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
Initial U.S. Approval: YYYY

---------- **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 16 years of age and older (1)

---------- **DOSAGE AND ADMINISTRATION** ----------
- For intramuscular injection only (2 2)
- COMIRNATY is administered intramuscularly as a series of 2 doses (0 3 mL each) 3 weeks apart (2 3)

---------- **DOSAGE FORMS AND STRENGTHS** ----------
Suspension for injection After preparation, 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** ----------
- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose (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 4)

---------- **ADVERSE REACTIONS** ----------
- In clinical studies of participants 16 through 55 years of age, the most commonly reported adverse reactions (≥10%) 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%)~~ (6 1)
- In clinical studies of participants 56 years of age and older, the most commonly reported adverse reactions (≥10%) 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%)~~ (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.

Revised: M/YYYY

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 16 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

2.1 Preparation for Administration

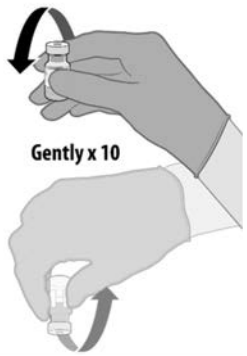
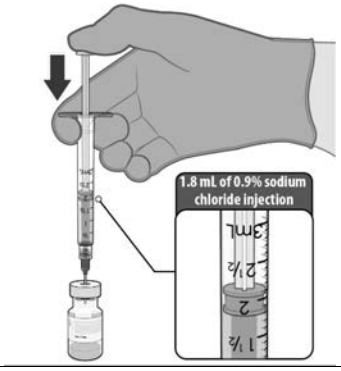
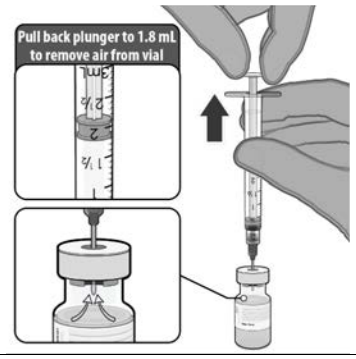
Prior to Dilution

- COMIRNATY Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (16)]*.
- Refer to thawing instructions in the panels below.

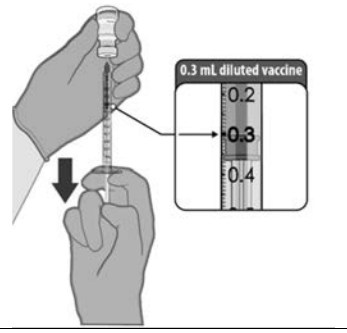
Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. Use the provided diluent or another sterile 0.9% Sodium Chloride Injection, USP as the diluent.
    - Provided diluent vials are single-use only; discard after 1.8 mL is withdrawn.
    - If another sterile 0.9% Sodium Chloride Injection, USP is used as the diluent, discard after 1.8 mL is withdrawn.
    - Do not use diluent vials to dilute multiple vials of COMIRNATY.
- After dilution, 1 vial of COMIRNATY contains 6 doses of 0.3 mL each.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of COMIRNATY before dilution either by: o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes.

	• Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake.</u> • Inspect the liquid in the vaccine vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. • Withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.
	• Equalize vial pressure before removing the needle from the vaccine vial by withdrawing 1.8 mL air into the empty diluent syringe.

	• Gently invert the vial containing COMIRNATY 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the COMIRNATY vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• Withdraw 0.3 mL of COMIRNATY preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in a single vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

After dilution, vials of COMIRNATY contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle,

- each dose must contain 0.3 mL of vaccine.
- if the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- do not pool excess vaccine from multiple vials.

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 an off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.

Administer a single 0.3 mL dose of COMIRNATY intramuscularly.

2.3 Vaccination Schedule

COMIRNATY is administered intramuscularly as a series of 2 doses (0.3 mL each) 3 weeks apart.

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination series. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination series.

A third dose of the COMIRNATY (0.3 mL) administered at least 28 days following the first 2 doses of this vaccine is authorized for administration to individuals at least 16 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

3 DOSAGE FORMS AND STRENGTHS

COMIRNATY is a suspension for injection. After preparation, 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 the COMIRNATY *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY.

