CLINICAL STUDY REPORT SYNOPSIS

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

Report Title: Interim Report – 6 Month Update: 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 SE

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 Date: 13 March 2021

Serology Completion Dates: 22 March 2021 (Phase 1, Visit 8 [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.

Date of Current Version: 29 April 2021

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

CLINICAL STUDY REPORT SYNOPSIS

OBJECTIVES

Study Objectives and Endpoints:

Phase 1

The study objectives, estimands, and endpoints presented in Table S1 are from Protocol Amendment 14. Only the primary safety (Dose 1 to unblinding date [up to approximately 6 months after Dose 2]) and partial secondary immunogenicity (6 months after Dose 2) objectives for the BNT162b2 30 µg or corresponding placebo are presented in this interim clinical study report (CSR). Exploratory objectives, estimands, and endpoints will be summarized at a later time.

Table S1. Phase 1 Objectives, Estimands, and Endpoints

Objectives	Estimands	Endpoints	Reference
Primary:	**Primary:**	**Primary:**	
To describe the safety and tolerability profiles of prophylactic BNT162 vaccines in healthy adults after 1 or 2doses	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 • Serious adverse events (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.	Interim data for local reactions and systemic events reported up to 7 days after each dose, and AEs and SAEs are reported from Dose 1 to 1 month after the last dose for all groups evaluated, and to the cutoff date after Dose 2 for the BNT162b2 30 µg group only in final analysis interim CSR dated 03 December 2020. AEs and SAEs from Dose 1 to the unblinding date for the BNT162b2 30 µg group only are reported in this CSR. Interim data are reported in final analysis interim CSR dated 03 December 2020.

CLINICAL STUDY REPORT SYNOPSIS

Table S1. Phase 1 Objectives, Estimands, and Endpoints

Objectives	Estimands	Endpoints	Reference
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	Interim data reported up to 1 month after Dose 2 in final analysis interim CSR dated 03 December 2020. Interim data up to 6 months after Dose 2 for the BNT162b2 30 µg group only are reported in this CSR.
	• 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	Interim data reported up to 1 month after Dose 2 in final analysis interim CSR dated 03 December 2020. Interim data of S1-binding IgG levels up to 6 months after Dose 2 for the BNT162b2 30 µg group only are reported in this CSR.
	• Geometric mean ratio (GMR), estimated by the ratio of the geometric mean of SARS-CoV-2neutralizing 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	Interim data reported up to 1 month after Dose 2 in final analysis interim CSR dated 03 December 2020. Interim data for SARS-CoV-2 neutralizing titers to S1-binding IgG levels up to 6 months after Dose 2 for the BNT162b2 30 µg group only are reported in this CSR.

CLINICAL STUDY REPORT SYNOPSIS

Table S1. Phase 1 Objectives, Estimands, and Endpoints

Objectives	Estimands	Endpoints	Reference
Exploratory:	**Exploratory:**	**Exploratory:**	
To describe the immune responses elicited by a third dose of prophylactic BNT162b2 administered to healthy adults 6 to 12 months after the second dose of either BNT162b1 or BNT162b2	• GMC/GMT and GMFR at the time of Dose 3 and 7 days and 1 month after Dose 3.	• SARS-CoV-2 reference-strain neutralizing titers • SARS-CoV-2 South African (SA)-variant neutralizing titers • Full-length S-binding or S1-binding IgG levels	Data will be reported at a later time.
	• GMR of SARS-CoV-2 reference-strain neutralizing titers 1 month after Dose 3 to 1 month after Dose 2	• SARS-CoV-2 reference-strain neutralizing titers	Data will be reported at a later time.
	• GMR of SARS-CoV-2 SA-variant neutralizing titers 1 month after Dose 3 to SARS-CoV-2 reference-strain neutralizing titers 1 month after Dose 2	• SARS-CoV-2 reference-strain neutralizing titers • SARS-CoV-2 SA-variant neutralizing titers	Data will be reported at a later time.
To describe the safety profile of a third dose of prophylactic BNT162b2 administered to healthy adults 6 to 12 months after the second dose of either BNT162b1 or BNT162b2	In participants receiving a third dose of BNT162b2, the percentage of participants reporting: • Local reactions for up to 7 days after Dose 3 • Systemic events for up to 7 days after Dose 3 • AEs and SAEs from Dose 3 to 1 month after Dose 3	• 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	Data will be reported at a later time.

