CLINICAL STUDY REPORT SYNOPSIS

Vaccine Name and Compound Number: BNT162 RNA-Based COVID-19 Vaccines, Compound Number: PF-07302048

Report Title: Final Analysis Interim Report: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals

Protocol Number: C4591001

Sponsor: BioNTech

Sponsor Agent: Pfizer Inc

Phase of Development: Phase 1/2/3

First Subject First Visit: 29 April 2020

Last Subject Last Visit: Not applicable

Data Cutoff Dates:

24 August 2020 (Phase 1 safety and immunogenicity data through 1 month after Dose 2)

02 September 2020 (Phase 2 safety data 7 days after Dose 2 only)

04 November 2020 (Phase 2/3 first interim analysis for efficacy)

14 November 2020 (Phase 2/3 final analysis for efficacy, safety data 1 month after Dose 2 for 37,586 participants with a median of at least 2 months of follow-up, and available safety data for all 43,252 participants)

Serology Completion Dates:

17 September 2020 (Phase 1, Visit 7 [post-Dose 2 blood draw] assay completed)

12 October 2020 (Phase 2, Visit 3 [post-Dose 2 blood draw] assay completed)

Coordinating Investigator(s): Stephen Thomas, MD, SUNY Upstate Medical University, 725 Irving Ave, Ste. 311, Syracuse, NY 13210

Refer to Appendix 16.1.4.1 for a list of investigators involved in this study.

Study Center(s): 131 in the United States, 9 in Turkey, 6 in Germany, 4 in South Africa, 2 in Brazil, and 1 in Argentina. Refer to Appendix 16.1.4.1 for a list of sites involved in this study.

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Date of Current Version: 03 December 2020

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

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OBJECTIVES

Study Objectives and Endpoints:

Phase 1

Note: The primary safety estimand of serious adverse events (SAEs) from Dose 1 to 6 months after the last dose is not presented in this interim clinical study report (CSR) but will be summarized when results are available.

Table S1. Phase 1 Objectives, Estimands, and Endpoints

Objectives	Estimands	Endpoints
Primary:	**Primary:**	**Primary:**
To describe the safety and tolerability profiles of prophylactic BNT162 vaccines in healthy adults after 1 or 2 doses	In participants receiving at least 1 dose of study intervention, 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 • Adverse events (AEs) from Dose 1 to 1 month after the last dose • SAEs from Dose 1 to 6 months after the last dose In addition, the percentage of participants with: • Abnormal hematology and chemistry laboratory values 1 and 7 days after Dose 1; and 7 days after Dose 2 • Grading shifts in hematology and chemistry laboratory assessments between baseline and 1 and 7 days after Dose 1; and before Dose 2 and 7 days 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 Hematology and chemistry laboratory parameters
Secondary:	**Secondary:**	**Secondary:**
To describe the immune responses elicited by prophylactic BNT162 vaccines in healthy adults after 1 or 2 doses	In participants complying with the key protocol criteria (evaluable participants) at the following time points after receipt of study intervention: 7 and 21 days after Dose 1; 7 and 14 days and 1, 6, 12, and 24 months after Dose 2 • Geometric mean titers (GMTs) at each time point • Geometric mean fold rise (GMFR) from before vaccination to each subsequent time point after vaccination • Proportion of participants achieving ≥4-fold rise from before vaccination to each subsequent time point after vaccination	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) neutralizing titers
	• Geometric mean concentrations (GMCs) at each time point • GMFR from prior to first dose of study intervention to each subsequent time point • Proportion of participants achieving ≥4-fold rise from before vaccination to each subsequent time point after vaccination	S1-binding immunoglobulin G (IgG) levels and receptor-binding domain (RBD)-binding IgG levels
	• Geometric mean ratio (GMR), estimated by the ratio of the geometric mean of SARS-CoV-2 neutralizing titers to the geometric mean of binding IgG levels at each time point	• SARS-CoV-2 neutralizing titers • S1-binding IgG levels • RBD-binding IgG levels

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Phase 2/3

Note: The objectives, estimands, and endpoints presented in Table S2 are from Protocol Amendment 9. The primary safety estimand of SAEs from Dose 1 to 6 months after the second dose in all participants in Phase 2/3, and most immunogenicity endpoints are not presented in this interim CSR but will be summarized at a later time. Only the exploratory immunogenicity estimand of GMTs/GMCs and GMFRs at 1 month after Dose 2 for Phase 2 participants are presented.

Table S2. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints
Primary Efficacy		
To evaluate the efficacy of prophylactic BNT162b2 against confirmed COVID-19 occurring from 7 days after the second dose in participants without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) at least 7 days after receipt of the second dose of study intervention: 100 × (1 – illness rate ratio [IRR]) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed nucleic acid amplification test (NAAT) in participants with no serological or virological evidence (up to 7 days after receipt of the second dose) of past SARS-CoV-2 infection
To evaluate the efficacy of prophylactic BNT162b2 against confirmed COVID-19 occurring from 7 days after the second dose in participants with and without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) at least 7 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT
Primary Safety		
To define the safety profile of prophylactic BNT162b2 in the first 360 participants randomized (Phase 2)	In participants receiving at least 1 dose of study intervention, 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 from Dose 1 to 7 days after the second dose • SAEs from Dose 1 to 7 days after the second 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

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Table S2. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints
To define the safety profile of prophylactic BNT162b2 in all participants randomized in Phase 2/3	In participants receiving at least 1 dose of study intervention, 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 from Dose 1 to 1 month after the second dose • SAEs from Dose 1 to 6 months after the second dose	• AEs • SAEs • In a subset of at least 6000 participants: o Local reactions (pain at the injection site, redness, and swelling) o Systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain)
To define the safety profile of prophylactic BNT162b2 in participants 12 to 15 years of age in Phase 3	In participants receiving at least 1 dose of study intervention, 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 from Dose 1 to 1 month after the second dose • SAEs from Dose 1 to 6 months after the second 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
Secondary Efficacy		
To evaluate the efficacy of prophylactic BNT162b2 against confirmed COVID-19 occurring from 14 days after the second dose in participants without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT in participants with no serological or virological evidence (up to 14 days after receipt of the second dose) of past SARS-CoV-2 infection
To evaluate the efficacy of prophylactic BNT162b2 against confirmed COVID-19 occurring from 14 days after the second dose in participants with and without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT
To evaluate the efficacy of prophylactic BNT162b2 against confirmed severe COVID-19 occurring from 7 days and from 14 days after the second dose in participants without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) • at least 7 days and • at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	Confirmed severe COVID-19 incidence per 1000 person-years of follow-up in participants with no serological or virological evidence (up to 7 days and up to 14 days after receipt of the second dose) of past SARS-CoV-2 infection

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Table S2. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints
To evaluate the efficacy of prophylactic BNT162b2 against confirmed severe COVID-19 occurring from 7 days and from 14 days after the second dose in participants with and without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) • at least 7 days and • at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	Confirmed severe COVID-19 incidence per 1000 person-years of follow-up
To describe the efficacy of prophylactic BNT162b2 against confirmed COVID-19 (according to the Centers for Disease Control and Prevention (United States) (CDC)-defined symptoms) occurring from 7 days and from 14 days after the second dose in participants without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) • at least 7 days and • at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT in participants with no serological or virological evidence (up to 7 days and up to 14 days after receipt of the second dose) of past SARS-CoV-2 infection
To describe the efficacy of prophylactic BNT162b2 against confirmed COVID-19 (according to the CDC-defined symptoms) occurring from 7 days and from 14 days after the second dose in participants with and without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) • at least 7 days and • at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT
Secondary Immunogenicity		
To demonstrate the noninferiority of the immune response to prophylactic BNT162b2 in participants 12 to 15 years of age compared to participants 16 to 25 years of age	GMR, estimated by the ratio of the geometric mean of SARS-CoV-2 neutralizing titers in the 2 age groups (12-15 years of age to 16-25 years of age) 1 month after completion of vaccination	SARS-CoV-2 neutralizing titers in participants with no serological or virological evidence (up to 1 month after receipt of the second dose) of past SARS-CoV-2 infection
Exploratory		
To evaluate the immune response over time to prophylactic BNT162b2 and persistence of immune response in participants with and without serological or virological evidence of SARS-CoV-2 infection before vaccination	GMC/GMT, GMFR, and percentage of participants with titers greater than defined threshold(s), at baseline and 1, 6, 12, and 24 months after completion of vaccination	• S1-binding IgG levels and/or RBD-binding IgG levels • SARS-CoV-2 neutralizing titers
To evaluate the immune response (non-S) to SARS-CoV-2 in participants with and without confirmed COVID-19 during the study		• SARS-CoV-2 nucleoprotein binding (N-binding) antibody
To describe the serological responses to the BNT vaccine candidate in cases of: • Confirmed COVID-19 • Confirmed severe COVID-19		• S1-binding IgG levels and/or RBD-binding IgG levels • SARS-CoV-2 neutralizing titers

