3 to 6 months after the most recent dose.

For Age 5 Years to 11 Years

COMIRNATY is given as an injection of 0.3 mL, preferably into a muscle of the upper arm.

Your child will receive 1 injection, regardless whether he/she has received a COVID-19 vaccine before.

If your child was previously vaccinated with a COVID-19 vaccine, he/she should not receive a dose of COMIRNATY until at least 6 months after the most recent dose.

For Age 6 Months to 4 Years

COMIRNATY is given as an injection of 0.3 mL, into a muscle of the thigh in infants from 6 to less than 12 months of age. In infants and children 1 year of age or older, it is given as an injection of 0.3 mL into a muscle of the thigh or into a muscle of the upper arm.

If your child has not completed a COVID-19 primary vaccination course, your child will receive a maximum of 3 injections (the total number of doses required as primary course). It is recommended to receive the second dose 3 weeks after the first dose followed by a third dose at least 8 weeks after the second dose to complete the three-dose course. If your child has started a three-dose course with COMIRNATY Omicron XBB.1.5, they may complete the three-dose course with COMIRNATY.

If your child has previously completed a COVID-19 primary vaccination course, your child will receive 1 injection. If your child was previously vaccinated with a COVID-19 vaccine, your child should not receive a dose of COMIRNATY until at least 6 months after the most recent dose.

If you have any further questions on the use of COMIRNATY, ask your healthcare professional.

Overdose:

Your healthcare professional may monitor you for 30 minutes in case of overdose. In the event of suspected overdose with COMIRNATY, contact your regional poison control centre.

Missed Dose:

If you forget to go back to your healthcare professional at the scheduled time for your/your child's next dose, ask your/your child's healthcare professional for advice.

What are possible side effects from using COMIRNATY?

Like all vaccines, COMIRNATY can cause side effects, although not everybody gets them.

Side effects may occur at the following frequencies:

Very common: may affect more than 1 in 10 people

- irritability (6 months to 23 months)
- injection site pain/tenderness, swelling
- tiredness
- headache
- muscle pain
- chills
- joint pain
- fever
- diarrhea

Common: may affect more than 1 in 100 and up to 1 in 10 people

- injection site redness ("very common" in 6 months to 11 years)
- nausea
- vomiting
- rash (6 months to 23 months)
- enlarged lymph nodes (more frequently observed after the booster dose)

Uncommon: may affect more than 1 in 1000 and up to 1 in 100 people

- feeling unwell
- arm pain
- feeling weak or lack of energy/sleepy
- decreased appetite ("very common" in 6 months to 23 months)
- excessive sweating
- night sweats

Non-severe allergic reactions (such as rash, itching, hives or swelling of the face), severe allergic reactions, facial paralysis / Bell's palsy, erythema multiforme (skin reaction or lesion; red spots or patches), hypoesthesia (reduced or loss of sensation) and paresthesia ("tingling sensation") have been reported.

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

These are not all the possible side effects you/your child may have when receiving COMIRNATY. If you/your child experience any side effects not listed here, tell your/your child's healthcare professional.

There is a remote chance that COMIRNATY could cause a severe allergic reaction. A severe allergic reaction would usually occur within a few minutes to one hour after getting a dose of COMIRNATY. For this reason, the vaccination provider may ask you/your child to stay at the place where the vaccine was received for monitoring after vaccination. Should you/your child develop any serious symptoms or symptoms that could be an allergic reaction, seek medical attention right away. Symptoms of an allergic reaction include:

- hives (bumps on the skin that are often very itchy)
- swelling of the face, tongue or throat
- difficulty breathing
- a fast heartbeat
- dizziness and weakness

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

Your/your child's health care provider should inform your local public health department of any serious side effects after vaccination.

Reporting Suspected Side Effects for Vaccines

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

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

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

Storage:

COMIRNATY should be stored, supplied and administered by a healthcare professional.

Keep out of reach and sight of children.

If you want more information about COMIRNATY**:**

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website [www.pfizer.ca], or by calling 1-800-463-6001 (Pfizer Medical Information)).

This leaflet was prepared by Pfizer Canada ULC.

Last Revised: July 13, 2026