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk has been highest in adolescent and young adult males under 40 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of

symptoms. Information is not yet available about potential long-term sequelae. The CDC has published considerations 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 the COMIRNATY.

5.5 Limitation of Effectiveness

COMIRNATY may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 16 through 55 years of age 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%).

In clinical studies, the most commonly reported (≥10%) adverse reactions in participants 56 years of age and older 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%).

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.

The safety of COMIRNATY was evaluated in participants 16 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 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 C4591001 (Study 2) is a multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection and efficacy study that has enrolled approximately 44,047 participants (22,026 COMIRNATY; 22,021 placebo) 16 years of age or older (including 378 and 376 participants 16 through 17 years of age in the vaccine and placebo groups, respectively). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses. 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.

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

Participants 16 years and older in the reactogenicity subset were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

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

Table 1 and Table 2 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days following each dose of COMIRNATY and placebo in the subset of participants 16 through 55 years of age included in the safety population who were monitored for reactogenicity with an electronic diary.

Table 3 and Table 4 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of COMIRNATY and placebo for participants 56 years of age and older.

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 1: 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

	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] (%)
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
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 2: 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)
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)

	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] (%)
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

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 3: 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

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 4: 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

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

	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] (%)

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.

In clinical studies, the adverse reactions occurring in <10% of participants 16 through 55 years of age following any dose were injection site redness (9.5%), nausea (1.4%), malaise (0.7%), lymphadenopathy (0.5%), asthenia (0.4%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In clinical studies, the adverse reactions occurring in <10% of participants 56 years of age and older following any dose were nausea (1.0%), malaise (0.5%), asthenia (0.3%), lymphadenopathy (0.2%), lethargy (0.2%), decreased appetite (0.1%), hyperhidrosis (0.1%), and night sweats (0.1%).

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, in 99 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported in recipients who were followed for 1 month following post Dose 3.

Unsolicited Adverse Events

Overall 51.1% of participants in the COMIRNATY group and 51.4% of 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 8.1% and 5.9% with ≥6 months of blinded follow-up time in the COMIRNATY and placebo groups, respectively.

~~Upon issuance of the EUA for COMIRNATY, participants were unblinded to offer placebo participants COMIRNATY.~~ Participants were unblinded in a phased manner over a period of months to offer placebo participants COMIRNATY. At the time of the updated efficacy analysis 54.5% of participants originally randomized to COMIRNATY had ≥6 months of follow-up from Dose 2 and 47.5% of original placebo participants had follow-up time between ≥1 month to <2 months after Dose 2 of COMIRNATY. ~~Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began~~

~~in a phased manner for participants in the study.~~ Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

Adverse events occurred in 28.8% of vaccine recipients who had a follow-up period of at least 6 months after Dose 2; 1.6% of the recipients had serious adverse events.

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (COMIRNATY =12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) ~~at an incidence rate of 2.1 per 100 person-years among~~ COMIRNATY recipients and 117 (0.9%)~~2.4 per 100 person-years among~~ placebo recipients. In a similar analysis, in participants 56 years of age and older (COMIRNATY =8931, placebo = 8895), serious adverse events were reported by 165 (1.8%)~~at an incidence rate of 4.9 per 100 person-years among~~ COMIRNATY recipients and 151 (1.7%)~~4.6 per 100 person-years among~~ 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%)~~at an incidence rate of 6.6 per 100 person-years among~~ COMIRNATY recipients and 2 (2%)~~6.9 per 100 person-years among~~ placebo recipients.

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.