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Table S2. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints
• SARS-CoV-2 infection without confirmed COVID-19		
To describe the safety, immunogenicity, and efficacy of prophylactic BNT162b2 in individuals with confirmed stable HIV disease		• All safety, immunogenicity, and efficacy endpoints described above
To describe the safety and immunogenicity of prophylactic BNT162b2 in individuals 16 to 55 years of age vaccinated with study intervention produced by manufacturing "Process 1" or "Process 2"		• All safety endpoints described above • SARS-CoV-2 neutralizing titers

a. HIV-positive participants in Phase 3 were not included in analyses of the objectives, with the exception of the specific exploratory objective.

METHODS

Study Design: This is a Phase 1/2/3, randomized, multinational, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in healthy individuals.

The study consists of 2 parts: Phase 1 to identify preferred vaccine candidate(s) and dose level(s); and Phase 2/3 as an expanded cohort and efficacy part. These parts, and the progression between them, are detailed in Figure S1.

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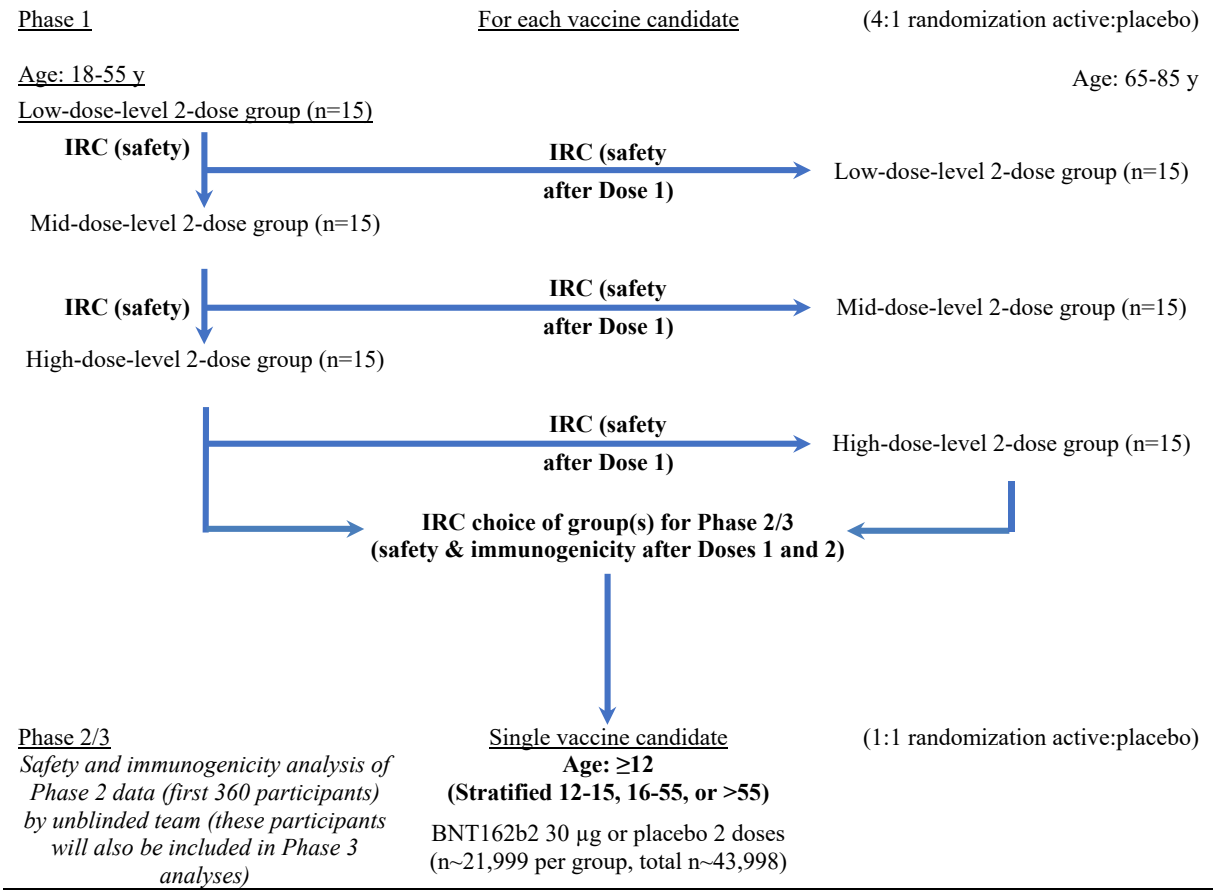
Figure S1. Study Schema



Abbreviation: IRC = internal review committee

The study evaluated the safety, tolerability, and immunogenicity of 2 different SARS-CoV-2 RNA vaccine candidates against COVID-19 and the Phase 2/3 efficacy of 1 selected candidate based on Phase 1 results:

- As a 2-dose (separated by 21 days) schedule;
- At various dose levels in Phase 1;
- In various age groups:
  - Phase 1: 18 to 55 years of age, 65 to 85 years of age;
  - Phase 2: ≥18 years of age (stratified as 18 to 55 years and >55 to 85 years);
  - Phase 3: ≥12 years of age (stratified as 12 to 15, 16 to 55, or >55 years of age).

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To facilitate rapid review of data in real time, Pfizer and BioNTech staff were unblinded to vaccine allocation for the participants in Phase 1 and remain blinded for the Phase 2/3 portion of study except those who were designated for unblinded activities following the protocol and the data blinding plan.

Phase 1

Each group (vaccine candidate/dose level/age group) was comprised of 15 participants randomized 4:1 to receive active vaccine or placebo (12 participants randomized to active vaccine and 3 to placebo, such that the placebo participants across the groups would produce a roughly comparably-sized cohort).

For each vaccine candidate/dose level/age group, safety precautions included: additional safety assessments, controlled enrollment, application of stopping rules, and IRC review of safety data to determine if dose escalation could proceed.

Groups of participants 65 to 85 years of age were not started until safety data for the RNA platform were deemed acceptable at the same, or a higher, dose level in the 18 to 55 years of age group by the IRC.

In this phase, 13 groups were studied, corresponding to a total of 195 participants.

Following review of all available safety and immunogenicity data through 14 days after Dose 2 for BNT162b1 and BNT162b2, both vaccine constructs were considered strong candidates to proceed to Phase 2/3.

Phase 2/3

Safety and immunogenicity data generated during the Phase 1 portion of this study and the BioNTech study conducted in Germany (BNT162-01) supported BNT162b2 at a dose of 30 μg as the vaccine candidate to proceed into Phase 2/3.

The Phase 2 part of the study was comprised of the first 360 participants enrolled (1:1 randomization between BNT162b2 and placebo, stratified by age groups [18 to 55 years and >55 to 85 years] with approximately 50% in each age stratum) to assess safety data through 7 days after Dose 2 and immunogenicity data. Enrollment continued during Phase 2 and these participants are included in the efficacy evaluation in the Phase 3 part of the study.