CLINICAL STUDY REPORT SYNOPSIS

Phase 2/3

The study objectives, estimands, and endpoints presented in Table S2 are from Protocol Amendment 14.

Based on a data cutoff date of 13 March 2021, this interim C4591001 CSR summarizes updated efficacy analyses on an accrued 927 COVID-19 cases for the first primary endpoint during blinded follow-up to evaluate duration of protection and the following immunogenicity and safety data:

- Blinded placebo-controlled follow-up period: from Dose 1 to 1 month after Dose 2 and to the date of unblinding:
    - Phase 2/3 safety analysis for participants ≥16 years of age, including participants with confirmed stable HIV disease, from Dose 1 to 1 month after Dose 2 (no exposure adjustment because all participants have the same follow-up period) and from Dose 1 to the unblinding date (exposure adjusted).
- Open-label observational follow-up period: from time of unblinding to the data cutoff date:
    - Phase 2/3 safety analysis for original BNT162b2 participants ≥16 years of age
    - Phase 2/3 safety analysis for original placebo participants ≥16 years of age who then received BNT162b2
- Cumulative safety from Dose 1 to at least 6 months after Dose 2: for Phase 2/3 original BNT162b2 participants ≥16 years of age (inclusive of blinded data and open-label data) that includes at least 3000 in each age group (16 through 55 years of age, >55 years of age)

CLINICAL STUDY REPORT SYNOPSIS

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

Objectives[a]	Estimands	Endpoints	Reference
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	Prespecified complete efficacy data are reported in final analysis interim CSR dated 03 December 2020. Updated efficacy data are reported in this CSR.
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	Interim data are reported in final analysis interim CSR dated 03 December 2020. Updated efficacy data are reported in this CSR.
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	Interim data are reported in final analysis interim CSR dated 03 December 2020.

CLINICAL STUDY REPORT SYNOPSIS

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

Objectives[a]	Estimands	Endpoints	Reference
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)	Interim data are reported up to 1 month after Dose 2 and to the data cutoff date (14 November 2020) in final analysis interim CSR dated 03 December 2020. Cumulative interim data up to the cutoff date are reported in this CSR.
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	Data will be reported separately.
To describe the safety and tolerability profile of BNT162b2$_{SA}$ given as 1 or 2 doses to BNT162b2-experienced participants, or as 2 doses to BNT162b2-naïve participants To describe the safety and tolerability profile of BNT162b2 given as a third dose to BNT162b2-experienced participants	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 last dose • SAEs from Dose 1 to 5 or 6 months after the last 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	Data will be reported at a later time.

CLINICAL STUDY REPORT SYNOPSIS

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

Objectives[a]	Estimands	Endpoints	Reference
Primary Immunogenicity *BNT162b2-experienced participants*			
To demonstrate the noninferiority of the anti–reference strain immune response after a third dose of BNT162b2 compared to after 2 doses of BNT162b2, in the same individuals	GMR of reference strain neutralizing titer (NT) 1 month after the third dose of BNT162b2 to 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the reference strain at 1 month after the third dose of BNT162b2 and 1 month after the second dose of BNT162b2	SARS-CoV-2 reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of the third dose of BNT162b2) of past SARS-CoV-2 infection	Data will be reported at a later time.
To demonstrate the noninferiority of the anti-SA immune response after 1 dose of $BNT162b2_{SA}$ compared to the anti–reference strain immune response after 2 doses of BNT162b2, in the same individuals	GMR of SA NT 1 month after 1 dose of $BNT162b2_{SA}$ to the reference strain NT 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the SA strain at 1 month after 1 dose of $BNT162b2_{SA}$ and seroresponse to the reference strain at 1 month after the second dose of BNT162b2	SARS-CoV-2 SA and reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of 1 dose of $BNT162b2_{SA}$) of past SARS-CoV-2 infection	Data will be reported at a later time.

