CLINICAL STUDY REPORT SYNOPSIS

Vaccine Name and Compound Number: PF-07302048

Report Title: Final Report: A Phase 3, Randomized, Observer-Blind Study to Evaluate the Safety, Tolerability, and Immunogenicity of Multiple Production Lots and Dose Levels of the Vaccine Candidate BNT162b2 Against COVID-19 in Healthy Participants 12 Through 50 Years of Age and the Safety, Tolerability, and Immunogenicity of BNT162b2 RNA-Based COVID-19 Vaccine Candidates as a Booster Dose in Healthy Participants 18 Through 50 Years of Age

Protocol Number: C4591017

Sponsor: BioNTech SE

Sponsor Agent: Pfizer Inc

Phase of Development: Phase 3

First Subject First Visit: 15 Feb 2021

Last Subject Last Visit: 22 Jul 2021

Serology Completion Date: Primary study IgG 17 Aug 2021

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Study Center(s): Refer to Appendix 16.1.4.1 for a list of investigators and sites involved in this study.

Date of Current Version: 06 January 2022

Date(s) of Previous Report(s): Not applicable

CLINICAL STUDY REPORT SYNOPSIS

OBJECTIVES

Primary and Secondary Study Objectives and Endpoints: The objectives and endpoints for primary and booster studies are listed in Table S1 and Table S2, respectively.

Table S1. Primary Study

Objectives	Estimands	Endpoints	Location of Results
Primary Immunogenicity – Lot Comparisons			
• To demonstrate that the immune responses induced by BNT162b2 are similar across the 3 US lots (Arms 1, 2, and 3) in participants without evidence of SARS-CoV-2 infection during the study.	In participants complying with the key protocol criteria (evaluable participants): • GMR from one US lot to another lot (Arm 1/Arm 2, Arm 1/Arm 3, and Arm 2/Arm 3) 1 month after Dose 2	• Full-length S-binding IgG concentrations	Final CSR
• To demonstrate that the immune response induced by the EU lot (Arm 4) of BNT162b2 is similar to the pooled US lots (Arms 1, 2, and 3) in participants without evidence of SARS-CoV-2 infection during the study.	In participants complying with the key protocol criteria (evaluable participants): • GMR from the EU lot (Arm 4) to the pooled US lots (Arm 4/pooled Arms 1, 2, and 3) 1 month after Dose 2	• Full-length S-binding IgG concentrations	Final CSR
Primary Immunogenicity – Dose Comparison			
• To demonstrate the noninferiority of the immune response to prophylactic BNT162b2 in participants receiving 20 µg compared to participants receiving the standard 30-µg dose (prepared from the same lot) without evidence of SARS-CoV-2 infection during the study.	In participants complying with the key protocol criteria (evaluable participants): • GMR, estimated by the ratio of the geometric mean of SARS-CoV-2 neutralizing titers in the 2 dose groups 1 month after Dose 2	• SARS-CoV-2 neutralizing titers	sCSR
Primary Safety			
• To evaluate the safety of BNT162b2 when administered on a 2-dose schedule in healthy participants 12 through 50 years of age.	In participants receiving at least 1 dose of study intervention from each vaccine group (individual and the pooled US lots, the EU lot, and the 20-µg dose), the percentage of participants reporting: • Local reactions for up to 7 days following each dose • Systemic events for up to 7 days following each dose • AEs and SAEs from Dose 1 to 1 month after Dose 2	• Local reactions (pain at the injection site, redness, and swelling) • Systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain) • AEs • SAEs	Final CSR

CLINICAL STUDY REPORT SYNOPSIS

Table S1. Primary Study

Objectives	Estimands	Endpoints	Location of Results
Secondary Immunogenicity			
• To describe the immune responses induced by different 30-µg dose lots of BNT162b2.	In evaluable participants from each vaccine group (individual and the pooled US lots, and the EU lot): • GMCs at baseline (before Dose 1) and 1 month after Dose 2 • GMFR from baseline (before Dose 1) to 1 month after Dose 2	• Full-length S-binding IgG concentrations	Final CSR
• To describe the immune responses induced by different doses of BNT162b2.	In evaluable participants from each vaccine group (20 µg and 30 µg from the same US lot): • GMTs at baseline (before Dose 1) and 1 month after Dose 2 • GMFR from baseline (before Dose 1) to 1 month after Dose 2	• SARS-CoV-2 neutralizing titers	sCSR

Abbreviations: AE = adverse event; CSR = clinical study report; EU = Europe; GMC = geometric mean concentration; GMFR = geometric mean fold rise; GMR = geometric mean ratio; GMT = geometric mean titer; IgG = immunoglobulin G; SAE = serious adverse event; SARS-COV-2 = severe acute respiratory syndrome coronavirus; sCSR = supplemental clinical study report; US = United States.
Note: "US lots" refers to lots of study vaccine containing drug substance manufactured in the US and the "EU lot" refers to the lot of study vaccine containing drug substance manufactured in Europe.