Participants in the ongoing Phase 3 part of the study are ≥12 years of age (stratified as 12 to 15, 16 to 55, or >55 years of age). The 12- to 15- year stratum will comprise up to approximately 2000 participants enrolled at selected investigational sites. It was planned to enroll a minimum of 40% of participants in the >55 years of age stratum. Participants in Phase 3 were randomized 1:1 to receive active vaccine or placebo.

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The Phase 2/3 part of the study is event-driven. Under the assumption of a true vaccine efficacy (VE) rate of ≥60%, a target of 164 primary-endpoint cases of confirmed COVID-19 occurring at least 7 days following the second dose of the primary series of the candidate vaccine will be sufficient to provide 90% power to conclude true VE >30% with high probability. The total number of participants enrolled in Phase 2/3 may vary depending on the incidence of COVID-19 at the time of the enrollment, the true underlying VE, and a potential early stop for efficacy or futility.

Assuming a COVID-19 attack rate of 1.3% per year in the placebo group, accrual of 164 first primary-endpoint cases within 6 months, an estimated 20% non-evaluable rate, and 1:1 randomization, the BNT162b2 vaccine candidate selected for Phase 2/3 is expected to comprise approximately 21,999 vaccine recipients per group, for a total sample size of 43,998. This is the number of participants initially targeted for Phase 2/3 and may be adjusted based on advice from DMC analyses of case accumulation and the percentage of participants who are seropositive at baseline. Dependent upon the evolution of the pandemic, it is possible that the COVID-19 attack rate may be higher, in which case accrual would be expected to be more rapid, enabling the study's primary endpoint to be evaluated sooner.

In Phase 3, noninferiority of immune response to prophylactic BNT162b2 in participants 12 to 15 years of age to response in participants 16 to 25 years of age will be assessed based on the GMR of SARS-CoV-2 neutralizing titers using a 1.5-fold margin.

The safety and immunogenicity of prophylactic BNT162b2 in individuals 16 to 55 years of age vaccinated with BNT162b2 manufactured with "Process 1" and each lot of BNT162b2 manufactured with "Process 2", which was developed to support an increased scale of manufacture, will be described.

It is planned that participants would participate for approximately 26 months.

Inclusion/Exclusion Criteria: Participants were eligible to be included in the study only if all of the following criteria apply:

Inclusion Criteria:

Age and Sex:

1. Male or female participants between the ages of 18 and 55 years, inclusive, 65 and 85 years, inclusive (Phase 1), or ≥12 years (Phase 2/3), at randomization. Note that participants <18 years of age cannot be enrolled in the EU.

Type of Participant and Disease Characteristics:

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

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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, could be included.

4. **Phase 2/3 only:** Participants who, in the judgment of the investigator, were at higher risk for acquiring COVID-19 (including, but not limited to, use of mass transportation, relevant demographics, and frontline essential workers).

Informed Consent:

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

Exclusion Criteria:

Participants were excluded from the study if any of the following criteria applied:

Medical Conditions:

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

2. **Phases 1 and 2 only:** 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. Receipt of medications intended to prevent COVID-19.

5. Previous clinical (based on COVID-19 symptoms/signs alone, if a SARS-CoV-2 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.

6. **Phase 1 only:** Individuals at high risk for severe COVID-19, including those with any of the following risk factors:

    - Hypertension

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- Diabetes mellitus
- Chronic pulmonary disease
- Asthma
- Current vaping or smoking
- History of chronic smoking within the prior year
- Chronic liver disease
- Stage 3 or worse chronic kidney disease (glomerular filtration rate <60 mL/min/1.73 m^2)
- Resident in a long-term facility
- Body mass index (BMI) >30 kg/m^2
- Anticipating the need for immunosuppressive treatment within the next 6 months

7. **Phase 1 only:** Individuals currently working in occupations with high risk of exposure to SARS-CoV-2 (eg, healthcare worker, emergency response personnel).

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

9. **Phase 1 only:** Individuals with a history of autoimmune disease or an active autoimmune disease requiring therapeutic intervention, including but not limited to: systemic or cutaneous lupus erythematosus, autoimmune arthritis/rheumatoid arthritis, Guillain-Barré syndrome, multiple sclerosis, Sjögren's syndrome, idiopathic thrombocytopenia purpura, glomerulonephritis, autoimmune thyroiditis, giant cell arteritis (temporal arteritis), psoriasis, and insulin-dependent diabetes mellitus (type 1).

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

11. Women who are pregnant or breastfeeding.

Prior/Concomitant Therapy:

12. Previous vaccination with any coronavirus vaccine.

13. Individuals who received treatment with immunosuppressive therapy, including cytotoxic agents or systemic corticosteroids, eg, for cancer or an autoimmune disease, or planned receipt throughout the study. If systemic corticosteroids were administered short term (<14 days) for treatment of an acute illness, participants should not have been enrolled into the study until corticosteroid therapy had been discontinued for at least 28 days before study intervention administration. Inhaled/nebulized (except for participants in Phase 1 – see exclusion criterion 14), intra-articular, intrabursal, or topical (skin or eyes) corticosteroids were permitted.

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14. **Phase 1 only:** Regular receipt of inhaled/nebulized corticosteroids.

15. 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:

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

17. Previous participation in other studies involving study intervention containing lipid nanoparticles.

Diagnostic Assessments:

18. **Phase 1 only:** Positive serological test for SARS-CoV-2 immunoglobulin M (IgM) and/or IgG antibodies at the screening visit.

19. **Phase 1 only:** Any screening hematology and/or blood chemistry laboratory value that meets the definition of a ≥ Grade 1 abnormality.

    Note: With the exception of bilirubin, participants with any stable Grade 1 abnormalities (according to the toxicity grading scale) may be considered eligible at the discretion of the investigator. (Note: A "stable" Grade 1 laboratory abnormality is defined as a report of Grade 1 on an initial blood sample that remains ≤ Grade 1 upon repeat testing on a second sample from the same participant.)

20. **Phase 1 only:** Positive test for HIV, hepatitis B surface antigen (HBsAg), hepatitis B core antibodies (HBc Abs), or hepatitis C virus antibodies (HCV Abs) at the screening visit.

21. **Phase 1 only:** SARS-CoV-2 NAAT-positive nasal swab within 24 hours before receipt of study intervention.

Other Exclusions:

22. 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.

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Vaccines Administered: The study evaluated a 2-dose (separated by 21 days) schedule of 2 investigational RNA vaccine candidates for active immunization against COVID-19 or saline placebo:

- BNT162b1 (BNT162 RNA-lipid nanoparticle (LNP) vaccine containing nucleoside-modified messenger ribonucleic acid (modRNA) that encodes the RBD): 10 µg, 20 µg, 30 µg, 100 µg
- BNT162b2 (BNT162 RNA-LNP vaccine containing modRNA that encodes SARS-CoV-2 full-length, P2 mutant, prefusion spike glycoprotein (P2 S): 10 µg, 20 µg, 30 µg
- Normal saline (0.9% sodium chloride solution for injection)

The vaccine candidate selected for Phase 2/3 evaluation was BNT162b2 at a dose of 30 µg.

A list of the study interventions administered in this study and their representative lot numbers is provided in Table S3.

