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

COMIRNATY® (COVID-19 Vaccine, mRNA) suspension for injection, for intramuscular use
2024-2025 Formula
Initial U.S. Approval: 2021

----------RECENT MAJOR CHANGES ----------
Dosage and Administration, Preparation for Administration: Plastic prefilled syringe is no longer available. (2.1) 8/2024
Warnings and Precautions, Myocarditis and Pericarditis (5.2) 6/2025

---------- INDICATIONS AND USAGE----------
COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 12 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
For intramuscular injection only. (2)

- COMIRNATY is administered as a single 0.3 mL dose. (2.2)
- For individuals previously vaccinated with any COVID-19 vaccine, administer the dose of COMIRNATY at least 2 months after the last dose of COVID-19 vaccine. (2.3)

---------- DOSAGE FORMS AND STRENGTHS----------
Suspension for injection. A single dose is 0.3 mL. (3)

---------- CONTRAINDICATIONS ----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY. (4)

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

- Analyses of postmarketing data from use of authorized or approved mRNA COVID-19 vaccines, including COMIRNATY, have demonstrated increased risks of myocarditis and pericarditis, with onset of symptoms typically in the first week following vaccination. The observed risk has been highest in males 12 years through 24 years of age. (5.2)
- Syncope (fainting) may occur in association with administration of injectable vaccines, including COMIRNATY. Procedures should be in place to avoid injury from fainting. (5.3)

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

- The most commonly reported adverse reactions (≥10%) after a dose of COMIRNATY were pain at the injection site (up to 90.5%), fatigue (up to 77.5%), headache (up to 75.5%), chills (up to 49.2%), muscle pain (up to 45.5%), joint pain (up to 27.5%), fever (up to 24.3%), injection site swelling (up to 11.8%), and injection site redness (up to 10.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

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

Revised: 6/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 12 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

2.1 Preparation for Administration

COMIRNATY Single Dose Glass Prefilled Syringes

- Verify that the glass prefilled syringe states 2024-2025 Formula.
- If glass prefilled syringe has been frozen, discard.
- Do not shake.
- Remove tip cap by slowly turning the cap counterclockwise while holding the Luer lock and attach a sterile needle. Use immediately. If COMIRNATY cannot be used immediately, it must be used within 4 hours.

COMIRNATY Single Dose Vials

- Verify that the vial states 2024-2025 Formula.
- If vial is frozen, thaw vial in the refrigerator [2ºC to 8ºC (35ºF to 46ºF) for up to 2 hours] or at room temperature [up to 25ºC (77ºF) for 30 minutes] *[see How Supplied/Storage and Handling (16)]*.
- Prior to use, mix by inverting vial gently 10 times. Do not shake.
- Withdraw a single 0.3 mL dose using a sterile needle and syringe.
- Discard vial and any excess volume.

2.2 Administration Information

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be a white to off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer the 0.3 mL dose intramuscularly immediately after preparation. For the prefilled syringe, administer the entire volume to deliver a single 0.3 mL dose.

2.3 Vaccination Schedule

COMIRNATY is administered as a single dose for individuals 12 years of age and older.

For individuals previously vaccinated with any COVID-19 vaccine, administer the dose of COMIRNATY at least 2 months after the last dose of COVID-19 vaccine.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. A single dose is 0.3 mL.

4 CONTRAINDICATIONS

Do not administer COMIRNATY to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY *[see Description (11)]* or to individuals who had a severe allergic reaction (e.g., anaphylaxis) following a previous dose of a Pfizer-BioNTech COVID-19 vaccine.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

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

5.2 Myocarditis and Pericarditis

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

Based on analyses of commercial health insurance claims data from inpatient and outpatient settings, the estimated unadjusted incidence of myocarditis and/or pericarditis during the period 1 through 7 days following administration of the 2023-2024 Formula of mRNA COVID-19 vaccines was approximately 8 cases per million doses in individuals 6 months through 64 years of age and approximately 27 cases per million doses in males 12 through 24 years of age.

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

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

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

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

5.3 Syncope

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

5.4 Altered Immunocompetence

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

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

An overview of clinical studies contributing to the safety assessment of COMIRNATY is provided in Table 1. Participants in these clinical studies received a 2-dose series, 3 weeks apart (referred to as a primary series) and subsequent doses referred to as booster doses.

Table 1: Clinical Studies

Study	Age Group	Vaccine Strain Composition	Dosing	Number of Participants
Primary Series				
Study 1 (NCT04380701)	18 through 55 years	Original[a]	Primary series	60
Study 2 (NCT04368728)	12 through 15 years of age	Original[a]	Primary series	1131[b]
	≥16 years of age	Original[a]	Primary series	22026[b]
Booster Dose				
Study 2 (NCT04368728)	12 through 15 years of age	Original[a]	1st booster	825
	18 through 55 years of age	Original[a]	1st booster	306
Study 4 (NCT04955626)	12 through 17 years of age	Original[a]	1st booster	65
	≥16 years of age	Original[a]	1st booster	5081[b]
Study 5 (NCT05472038)	≥12 years of age	Original and Omicron BA.4/BA.5[c]	2nd booster	726
Concomitant Administration				
Study 8 (NCT05310084)	18 through 64 years of age	Original[a]	2nd booster administered alone or concomitantly with Influenza Vaccine[d]	1128

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

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

b. Received COMIRNATY during placebo-control period.

c. Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original) and Omicron variant lineages BA.4 and BA.5 (Omicron BA.4/BA.5), authorized as Pfizer-BioNTech COVID-19 Vaccine, Bivalent.

d. Influenza Vaccine (Afluria Quadrivalent).

Primary Series with COMIRNATY

Participants 12 through 15 years of age in Study 2: the most commonly reported adverse reactions (≥8%) following any dose were pain at the injection site (90.5%), fatigue (77.5%), headache (75.5%), chills (49.2%), muscle pain (42.2%), fever (24.3%), joint pain (20.2%), injection site swelling (9.2%), and injection site redness (8.6%).

Participants 16 through 55 years of age in Study 2: the most commonly reported adverse reactions (≥10%) following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%).

Participants 56 years of age and older in Study 2: the most commonly reported adverse reactions (≥10%) following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

Booster Dose with COMIRNATY

Participants 12 years of age and older in Studies 2 and 4: the most commonly reported adverse reactions (≥5%) following administration of a first booster dose with COMIRNATY were similar to those reported by participants who received COMIRNATY in the primary series.

Booster Dose With Pfizer-BioNTech COVID-19 Vaccine, Bivalent

Participants 12 years of age and older in Study 5: the most commonly reported adverse reactions (≥5%) following administration of a second booster dose with Pfizer-BioNTech COVID-19 Vaccine, Bivalent were pain at the injection site (67.3%), fatigue (52.6%), headache (40.5%), muscle pain (24.6%), chills (18.0%), joint pain (13.3%), fever (5.3%), injection site swelling (5.3%), and injection site redness (5.3%).

6.1 Clinical Trials Experience

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

Primary Series With COMIRNATY

The safety of a 2-dose primary series of COMIRNATY was evaluated in participants 12 years of age and older in 2 clinical studies conducted in Germany (Study 1), United States, Argentina, Brazil, Turkey, South Africa, and Germany (Study 2). Study BNT162-01 (Study 1) was a Phase 1/2, 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age and 36 participants, 56 through 85 years of age. Study 2 was a Phase 1/2/3 multicenter, randomized, saline placebo-controlled, double-blinded (Phase 2/3), dose finding-, vaccine candidate-selection and efficacy study that enrolled approximately 46,000 participants 12 years of age or older. Of these, approximately 2,260 participants were 12 through 15 years of age (1,131 COMIRNATY; 1,129 placebo) and 754 were 16 through 17 years of age (378 COMIRNATY; 376 placebo). In all, 44,047 participants in Phase 2/3 were 16 years of age or older (22,026 COMIRNATY; 22,021 placebo).

Study 2 included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection. Confirmed stable HIV infection was defined as documented viral load <50 copies/mL and CD4 count >200 cells/mm^3 within 6 months before enrollment, and on stable antiretroviral therapy for at least 6 months.

HIV-positive participants are included in the safety population but are summarized separately in the safety analyses.

In Study 2, participants 12 years and older in the reactogenicity subset were monitored using an electronic diary for solicited local and systemic reactions and use of antipyretic medication after each vaccination. Participants were also monitored for unsolicited adverse events throughout the study (from Dose 1 through 1 month [all unsolicited adverse events] or through 6 months [serious adverse events] after the last vaccination). Tables 2 and 3 present the frequency and severity of solicited local and systemic reactions, respectively, within 7 days following any dose of COMIRNATY.