CLINICAL STUDY REPORT SYNOPSIS

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

Objectives[a]	Estimands	Endpoints	Reference
BNT162b2-naïve participants			
To demonstrate the noninferiority of the anti-SA immune response after 2 doses of BNT162b2$_{SA}$ compared to the anti–reference strain immune response after 2 doses of BNT162b2	GMR of SA NT 1 month after the second dose of BNT162b2$_{SA}$ to the reference strain NT 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the SA strain at 1 month after the second dose of BNT162b2$_{SA}$ and seroresponse to the reference strain at 1 month after the second dose of BNT162b2	SARS-CoV-2 SA and reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of the second dose of BNT162b2$_{SA}$ or BNT162b2 as appropriate) of past SARS-CoV-2 infection	Data will be reported at a later time.
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	Prespecified complete efficacy data are reported in final analysis interim CSR dated 03 December 2020.
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	Prespecified complete efficacy data are reported in final analysis interim CSR dated 03 December 2020.
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	Prespecified complete efficacy data are reported in final analysis interim CSR dated 03 December 2020. Updated efficacy data occurring from at least 7 days after the second dose only are reported in this CSR.

CLINICAL STUDY REPORT SYNOPSIS

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

Objectives[a]	Estimands	Endpoints	Reference
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	Prespecified complete efficacy data are reported in final analysis interim CSR dated 03 December 2020. Updated efficacy data occurring from at least 7 days after the second dose only are reported in this CSR.
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 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	Prespecified complete efficacy data are reported in final analysis interim CSR dated 03 December 2020.
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 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	Prespecified complete efficacy data are reported in final analysis interim CSR dated 03 December 2020.
To evaluate the efficacy of prophylactic BNT162b2 against non-S seroconversion to SARS-CoV-2 in participants without evidence of infection or confirmed COVID-19	In participants complying with the key protocol criteria (evaluable participants): 100 × (1 – IRR) [ratio of active vaccine to placebo]	Incidence of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on SARS-CoV-2 nucleoprotein (N)-binding antibody seroconversion in participants with no serological or virological evidence of past SARS-CoV-2 infection or confirmed COVID-19	Data will be reported at a later time.
To evaluate the efficacy of prophylactic BNT162b2 against asymptomatic SARS-CoV-2 infection in participants without evidence of infection up to the start of the asymptomatic surveillance period	In participants complying with the key protocol criteria (evaluable participants): 100 × (1 – IRR) [ratio of active vaccine to placebo]	Incidence of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on central laboratory–confirmed NAAT in participants with no serological or virological evidence (up to the start of the	Data will be reported at a later time.

CLINICAL STUDY REPORT SYNOPSIS

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

Objectives[a]	Estimands	Endpoints	Reference
		asymptomatic surveillance period) of past SARS-CoV-2 infection	
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	Data will be reported separately.
BNT162b2-experienced participants			
To demonstrate the noninferiority of the anti-SA immune response after a third dose of BNT162b2 compared to the anti–reference strain immune response after 2 doses of BNT162b2, in the same individuals	GMR of SA NT 1 month after the third dose of BNT162b2 to the reference strain NT 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the SA strain at 1 month after the third dose of BNT162b2 and seroresponse to the reference strain at 1 month after the second dose of BNT162b2	SARS-CoV-2 SA and reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of the third dose of BNT162b2) of past SARS-CoV-2 infection	Data will be reported at a later time.
To demonstrate the noninferiority of the anti–reference strain immune response after 1 dose of BNT162b2$_{SA}$ compared to after 2 doses of BNT162b2, in the same individuals	GMR of reference strain NT 1 month after 1 dose of BNT162b2$_{SA}$ to 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the reference strain at 1 month after 1 dose of BNT162b2$_{SA}$ and 1 month after the second dose of BNT162b2	SARS-CoV-2 reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of 1 dose of BNT162b2$_{SA}$) of past SARS-CoV-2 infection	Data will be reported at a later time.
To descriptively compare the anti-SA immune response after 1 dose of BNT162b2$_{SA}$ and a third dose of BNT162b2	GMR of SA NT 1 month after 1 dose of BNT162b2$_{SA}$ to 1 month after the third dose of BNT162b2 The difference in percentages of participants with seroresponse to the SA strain at 1 month after 1 dose of	SARS-CoV-2 SA NT in participants with no serological or virological evidence (up to 1 month after receipt of 1 dose of BNT162b2$_{SA}$ or the third dose of BNT162b2) of past SARS-CoV-2 infection	Data will be reported at a later time.