Table S3. Investigational Product Lot Numbers – Final Analysis Interim

Investigational Product	Phase	Manufacturer	Vendor Lot Number (Manufacturer)	Lot Number[a] (Pfizer)
BNT162b1 (10 µg, 20 µg, 30 µg, and 100 µg)	1	BioNTech	BCV10320-A	E220395-0001L
BNT162b2 (10 µg, 20 µg, and 30 µg)	1	BioNTech	BCV40420-A	E220395-0004L
Normal saline (0.9% sodium chloride solution for injection)	1	Pfizer	DK1589	20-001592
BNT162b2 (30 µg)	2/3	BioNTech	BCV40420-A	E220395-0006L003/P220395-0012L
			BCV40420-A	E220395-0035L002/P220395-0048L
			BCV40420-A	E220395-0035L003/P220395-0048L
			BCV40420-A	EU2065896/E220395-0004L
			BCV40420-A	PA2070104/P220395-0008L
			BCV40620-A	PA2071394/P220395-0029L
			BCV40620-A	PA2072393/P220395-

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Table S3. Investigational Product Lot Numbers – Final Analysis Interim

				0019L
			BCV40620-B	PA2071395/P220395-0016L
			BCV40620-B	PA2072396/P220395-0016L
			BCV40620-C	PA2071396/P220395-0047L
			BCV40620-C	PA2072439/P220395-0047L
			BCV40620-D	PA2072442/P220395-0042L
			BCV40620-D	PA2072765/P220395-0042L
			BCV40720-A	PA2074172/P220395-0053L
			BCV40720-A	PA2074998/P220395-0060L
			BCV40720-B	PA2074173/P220395-0051L
			BCV40720-C	PA2074071/P220395-0052L
			ED3938	PA2074300/P220395-0021L
			ED3938	EU2074330/E220395-0036L
			ED3938	PA2074300/P220395-0022L
			ED3938	PA2074300/P220395-0023L
			EE3813	PA2074838/P220395-0024L
			EE3813	PA2074838/P220395-0020L
			EE8493Z	PA2077905/P220395-0026L
Normal saline (0.9% sodium chloride solution for injection)	2/3	Pfizer	DK1589;20 - 001592	PA2064251/P220395-0005L
			DK1589;20 - 001776	PA2065311/P220395-0007L
			DK2074;20 - 002029	PA2067775/P220395-0030L
			DK2074;20 - 002108	PA2067774/P220395-0013L
			DK2074;20 - 002221	PA2069407/P220395-0031L
			DK2074;20 - 002221	PA2069407/P220395-0032L
			DK2074;20 - 002221	PA2069407/P220395-0033L
			DK2074;20 - 002221	PA2069407/P220395-

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Table S3. Investigational Product Lot Numbers – Final Analysis Interim

	0034L
DK2074;20 - 002221	PA2069407/P220395-0044L
DK2074;20 - 002221	PA2069407/P220395-0045L
DK2074;20 - 002221	PA2069407/P220395-0046L
DK2074;20 - 002221	PA2069407/P220395-0054L
DK2074;20 - 002221	PA2069407/P220395-0055L
DK2074;20 - 002221	PA2069407/P220395-0056L
DK2074;20 - 002221	PA2069407/P220395-0062L
DK2074;20 - 002221	PA2069407/P220395-0065L
DK2074;20 - 002221	PA2069407OTH/E220395-0049L

Note: C4591001 End of Study Information and Quality Control (QC) Record for Study Drug Appendix (Section D) dated 19Nov2020 was used to create this table.
a. Lot number assigned to the investigational product by Pfizer Global Clinical Supply.
Protocol C4591001 Investigational Product Lot Numbers Table – Final Analysis Interim, Final, Version 1.0, 19Nov2020.

Efficacy and Immunogenicity Evaluations: Efficacy was assessed for potential cases of COVID-19.

- Confirmed severe COVID-19: confirmed COVID-19 and presence of at least 1 of the following:
  - Clinical signs at rest indicative of severe systemic illness (RR ≥30 breaths per minute, HR ≥125 beats per minute, SpO2 ≤93% on room air at sea level, or PaO2/FiO2 <300 mm Hg);
  - Respiratory failure (defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation, or ECMO);
  - Evidence of shock (SBP <90 mm Hg, DBP <60 mm Hg, or requiring vasopressors);
  - Significant acute renal, hepatic, or neurologic dysfunction*;
  - Admission to an ICU;
  - Death.

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For immunogenicity testing, the following assays were performed in Phase 1 and Phase 2 and will be performed in Phase 2/3, with the exception of the RBD-binding IgG assay:

- SARS-CoV-2 neutralizing titers
- Antigen binding antibodies specific to SARS-CoV-2
    - RBD-binding IgG levels (most relevant to BNT162b1, which encodes the RBD)
    - S1-binding IgG levels (most relevant to BNT162b2 which encodes P2 S)
    - N-binding antibody (Phase 2/3 only)

Safety Evaluations:

Clinical Safety Laboratory Assessments (Phase 1 only): All protocol-required laboratory assessments, were conducted in accordance with the laboratory manual and the Schedule of Activities. Unscheduled clinical laboratory measurements were obtained at any time during the study to assess any perceived safety issues.

The investigator reviewed the laboratory report, documented this review, and recorded any clinically relevant changes occurring during the study in the AE section of the case report form (CRF). All laboratory tests with values considered clinically significantly abnormal during participation in the study or within 28 days after the last dose of study intervention were repeated until the values returned to normal or baseline or were no longer considered clinically significant by the investigator or medical monitor. If such values did not return to normal/baseline within a period of time judged reasonable by the investigator, the etiology was identified, and Pfizer and BioNTech notified.

Local Reactions and Systemic Events: All participants in Phase 1 and a subset of at least the first 6000 participants randomized in Phase 2/3 were asked to monitor and record local reactions, systemic events, and antipyretic/pain medication usage for 7 days following administration of the study intervention using an e-diary. Any participants in Phase 3 who are HIV-positive or 12 to 15 years of age may also have been included in this subset (will be reported at a later time). In addition, participants 16 through 17 years of age enrolled under Protocol Amendment 9 (finalized 29 October 2020) and onwards will be included in the reactogenicity subset. For participants who are not in the reactogenicity subset, local reactions and systemic events consistent with reactogenicity were detected and reported as AEs.

For local reactogenicity, during the reactogenicity e-diary reporting period, participants were asked to assess redness, swelling, and pain at the injection site and to record the symptoms in the reactogenicity e-diary. If a local reaction persisted beyond the end of the reactogenicity e-diary period following vaccination, the participant was requested to report that information. Redness and swelling were measured and recorded in measuring device units (range: 1 to 21)

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and then categorized during analysis as absent, mild, moderate, or severe based on the grading scale. Pain at the injection site was assessed by the participant as absent, mild, moderate, or severe according the grading scale.

For systemic reactogenicity, during the reactogenicity e-diary reporting period, participants were asked to assess vomiting, diarrhea, headache, fatigue, chills, new or worsened muscle pain, and new or worsened joint pain and to record the symptoms in the reactogenicity e-diary. The symptoms were assessed by the participant as absent, mild, moderate, or severe according to the grading scale.

Temperature was collected in the reactogenicity e-diary in the evening daily during the reactogenicity e-diary reporting period and at any time during the reactogenicity e-diary data collection periods when fever was suspected. Fever is defined as an oral temperature of ≥38.0°C (100.4°F). The highest temperature for each day was recorded in the reactogenicity e-diary.

The investigator or designee obtained stop dates from the participant for any ongoing local reactions, systemic events, or use of antipyretic medication on the last day that the reactogenicity e-diary was completed.

AEs and SAEs: AEs were reported by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally authorized representative). The time period for actively eliciting and collecting AEs and SAEs ("active collection period") for each participant began from the time the participant provided informed consent, which was obtained before the participant's participation in the study (ie, before undergoing any study-related procedure and/or receiving study intervention), through and including Visit 7 (1 month after Dose 2) for Phase 1 participants, and Visit 3 (1 month after Dose 2) for Phase 2/3 participants. In addition, any AEs occurring up to 48 hours after each subsequent blood draw were recorded on the CRF. SAEs were collected from the time the participant provides informed consent to approximately 6 months after the last dose of study intervention (Visit 8 for Phase 1 participants and Visit 4 for Phase 2/3 participants).