CLINICAL STUDY REPORT SYNOPSIS

Table S2. Booster Study

Objectives	Estimands	Endpoints	Location of Results
Primary Safety			
To evaluate the safety and tolerability profile of a third dose of study intervention (either BNT162b2 30 µg or BNT162b2 [B.1.351]* 30 µg) administered to participants (18 through 50 years of age) who received two 30-µg doses of BNT162b2, approximately 3 months after Dose 2.	In participants receiving the third dose of study intervention, the percentage of participants reporting: • Local reactions for up to 7 days following the booster dose • Systemic events for up to 7 days following the booster dose • AEs and SAEs from the booster dose to 1 month after the booster dose	• Local reactions (pain at the injection site, redness, and swelling) • Systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain) • AEs • SAEs	Final CSR
Primary Immunogenicity			
To describe the immune response induced by a third dose of study intervention (either BNT162b2 30 µg or BNT162b2 [B.1.351]* 30 µg).	In evaluable participants from each vaccine group (either BNT162b2 30 µg or BNT162b2 [B .1.351] 30 µg): • Geometric mean neutralizing titers at baseline (before Dose 1), 1 month after Dose 2, before Dose 3, and 1 week after and 1 month after Dose 3 • Geometric mean IgG concentrations at baseline (before Dose 1), 1 month after Dose 2, before Dose 3, and 1 week after and 1 month after Dose 3 • GMFRs from 1 month after Dose 2 to 1 week after and 1 month after Dose 3 and from before Dose 3 to 1 week after and 1 month after Dose 3 • The percentages of participants with seroresponse§ (based on neutralizing titers) to the reference strain at 1 month after Dose 2, before Dose 3, and 1 week after and 1 month after Dose 3 • The percentages of participants with seroresponse§ (based on neutralizing titers) to the B.1.351 variant strain at 1 month after Dose 2, before Dose 3, and 1 week after and 1 month after Dose 3	• SARS-CoV-2 reference-strain neutralizing titer† • SARS-CoV-2 B.1.351-strain neutralizing titer†† • Full-length S-binding IgG concentrations	sCSR

Abbreviations: AE = adverse event; GMFR = geometric mean fold rise; IgG = immunoglobulin G; LLOQ = lower limit of quantitation; S = spike protein; SAE = serious adverse event; SARS-COV-2 = severe acute respiratory syndrome coronavirus; sCSR = supplemental clinical study report.
* BNT162 (B.1.351). = BNT162b2s01 vaccine encoding for the full-length spike protein of South African–origin variant B.1.351 (formerly referred to as BNT162b2$_{SA}$ and BNT162b2.B.1.351).
† SARS-CoV-2 reference-strain neutralizing titers = neutralizing titers against SARS-CoV-2 USA-WA1/2020 virus.
†† SARS-CoV-2 B.1.351-strain neutralizing titers = neutralizing titers against SARS-CoV-2 virus with B.1.351 spike.
§ Seroresponse is defined as ≥4-fold increase from baseline (before Dose 1) to the specified time point. If the baseline measurement is below LLOQ, a postvaccination measurement of ≥4 × LLOQ is considered a seroresponse.

CLINICAL STUDY REPORT SYNOPSIS

METHODS

Study Design:

Primary Study: This was a Phase 3, randomized, observer-blind study to evaluate the safety, tolerability, and immunogenicity of 4 manufacturing lots of BNT162b2 at a 30-µg dose and an additional 20-µg dose arm of US Lot 1. BNT162b2 is a ribonucleic acid (RNA)-based coronavirus disease 2019 (COVID-19) vaccine, administered on a 2-dose schedule in healthy participants 12 through 50 years of age.

The study was conducted in the United States (US). Participants were randomized to 1 of 5 arms in a 2:2:2:1:2 ratio (Arm 1: Arm 2: Arm 3: Arm 4: Arm 5), where Arms 1, 2, and 3 contained US-manufactured drug substance for 30-µg dosing; Arm 4 contained Europe (EU)-manufactured drug substance for 30-µg dosing; and Arm 5 contained US-manufactured drug substance for 20-µg dosing (US Lot 1). In order to allow for balanced age representation across all arms, the randomization was stratified by age groups: 12 through 17, 18 through 30, and 31 through 50 years.