Non-Serious Adverse Events

Overall in Study 2 in which 12,995 participants 16 through 55 years of age received COMIRNATY and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 4396 (33.8%)~~at an incidence rate of 88.4 per 100 person- years among~~ participants who received COMIRNATY and 2136 (16.4%)~~43.5 per 100 person-years among~~ participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (COMIRNATY = 8931, placebo = 8895), all events, which include nonserious adverse events were reported by 2551 (28.6%)~~at an incidence rate of 75.7 per 100 person-years among~~ participants who received COMIRNATY and 1432 (16.1%)~~43.3 per 100 person-years among~~ participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 29 (29%)~~at an incidence rate of 95.8 per 100 person-years among~~ participants who received COMIRNATY and 15 (15%)~~52.0 per 100 person-years among~~ participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among COMIRNATY recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse

events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Table 3 and Table 4.

From Dose 1 up to the participant unblinding date, reports of lymphadenopathy were imbalanced with notably more cases in the COMIRNATY group (87) versus the placebo group (8).

Throughout the placebo-controlled safety follow-up period to date, 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. 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.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of COMIRNATY, including under Emergency Use Authorization. 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)

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 on four 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)*.

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Comirnaty during pregnancy. Women who are vaccinated with COMIRNATY during pregnancy are encouraged to enroll in the registry by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.

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 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 16 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 16 years of age have not been established.

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 = 4552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older *[see Clinical Studies (14.1)]*. No overall differences in safety or effectiveness were observed between these recipients and younger recipients.

8.6 Immunocompromised Use

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, safety and effectiveness of a third dose of COMIRNATY have been evaluated in persons that received solid organ transplants. The administration of a third dose of vaccine appears to be only moderately effective in increasing potentially protective antibody titers. Patients should still be counselled to maintain physical precautions to help prevent COVID-19. In addition, close contacts of immunocompromised persons should be vaccinated as appropriate for their health status.

11 DESCRIPTION

COMIRNATY (COVID-19 Vaccine, mRNA) is a sterile suspension for injection for intramuscular use. COMIRNATY is supplied as a frozen suspension in multiple dose vials ; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY

contains 30 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the 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 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain preservative.

The vial stoppers 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 there were no vaccine-related effects on female fertility *[see Use in Special Populations (8.1)]*.

14 CLINICAL STUDIES

Efficacy in Participants 16 Years of Age and Older

Formatted: Underline

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 16 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 50.35% were male and 48.6% or 49.75% were female, ~~75~~79.1% or ~~75~~79.21% were 16 through 64 years of age, 20.91% or 20.83% were 65 years of age and older, ~~16.1% or 16.3% were 65 through 74 years of age, 4.0% or 4.0% 75 years of age and~~

~~older, 82~~81.9% or 82.1% were White, ~~9~~8.5% or ~~9~~8.6% were Black or African American, ~~0.9~~1.0% or 0.9% were American Indian or Alaska Native, 4.~~4~~6% or 4.~~3~~5% were Asian, 0.3% or 0.~~1~~2% Native Hawaiian or other Pacific Islander, 2~~5~~4.~~9~~6% or 2~~5~~4.~~4~~6% were Hispanic/Latino, 7~~3~~4.~~6~~9% or 74.~~1~~8% were non-Hispanic/Latino, 0.5% or 0.5% did not report ethnicity, 4~~4~~6.~~6~~0% or 4~~5~~4.~~7~~4% 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 one of the Charlson comorbidity index category or body mass index (BMI) ≥30 kg/m^2], respectively. The mean age at vaccination was 4~~9~~8.~~8~~3 or 4~~9~~8.~~7~~2 years and median age was 5~~1~~0.0 or 5~~1~~0.0 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.