Acute reactions (immediate AEs) were collected within the first 4 hours after administration of the study intervention (for the first 5 participants vaccinated in each Phase 1 group), and within the first 30 minutes (for the remainder of participants).

Statistical Methods:

Efficacy Analysis: The efficacy assessment in Phase 2/3 portion of the study was event-driven. Initially, 4 interim analyses were planned to be performed by an unblinded statistical team supporting the DMC after accrual of at least 32, 62, 92, and 120 confirmed COVID-19 cases, with the final analysis performed after accrual of at least 164 cases. For operational reasons, the first planned IA (after at least 32 cases) was not performed. Protocol Amendment 9 eliminated the planned interim analysis with at least 32 cases and provided for 3 interim analyses to be performed after accrual of at least 62, 92, and 120 cases. At each of

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the IAs, vaccine efficacy with respect to the first primary efficacy endpoint was to be assessed. At the final analysis (at least 164 cases) vaccine efficacy with respect to all efficacy endpoints was to be assessed.

Assessment of VE of BNT162b2 for the first primary efficacy endpoint was performed for confirmed COVID-19 cases observed at least 7 days after the receipt of Dose 2 onwards among participants without serological or virological evidence (up to 7 days after receipt of the second dose) of past SARS-CoV-2 infection. VE was estimated by 100% × (1 – IRR), where IRR was the ratio of COVID-19 illness rate in the BNT162b2 group to the corresponding illness rate in the placebo group. The Bayesian 95% credible interval and the posterior probability for the true vaccine efficacy greater than 30% conditioning on the available data, i.e. P[VE >30%|data], were calculated using a beta-binomial model and a pre-specified minimally informative beta distribution as prior. The calculation of posterior probability and 95% credible interval were adjusted for surveillance time. All efficacy endpoints were to be analyzed using the same Bayesian approach unless stated otherwise.

If the posterior probability of VE>30% is greater than 99.5% at any pre-planned interim analysis, or greater than 98.6% at the final analysis, the vaccine efficacy of BNT162b2 would be declared.

If the predicted posterior probability of demonstrating vaccine efficacy at the final analysis is less than 5.0% at any of the first 2 planned interim analyses, the study would stop for lack of benefit (futility).

For the subgroup analyses of the efficacy endpoints, and for the analyses of efficacy for COVID-19 cases determined according to the CDC-defined symptoms, VE and the 2-sided 95% confidence interval (CI) for VE was derived based on the Clopper and Pearson method adjusted for surveillance time.

Immunogenicity Analysis: For immunogenicity results of SARS-CoV-2 neutralizing titers and S1- or RBD-binding IgG concentrations, the GMT or GMCs were computed along with associated 95% confidence intervals (CIs). The GMT and GMC were calculated as the means of assay results after making the logarithm transformation and then exponentiating the means to express results on the original scale. Two-sided 95% CIs were obtained by taking log transforms of assay results, calculating the 95% CIs with reference to Student's t-distribution, and then exponentiating the confidence limits.

The GMFR was calculated by exponentiating the mean of the difference of logarithmically transformed assay results (later time point – earlier time point). Two-sided CIs were 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 GMR was calculated as the mean of the difference of logarithmically transformed assay results (eg, SARS-CoV-2 neutralizing titers minus S1-binding IgG levels for each participant) and exponentiating the mean. Two-sided CIs were 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 exact 95% CIs for binary endpoints were computed using the F distribution (Clopper-Pearson method).

Titers/concentrations below the lower limit of quantitation (LLOQ) or denoted as below the level of quantitation (BLQ) were set to 0.5 × LLOQ for analysis.

For participants with no serological or virological evidence (up to 1 month after receipt of the second dose) of past SARS-CoV-2 infection, the GMR of SARS-CoV-2 neutralizing titers in participants 12 to 15 years of age to those in participants 16 to 25 years of age and 2-sided 95% CIs will be provided at 1 month after Dose 2 for noninferiority assessment. The GMR and its 2-sided 95% CI will be derived by calculating differences in means and CIs on the natural log scale of the titers based on the Student's t-distribution and then exponentiating the results. The difference in means on the natural log scale will be 12 to 15 years minus 16 to 25 years. Noninferiority will be declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67.

Safety Analysis: The primary safety objective was evaluated by descriptive summary statistics for local reactions, systemic events, AEs/SAEs, and abnormal hematology and chemistry laboratory parameters (Phase 1 only), for each vaccine group. A 3-tier approach was used to summarize AEs in Phase 2/3. Under this approach, AEs were classified into 1 of 3 tiers:

- Tier 1 events are prespecified events of clinical importance and are identified in a list in the product's Safety Review Plan; there are no Tier 1 AEs identified for this program.
- Tier 2 events were those that were not Tier 1 but were considered "relatively common"; a MedDRA preferred term is defined as a Tier 2 event if there are at least 1% of participants with the AE term in at least 1 vaccine group.
- Tier 3 events were those that were neither Tier 1 nor Tier 2.

Other Analysis: The safety and immunogenicity results for individuals with confirmed stable HIV disease will be summarized descriptively at a later time. Furthermore, VE may be assessed if there is a sufficient number of COVID-19 cases in this group of participants.

The safety and immunogenicity results for individuals 16 to 55 years of age vaccinated with study intervention produced by manufacturing "Process 1" or "Process 2" will be summarized descriptively.

All severe COVID-19 cases occurring after Dose 1 were summarized descriptively.

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RESULTS – PHASE 1

Participant Disposition and Demography: BNT162b1: In the younger age group, all participants randomized to the 10-µg, 20-µg, and 30-µg dose groups received both doses of BNT162b1 or placebo. All participants randomized to the 100-µg dose group received Dose 1 of BNT162b1 or placebo. The IRC determined not to administer the second dose of 100 µg due to reactogenicity. At the time of the data cutoff date (24 August 2020), 11 of 12 participants in this group received Dose 2 of BNT162b1 at 10 µg but results for Dose 2 are not yet available at the time of this report. After the data cutoff date (24 August 2020), the remaining participant received Dose 2 of BNT162b1 at 10 µg. All participants in the older age group randomized to each dose group received both doses of BNT162b1 or placebo.

Overall, for the safety population, most participants were White (37 [82.2%]; 14 [93.3%] for the 100-µg dose group) in both the younger age group and older age group. Median age was 35.0 years in the younger age group (35.0 years for the 100-µg dose group) and 69.0 years in the older age group. There was a higher representation of males in the younger age group (up to 30 µg) (28 [62.2%]). There was a higher representation of females in younger 100-µg dose group (9 [60.0%]) and in the older age group (32 [71.1%]).

BNT162b2: All participants randomized to each dose group in the younger and older age groups received both doses of BNT162b2 or placebo.

Overall, most participants were White in the younger age group (39 [86.7%]), and all participants were White in the older age group (45 [100%]). Median age was 37.0 years in the younger age group and 68.0 years in the older age group. There was a higher representation of females in both the younger (26 [57.8%]) and older (28 [62.2%]) age groups.

Immunogenicity Results: In general, a modest neutralizing immune response was observed in both the younger and older age groups after the first dose. A much more robust immune response was observed 7 days after the second dose of either BNT162b1 or BNT162b2 at all dose levels in both the younger and older age groups. Antibody levels at the last time point tested were still substantially above those at baseline.

In the younger age group:

- At 7 days after Dose 2, SARS-CoV-2 50% neutralizing GMTs in the 20-µg and 30-µg dose groups were higher for BNT162b2 recipients than for BNT162b1 recipients. The GMTs were similar in the 10-µg dose group for both recipients. At 1 month after Dose 2 (Day 52), GMTs remained substantially higher than those at the earlier time points after Dose 1 for both BNT162b1 and BNT162b2 recipients.

- From before vaccination to 7 days after Dose 2, GMFRs of SARS-CoV-2 50% neutralizing titers were substantially high for BNT162b1 and BNT162b2 recipients at the 30-µg dose level.