Booster Study: A booster study in which a subset of the adult participants (18 through 50 years of age) who each received two 30-µg doses of the designated US lot(s) were randomly assigned to 1 of 2 arms in a 1:1 ratio (Booster 1: Booster 2), where Booster 1 was BNT162b2 at 30 µg and Booster 2 was BNT162b2 (B.1.351) at 30 µg. The third dose was administered approximately 3 months after BNT162b2 Dose 2 of the primary study.

Inclusion/Exclusion Criteria:

Inclusion Criteria:

Age and Sex:

1. Primary study: Male or female participants between the ages of 12 and 50 years, inclusive, at Visit 1 (Day 1).

   Booster study: Male or female participants between the ages of 18 and 50 years, inclusive, at rerandomization.

Type of Participant and Disease Characteristics:

2. Participants who were willing and able to comply with all scheduled visits, treatment plan, laboratory tests, lifestyle considerations, and other study procedures.

CLINICAL STUDY REPORT SYNOPSIS

3. Healthy participants who were determined by medical history, physical examination (if required), and clinical judgment of the investigator to be eligible for inclusion in the study.

   Note: Healthy 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.

Informed Consent:

4. Capable of giving personal signed informed consent/have parent(s)/legal guardian capable of giving signed informed consent which includes compliance with the requirements and restrictions listed in the informed consent document (ICD) and in this protocol.

Exclusion Criteria:

Medical Conditions:

1. Other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation or, in the investigator's judgment, make the participant inappropriate for the study.

2. Known infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV).

3. History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the study intervention(s).

4. Previous clinical (based on COVID-19 symptoms/signs alone, if a severe acute respiratory syndrome coronavirus (SARS-CoV-2) nucleic acid amplification test [NAAT] result was not available) or microbiological (based on COVID-19 symptoms/signs and a positive SARS-CoV-2 NAAT result) diagnosis of COVID-19.

5. Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination.

6. Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection.

7. Women who were pregnant or breastfeeding.

Prior/Concomitant Therapy:

8. Primary study: Previous vaccination with any coronavirus vaccine.

CLINICAL STUDY REPORT SYNOPSIS

Booster study: Previous vaccination with any coronavirus vaccine outside of this study.

9. Receipt of medications intended to prevent COVID-19.

10. Individuals who received treatment with radiotherapy or immunosuppressive therapy, including cytotoxic agents or systemic corticosteroids (if systemic corticosteroids are administered for ≥14 days at a dose of ≥20 mg/day of prednisone or equivalent), eg, for cancer or an autoimmune disease, or planned receipt throughout the study. Inhaled/nebulized, intra-articular, intrabursal, or topical (skin or eyes) corticosteroids were permitted.

11. Receipt of blood/plasma products or immunoglobulin, from 60 days before study intervention administration or planned receipt throughout the study.

Prior/Concurrent Clinical Study Experience:

12. Participation in other studies involving study intervention within 28 days prior to study entry and/or during study participation.

13. Previous participation in other studies involving study intervention containing lipid nanoparticles (LNPs).

Other Exclusions:

14. Investigator site staff or Pfizer/BioNTech employees directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members.

Additional Exclusion Criteria Specific to the Booster Study:

1. Current febrile illness (body temperature ≥100.4°F [≥38.0°C]) or other acute illness within 48 hours before study intervention administration.

2. Receipt of any seasonal or pandemic influenza vaccine within 14 days, or any other nonstudy vaccine within 28 days, before study intervention administration.

3. Anticipated receipt of any seasonal or pandemic influenza vaccine within 14 days, or any other nonstudy vaccine within 28 days, after study intervention administration.

4. Receipt of short-term (<14 days) systemic corticosteroids. Inhaled/nebulized, intra-articular, intrabursal, or topical (skin or eyes) corticosteroids were permitted.

CLINICAL STUDY REPORT SYNOPSIS

Vaccines Administered: In the primary study, study intervention refers to BNT162b2, an RNA-based vaccine for immunization against COVID-19. All 4 production lots were administered at a 30-µg dose and 1 of the lots was also administered at a 20-µg dose, with the group names Arms 1, 2, 3, 4, and 5, respectively. The study evaluated a 2-dose (separated by 21 days) schedule in healthy participants 12 through 50 years of age.