Adolescents 12 Through 15 Years of Age

In Study 2, 2,260 adolescents (1,131 COMIRNATY; 1,129 placebo) were 12 through 15 years of age. At the time of the analysis of the ongoing Study 2 with a data cutoff of September 2, 2021, there were 1,559 (69.0%) adolescents (786 COMIRNATY and 773 placebo) 12 through 15 years of age followed for ≥4 months after the second dose.

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among adolescents who received COMIRNATY and those who received placebo. Overall, among the adolescents who received COMIRNATY, 50.1% were male and 49.9% were female, 85.8% were White, 4.6% were Black or African American, 11.7% were Hispanic/Latino, 6.4% were Asian, and 0.4% were American Indian/Alaska Native.

Local and Systemic Adverse Reactions Solicited in Study 2

In adolescents 12 through 15 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 11 days), for redness 1.8 days (range 1 to 5 days), and for swelling 1.6 days (range 1 to 5 days) in the COMIRNATY group.

Table 2: Study 2 – Frequency and Percentages of Adolescents With Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Adolescents 12 Through 15 Years of Age – Safety Population*

	COMIRNATY† Dose 1 N[a]=1127 n[b] (%)	**Placebo Dose 1 N[a]=1127 n[b] (%)**	**COMIRNATY† Dose 2 N[a]=1097 n[b] (%)**	**Placebo Dose 2 N[a]=1078 n[b] (%)**
Redness[c]				
Any (>2 cm)	65 (5.8)	12 (1.1)	55 (5.0)	10 (0.9)
Mild	44 (3.9)	11 (1.0)	29 (2.6)	8 (0.7)
Moderate	20 (1.8)	1 (0.1)	26 (2.4)	2 (0.2)
Severe	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Swelling[c]				
Any (>2 cm)	78 (6.9)	11 (1.0)	54 (4.9)	6 (0.6)
Mild	55 (4.9)	9 (0.8)	36 (3.3)	4 (0.4)
Moderate	23 (2.0)	2 (0.2)	18 (1.6)	2 (0.2)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	COMIRNATY† Dose 1 N[a]=1127 n[b] (%)	Placebo Dose 1 N[a]=1127 n[b] (%)	COMIRNATY† Dose 2 N[a]=1097 n[b] (%)	Placebo Dose 2 N[a]=1078 n[b] (%)
Pain at the injection site[d]				
Any	971 (86.2)	263 (23.3)	866 (78.9)	193 (17.9)
Mild	467 (41.4)	227 (20.1)	466 (42.5)	164 (15.2)
Moderate	493 (43.7)	36 (3.2)	393 (35.8)	29 (2.7)
Severe	11 (1.0)	0 (0.0)	7 (0.6)	0 (0.0)

Note: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

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

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 3: Study 2 – Frequency and Percentages of Adolescents With Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Adolescents 12 Through 15 Years of Age – Safety Population*

	COMIRNATY† Dose 1 N[a]=1127 n[b] (%)	Placebo Dose 1 N[a]=1127 n[b] (%)	COMIRNATY† Dose 2 N[a]=1097 n[b] (%)	Placebo Dose 2 N[a]=1078 n[b] (%)
Fever				
≥38.0°C	114 (10.1)	12 (1.1)	215 (19.6)	7 (0.6)
≥38.0°C to 38.4°C	74 (6.6)	8 (0.7)	107 (9.8)	5 (0.5)
>38.4°C to 38.9°C	29 (2.6)	2 (0.2)	83 (7.6)	1 (0.1)
>38.9°C to 40.0°C	10 (0.9)	2 (0.2)	25 (2.3)	1 (0.1)
>40.0°C	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Fatigue[c]				
Any	677 (60.1)	457 (40.6)	726 (66.2)	264 (24.5)
Mild	278 (24.7)	250 (22.2)	232 (21.1)	133 (12.3)
Moderate	384 (34.1)	199 (17.7)	468 (42.7)	127 (11.8)
Severe	15 (1.3)	8 (0.7)	26 (2.4)	4 (0.4)
Headache[c]				
Any	623 (55.3)	396 (35.1)	708 (64.5)	264 (24.5)
Mild	361 (32.0)	256 (22.7)	302 (27.5)	170 (15.8)
Moderate	251 (22.3)	131 (11.6)	384 (35.0)	93 (8.6)
Severe	11 (1.0)	9 (0.8)	22 (2.0)	1 (0.1)
Chills[c]				
Any	311 (27.6)	109 (9.7)	455 (41.5)	74 (6.9)
Mild	195 (17.3)	82 (7.3)	221 (20.1)	53 (4.9)
Moderate	111 (9.8)	25 (2.2)	214 (19.5)	21 (1.9)
Severe	5 (0.4)	2 (0.2)	20 (1.8)	0 (0.0)
Vomiting[d]				
Any	31 (2.8)	10 (0.9)	29 (2.6)	12 (1.1)
Mild	30 (2.7)	8 (0.7)	25 (2.3)	11 (1.0)
Moderate	0 (0.0)	2 (0.2)	4 (0.4)	1 (0.1)
Severe	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)

	COMIRNATY† Dose 1 N[a]=1127 n[b] (%)	Placebo Dose 1 N[a]=1127 n[b] (%)	COMIRNATY† Dose 2 N[a]=1097 n[b] (%)	Placebo Dose 2 N[a]=1078 n[b] (%)
Diarrhea[e]				
Any	90 (8.0)	82 (7.3)	65 (5.9)	44 (4.1)
Mild	77 (6.8)	72 (6.4)	59 (5.4)	39 (3.6)
Moderate	13 (1.2)	10 (0.9)	6 (0.5)	5 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
New or worsened muscle pain[c]				
Any	272 (24.1)	148 (13.1)	355 (32.4)	90 (8.3)
Mild	125 (11.1)	88 (7.8)	152 (13.9)	51 (4.7)
Moderate	145 (12.9)	60 (5.3)	197 (18.0)	37 (3.4)
Severe	2 (0.2)	0 (0.0)	6 (0.5)	2 (0.2)
New or worsened joint pain[c]				
Any	109 (9.7)	77 (6.8)	173 (15.8)	51 (4.7)
Mild	66 (5.9)	50 (4.4)	91 (8.3)	30 (2.8)
Moderate	42 (3.7)	27 (2.4)	78 (7.1)	21 (1.9)
Severe	1 (0.1)	0 (0.0)	4 (0.4)	0 (0.0)
Use of antipyretic or pain medication[f]	413 (36.6)	111 (9.8)	557 (50.8)	95 (8.8)

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

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

a. N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. 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.

f. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events in Study 2

In Study 2, 2,260 adolescents (1,131 COMIRNATY; 1,129 placebo) were 12 through 15 years of age. Of these, 634 (56.1%) participants in the COMIRNATY group and 629 (55.7%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 152 (13.4%) and 144 (12.8%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 1,113 (98.4%) participants 12 through 15 years of age originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2. An analysis of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date was conducted. Among participants 12 through 15 years of age who received at least 1 dose of study vaccine, unsolicited adverse events were reported by 95 (8.4%) participants in the COMIRNATY group and 113 (10.0%) participants in the placebo group.

In an analysis of all unsolicited adverse events reported during blinded follow-up from Dose 1 through 1 month after Dose 2, in adolescents 12 to 15 years of age, those assessed as adverse reactions not already captured by solicited local and systemic reactions were lymphadenopathy (9 vs. 2), and nausea (5 vs. 2).

In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of unsolicited adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

In Study 2, among participants 12 through 15 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY = 1,131; placebo = 1,129), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 10 (0.9%) COMIRNATY recipients and 2 (0.2%) placebo recipients. In these analyses, 69.0% of study participants had at least 4 months of follow-up after Dose 2. In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

Participants 16 Years of Age and Older

At the time of the analysis of Study 2 with a data cutoff of March 13, 2021, there were 25,651 (58.2%) participants (13,031 COMIRNATY; 12,620 placebo) 16 years of age and older followed for ≥4 months after the second dose.

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received COMIRNATY and those who received placebo. Overall, among the total participants who received either COMIRNATY or placebo, 50.9% were male, 49.1% were female, 79.3% were 16 through 64 years of age, 20.7% were 65 years of age and older, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Local and Systemic Adverse Reactions Solicited in the Study 2
In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the COMIRNATY group.