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- From before vaccination to 7 days after Dose 2, all participants at the 30-µg dose level who received BNT162b1 or BNT162b2 achieved a ≥4-fold rise in SARS CoV-2 50% neutralizing titers.

In the older age group:

- At 7 days after Dose 2, SARS-CoV-2 50% neutralizing GMT in the 30-µg dose group was higher for BNT162b2 recipients than for BNT162b1 recipients. At 1 month after Dose 2 (Day 52), the SARS-CoV-2 50% neutralizing GMTs in the 30-µg dose group were similar for both BNT162b1 and BNT162b2 recipients.

- From before vaccination to 7 days after Dose 2, the GMFR of SARS-CoV-2 50% neutralizing titers were substantially high for BNT162b1 and BNT162b2 recipients at the 30-µg dose level.

- From before vaccination to 7 days after Dose 2, most participants who received BNT162b1 or BNT162b2 at the 30-µg dose level achieved a ≥4-fold rise in SARS-CoV-2 50% neutralizing titers.

Immunogenicity Conclusions:

- Both BNT162b1 and BNT162b2 elicited robust SARS-CoV-2 neutralizing antibody response 7 days after Dose 2 in younger and older adults, based on GMTs, GMFRs, proportions of participants achieving a ≥4-fold rise in neutralizing titers, and reverse cumulative distribution curves (RCDCs). Neutralizing antibody response was maintained through Day 52 and was similar for the candidates within the corresponding age and dose groups.

- Both BNT162b1 and BNT162b2 elicited substantial rises in antigen binding IgG levels 7 days after Dose 2, based on GMCs, GMFRs, and proportions of participants achieving a ≥4-fold rise in IgG-antigen specific binding. Responses were maintained through Day 52.

- In the 100-µg dose group, SARS-CoV-2 neutralizing antibody response modestly increased by 3 weeks after Dose 1 of BNT162b1, but neutralizing antibody response returned to levels similar to baseline by 7 weeks after Dose 1.

- These data support the need for a 2-dose vaccination series.

Safety Results: Overall, reactogenicity events were well tolerated and short-lived (median durations 1.0 to 4.0 days). All participants returned to receive their second dose. All AEs as a result of reactogenicity events resolved without sequelae.

- For local reactions in both age groups, pain at the injection site (58.3% to 100.0%), redness (0% to 16.7%), and swelling (0% to 25.0%) were reported for BNT162b1

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recipients, which were more frequent than for BNT162b2 recipients: pain at the injection site (33.3% to 91.7%), redness (0% to 8.3%), and swelling (0% to 16.7%). In general, frequencies of local reactions were observed to be higher with increased dose level.

- The frequency of local reactions was lower in the older age group compared to the younger age group. The frequency of pain at the injection site, the most frequently reported local reaction, was lower in the older age groups after 30 µg BNT162b1 (91.7% and 75.0%) and after 30 µg of BNT162b2 (75.0% and 66.7% for Dose 1 and Dose 2, respectively), compared to the younger age groups after 30 µg of BNT162b1 (100.0% for both Dose 1 and Dose 2) and 30 µg of BNT162b2 (91.7% and 83.3% for Dose 1 and Dose 2, respectively).

- BNT162b2 recipients in the older age group reported lower frequencies of local reactions compared with BNT162b1 recipients in the older age group. In the older 30-µg BNT162b2 group, pain at the injection site was lower after Dose 1 (75.0%) and Dose 2 (66.7%) than in the older 30-µg BNT162b1 group after Dose 1 (91.7%) and Dose 2 (75.0%).

- Common systemic events in both age groups after either Dose 1 or Dose 2 included fatigue (16.7% to 83.3%), headache (25.0% to 100%), chills (8.3% to 66.7%), fever (0% to 75.0%), and muscle pain (8.3% to 75.0%) for BNT162b1 recipients up to 30 µg, which were more frequent than BNT162b2 recipients up to 30 µg: fatigue (8.3% to 75.0%), headache (0% to 66.7%), chills (0% to 58.3%), fever (0% to 16.7%), and muscle pain (0% to 58.3%). In general, frequencies of systemic events were observed to be higher with increased dose level.

- The frequency of systemic events was lower in the older age group compared to the younger age group. The frequency of fatigue was lower in the older age groups after 30 µg of BNT162b1 (50.0% and 66.7%) and after 30 µg of BNT162b2 (25.0% and 41.7% for Dose 1 and Dose 2, respectively), compared to the younger age groups after 30 µg of BNT162b1 (50.0% and 83.3%) and after 30 µg of BNT162b2 (41.7% and 75.0%) for Dose 1 and Dose 2, respectively.

- BNT162b2 recipients in the older age group reported lower frequencies of systemic events compared with BNT162b1 recipients in the older age group. The frequency of fatigue was lower in the older 30-µg BNT162b2 group (25.0% and 41.7% for Dose 1 and Dose 2, respectively) than in the older 30-µg BNT162b1 group (50.0% and 66.7% for Dose 1 and Dose 2, respectively).

Most AEs were mild or moderate in severity. Most related AEs were similar to the solicited reactogenicity events reported in the e-diary. Few severe AE were reported but were considered not related to study intervention.

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There were no SAEs reported in the BNT162b1 groups (across all dose levels). There was 1 SAE reported in the BNT162b2 30-µg younger age group (neuritis).

Transient decrease in lymphocytes were observed in all age and dose groups 1 to 3 days after Dose 1, which resolved by 6 to 8 days after Dose 1.

There were no clinically important findings from physical examinations.

BNT162b2 demonstrated a favorable reactogenicity and safety profile compared with BNT162b1, contributing to the selection of BNT162b2 for Phase 2/3 development.

Safety Conclusions:

- All doses tested for BNT162b1 and BNT162b2 (10 µg, 20 µg, and 30 µg) were safe and well tolerated except for BNT162b1 at 100 µg, which was discontinued after the first dose due to the reactogenicity profile.
- Reactogenicity was generally higher after Dose 2 than Dose 1.
- The frequency of local and systemic reactogenicity was generally lower for BNT162b2 compared to BNT162b1 especially after the second dose.
- Reactogenicity events after each dose for both BNT162b1 and BNT162b2 in older adults were milder and less frequent than those observed in younger adults. The majority of reactogenicity events were mild or moderate in severity.
- Most AEs were mild or moderate. There were discontinuations because of AEs. There was 1 SAE (neuritis; unrelated to vaccination) reported in a younger participant in the BNT162b2 30 µg group.
- Overall, fewer AEs were experienced by participants who received BNT162b2 compared with those who received BNT162b1, with the least number of participants experiencing AEs in the BNT162b2 older age group. Few severe AEs in the older age group after BNT162b2 were observed, and all were considered unrelated to study intervention.
- Clinical laboratory evaluations showed a transient decrease in lymphocytes that was observed in all age and dose groups after Dose 1, which resolved within a few days, were not associated with any other clinical sequelae, and were not considered clinically relevant.
- BNT162b2 at 30 µg was selected to proceed into the Phase 2/3 portion of the study because this dose and construct provided the optimum combination of a favorable reactogenicity profile and a robust immune response.

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RESULTS – PHASE 2

Participant Disposition and Demography: The first 360 participants enrolled as part of Phase 2 were randomized 1:1 (180 participants each) to the BNT162b2 and placebo groups. Among participants randomized to the BNT162b2 group, 88 participants were in the younger age group (18 to 55 years of age) and 92 participants were in the older age group (56 to 85 years of age).

Except for 1 participant in the BNT162b2 younger age group who was withdrawn after Dose 1 but before Dose 2 and 1 participant in the placebo group (who had not yet received Dose 2 at the time of data cutoff date [02 September 2020]), all other participants received both doses of study intervention. One participant noted above in the BNT162b2 younger age group was withdrawn from the study (after Dose 1 but before Dose 2) because of an SAE of gastric adenocarcinoma 23 days after receiving Dose 1.