In the booster study, study intervention refers to BNT162b2 or BNT162b2 (B.1.351), RNA-based vaccines for immunization against COVID-19. The study evaluated a single 30-µg dose administered 3 months after Dose 2 in the primary study to healthy participants 18 through 50 years of age.

Immunogenicity Evaluations: Serum samples were obtained for testing via the full-length spike protein (S)-binding immunoglobulin G (IgG)-concentration assay. SARS-CoV-2 neutralizing titers for the primary study and all immunogenicity in the booster study are not included in this clinical study report (CSR) and will be presented in the supplemental CSR (sCSR). Nasal (midturbinate) swabs were obtained in order to detect SARS-CoV-2 via reverse transcription–polymerase chain reaction (RT-PCR) (NAAT) as one of the determinations for participants to be included in the evaluable immunogenicity analysis.

Safety Evaluations: Participants used a reactogenicity e-diary and recorded local reactions, systemic events, and antipyretic medication usage for 7 days from the day of administration of the study intervention.

During the primary study, adverse events (AEs) and serious adverse events (SAEs) were collected during the study from the signing of the ICD through and including Visit 3 (1-month follow-up). In addition, any AEs occurring up to 48 hours after the blood draw and nasal swab collection at Visit 3 reported by the participant were collected.

During the booster study, AEs and SAEs were collected during the study from the signing of the ICD at Visit 4 through and including Visit 6 (1-month follow-up). In addition, any AEs occurring up to 48 hours after the blood draw and nasal swab collection at Visit 6 reported by the participant were collected.

Statistical Methods: For all the immunogenicity endpoints, the analysis was based on the evaluable immunogenicity population. An additional analysis was performed based on the all-available immunogenicity population if there was a 10% difference in sample size between the all-available immunogenicity population and the evaluable immunogenicity population.

CLINICAL STUDY REPORT SYNOPSIS

The 3 primary immunogenicity objectives are to be assessed sequentially in the following order to control studywise type I error: 1) similarity across the 3 US lots, 2) noninferiority of the 20-µg dose level to the 30-µg dose level, and 3) similarity between the EU lot and the pooled US lots. The primary immunogenicity objective of similarity between the EU lot and the pooled US lots is to be assessed only if the other 2 primary objectives are met. The second objective of noninferiority of the 20-µg dose level to the 30-µg dose level will be analyzed in the sCSR, so the third objective of similarity between the EU lot and the pooled US lots cannot be formally assessed in this CSR.

Model-Based: As the main approach in the primary study, the GMR and associated 95% confidence interval (CI) were calculated by exponentiating the difference in LS means and the corresponding CIs based on analysis of logarithmically transformed assay results using a linear regression model with terms of age and vaccine group.

Unadjusted: The GMRs in the primary study were calculated as the mean of the difference of logarithmically transformed assay results between 2 vaccine groups and exponentiating the mean. Two-sided CIs will be obtained by calculating CIs using Student's t-distribution for the mean difference of the logarithmically transformed assay results and exponentiating the confidence limits.

The analysis of S-binding IgG in the primary study presented in this CSR is summarized below.

- Geometric mean ratios (GMRs) of full-length S-binding IgG concentrations between the US lots
    - For full-length S-binding levels, the GMRs for each between-lot comparison (Arm 1/Arm 2, Arm 1/Arm 3, and Arm 2/Arm 3) at 1 month after Dose 2 will be provided along with associated 2-sided 95% Cis.
    - Using a 1.5-fold equivalence margin, 2 lots will be considered similar if the 2-sided 95% CI for each GMR is contained in the interval (0.67, 1.5). The 3 US lots will be considered similar if the 1.5-fold equivalence criterion is met for all 3 between-lot comparisons (Arm 1 to Arm 2, Arm 1 to Arm 3, and Arm 2 to Arm 3).
- GMR of full-length S-binding IgG concentrations between the EU lot and the 3 US lots
    - The GMR of the EU lot (Arm 4) to the pooled US lots (Arm 4/pooled Arms 1, 2, and 3) at 1 month after Dose 2 will be provided along with associated 2-sided 95% CIs.
    - Using a 1.5-fold equivalence margin, the EU lot (Arm 4) and the pooled US lots (Arms 1-3) will be considered similar if the 2-sided 95% CI for the GMR is contained in the interval (0.67, 1.5) and primary objectives on the US lot similarity and dose comparison are both met.