In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the COMIRNATY group.

Table 4: Study 2 – Frequency and Percentages of Participants With Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY† Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY† Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Redness[c]				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling[c]				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0
Pain at the injection site[d]				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

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

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 5: Study 2 – Frequency and Percentages of Participants With Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	COMIRNATY† Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY† Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue[c]				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)

	COMIRNATY† Dose 1 N[a]=2899 n[b] (%)	Placebo Dose 1 N[a]=2908 n[b] (%)	COMIRNATY† Dose 2 N[a]=2682 n[b] (%)	Placebo Dose 2 N[a]=2684 n[b] (%)
Headache[c]				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills[c]				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)
Vomiting[d]				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea[e]				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain[c]				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication[f]	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

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

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. 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.

f. Severity was not collected for use of antipyretic or pain medication.

Table 6: Study 2 – Frequency and Percentages of Participants With Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY† Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY† Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Redness[c]				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling[c]				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

Notes: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

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

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 7: Study 2 – Frequency and Percentages of Participants With Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	COMIRNATY† Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY† Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0

	COMIRNATY† Dose 1 N[a]=2008 n[b] (%)	Placebo Dose 1 N[a]=1989 n[b] (%)	COMIRNATY† Dose 2 N[a]=1860 n[b] (%)	Placebo Dose 2 N[a]=1833 n[b] (%)
Fatigue[c]				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache[c]				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills[c]				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting[d]				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea[e]				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain[c]				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication[f]	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

Notes: Reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention. Participants with chronic, stable HIV infection were excluded.

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

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. N for each reaction or use of antipyretic or pain medication was the same, therefore was included in the column header.

b. n = Number of participants with the specified reaction.
c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
e. 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 or hospitalization for severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

In participants with chronic, stable HIV infection the frequencies of solicited local and systemic adverse reactions were similar to or lower than those observed for all participants 16 years of age and older.

Unsolicited Adverse Events

Overall, 11,253 (51.1%) participants 16 years of age and older in the COMIRNATY group and 11,316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 in the blinded placebo-controlled follow-up period with an additional 1,778 (8.1%) and 1,304 (5.9%) with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

A total of 12,006 (54.5%) participants originally randomized to COMIRNATY had ≥6 months total (blinded and unblinded) follow-up after Dose 2.

In an analysis of all unsolicited adverse events reported following any dose, through 1 month after Dose 2, in participants 16 years of age and older (N = 43,847; 21,926 COMIRNATY group vs. 21,921 placebo group), those assessed as adverse reactions not already captured by solicited local and systemic reactions were nausea (274 vs. 87), malaise (130 vs. 22), lymphadenopathy (83 vs. 7), asthenia (76 vs. 25), decreased appetite (39 vs. 9), hyperhidrosis (31 vs. 9), lethargy (25 vs. 6), and night sweats (17 vs. 3).

In analyses of all unsolicited adverse events in Study 2 from Dose 1 up to the participant unblinding date, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants 16 through 55 years of age who received at least 1 dose of study vaccine, 12,995 of whom received COMIRNATY and 13,026 of whom received placebo, unsolicited adverse events were reported by 4,396 (33.8%) participants in the COMIRNATY group and 2,136 (16.4%) participants in the placebo group. In a similar analysis in participants 56 years of age and older that included 8,931 COMIRNATY recipients and 8,895 placebo recipients, unsolicited adverse events were reported by 2,551 (28.6%) participants in the COMIRNATY group and 1,432 (16.1%) participants in the placebo group. Among participants with confirmed stable HIV infection that included 100 COMIRNATY recipients and 100 placebo recipients, unsolicited adverse events were reported by 29 (29%) participants in the COMIRNATY group and 15 (15%) participants in the placebo group. The higher frequency of reported unsolicited adverse events among COMIRNATY recipients compared to placebo recipients was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset (Table 6 and Table 7).

Throughout the placebo-controlled safety follow-up period, Bell's palsy (facial paralysis) was reported by 4 participants in the COMIRNATY group and 2 participants in the placebo group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. In the placebo group the onset of facial paralysis was Day 32 and Day 102. Currently available information is insufficient to determine a causal relationship with the vaccine. In the analysis of blinded, placebo-controlled follow-up, there were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no

notable patterns of specific categories of non-serious adverse events that would suggest a causal relationship to COMIRNATY.

Serious Adverse Events

Participants 16 through 55 years of age in Study 2 who had received at least 1 dose of vaccine or placebo (COMIRNATY = 12,995; placebo = 13,026), reported serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up as follows: 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis, in participants 56 years of age and older (8,931 COMIRNATY group and 8,895 placebo group), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 2 (2%) COMIRNATY recipients and 2 (2%) placebo recipients.

In the analysis of blinded, placebo-controlled follow-up, there were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY. In the analysis of unblinded follow-up, there were no notable patterns of specific categories of serious adverse events that would suggest a causal relationship to COMIRNATY.

First Booster Dose With COMIRNATY Following the Primary Series

12 Through 15 Years of Age

A subset of 825 Study 2 Phase 2/3 participants 12 through 15 years of age received a booster dose of COMIRNATY 11.2 months (median time, range 6.3 to 20.1 months) after completing the primary series and had a median follow-up time of 9.5 months up to a data cutoff date of November 3, 2022. The median age of participants was 14.0 years (range 13 through 15 years of age), 49.3% were male and 50.7% were female, 83.5% were White, 10.8% were Hispanic/Latino, 4.6% were Black or African American, 7.5% were Asian, and 0.4% were American Indian/Alaska Native.

Adverse reactions reported in participants receiving a booster dose of COMIRNATY were similar to those previously observed in participants receiving COMIRNATY as part of the primary series. Lymphadenopathy occurred in 8 (1.0%) participants who received a booster dose of COMIRNATY and in 9 (0.8%) participants who received COMIRNATY as a primary series.

12 Through 17 Years of Age

A subset of 65 Study 4 participants 12 through 17 years of age received a booster dose of COMIRNATY 13.3 months (median time, range 6.5 to 16.9 months) after completing the primary series and had a median follow-up time of 5.6 months up to a data cutoff date of July 14, 2022. The median age of participants was 14 years (range 12 through 17 years of age), 49.2% were male and 50.8% were female, 76.9% were White, 16.9% were Hispanic/Latino, 13.8% were Black or African American, 7.7% were Asian, and 1.5% were American Indian/Alaska Native.

Adverse reactions reported in participants receiving a booster dose of COMIRNATY were similar to those previously observed in participants receiving COMIRNATY as part of the primary series. There were no cases of lymphadenopathy reported in participants who received a booster dose of COMIRNATY.

16 Years of Age and Older

In Study 4, a double-blind placebo-controlled booster study, 5,081 participants 16 years of age and older recruited from Study 2 received a booster dose of COMIRNATY 10.8 months (median time, range of 5.0 to 12.6 months) after completing the primary series of COMIRNATY series and had a median follow-up time of 2.9 months based on data up to the cutoff date of February 8, 2022. The median age of participants who received COMIRNATY or placebo was 53.0 years (range 16 through 87 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.

Adverse reactions reported in participants receiving a booster dose of COMIRNATY were similar to those previously observed in participants receiving COMIRNATY as part of the primary series. Lymphadenopathy occurred in 141 (2.8%) participants who received a booster dose of COMIRNATY and in 83 (0.4%) participants who received COMIRNATY as a primary series.

18 Through 55 Years of Age

A subset of 306 Study 2 Phase 2/3 participants 18 through 55 years of age received a booster dose of COMIRNATY 6.8 months (median time, range 4.8 to 8.0 months) after completing the primary series. These participants had a median follow-up time of 8.3 months up to a data cutoff date of November 22, 2021. Among the 306 participants, the median age was 42 years (range 19 through 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.

Adverse reactions reported in participants receiving a booster dose of COMIRNATY were similar to those previously observed in participants receiving COMIRNATY as part of the primary series. Lymphadenopathy occurred in 16 (5.2%) of participants who received a booster dose of COMIRNATY and 83 (0.4%) in participants who received COMIRNATY as a primary series.

Second Booster With Pfizer-BioNTech COVID-19 Vaccine, Bivalent

12 Years of Age and Older

A subset of 107 Study 5 Phase 2/3 participants 12 through 17 years of age, 313 participants 18 through 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, went on to receive a second booster dose with Pfizer-BioNTech COVID-19 Vaccine, Bivalent.

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 up to a data cutoff date of October 31, 2022. 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.