From 7 days after Dose 2 to the data cutoff date of 14 November 2020, 1 additional participant in the BNT162b2 older age group was withdrawn from the study because of an SAE of cardiac arrest 60 days after receiving Dose 2, which resulted in death. The death was assessed by the investigator as not related to the study intervention.

Demographic characteristics for Phase 2 were similar in the BNT162b2 group and the placebo group for the safety population. The male/female split was approximately 50/50 for both vaccine groups and also for both age groups within the BNT162b2 group.

Overall, most participants were White (85.8%), followed by Black or African American (9.2%). The proportions of Hispanic/Latino participants were similar in the BNT162b2 and placebo groups (8.9% and 11.1%, respectively). Within the BNT162b2 group, the younger age group had 14.8% of Hispanic/Latino participants and the older age group had 3.3%.

The median age was 56.0 years overall. Median age was 44.0 years for the BNT162b2 younger age group and 65.0 years for the BNT162b2 older age group.

Demographic characteristics for the 336 participants included in the Dose 2 evaluable immunogenicity population were similar to those in the safety population in Phase 2. Demographic characteristics for the Dose 2 all-available immunogenicity population were similar to those in the Dose 2 evaluable immunogenicity population.

Immunogenicity Results:

- Immunogenicity results from 360 participants in Phase 2 of this study demonstrated that BNT162b2 at 30 µg elicited robust SARS-CoV-2 neutralization and S1-binding IgG antibody responses at 1 month after Dose 2 similar to those previously observed in Phase 1 of the study. Notably, SARS-CoV-2 neutralizing titers were higher in the younger age cohort compared with the older age cohort.

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- S1-binding GMCs were generally higher in the younger age cohort compared to the older age cohort, again concordant with observations in the Phase 1 portion of the study.

Safety Results:

- Across age groups, local reactions were generally similar in frequency after each dose, and systemic events generally increased in frequency and severity after Dose 2 compared to Dose 1. Local and systemic reactogenicity events were well-tolerated and short-lived.

- Reactogenicity events after each dose of BNT162b2 in older adults were generally milder and less frequent than those observed in younger adults. The majority of reactogenicity events were mild or moderate in severity. No Grade 4 events were reported.

- AEs in participants were low in frequency, and most AEs were mild or moderate in severity. There were no SAEs or discontinuations because of AEs that were assessed as related by the investigator. There was 1 death in the BNT162b2 group (cardiac arrest) that was assessed as not related to study intervention.

- The reactogenicity and AE profile after BNT162b2 30 µg evaluated in 360 participants was consistent with the safety profile observed after BNT162b2 30 µg in Phase 1.

- BNT162b2 at 30 µg was safe and well tolerated up to 7 days after Dose 2 and up to at least 2 months of follow-up.

RESULTS – PHASE 2/3

Participant Disposition and Demography: The disposition of the first 37,796 participants (including the 360 participants in Phase 2) randomized was similar in the BNT162b2 and placebo groups. Most participants randomized (≥98.1%) received Dose 1 and Dose 2. There were 121 (0.6%) participants in the BNT162b2 group and 111 (0.6%) participants in the placebo group discontinued from the vaccination period who are continuing in the study to be followed for safety. The most frequently reported reasons for discontinuation from the vaccination period included: no longer meets eligibility criteria, withdrawal by subject, and AE. Few participants in the BNT162b2 and placebo groups were withdrawn from the study (1.0% and 1.4%, respectively), and most were withdrawals by the participant, or they were lost to follow-up. Eight participants in the BNT162b2 group and 5 participants in the placebo group were withdrawn due to an AE.

One participant was randomized but did not sign an ICD and is not included in any analysis population. HIV-positive participants (120 participants) are included in this summary but were not included in the analyses of the overall study objectives. Because of a dosing error, 2 participants received an additional dose of BNT162b2 (30 µg) at an unscheduled visit after receiving 1 dose of BNT162b2 (30 µg) and 1 dose of placebo.

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Due to a data-related issue for this ongoing study that is being corrected, 2 participants were reported as 'discontinued from the vaccination period but continue in the study' with the reason as lost to follow-up, although the participants discontinued from the study.

The total of 37,796 participants excluded 4 participants (5 participant identification numbers) with special data issues: 2 participant identification numbers from 1 multi-enrolled participant and 3 participants whose actual treatment was not confirmed in IRT at the time of data cutoff.

From Dose 1 to the data cutoff date (14 November 2020), disposition of all 43,548 participants randomized (which excludes 3 participants whose actual treatment was not confirmed in IRT at the time of the data cutoff and 2 additional participant identification numbers from 1-multi-enrolled participant) was generally similar in the BNT162b2 and placebo groups. Almost all participants randomized received Dose 1 (99.8%) and approximately 94.2% of participants received Dose 2 at the cutoff date for the analyses in this CSR. At the time of the data cutoff, 137 (0.6%) participants in the BNT162b2 group and 129 (0.6%) participants in the placebo group were discontinued from the vaccination period but were continuing in the study for safety follow-up. The most frequently reported reasons for discontinuation from the vaccination period included: no longer meets eligibility criteria, withdrawal by participant, and AE.

Of the 181 (0.8%) and 263 (1.2%) participants who were withdrawn from the study in the BNT162b2 and placebo groups, respectively, most were withdrawn after Dose 1 and before Dose 2 (133 [0.6%] in the BNT162b2 group and 168 [0.8%] in the placebo group). Most of these were withdrawals by the participant, or they were lost to follow-up. Eight participants in the BNT162b2 group and 6 participants in the placebo group were withdrawn because of an AE. Nine participants withdrew from the study due to pregnancies. There were 6 deaths: 2 in the BNT162b2 group and 4 in the placebo group. None of the deaths were assessed by the investigator as related to study intervention.

Due to a data-related issue for this ongoing study that is being corrected, a total of 3 participants were reported as 'discontinued from the vaccination period but continue in the study' with the reason as lost to follow-up (inclusive of the 2 participants who were part of the ~38,000 participants), although the participants discontinued from the study.

The Phase 2/3 total of 43,548 randomized participants excluded 4 participants (5 participant identification numbers) with special data issues: 1 multi-enrolled participant (2 participant identification numbers) and 3 participants whose actual treatment was not confirmed in IRT at the time of data cutoff. All 4 participants (5 participant numbers) were part of the ~38,000 population.

Demographic characteristics for the 37,706 Phase 2/3 participants (who had a median 2 months of follow-up after Dose 2) were similar in the BNT162b2 and placebo groups. Overall, most participants were White (82.9%), with 9.3% Black participants and 4.3% Asian participants, and other racial groups were <3%. There were 28% Hispanic/Latino

participants. Median age was 52 years and 50.6% of participants were male. The younger and older age groups were 57.8% and 42.2% of participants, respectively. Obese participants made up 35.1% of this safety population.

Within each age group, most demographic characteristics were similar in the BNT162b2 group and the placebo group. There was a lower proportion of non-Hispanic/non-Latino participants in the younger BNT162b2 and placebo groups (65.4% and 65.6%, respectively) than in the older BNT162b2 and placebo groups (79.8% and 79.4%, respectively).

Demographic characteristics for all 43,448 Phase 2/3 participants included in the safety population to date were similar in the BNT162b2 and placebo groups for the safety population. Overall, most participants were White (82.2%) and non-Hispanic/non-Latino (73.3%), median age was 51.0 years, and 49.1% were female. There were 9.7% Black or African American, 4.3% Asian, 2.4% Multiracial, 0.7% American Indian or Alaskan native, and 0.2% Native Hawaiian or other Pacific Islander participants included in the safety population. Race was not reported for 0.5% of the participants. There were 58.9% of participants in the younger age group. Obese participants made up 34.7% of this safety population.

Within each age group, most demographic characteristics were similar in the BNT162b2 group and the placebo group. There was a lower proportion on non-Hispanic/non-Latino participants in the younger BNT162b2 and placebo groups (68.1% and 68.3%, respectively) than in the older BNT162b2 and placebo groups (80.9% and 80.6%, respectively).