CLINICAL STUDY REPORT SYNOPSIS

- GMCs of full-length S-binding IgG concentrations
    - The GMCs and 2-sided 95% CIs were provided for each vaccine group (individual US lots, the pooled US lots, and the EU lot) at baseline (before Dose 1) and at 1 month after Dose 2.
- Geometric mean fold rise (GMFR) of full-length S-binding IgG concentrations
    - The GMFRs and 2-sided 95% CIs were provided for each vaccine group (individual US lots, the pooled US lots, and the EU lot) from baseline (before Dose 1) to 1 month after Dose 2.

The safety analyses were based on the safety population. Descriptive statistics are provided for each reactogenicity endpoint for each dose and vaccine group. Local reactions and systemic events from Day 1 through Day 7 after each vaccination are presented by severity and cumulatively across severity levels. Descriptive summary statistics included counts and percentages of participants with the indicated endpoint and the associated Clopper-Pearson 95% CIs.

AEs and SAEs were categorized according to Medical Dictionary for Regulatory Activities (MedDRA) terms. Counts, percentages, and the associated Clopper-Pearson 95% CIs of AEs and SAEs from Dose 1 to 1 month after Dose 2 are provided for each vaccine group.

RESULTS

Subject Disposition and Demography:

Primary Study

A total of 1574 participants were randomized across all vaccine groups in the primary study (1573 participants were vaccinated at Dose 1 and 1570 participants were vaccinated at Dose 2) (Table S3). Greater than 98% of participants within each vaccine group completed the study. A total of 2 participants in the primary study were discontinued from receiving Dose 2 but continued in the study for safety follow-up (1 due to AEs of dermatitis and angioedema and 1 because of pregnancy). A total of 16 participants were withdrawn from the study (1 participant was withdrawn after Dose 1 and before Dose 2 and 15 participants were withdrawn after Dose 2). The most common reasons overall for withdrawal from the study across all vaccine groups was withdrawal by participant (6 [0.4%] participants), lost to follow-up (5 [0.3%] participants), and Other (4 [0.3%] participants).

Overall, the safety population in the primary study was similarly distributed between male and female participants (51.8% and 48.2%, respectively) and consisted of participants similarly distributed across age groups (12 to 17 years of age [28.3% of participants], 18 to 30 years of age [34.5% of participants], and 31 to 50 years of age [37.2% of participants]). The majority of participants were White and non-Hispanic/non-Latino.

CLINICAL STUDY REPORT SYNOPSIS

Table S3. Disposition of All Randomized Participants – Primary Study

	Vaccine Group (as Randomized)						
	Arm 1 (US Lot 1) (N^a=351) n^b (%)	Arm 2 (US Lot 2) (N^a=352) n^b (%)	Arm 3 (US Lot 3) (N^a=347) n^b (%)	Pooled US Lots (N^a=1050) n^b (%)	Arm 4 (EU Lot) (N^a=173) n^b (%)	Arm 5 (20 µg) (N^a=351) n^b (%)	Total (N^a=1574) n^b (%)
Randomized	351 (100.0)	352 (100.0)	347 (100.0)	1050 (100.0)	173 (100.0)	351 (100.0)	1574 (100.0)
Not vaccinated	0	0	1 (0.3)	1 (0.1)	0	0	1 (0.1)
Vaccinated							
Dose 1	351 (100.0)	352 (100.0)	346 (99.7)	1049 (99.9)	173 (100.0)	351 (100.0)	1573 (99.9)
Dose 2	351 (100.0)	352 (100.0)	344 (99.1)	1047 (99.7)	173 (100.0)	350 (99.7)	1570 (99.7)
Completed the study	347 (98.9)	346 (98.3)	344 (99.1)	1037 (98.8)	171 (98.8)	349 (99.4)	1557 (98.9)
Discontinued from receiving Dose 2 but continued in the study for safety follow-up	0	0	1 (0.3)	1 (0.1)	0	1 (0.3)	2 (0.1)
Reason for discontinuation							
Adverse event	0	0	0	0	0	1 (0.3)	1 (0.1)
Pregnancy	0	0	1 (0.3)	1 (0.1)	0	0	1 (0.1)
Withdrawn from the study	4 (1.1)	6 (1.7)	2 (0.6)	12 (1.1)	2 (1.2)	2 (0.6)	16 (1.0)
Withdrawn after Dose 1 and before Dose 2	0	0	1 (0.3)	1 (0.1)	0	0	1 (0.1)
Withdrawn after Dose 2	4 (1.1)	6 (1.7)	1 (0.3)	11 (1.0)	2 (1.2)	2 (0.6)	15 (1.0)
Reason for withdrawal							
Lost to follow-up	1 (0.3)	1 (0.3)	2 (0.6)	4 (0.4)	1 (0.6)	0	5 (0.3)
Other	1 (0.3)	2 (0.6)	0	3 (0.3)	0	1 (0.3)	4 (0.3)
Withdrawal by subject	2 (0.6)	3 (0.9)	0	5 (0.5)	0	1 (0.3)	6 (0.4)
Withdrawal by parent/guardian	0	0	0	0	1 (0.6)	0	1 (0.1)