Local and Systemic Adverse Reactions Solicited in Study 5

Table 8 and Table 9 present the frequency and severity of reported solicited local reactions and systemic reactions, respectively, within 7 days of a second booster dose of Pfizer-BioNTech COVID-19 Vaccine, Bivalent.

In participants 12 years of age and older who received a second booster dose, the mean duration of injection site pain was 2.1 to 2.4 days (range 1 to 11 days), injection site redness was 1.5 to 2.5 days (range 1 to 4 days), and injection site swelling was 1.3 to 1.9 days (range 1 to 4 days), respectively.

Table 8: Study 5 – Frequency and Percentages of Participants With Solicited Local Reactions, by Maximum Severity, Within 7 Days After a Second Booster Dose – Participants 12 Years of Age and Older – Safety Population

	Pfizer-BioNTech COVID-19 Vaccine, Bivalent*		
	12 Through 17 Years of Age N[a]=107 n[b] (%)	18 Through 55 Years of Age N[a]=309[†] n[b] (%)	56 Years of Age and Older N[a]=300[†] n[b] (%)
Redness[c]			
Any (>2 cm)	6 (5.6)	21 (6.8%)	11 (3.7%)
Mild	4 (3.7)	16 (5.2%)	7 (2.3)
Moderate	2 (1.9)	5 (1.6)	4 (1.3%)
Severe	0	0	0
Swelling[c]			
Any (>2 cm)	8 (7.5)	23 (7.4%)	8 (2.7)
Mild	6 (5.6)	19 (6.1%)	5 (1.7)
Moderate	2 (1.9)	4 (1.3)	3 (1.0)
Severe	0	0	0
Pain at the injection site[d]			
Any	75 (70.1)	236 (76.1)	172 (57.1)
Mild	45 (42.1)	178 (57.4)	147 (48.8)
Moderate	29 (27.1)	58 (18.7)	24 (8.0)
Severe	1 (0.9)	0	1 (0.3)

Note: Adverse Reactions were collected in the electronic diary (e-diary) from day of vaccination (Day 1) through Day 7 after the study vaccination.

* Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original) and Omicron variant lineages BA.4 and BA.5 (Omicron BA.4/BA.5).

† N = 310 for redness and pain at injection site in participants 18 through 55 years of age; N = 301 for pain at injection site in participants 56 years of age and older.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the study vaccination.

b. n = Number of participants with the specified adverse reaction.

c. Mild: >2.0 to 5.0 cm; Moderate: >5.0 to 10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 9: Study 5 – Frequency and Percentages of Participants With Solicited Systemic Adverse Reactions, by Maximum Severity, Within 7 Days After a Second Booster Dose – Participants 12 Years of Age and Older – Safety Population

	Pfizer-BioNTech COVID-19 Vaccine, Bivalent*		
	12 Through 17 Years of Age N[a]=107 n[b] (%)	18 Through 55 Years of Age N[a]=309 n[b] (%)	56 Years of Age and Older N[a]=300[†] n[b] (%)
Fever			
≥38.0°C	10 (9.3)	15 (4.9)	14 (4.7)
≥38.0°C to 38.4°C	7 (6.5)	9 (2.9)	10 (3.3)
>38.4°C to 38.9°C	2 (1.9)	6 (1.9)	3 (1.0)
>38.9°C to 40.0°C	1 (0.9)	0	0
>40.0°C	0	0	0
Fatigue[c]			
Any	72 (67.3)	189 (61.2)	116 (38.5)
Mild	27 (25.2)	83 (26.9)	56 (18.6)
Moderate	45 (42.1)	100 (32.4)	56 (18.6)
Severe	0	6 (1.9)	4 (1.3)
Headache[c]			
Any	54 (50.5)	144 (46.6)	92 (30.7)
Mild	28 (26.2)	87 (28.2)	62 (20.7)
Moderate	26 (24.3)	55 (17.8)	30 (10.0)
Severe	0	2 (0.6)	0
Chills[c]			
Any	25 (23.4)	68 (22.0)	36 (12.0)
Mild	19 (17.8)	38 (12.3)	21 (7.0)
Moderate	6 (5.6)	28 (9.1)	14 (4.7)
Severe	0	2 (0.6)	1 (0.3)
Vomiting[d]			
Any	3 (2.8)	6 (1.9)	2 (0.7)
Mild	3 (2.8)	5 (1.6)	2 (0.7)
Moderate	0	1 (0.3)	0
Severe	0	0	0
Diarrhea[e]			
Any	7 (6.5)	33 (10.7)	29 (9.6)
Mild	7 (6.5)	27 (8.7)	23 (7.6)
Moderate	0	5 (1.6)	6 (2.0)
Severe	0	1 (0.3)	0
New or worsened muscle pain[c]			
Any	28 (26.2)	94 (30.4)	54 (18.0)
Mild	12 (11.2)	47 (15.2)	30 (10.0)
Moderate	16 (15.0)	47 (15.2)	24 (8.0)
Severe	0	0	0

	Pfizer-BioNTech COVID-19 Vaccine, Bivalent*		
	12 Through 17 Years of Age N[a]=107 n[b] (%)	**18 Through 55 Years of Age N[a]=309 n[b] (%)**	**56 Years of Age and Older N[a]=300[†] n[b] (%)**
New or worsened joint pain[c]			
Any	13 (12.1)	46 (14.9)	36 (12.0)
Mild	9 (8.4)	21 (6.8)	20 (6.7)
Moderate	4 (3.7)	25 (8.1)	16 (5.3)
Severe	0	0	0
Use of antipyretic or pain medication[f]	36 (33.6)	105 (34.0)	74 (24.7)

Note: Adverse reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from day of vaccination (Day 1) through Day 7 after the study vaccination.

* Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original) and Omicron variant lineages BA.4 and BA.5 (Omicron BA.4/BA.5).

† N = 301 for fever, fatigue and diarrhea in participants 56 years of age and older.

a. N = Number of participants reporting at least 1 yes or no response for the specified adverse reaction after the study vaccination.

b. n = Number of participants with the specified adverse reaction.

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. 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.

f. 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 48 (6.6%) participants who received a second booster dose through 1 month after the booster dose. Lymphadenopathy occurred in 7 (1.0%) participants.

Concomitant Administration of COMIRNATY With Influenza Vaccine in Individuals 18 Through 64 Years of Age

In Study 8 (NCT05310084), a Phase 3 study, participants 18 through 64 years of age who received COMIRNATY concomitantly administered with Influenza Vaccine (Afluria Quadrivalent) followed 1 month later by saline placebo (n = 564) were compared to participants who received influenza vaccine with saline placebo followed 1 month later by COMIRNATY (n = 564).

Demographic characteristics in Study 8 among the participants in the concomitant administration and separate administration groups were similar with regard to age, sex, race, and ethnicity. Among the 564 participants in the concomitant administration group, the median age was 39.0 years (range 18 through 64 years of age), 36.9% were male and 63.1% were female, 79.1% were White, 12.9% were Asian, and 0.9% were Hispanic/Latino.

Solicited local and systemic adverse reactions were reported more frequently by participants who received COMIRNATY concomitantly with influenza vaccine, compared to participants who received COMIRNATY alone. The most common adverse reactions reported in the concomitant administration group and after COMIRNATY alone were injection site pain (COMIRNATY injection site) (86.2% and 84.4%, respectively), fatigue (64.0% and 50.8%, respectively), and headache (47.2% and 37.8%, respectively).

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, Pfizer-BioNTech COVID-19 Vaccine and Pfizer-BioNTech COVID-19 Vaccine, Bivalent. 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 vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)
Nervous System Disorders: syncope, dizziness

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

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

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

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

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

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

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

A developmental toxicity study has been performed in female rats administered the equivalent of a single human dose of COMIRNATY [encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain

(Original)] on 4 occasions, twice prior to mating and twice during gestation. These studies revealed no evidence of harm to the fetus due to the vaccine *(see Animal Data)*.

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk

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

Data

Animal Data

In a developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of COMIRNATY [encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original)] was administered to female rats by the intramuscular route on 4 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.

8.2 Lactation

Risk Summary

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

8.4 Pediatric Use

Safety and effectiveness of COMIRNATY in individuals 12 through 17 years of age is based on safety and effectiveness data in this age group and in adults *[see Adverse Reactions (6) and Clinical Studies (14.1)]*.

The safety and effectiveness of COMIRNATY in individuals younger than 12 years of age have not been established. Evidence from clinical studies in individuals 6 months through 4 years of age strongly suggests that a single dose of COMIRNATY would be ineffective in individuals younger than 6 months of age.