Demographics of participants in the final analysis evaluable efficacy population for participants without evidence of infection prior to 7 days after Dose 2 were similar in BNT162b2 and placebo groups. This analysis population had generally similar demographics compared to the safety population.

Demographic characteristics for the final analysis Dose 2 all-available efficacy population and the evaluable population without evidence of infection prior to 14 days after Dose 2 were similar to the Dose 2 evaluable efficacy (7 days) population

Efficacy Results:

Interim Analysis 1

- The first primary efficacy objective met success criteria. BNT162b2 achieved vaccine efficacy of 95.5% with a 95% credible interval of 88.8% to 98.4% among participants without evidence of infection before and during vaccination regimen, and a >99.99% posterior probability for the true vaccine efficacy greater than 30% conditioning on available data.

- All 7 severe COVID-19 cases (after Dose 1) were observed in the placebo group, as of the interim analysis cutoff dates.

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Final Analysis

Evaluable Efficacy Population

In the final efficacy analysis, among participants without evidence of SARS-CoV-2 infection before and during vaccination regimen, VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0%, with 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%.

For the second primary endpoint, VE against confirmed COVID-19 occurring at least 7 days after Dose 2 in participants with or without evidence of SARS-CoV-2 infection before and during vaccination regimen was 94.6%, with 9 and 169 cases in the BNT162b2 and placebo groups respectively. The posterior probability of >99.99% for the true VE greater than 30% met the prespecified success criterion of >98.6% for this endpoint. The 95% credible interval for the vaccine efficacy was 89.9% to 97.3%.

Observed VE was very high for the first primary efficacy endpoint across subgroups of age, sex, race/ethnicity, and country, as VE was >93% in all subgroups, with the exception of "all others" race group (89.3% VE) and Brazil (87.7% VE).

For the secondary efficacy endpoint, observed VE against confirmed COVID-19 occurring at least 14 days after Dose 2 in participants without evidence of SARS-CoV-2 infection before and during vaccination regimen, was 94.2%, with 8 and 139 cases in the BNT162b2 and placebo groups, respectively. The posterior probability of >99.99% for the true VE greater than 30% met the prespecified success criterion of >98.6% for this endpoint. The 95% credible interval for the vaccine efficacy was 88.7% to 97.2%.

Similarly, among participants with or without evidence of SARS-CoV-2 infection before and during vaccination regimen, VE against confirmed COVID-19 occurring at least 14 days after Dose 2 was 94.4%, with 8 and 144 cases in the BNT162b2 and placebo groups respectively. The posterior probability of >99.99% for the true VE greater than 30% met the prespecified success criterion of >98.6% for this endpoint. The 95% credible interval for the vaccine efficacy was 89.1% to 97.3%.

Among participants without evidence of SARS-CoV-2 infection before and during vaccination regimen, observed VE of 66.3% against severe COVID-19 occurring at least 7 days after Dose 2 did not meet the prespecified success criterion of the posterior probability >98.6%, due to the small number of severe cases (1 in the BNT162b2 group, 3 in the placebo group) observed within the prespecified timeframe of ≥7 days after Dose 2 in the study.

The efficacy analyses using CDC defined symptoms to identify a COVID-19 case gave similar efficacy results as the primary endpoint.

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All-Available Efficacy Population

The early onset of protection is readily apparent from cumulative incidence curves, which show that disease onset tracks conjointly for BNT162b2 and placebo until approximately 14 days after Dose 1, at which point the curves diverge, with cases steadily accumulating in the placebo group, while remaining virtually flat after BNT162b2.

Among all participants (regardless of evidence of infection before or during the vaccination regimen) 50 cases of COVID-19 occurred after Dose 1 in the BNT162b2 group compared with 275 cases in the placebo group, indicating an estimated VE of 82% (2-sided 95% CI: 75.6%, 86.9%) against confirmed COVID-19 occurring after Dose 1, with VE of 52.4% (95% CI: 29.5%, 68.4%) between Dose 1 and Dose 2.

Among the total of 10 severe COVID-19 cases observed after Dose 1, only 1 severe case was seen in BNT162b2 recipients compared to 9 severe COVID-19 cases in placebo recipients; these results, as well as case splits between Dose 1 and Dose 2 and after Dose 2, were consistent with overall efficacy seen against COVID-19.

In conclusion, the final efficacy results show that BNT162b2 at 30 µg provided protection against COVID-19 in participants who had no evidence of prior infection with SARS-CoV-2, including across demographic subgroups, with severe cases observed predominantly in the placebo group.

Safety Results:

- Across age groups, local reactions were generally similar in frequency after each dose, and systemic events generally increased in frequency and severity after Dose 2 compared to Dose 1. Local and systemic reactogenicity events were well-tolerated and short-lived (median durations of 1.0 to 2.0 days).

- Reactogenicity events after each dose of BNT162b2 in older adults were generally milder and less frequent than those observed in younger adults. The majority of reactogenicity events were mild or moderate in severity. No Grade 4 events were reported other than fever in 2 participants: 1 participant in the younger BNT162b2 group that began on Day 2 after Dose 2 and lasted 1 day, and 1 participant in the older BNT162b2 group that began on Day 4 after Dose 1 and lasted for 1 day.

- The reactogenicity profile after BNT162b2 30 µg evaluated in 8183 participants was consistent with the reactogenicity profile observed after BNT162b2 30 µg in Phase 1 and Phase 2.

- In the ~38,000 participants in Phase 2/3 with a median follow-up of at least 2 months after Dose 2, AEs were reported in 27.0% of participants in the BNT162b2 group, and most AEs were mild or moderate in severity. At the time of the data cutoff date, the number of participants with AEs in the BNT162b2 group was greater as compared with

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the placebo group (12.5%), which upon analysis, was attributed to reactogenicity events reported as AEs within 7 days after each dose.

- Analyses of the data for each population at the data cutoff date of 14 November 2020 (~38,000 with a median follow-up of 2 months after Dose 2, ~19,000 with at least 2 months of follow-up after Dose 2, and ~44,000 enrolled participants with variable length of follow-up) did not identify any new safety signals with longer follow-up or by examining all of the AEs reported in the database.

- At the time of the data cutoff date, there were 4 related SAEs in the BNT162b2 group (lymphadenopathy; shoulder injury related to vaccine administration [SIRVA], erroneously administered into or near the shoulder joint capsule; ventricular arrhythmia; and lower back pain and bilateral lower extremity pain with radicular paresthesia [uncoded term]), and few participants in the BNT162b2 group (0.2%) were withdrawn because of AEs. There were 2 deaths in the BNT162b2 group (arteriosclerosis and cardiac arrest) and 4 deaths in the placebo group that were assessed as not related to study intervention.

- Overall, BNT162b2 at 30 µg was well tolerated with a maximum follow-up time of up to 14 weeks after Dose 2.

Overall Conclusion(s):

- In Phase 1, BNT162b2 at 30 µg induced a robust immune response in both younger and older adults, and the reactogenicity profile was also satisfactory in both younger and older adults. BNT162b2 at 30 µg was selected for further development in the Phase 2/3 part of the study.

- In Phase 2, BNT162b2 at 30 µg elicited robust SARS-CoV-2 neutralization and S1-binding IgG antibody responses, consistent with results observed in Phase 1.

- In Phase 2/3, BNT162b2 at 30 µg provided protection against COVID-19 in participants irrespective of evidence of prior infection with SARS-CoV-2, including across demographic subgroups, with severe cases observed predominantly in the placebo group. The tolerability and safety profile of BNT162b2 30 µg was acceptable, and no clinically significant safety findings other than mild or moderate reactogenicity and mild and reversible lymphadenopathy were identified.

- Overall, the risk-benefit of BNT162b2 30 µg remains favorable.