CLINICAL STUDY REPORT SYNOPSIS

Table S3. Disposition of All Randomized Participants – Primary Study

	Vaccine Group (as Randomized)						
	Arm 1 (US Lot 1) (N[a]=351) n[b] (%)	Arm 2 (US Lot 2) (N[a]=352) n[b] (%)	Arm 3 (US Lot 3) (N[a]=347) n[b] (%)	Pooled US Lots (N[a]=1050) n[b] (%)	Arm 4 (EU Lot) (N[a]=173) n[b] (%)	Arm 5 (20 µg) (N[a]=351) n[b] (%)	Total (N[a]=1574) n[b] (%)

Note: A 30-µg dose of BNT162b2 was administered in Arms 1, 2, 3, and 4, and a 20-µg dose of BNT162b2 was administered in Arm 5. Arm 5 study vaccine was from US Lot 1.
Note: Participant [redacted] was randomized to Arm 5 (Lot 1 [20 µg]). At Vaccination 2 the participant received a 20-µg dose of the investigational product but may have received the dose from a different arm/lot to which the participant was randomized.
a. N = number of participants in the specified group, or the total sample. This value is the denominator for the percentage calculations.
b. n = Number of participants with the specified characteristic.
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CLINICAL STUDY REPORT SYNOPSIS

Booster Study

A total of 62 participants were randomized and vaccinated (Dose 3) in the booster study. All 62 participants completed the booster study (Table S4). The study population in the booster study was similar to the primary study with the exception of participant age as the booster study only contained adult participants (18 to 30 years of age: 26 [41.9%] and 31 to 50 years of age: 36 [58.1%] participants). Males and females were similarly distributed.

Table S4. Disposition of All Randomized Participants – Booster Study

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=31) n[b] (%)	**BNT162b2.B.1.351 (30 µg) (N[a]=31) n[b] (%)**	**Total (N[a]=62) n[b] (%)**
Randomized	31 (100.0)	31 (100.0)	62 (100.0)
Not vaccinated	0	0	0
Vaccinated			
Dose 3	31 (100.0)	31 (100.0)	62 (100.0)
Completed the study	31 (100.0)	31 (100.0)	62 (100.0)

a. N = number of participants in the specified group, or the total sample. This value is the denominator for the percentage calculations.
b. n = Number of participants with the specified characteristic.
PFIZER CONFIDENTIAL SDTM Creation: 29OCT2021 (01:07) Source Data: adds Table Generation: 03NOV2021 (22:36)
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CLINICAL STUDY REPORT SYNOPSIS

Immunogenicity Results:

- The 3 US lots met the 1.5-fold equivalence criteria for all 3 between-lot full-length S-binding IgG comparisons and were considered similar (model-based GMR [95% CI] estimates were contained in the interval [0.67, 1.5]: US Lot 1 to US Lot 2: 1.01 [0.91, 1.13]; US Lot 1 to US Lot 3: 0.93 [0.83, 1.04]; and US Lot 2 to US Lot 3: 0.92 [0.82, 1.03]) (Table S5).

- The similarity of the EU lot to the pooled US lots cannot be formally declared until the dose comparison analysis is conducted in the sCSR, however the full-length S-binding IgG GMR (95% CI) of the EU lot to the pooled US lots was contained in the interval (0.67, 1.5) defined by the 1.5-fold equivalence margin.

- Full-length S-binding IgG GMFRs (95% CI) from baseline to 1 month after Dose 2 were similar for all the US lots. Full-length S-binding IgG GMFRs (95% CI) from baseline to 1 month after Dose 2 were similar for the EU lot and the pooled US lots.