8.5 Geriatric Use

Of the total number of COMIRNATY recipients in Study 2 as of March 13, 2021 (N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. In Study 4, of 5081 recipients who received COMIRNATY as the first booster dose, 23.1% (n = 1175) were 65 years of age and older and 5.2% (n = 265) were 75 years of age and older. In Study 5, of 726 recipients who received Pfizer-BioNTech COVID-19 Vaccine, Bivalent as the second booster dose, 21.9% (n = 159) were 65 years of age and older and 4.8% (n = 35) were 75 years of age and older. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

8.6 Immunocompromised Individuals

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

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use.

Each 0.3 mL dose of COMIRNATY (2024-2025 Formula) is formulated to contain 30 mcg of a nucleoside-modified messenger RNA (modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2 Omicron variant lineage KP.2.

Each 0.3 mL dose of COMIRNATY also includes the following ingredients:
lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate),
0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide,
0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.19 mg cholesterol), 0.06 mg tromethamine,
0.4 mg tromethamine hydrochloride, and 31 mg sucrose.

COMIRNATY does not contain preservatives.

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.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The nucleoside-modified mRNA in COMIRNATY is formulated in lipid particles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

COMIRNATY has not been evaluated for the potential to cause carcinogenicity, genotoxicity, or impairment of male fertility. In a developmental toxicity study in rats with COMIRNATY [encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original)] there were no vaccine-related effects on female fertility *[see Use in Specific Populations (8.1)]*.

14 CLINICAL STUDIES

14.1 Immunogenicity Data Supporting the Use of a Single Dose of COMIRNATY in Seropositive, Vaccine-Naïve Individuals

In a post-hoc analysis in a subset of participants 18 through 85 years of age enrolled in Study 7 (NCT05004181), immunogenicity of a single 30 mcg dose of a Pfizer-BioNTech bivalent COVID-19 vaccine

containing equal quantities of modRNA encoding the viral spike (S) glycoprotein for the Alpha and Delta SARS-CoV-2 variants [not authorized or approved in the U.S., hereafter referred to as bivalent vaccine (Alpha and Delta)] was assessed in COVID-19 vaccine-naïve participants with evidence of prior SARS-CoV-2 infection (n = 262) compared to participants without prior SARS-CoV-2 infection who received 2 doses of COMIRNATY in Study 2 (n = 275). Among Study 7 participants, 253 were from study sites in South Africa and 9 were from study sites in the U.S. The immunogenicity of the bivalent Alpha and Delta vaccine is relevant to COMIRNATY because these vaccines are manufactured using the same process with differences only in the encoded spike proteins.

Table 10 presents demographic characteristics for participants in the immunogenicity analysis set.

Table 10: Demographic Characteristics – Subset of Participants from Study 7 and Study 2 – Reference Strain Neutralization – Immunogenicity Analysis Set

	Study 7 Single Dose of Bivalent Vaccine (Alpha and Delta) With Evidence of Prior Infection (N[a]=262) N[b] (%)	**Study 2 Two Doses of COMIRNATY* Without Evidence of Infection (N[a]=275) N[b] (%)**
Sex		
Male	109 (41.6)	113 (41.1)
Female	153 (58.4)	162 (58.9)
Age at Vaccination (Years)		
Mean (SD)	42.9 (16.21)	42.7 (16.08)
Median	41.0	40.0
Min, max	(18,84)	(18, 84)
Race		
White	4 (1.5)	230 (83.6)
Black or African American	169 (64.5)	25 (9.1)
American Indian or Alaska Native	0	2 (0.7)
Asian	0	7 (2.5)
Other[c]	89 (34.0)	11 (4.0)
Ethnicity		
Hispanic or Latino	5 (1.9)	83 (30.2)
Not Hispanic or Latino	255 (97.3)	192 (69.8)
Not reported	2 (0.8)	0

* 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. This value is the denominator for the percentage calculations.
b. n = Number of participants with the specified characteristic.
c. Includes multiracial and not reported.

The objective of this analysis was to assess noninferiority with respect to level of 50% neutralizing titer (NT50) and to the seroresponse rate to the reference strain induced by a single dose of the bivalent Alpha and Delta vaccine in COVID-19 vaccine-naïve participants with evidence of prior infection relative to participants without evidence of SARS-CoV-2 infection who received 2 doses of COMIRNATY.

Noninferiority of the reference strain immune response with respect to level of NT50 was met, as the lower bound of the 2-sided 95% CI for the geometric mean ratio (GMR) was >0.67 (Table 11). Noninferiority of the seroresponse rate to the reference strain was not met, as the lower bound of the 2-sided 95% CIs for the

difference in seroresponse rate of reference strain was -10.04%, below the noninferiority margin of -10% (Table 12).

Table 11: Geometric Mean Ratios – Single Dose of Bivalent Vaccine (Alpha and Delta) in Vaccine-Naïve Participants from Study 7 With Evidence of Prior SARS-CoV-2 Infection Compared to 2 Doses of COMIRNATY in a Subset of Participants from Study 2 Without Evidence of SARS-CoV-2 Infection – Reference Strain Neutralization – Immunogenicity Analysis Set

	Study 7 Single Dose of Bivalent Vaccine (Alpha and Delta) With Evidence of Prior Infection[a] 3 Weeks After Dose 1[b]		Study 2 Two Doses of COMIRNATY* Without Evidence of Infection[c] 1 Month After Dose 2[b]		Bivalent Vaccine (Alpha and Delta) With Evidence of Prior Infection[b] / COMIRNATY Without Evidence of Infection[c]
SARS-CoV-2 Neutralization Assay	**n[d]**	**GMT[e] (95% CI[e])**	**n[d]**	**GMT[e] (95% CI[e])**	**GMR[f] (95% CI[f])**
Reference strain - NT50 (titer)[g]	262	17404.2 (15485.1, 19561.1)	275	1328.1 (1183.1, 1491.0)	13.12 (11.14, 15.45)[h]

Abbreviations: CI = confidence interval; GMR = geometric mean ratio; GMT = geometric mean titer; LLOQ = lower limit of quantitation; N-binding = SARS-CoV-2 nucleoprotein–binding; 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. Participants with positive N-binding antibody result at baseline, positive NAAT result prior to vaccination, or medical history or adverse event of COVID-19 prior to vaccination.

b. Protocol-specified timing for blood sample collection.

c. Participants who had no serological or virological evidence (up to the 1-month post–Dose 2 blood sample collection) of past SARS-CoV-2 infection (i.e., negative N-binding antibody [serum] result at the Dose 1 and 1-month post–Dose 2 visits, negative NAAT [nasal swab] at the Dose 1 and Dose 2 visits, and any unscheduled visit [up to the 1-month post–Dose 2 blood sample collection]) and had no medical history of COVID-19 were included in the analysis.

d. n = Number of participants with valid and determinate assay results for the specified assay at the given sampling time point.

e. 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.

f. GMRs and 2-sided 95% CIs were calculated by exponentiating the difference of LS means and corresponding CIs based on the analysis of logarithmically transformed neutralizing titers using a linear regression model with terms of age, sex, and group. Assay results below the LLOQ were set to 0.5 × LLOQ.

g. SARS-CoV-2 NT50 were determined using a validated 384-well assay platform (original strain [USA-WA1/2020, isolated in January 2020]).