~~The vaccine efficacy information is presented in Table 5.~~

~~**Table 5: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population**~~

~~**First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection***~~			
~~**Subgroup**~~	~~**COMIRNATY N[a]=18,198 Cases n1[b] Surveillance Time[c] (n2[d])**~~	~~**Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])**~~	~~**Vaccine Efficacy % (95% CI)**~~
~~All participants[e]~~	~~8 2.214 (17,411)~~	~~162 2.222 (17,511)~~	~~95.0 (90.3, 97.6)[f]~~
~~16 to 64 years~~	~~7 1.706 (13,549)~~	~~143 1.710 (13,618)~~	~~95.1 (89.6, 98.1)[g]~~
~~65 years and older~~	~~1 0.508 (3848)~~	~~19 0.511 (3880)~~	~~94.7 (66.7, 99.9)[g]~~
~~65 to 74 years~~	~~1 0.406 (3074)~~	~~14 0.406 (3095)~~	~~92.9 (53.1, 99.8)[g]~~
~~75 years and older~~	~~0 0.102 (774)~~	~~5 0.106 (785)~~	~~100.0 (-13.1, 100.0)[g]~~
~~**First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection**~~			
~~**Subgroup**~~	~~**COMIRNATY N[a]=19,965 Cases n1[b] Surveillance Time[c] (n2[d])**~~	~~**Placebo N[a]=20,172 Cases n1[b] Surveillance Time[c] (n2[d])**~~	~~**Vaccine Efficacy % (95% CI)**~~
~~All participants[e]~~	~~9~~	~~169~~	~~94.6~~

	2.332 (18,559)	2.345 (18,708)	(89.9, 97.3)[f]
16 to 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1 0.530 (4044)	19 0.532 (4067)	94.7 (66.8, 99.9)[g]
65 to 74 years	1 0.424 (3239)	14 0.423 (3255)	92.9 (53.2, 99.8)[g]
75 years and older	0 0.106 (805)	5 0.109 (812)	100.0 (12.1, 100.0)[g]

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.

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

f. Two-sided credible interval for vaccine efficacy was calculated using a beta-binomial model with a beta (0.700102, 1) prior for θ=r(1-VE)/(1+r(1-VE)), where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.

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

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%. The case split was 8 COVID-19 cases in the BNT162b2 group compared to 162 COVID-19 cases in the placebo group. The 95% credible interval for the vaccine efficacy was 90.3% to 97.6%, indicating that the true vaccine efficacy is at least 90.3% with a 97.5% probability, which met the pre-specified success criterion.

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 ≥4 months after Dose 2 in the blinded placebo-controlled follow-up period.

The updated vaccine efficacy information is presented in Table 5~~6~~.

Table 5~~6~~: 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 participantsf	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

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 the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, geographies, and participants with medical comorbidities and obesity associated with high risk of severe COVID-19.

Efficacy Against Severe COVID-19

Efficacy analyses of secondary efficacy endpoints supported 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 ~~7~~6) 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 ~~6~~7: 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

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

Immunogenicity in Solid Organ Transplant Recipients

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, a single arm study has been conducted in

101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously. A third dose of COMIRNATY was administered to 99 of these individuals approximately 2 months after they had received a second dose. Among the 59 patients who had been seronegative before the third dose, 26 (44%) were seropositive at 4 weeks after the third dose. All 40 patients who had been seropositive before the third dose were still seropositive 4 weeks later. The prevalence of anti-SARS-CoV-2 antibodies was 68% (67 of 99 patients) 4 weeks after the third dose.

16 HOW SUPPLIED/STORAGE AND HANDLING

COMIRNATY Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 0069-1000-03) or 195 multiple dose vials (NDC 0069-1000-02). A 0.9% Sodium Chloride Injection, USP diluent is provided but shipped separately, and should be stored at controlled room temperature 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02).

After dilution, 1 vial contains 6 doses of 0.3 mL.

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

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of COMIRNATY Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -8090ºC to -60ºC (-112ºF 130ºF to -76ºF) until the expiry date printed on the label. Alternatively, vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned 1 time to the recommended storage condition of -8090ºC to -60ºC (-112ºF 130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which COMIRNATY arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned 1 time to the recommended storage condition of -8090ºC to -60ºC (-112ºF 130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of 1 or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

17 PATIENT COUNSELING INFORMATION

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

Inform vaccine recipient of the importance of completing the two dose vaccination series.

There is a pregnancy exposure registry for COMIRNATY. Encourage individuals exposed to COMIRNATY around the time of conception or during pregnancy to register by visiting https://mothertobaby.org/ongoing-study/covid19-vaccines/.
~~calling …..~~

Advise vaccine recipient 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 www.comirnatyglobal.com.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1448-0.~~3~~4

US Govt. License No. x