CLINICAL STUDY REPORT SYNOPSIS

Table S5. Geometric Mean Ratios of Full-Length S-Binding IgG Concentrations (U/mL) Between Individual US Lots – 1 Month After Dose 2 – Linear Regression – Primary Study – Evaluable Immunogenicity Population

Vaccine Group (as Randomized)								
Arm 1 (US Lot 1)		Arm 2 (US Lot 2)		Arm 3 (US Lot 3)		Comparison GMR[a] (95% CI[a])		
n[b]	GMC[c] (95% CI[c])	n[b]	GMC[c] (95% CI[c])	n[b]	GMC[c] (95% CI[c])	Arm 1 (US Lot 1) /Arm 2 (US Lot 2)	Arm 1 (US Lot 1) /Arm 3 (US Lot 3)	Arm 2 (US Lot 2) /Arm 3 (US Lot 3)
324	6299.5 (5835.4, 6800.5)	311	6231.9 (5763.7, 6738.2)	310	6774.8 (6264.9, 7326.1)	1.01 (0.91, 1.13)	0.93 (0.83, 1.04)	0.92 (0.82, 1.03)

Abbreviations: GMC = geometric mean concentration; GMR = geometric mean ratio; IgG = immunoglobulin G; LLOQ = lower limit of quantitation; LS=least squares; S = spike protein.
Note: A 30-µg dose of BNT162b2 was administered in Arms 1, 2, 3.
a. GMRs and the corresponding 2-sided 95% CIs were calculated by exponentiating the difference in LS means and corresponding CIs based on analysis of logarithmically transformed assay results using a linear regression model with terms of age and vaccine group.
b. n = Number of participants with valid and determinate assay results for the specified assay at the given sampling time point.
c. GMCs and 2-sided 95% CIs were calculated by exponentiating the LS mean of the concentrations and corresponding CIs based on the same linear regression model as above. Assay results below the LLOQ were set to 0.5 × LLOQ.
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(Database Snapshot Date : 26OCT2021) Output File: ./C4591017_SEC/C4591017_CSR/adva_s004_gmrc1_lr_eval

CLINICAL STUDY REPORT SYNOPSIS

Safety Results:

- In general, the proportion of participants reporting local reactions and systemic events in the primary study and booster study was similar across all vaccine groups. The most common local reaction in the primary study and booster study was pain at the injection site. The most common systemic events in the primary study and booster study were fatigue, headache, and new or worsened muscle pain. Most local reactions and systemic events were mild or moderate with no Grade 4 events reported.

- The proportion of participants in the primary study who reported local reactions, in general, were similar after Dose 1 and Dose 2. In general, in the primary study a higher proportion of participants reported systemic events and antipyretic/analgesic medication use after Dose 2 than Dose 1. The proportion of participants in the booster study who reported pain at the injection site was higher after Dose 3 compared to after Dose 2, but similar for redness and swelling. In the booster study similar proportions of participants reported systemic events after Dose 3 and Dose 2.

- The incidence of any AE from Dose 1 to 1 month after Dose 2 in the primary study ranged from 5.2% (US Lot 3) to 10.4% (EU Lot) (Table S6). A total of 3 AEs were reported in the booster study from Dose 3 to 1 month after Dose 3 (Table S7). No participants in the booster study reported any severe or immediate AEs.

CLINICAL STUDY REPORT SYNOPSIS

Table S6. Number (%) of Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2 – Primary Study – Safety Population

	Vaccine Group (as Administered)					
	Arm 1 (US Lot 1) (N[a]=351)	Arm 2 (US Lot 2) (N[a]=352)	Arm 3 (US Lot 3) (N[a]=346)	Pooled US Lots (N[a]=1049)	Arm 4 (EU Lot) (N[a]=173)	Arm 5 (20 µg) (N[a]=351)
Adverse Event	n[b] (%)	n[b] (%)	n[b] (%)	n[b] (%)	n[b] (%)	n[b] (%)
Any adverse event	19 (5.4)	21 (6.0)	18 (5.2)	58 (5.5)	18 (10.4)	24 (6.8)
Related[c]	2 (0.6)	5 (1.4)	7 (2.0)	14 (1.3)	5 (2.9)	8 (2.3)
Severe	4 (1.1)	1 (0.3)	2 (0.6)	7 (0.7)	1 (0.6)	1 (0.3)
Life-threatening	0	0	0	0	0	0
Any serious adverse event	0	0	1 (0.3)	1 (0.1)	1 (0.6)	0
Related[c]	0	0	0	0	0	0
Severe	0	0	1 (0.3)	1 (0.1)	1 (0.6)	0
Life-threatening	0	0	0	0	0	0
Any nonserious adverse event	19 (5.4)	21 (6.0)	18 (5.2)	58 (5.5)	18 (10.4)	24 (6.8)
Related[c]	2 (0.6)	5 (1.4)	7 (2.0)	14 (1.3)	5 (2.9)	8 (2.3)
Severe	4 (1.1)	1 (0.3)	1 (0.3)	6 (0.6)	0	1 (0.3)
Life-threatening	0	0	0	0	0	0
Any adverse event leading to withdrawal	0	0	1 (0.3)	1 (0.1)	0	1 (0.3)
Related[c]	0	0	0	0	0	1 (0.3)
Severe	0	0	0	0	0	0
Life-threatening	0	0	0	0	0	0
Death	0	0	0	0	0	0