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

Table 12: Difference in Percentages of Participants With Seroresponse – Bivalent Vaccine (Alpha and Delta) in Vaccine-Naïve Participants from Study 7 With Evidence of Prior SARS-CoV-2 Infection Compared to 2 Doses of COMIRNATY in a Subset of Participants from Study 2 Without Evidence of Prior SARS-CoV-2 Infection– Reference Strain Neutralization – Immunogenicity Analysis Set

	Study 7 Bivalent Vaccine (Alpha and Delta) With Evidence of Prior Infection[a] 3 Weeks After Dose 1[b]		Study 2 COMIRNATY* Without Evidence of Prior Infection[c] 1 Month After Dose 2[b]		Bivalent Vaccine (Alpha and Delta) With Evidence of Prior Infection[a] Minus COMIRNATY Without Evidence of Prior Infection[c]	
SARS-CoV-2 Neutralization Assay	**N[d]**	**n[e] (%) (95% CI[f])**	**N[d]**	**n[e] (%) (95% CI[f])**	**Difference %[g]**	**95% CI[h]**
Reference strain – NT50 (titer)[i]	260	223 (85.8) (80.9, 89.8)	275	249 (90.5) (86.5, 93.7)	-4.55	(-10.04, 0.83)[j]

Abbreviations: CI = confidence interval; N-binding = SARS-CoV-2 nucleoprotein–binding; 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. Participants with positive N-binding antibody result at baseline, positive NAAT result prior to vaccination, or medical history or adverse event of COVID-19 prior to vaccination.

b. Protocol-specified timing for blood sample collection.

c. Participants who had no serological or virological evidence (up to the 1-month post–Dose 2 blood sample collection) of past SARS-CoV-2 infection (i.e., negative N-binding antibody [serum] result at the Dose 1 and 1-month post–Dose 2 visits, negative NAAT [nasal swab] at the Dose 1 and Dose 2 visits, and any unscheduled visit [up to the 1-month post–Dose 2 blood sample collection]) and had no medical history of COVID-19 were included in the analysis.

d. N = number of participants with valid and determinate assay results for the specified assay at both the pre-vaccination time point and the given sampling time point. This value is the denominator for the percentage calculation.

e. n = Number of participants with seroresponse for the given assay at the given sampling time point.

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

g. Adjusted difference in proportions estimated using minimum risk weights and stratified by sex and age group (18 to 55 years, 56 to 85 years), expressed as a percentage.

h. 2-Sided CI based on the Newcombe method stratified by sex and age group (18 to 55 years, 56 to 85 years) with minimum risk weights for the difference in proportions.

i. SARS-CoV-2 NT50 were determined using a validated 384-well assay platform (original strain [USA-WA1/2020, isolated in January 2020]).

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

14.2 Primary Series With COMIRNATY – Efficacy in Participants 16 Years of Age and Older

Study 2 is an ongoing, multicenter, multinational, 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 through 15 years of age, 16 through 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 preexisting 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 HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

In Study 2, based on data accrued through March 13, 2021, approximately 44,000 participants 12 years of age and older were randomized equally and received 2 doses of COMIRNATY or placebo. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

Overall, among the total participants who received COMIRNATY or placebo, 51.4% or 50.3% were male and 48.6% or 49.7% were female, 79.1% or 79.2% were 16 through 64 years of age, 20.9% or 20.8% were 65 years of age and older, 81.9% or 82.1% were White, 9.5% or 9.6% were Black or African American, 1.0% or 0.9% were American Indian or Alaska Native, 4.4% or 4.3% were Asian, 0.3% or 0.2% Native Hawaiian or other Pacific Islander, 25.6% or 25.4% were Hispanic/Latino, 73.9% or 74.1% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 46.0% or 45.7% had comorbidities [participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least 1 of the Charlson comorbidity index category or body mass index (BMI) $\geq$30 kg/m^2], respectively. The mean age at vaccination was 49.8 or 49.7 years and median age was 51.0 or 51.0 in participants who received COMIRNATY or placebo, respectively.

Efficacy Against COVID-19

The population for the analysis of the protocol pre-specified primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the COMIRNATY group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. The population in the protocol pre-specified primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.3, 97.6), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the COMIRNATY group compared to 162 COVID-19 cases in the placebo group.

The population for the updated vaccine efficacy analysis included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2. There were 12,796 (60.8%) participants in the COMIRNATY group and 12,449 (58.7%) in the placebo group followed for $\geq$4 months after Dose 2 in the blinded placebo-controlled follow-up period.

SARS-CoV-2 variants of concern identified from COVID-19 cases for this age group from this data cutoff include B.1.1.7 (Alpha) and B.1.351 (Beta). Representation of identified variants among cases in vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

The updated vaccine efficacy information is presented in Table 13.

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

First COVID-19 occurrence from 7 days after Dose 2 in participants Without evidence of prior SARS-CoV-2 infection*			
Subgroup	**COMIRNATY† Na=19,993 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=20,118 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
All participants	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
First COVID-19 occurrence from 7 days after Dose 2 in participants With or without* evidence of prior SARS-CoV-2 infection			
Subgroup	**COMIRNATY† Na=21,047 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=21,210 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and 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).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2) and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† 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.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

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

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported the benefit of COMIRNATY in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 14) as 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.

Table 14: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† or Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence			
	COMIRNATY§ Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	COMIRNATY§ Cases n1[a] Surveillance Time[b] (n2[c])	**Placebo Cases n1[a] Surveillance Time[b] (n2[c])**	**Vaccine Efficacy % (95% CI[d])**
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and 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).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2) and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing high flow oxygen, noninvasive ventilation, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

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

a. n1 = Number of participants meeting the endpoint definition.

b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

c. n2 = Number of participants at risk for the endpoint.

d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

14.3 Primary Series With COMIRNATY – Efficacy and Immunogenicity in Adolescents 12 Through 15 Years of Age

A descriptive efficacy analysis of Study 2 has been performed in 2,260 adolescents 12 through 15 years of age evaluating confirmed COVID-19 cases accrued up to a data cutoff date of September 2, 2021.

The vaccine efficacy information in adolescents 12 through 15 years of age is presented in Table 15.

Table 15: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2: Without Evidence of Infection and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period, Adolescents 12 Through 15 Years of Age Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in adolescents 12 through 15 years of age without evidence of prior SARS-CoV-2 infection*			
	COMIRNATY† N[a]=1057 Cases n1[b] Surveillance Time[c] (n2[d])	**Placebo N[a]=1030 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
Adolescents 12 through 15 years of age	0 0.343 (1043)	28 0.322 (1019)	100.0 (86.8, 100.0)
First COVID-19 occurrence from 7 days after Dose 2 in adolescents 12 through 15 years of age With or without evidence of prior SARS-CoV-2 infection			
	COMIRNATY† N[a]=1119 Cases n1[b] Surveillance Time[c] (n2[d])	**Placebo N[a]=1109 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
Adolescents 12 through 15 years of age	0 0.362 (1098)	30[f] 0.345 (1088)	100.0 (87.5, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and 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).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2) and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† 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.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1,000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

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

f. The only SARS-CoV-2 variant of concern identified from COVID-19 cases in this age group from this data cutoff was B.1.1.7 (Alpha).

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 demonstrated non-inferior immune responses (within 1.5-fold) comparing adolescents 12 through 15 years of age to participants 16 through 25 years of age who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after Dose 2 (Table 16).

Table 16: Summary of Geometric Mean Ratio for 50% Neutralizing Titer – Comparison of Adolescents 12 Through 15 Years of Age to Participants 16 Through 25 Years of Age (Immunogenicity Subset) – Participants Without Evidence of Infection up to 1 Month After Dose 2 – Dose 2 Evaluable Immunogenicity Population

		COMIRNATY*		12 Through 15 Years/ 16 Through 25 Years	
		12 Through 15 Years n[a]=190	16 Through 25 Years n[a]=170		
Assay	Time Point[b]	GMT[c] (95% CI[c])	GMT[c] (95% CI[c])	GMR[d] (95% CI[d])	Met Noninferiority Objective[e] (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)[f]	1 month after Dose 2	1253.6 (1117.7, 1406.1)	708.1 (625.9, 801.1)	1.77 (1.50, 2.09)	Y

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.

Note: Participants who had no serological or virological 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 SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit up to 1 month after Dose 2 were included in the analysis.

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

a. n = Number of participants with valid and determinate assay results for the specified assay at the given dose/sampling time point.

b. Protocol-specified timing for blood sample collection.

c. 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.

d. GMRs and 2-sided 95% CIs were calculated by exponentiating the mean difference of the logarithms of the titers (Group 1 [12 through 15 years of age] – Group 2 [16 through 25 years of age]) and the corresponding CI (based on the Student t distribution).

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

f. SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

14.4 Booster Dose With COMIRNATY – Immunogenicity of a First Booster Dose in Individuals 18 Through 55 Years of Age

Effectiveness of a booster dose of COMIRNATY was based on an assessment of 50% neutralizing antibody titers (NT50) against SARS-CoV-2 reference strain (USA_WA1/2020) in Study 2 participants 18 through 55 years of age (n = 200 – 212) who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after the booster vaccination. Analyses of NT50 1 month after the booster dose compared to 1 month after the primary series demonstrated noninferiority for both geometric mean ratio (GMR) [3.26 (97.5% CI: 2.76, 3.86)] and difference in seroresponse rates (percentage) [4.5% (97.5% CI: 1.0, 7.9)]. Seroresponse for a participant was defined as achieving a ≥4-fold rise in NT50 from baseline (before primary series).