Note: A 30-µg dose of BNT162b2 was administered in Arms 1, 2, 3, and 4, and a 20-µg dose of BNT162b2 was administered in Arm 5. Arm 5 study vaccine was from US Lot 1.
a. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of participants reporting at least 1 occurrence of the specified adverse event. For "any event," n = number of participants reporting at least 1 occurrence of any adverse event.
c. Assessed by the investigator as related to investigational product.
PFIZER CONFIDENTIAL SDTM Creation: 29OCT2021 (02:44) Source Data: adae Table Generation: 03NOV2021 (07:42)
(Database Snapshot Date : 26OCT2021) Output File: ./C4591017_SEC/C4591017_CSR/adae_s091_1md2_saf

CLINICAL STUDY REPORT SYNOPSIS

Table S7. Number (%) of Participants Reporting at Least 1 Adverse Event From Dose 3 to 1 Month After Dose 3 – Booster Study – Safety Population

	Vaccine Group (as Administered)	
Adverse Event	**BNT162b2 (30 µg) (N[a]=31) n[b] (%)**	**BNT162b2.B.1.351 (30 µg) (N[a]=31) n[b] (%)**
Any adverse event	2 (6.5)	1 (3.2)
Related[c]	1 (3.2)	0
Severe	0	0
Life-threatening	0	0
Any serious adverse event	0	0
Related[c]	0	0
Severe	0	0
Life-threatening	0	0
Any nonserious adverse event	2 (6.5)	1 (3.2)
Related[c]	1 (3.2)	0
Severe	0	0
Life-threatening	0	0
Any adverse event leading to withdrawal	0	0
Related[c]	0	0
Severe	0	0
Life-threatening	0	0
Death	0	0

a. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of participants reporting at least 1 occurrence of the specified adverse event. For "any event," n = number of participants reporting at least 1 occurrence of any adverse event.
c. Assessed by the investigator as related to investigational product.
PFIZER CONFIDENTIAL SDTM Creation: 29OCT2021 (02:44) Source Data: adae Table Generation: 03NOV2021 (07:42)
(Database Snapshot Date : 26OCT2021) Output File: ./C4591017_SEC/C4591017_CSR/adae_s091_1md2_bstr

CLINICAL STUDY REPORT SYNOPSIS

- There was a total of 2 SAEs in the primary study (1 participant who experienced an AE of exposure during pregnancy followed by an SAE of spontaneous abortion and 1 participant who experienced status migrainosus), both of which were severe, but neither were related to the study vaccine. No participants in the booster study reported an SAE.

- There were 2 participants in the primary study who received US Lot 2 who were diagnosed with COVID-19, defined as an AE of special interest, with onset between Dose 1 and Dose 2 (mild to moderate severities). No participants in the booster study reported an AE of special interest (COVID-19). There were no cases of multisystem inflammatory syndrome in children (MIS-C) in the primary study.

- In the primary study lymphadenopathy from Dose 1 to 1 month after Dose 2 was reported by 1 participant who received US Lot 1, 3 participants who received US Lot 2, 1 participant who received the EU Lot, and 2 participants who received 20 µg of US Lot 1 (Arm 5). In the booster study 1 participant who received BNT162b2 reported lymphadenopathy from Dose 3 to 1 month after Dose 3.

- Two participants were withdrawn from the primary study for safety-related reasons, 1 of which had AEs assessed as related to the investigational product (dermatitis and angioedema). No participants in the booster study were withdrawn.

- There were no deaths in the primary study or booster study.

Conclusions: The 3 US lots in the primary study met the 1.5-fold equivalence criteria for all 3 between-lot comparisons based on full-length S-binding IgG levels and were considered similar.

Safety profiles across all vaccine groups were similar with no safety concerns identified in both the primary and booster study.

- Vaccines in all arms of the study were well-tolerated in both the primary and booster study.

- The safety profile was consistent with previous studies.