14.5 Booster Dose With Pfizer-BioNTech COVID-19 Vaccine, Bivalent – Immunogenicity of a Second Booster Dose in Individuals 12 Years of Age and Older

In an analysis of a subset from Study 5, 105 participants 12 through 17 years of age, 297 participants 18 through 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 received a second booster dose of Pfizer-BioNTech COVID-19

Vaccine, Bivalent. In participants 12 through 17 years of age, 18 through 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 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 Pfizer-BioNTech COVID-19 Vaccine, Bivalent in Study 5 compared to a subset of participants from Study 4 who received a second booster dose of COMIRNATY demonstrated superiority of Pfizer-BioNTech COVID-19 Vaccine, Bivalent to COMIRNATY based on GMR and 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 17 and Table 18).

Analyses of NT50 against Omicron BA.4/BA.5 among participants 18 through 55 years of age compared to participants 56 years of age and older who received a second booster dose of Pfizer-BioNTech COVID-19 Vaccine, Bivalent in Study 5 demonstrated noninferiority of anti-Omicron BA.4/BA.5 response among participants 18 through 55 years of age to participants 56 years of age and older for both GMR and difference in seroresponse rates (Table 17 and Table 18).

The study also assessed the level of NT50 against the anti-Omicron BA.4/BA.5 and original SARS-CoV-2 strains pre-vaccination and 1 month after vaccination in participants who received a second booster dose (Table 19).

Table 17: Geometric Mean Titer Ratios – Study 5 COMIRNATY – Participants With or Without Evidence of Infection – Evaluable Immunogenicity Population

		Pfizer-BioNTech COVID-19 Vaccine, Bivalent* Study 5				COMIRNATY† Subset of Study 4		Age Group Comparison	Vaccine Group Comparison
		18 Through 55 Years of Age		56 Years of Age and Older		56 Years of Age and Older		Pfizer-BioNTech COVID-19 Vaccine, Bivalent* 18 Through 55 Years of Age/≥56 Years of Age	≥56 Years of Age Pfizer-BioNTech COVID-19 Vaccine, Bivalent* / COMIRNATY†
SARS-CoV-2 Neutralization Assay	Sampling Time Point[a]	n[b]	GMT[c] (95% CI[c])	n[b]	GMT[c] (95% CI[c])	n[b]	GMT[c] (95% CI[c])	GMR[d] (95% CI[d])	GMR[d] (95% CI[d])
Omicron BA.4/BA.5 - NT50 (titer)[e]	1 Month	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)[f]	2.91 (2.45, 3.44)[g]
Reference Strain – NT50 (titer)[e]	1 Month	-	-	286	16250.1 (14499.2, 18212.4)	289	10415.5 (9366.7, 11581.8)	-	1.38 (1.22, 1.56)[h]

Abbreviations: GMT = geometric mean titer; LLOQ = lower limit of quantitation; N-binding = SARS-CoV-2 nucleoprotein–binding; 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) and Omicron variant lineages BA.4 and BA.5 (Omicron BA.4/BA.5).

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

a. Protocol-specified timing for blood sample collection.

b. n = Number of participants with valid and determinate assay results for the specified assay at the given sampling time point.

c. 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.

d. GMRs and 2-sided 95% CIs were calculated by exponentiating the difference of LS means and corresponding CIs based on analysis of logarithmically transformed neutralizing titers using a linear regression model with terms of baseline neutralizing titer (log scale) and vaccine group or age group.

e. SARS-CoV-2 NT50 were determined using a validated 384-well assay platform (original strain [USA-WA1/2020, isolated in January 2020] and Omicron B.1.1.529 subvariant BA.4/BA.5).
f. Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67.
g. Superiority is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 1.
h. 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 18: Difference in Percentages of Participants With Seroresponse – Pfizer-BioNTech COVID-19 Vaccine, Bivalent from Study 5 and COMIRNATY from Subset of Study 4 – Participants With or Without Evidence of Infection – Evaluable Immunogenicity Population

SARS-CoV-2 Neutralization Assay	Sampling Time Point[a]	Pfizer-BioNTech COVID-19 Vaccine, Bivalent* Study 5				COMIRNATY† Subset of Study 4		Age Group Comparison	Vaccine Group Comparison ≥56 Years of Age
		18 Through 55 Years of Age		56 Years of Age and Older		56 Years of Age and Older		Pfizer-BioNTech COVID-19 Vaccine, Bivalent* 18 Through 55 Years of Age/≥56 Years of Age	Pfizer-BioNTech COVID-19 Vaccine, Bivalent* / COMIRNATY†
		n[b]	N[c] (%) (95% CI[d])	n[b]	N[c] (%) (95% CI[d])	n[b]	N[c] (%) (95% CI[d])	Difference[e] (95% CI[f])	Difference[e] (95% CI[f])
Omicron BA.4/BA.5 - NT50 (titer)[g]	1 Month	294	180 (61.2) (55.4, 66.8)	282	188 (66.7) (60.8, 72.1)	273	127 (46.5) (40.5, 52.6)	-3.03 (-9.68, 3.63)[h]	26.77 (19.59, 33.95)[i]

Abbreviations: LLOQ = lower limit of quantitation; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Seroresponse is defined as achieving a ≥4-fold rise from baseline. If the baseline measurement is below the LLOQ, a postvaccination assay result ≥4 × LLOQ is considered a seroresponse.
* Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original) and Omicron variant lineages BA.4 and BA.5 (Omicron BA.4/BA.5).
† Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original).
a. Protocol-specified timing for blood sample collection.
b. N = Number of participants with valid and determinate assay results for the specified assay at both the pre-vaccination time point and the given sampling time point. This value is the denominator for the percentage calculation.
c. n = Number of participants with seroresponse for the given assay at the given sampling time point.
d. Exact 2-sided CI, based on the Clopper and Pearson method.
e. Difference in proportions, expressed as a percentage.
f. 2-Sided CI based on the Miettinen and Nurminen method stratified by baseline neutralizing titer category (<median, ≥ median) for the difference in proportions. The median of baseline neutralizing titers was calculated based on the pooled data in 2 comparator groups.
g. SARS-CoV-2 NT50 were determined using a validated 384-well assay platform (Omicron B.1.1.529 subvariant BA.4/BA.5).
h. Noninferiority is declared if the lower bound of the 2-sided 95% CI for the difference in percentages of participants with seroresponse is >-10%.
i. 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 19: Geometric Mean Titers – Pfizer-BioNTech COVID-19 Vaccine, Bivalent Groups Subset of Study 5 – Prior to and 1 Month After Second Booster – Participants 12 Years of Age and Older – Evaluable Immunogenicity Population

SARS-CoV-2 Neutralization Assay	Sampling Time Point[a]	Pfizer-BioNTech COVID-19 Vaccine, Bivalent*					
		12 Through 17 Years of Age		18 Through 55 Years of Age		56 Years of Age and Older	
		n[b]	GMT[c] (95% CI[c])	n[b]	GMT[c] (95% CI[c])	n[b]	GMT[c] (95% CI[c])
Omicron BA.4/BA.5 - NT50 (titer)[d]	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)
Reference strain - NT50 (titer)[d]	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)

Abbreviations: GMT = geometric mean titer; LLOQ = lower limit of quantitation; N-binding = SARS-CoV-2 nucleoprotein–binding; 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) and Omicron variant lineages BA.4 and BA.5 (Omicron BA.4/BA.5).

a. Protocol-specified timing for blood sample collection.

b. n = Number of participants with valid and determinate assay results for the specified assay at the given sampling time point.

c. 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.

d. SARS-CoV-2 NT50 were determined using a validated 384-well assay platform (original strain [USA-WA1/2020, isolated in January 2020] and Omicron B.1.1.529 subvariant BA.4/BA.5).

14.6 Concomitant Administration of COMIRNATY With Influenza Vaccine in Individuals 18 Through 64 Years of Age

In Study 8 (NCT05310084), a Phase 3 multicenter, randomized, observer-blind study, 1,134 participants 18 through 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 concomitantly administered with Influenza Vaccine (Afluria Quadrivalent) followed 1 month later by placebo (Group 1, n = 568) or influenza vaccine with placebo followed 1 month later with COMIRNATY (Group 2, n = 566).

Full-length spike (S)-binding IgG responses to COMIRNATY and influenza strain-specific hemagglutination inhibition (HAI) titers were assessed 1-month post-vaccination in each group.

The non-inferiority criteria (lower bound of the 2-sided 95% CI > 0.67) for the comparison of concomitant administration versus separate administration were met. The GMC ratio of full-length S-binding IgG levels of SARS-CoV-2 Wuhan-Hu-1 strain (Original) (Group 1/Group 2) was 0.83 [95% CI: 0.77, 0.89]. The GMT ratio (Group 1/Group 2) for the 4 strain-specific influenza HAI titers were H1N1 A/Victoria: 0.95 [95% CI: 0.83, 1.09]; H3N2 A/Darwin: 0.96 [95% CI: 0.85, 1.09]; B/Austria: 0.89 [95% CI: 0.77, 1.04]; B/Phuket: 1.00 [95% CI: 0.89, 1.13].

SARS-CoV-2 Wuhan-Hu-1 strain (Original) neutralizing GMTs were descriptively assessed in a subset of participants, 100 participants from Group 1 and 100 participants from Group 2.

The SARS-CoV-2 neutralization assay (NT50 titer) GMTs increased from baseline to 1 month after vaccination with COMIRNATY from 2755.9 to 6773.9 in Group 1 and from 2421.2 to 7886.6 in Group 2.

15 REFERENCES

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

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY is a suspension for intramuscular injection and is supplied as follows:

- Glass Prefilled Syringes
  - Carton of 10 single dose prefilled syringes: NDC 0069-2432-10
  - Single dose prefilled syringe: NDC 0069-2432-01

- Vials
  - Carton of 10 single dose vials: NDC 0069-2403-10
  - Single dose vial: NDC 0069-2403-01

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.

Storage Prior to Use

Glass Prefilled Syringes

Store COMIRNATY glass prefilled syringes refrigerated at 2°C to 8°C (35°F to 46°F). DO NOT FREEZE.

The total time out of refrigeration (at temperatures between 8°C and 25°C (46°F and 77°F)) must not exceed 12 hours.

Single Dose Vials

COMIRNATY single dose vials may arrive frozen at ultra-cold conditions in thermal containers with dry ice. Once received, frozen vials may be immediately transferred to the refrigerator at 2ºC to 8ºC (35ºF to 46ºF), thawed and stored for up to 10 weeks. The 10-week refrigerated expiry date should be recorded on the carton at the time of transfer. Cartons of 10 single dose vials may take up to 2 hours to thaw at this temperature. Once thawed, they should not be refrozen.

Alternatively, single dose vials may be stored in an ultra-low temperature freezer at -90ºC to -60ºC (-130ºF to -76ºF). Do not store vials at -25°C to -15°C (-13°F to 5°F).

Cartons of COMIRNATY single dose vials may be received at 2°C to 8°C (35ºF to 46ºF), and they should be stored at 2°C to 8°C (35ºF to 46ºF). Check that the carton has been previously updated to reflect the 10-week refrigerated expiry date.

The total time out of refrigeration (at temperatures between 8°C and 25°C (46°F and 77°F)) must not exceed 12 hours.

17 PATIENT COUNSELING INFORMATION

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

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

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

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

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LAB-1490-11.0

US Govt. License No. 2229

INFORMATION FOR RECIPIENTS AND CAREGIVERS
COMIRNATY (Cuh-mir'-na-tee)
(COVID-19 VACCINE, mRNA)
(2024-2025 Formula)

This summary is not intended to take the place of talking with your healthcare provider. If you have questions or would like more information, please talk with your healthcare provider.

What is COMIRNATY?
COMIRNATY is a vaccine for use in people 12 years of age and older to protect against COVID-19.

COMIRNATY may not protect all people who receive the vaccine.

COMIRNATY does not contain SARS-CoV-2, the virus that causes COVID-19. COMIRNATY cannot give you COVID-19.

Who should not get COMIRNATY?
You should not get COMIRNATY if you had:

- a severe allergic reaction after a previous dose of COMIRNATY or any Pfizer-BioNTech COVID-19 vaccine
- a severe allergic reaction to any ingredient in these vaccines (see **What are the ingredients in COMIRNATY?**).

Before getting COMIRNATY, tell your vaccination provider about all of your medical conditions, including if you:

- have any allergies
- had a severe allergic reaction after receiving a previous dose of any COVID-19 vaccine
- have had myocarditis (inflammation of the heart muscle) or pericarditis (inflammation of the lining outside the heart)
- have a fever
- have a bleeding disorder or are on a blood thinner
- are immunocompromised or are on a medicine that affects your immune system
- are pregnant or plan to become pregnant
- are breastfeeding
- have received another COVID-19 vaccine
- have ever fainted in association with an injection

How is COMIRNATY given?
COMIRNATY is given as an injection into the muscle.

What are the risks of COMIRNATY?
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 1 hour after getting a dose. For this reason, your vaccination provider may ask you to stay at the place where you received your vaccine for monitoring after vaccination. Signs of a severe allergic reaction can include:

- Difficulty breathing
- Swelling of your face and throat
- A fast heartbeat
- A bad rash all over your body
- Dizziness and weakness

Myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) have occurred in some people who have received mRNA COVID-19 vaccines, including COMIRNATY and Pfizer-BioNTech COVID-19 vaccines. Myocarditis and pericarditis following administration of mRNA COVID-19 vaccines have occurred most commonly in males 12 years through 24 years of age. In most of these people, symptoms began within a week following vaccination. Based on available data, estimated rates of myocarditis and/or pericarditis from 1 through 7 days after getting a dose of the 2023-2024 Formula of mRNA COVID-19 vaccines were approximately 8 cases per million doses in people 6 months through 64 years of age and approximately 27 cases per million doses in males 12 years through 24 years of age.

In most people who have had myocarditis or pericarditis after receiving an mRNA COVID-19 vaccine, symptoms have gone away a few days after receiving treatment with medicines used to reduce inflammation.

In a study, follow-up information was collected on people who developed myocarditis after receiving the original formula of a COVID-19 vaccine; most people had received an mRNA COVID-19 vaccine. Some people in the study reported having heart symptoms approximately 3 months after developing myocarditis. Some people in the study had heart MRIs (scans that show detailed images of the heart muscle) initially after developing myocarditis and again approximately 5 months later. The initial and follow-up heart MRIs commonly showed signs of injury to the heart muscle, with improvement over time in most people. It is not known if these heart MRI findings might predict long-term heart effects of myocarditis. Studies are underway to find out if there are long-term heart effects in people who have had myocarditis after receiving an mRNA COVID-19 vaccine.

You should seek medical attention right away if you or your child have any of the following symptoms after receiving COMIRNATY, particularly during the 2 weeks after receiving a dose of the vaccine:

- Chest pain
- Shortness of breath
- Feelings of having a fast-beating, fluttering, or pounding heart

These could be symptoms of myocarditis or pericarditis.

Side effects that have been reported with COMIRNATY or Pfizer-BioNTech COVID-19 vaccines include:

- Severe allergic reactions
- Non-severe allergic reactions such as rash, itching, hives, or swelling of the face
- Myocarditis (inflammation of the heart muscle)

- Pericarditis (inflammation of the lining outside the heart)
- Injection site reactions: pain, swelling, redness, arm pain
- General side effects: tiredness, headache, muscle pain, chills, joint pain, fever, nausea, feeling unwell, swollen lymph nodes (lymphadenopathy), decreased appetite, diarrhea, vomiting, dizziness
- Fainting in association with injection of the vaccine

These may not be all the possible side effects of COMIRNATY. Ask your healthcare provider about any side effects that concern you.

Report vaccine side effects to FDA/CDC Vaccine Adverse Event Reporting System (VAERS). The VAERS toll-free number is 1-800-822-7967 or report online to https://vaers.hhs.gov/reportevent.html.

In addition, you can report side effects to Pfizer Inc. at 1-800-438-1985 or www.pfizersafetyreporting.com.

What if you are pregnant or breastfeeding?
If you are pregnant or breastfeeding, discuss your options with your healthcare provider.

What are the ingredients in COMIRNATY?
COMIRNATY contains the following ingredients:

- messenger ribonucleic acid (mRNA)
- lipids (((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 2 [(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 1,2-distearoyl-sn-glycero-3-phosphocholine, and cholesterol)
- tromethamine
- tromethamine hydrochloride
- sucrose

COMIRNATY does not contain preservatives.

This Information for Recipients and Caregivers may have been updated. For the most recent Information for Recipients and Caregivers, please visit https://dailymed.nlm.nih.gov/dailymed/.

If you have questions, talk to your healthcare provider or visit www.COMIRNATY.com or call 1-877-VAX-CO19 (1-877-829-2619).

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