CLINICAL STUDY REPORT SYNOPSIS

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

Objectives[a]	Estimands	Endpoints	Reference
	BNT162b2$_{SA}$ and 1 month after the third dose of BNT162b2		
To descriptively compare the anti-SA immune response after 2 doses of BNT162b2$_{SA}$ and the anti–reference strain immune response after 2 doses of BNT162b2, in the same individuals	GMR of SA NT 1 month after the second dose of BNT162b2$_{SA}$ to the reference strain NT 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the SA strain at 1 month after the second dose of BNT162b2$_{SA}$ and seroresponse to the reference strain at 1 month after the second dose of BNT162b2	SARS-CoV-2 SA and reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of the second dose of BNT162b2$_{SA}$) of past SARS-CoV-2 infection	Data will be reported at a later time.
BNT162b2-naïve participants			
To demonstrate a statistically greater anti-SA immune response after 2 doses of BNT162b2$_{SA}$ compared to after 2 doses of BNT162b2	GMR of SA NT 1 month after the second dose of BNT162b2$_{SA}$ to 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the SA strain at 1 month after the second dose of BNT162b2$_{SA}$ and 1 month after the second dose of BNT162b2	SARS-CoV-2 SA NTs in participants with no serological or virological evidence (up to 1 month after receipt of the second dose of BNT162b2$_{SA}$ or BNT162b2 as appropriate) of past SARS-CoV-2 infection	Data will be reported at a later time.
To descriptively compare the anti–reference strain immune response after 2 doses of BNT162b2$_{SA}$ and after 2 doses of BNT162b2	GMR of reference strain NT 1 month after the second dose of BNT162b2$_{SA}$ to 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to reference strain at 1 month after the second dose of BNT162b2$_{SA}$ and 1 month after the second dose of BNT162b2	SARS-CoV-2 reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of the second dose of BNT162b2$_{SA}$ or BNT162b2 as appropriate) of past SARS-CoV-2 infection	Data will be reported at a later time.

CLINICAL STUDY REPORT SYNOPSIS

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

Objectives[a]	Estimands	Endpoints	Reference
Exploratory			
To describe the efficacy of prophylactic BNT162b2 against confirmed COVID-19 occurring from 7 days after the second dose through the blinded follow-up period in participants without, and with and without, evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) 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 blinded follow-up based on central laboratory or locally confirmed NAAT	Interim data are reported in this CSR.
To describe the incidence of confirmed COVID-19 through the entire study follow-up period in participants who received BNT162b2 at initial randomization or subsequently	In participants who received BNT162b2 (at initial randomization or subsequently): Incidence per 1000 person-years of follow-up	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT	Data will be reported at a later time.
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 and GMFR at baseline and 1, 6, 12, and 24 months after completion of vaccination	• Full-length S-binding or S1-binding IgG levels • SARS-CoV-2 neutralizing titers	Interim data for Phase 2 (first 360 participants) only up to 1 month after Dose 2 are reported for S1-binding IgG levels and SARS-CoV-2 neutralizing titers in final analysis interim CSR dated 03 December 2020. Phase 2/3 data will be reported at a later time
To describe the incidence of non-S seroconversion to SARS-CoV-2 through the entire study follow-up period in participants who received BNT162b2 at initial randomization	In participants who received BNT162b2 at initial randomization: Incidence per 1000 person-years of follow-up	Incidence of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on N-binding antibody seroconversion in participants with no serological or virological evidence of past SARS-CoV-2 infection or confirmed COVID-19	Data will be reported at a later time.
To describe the efficacy of prophylactic BNT162b2 against asymptomatic SARS-CoV-2 infection in participants with evidence of infection up to the start of the asymptomatic surveillance period	In participants complying with the key protocol criteria (evaluable participants): 100 × (1 – IRR) [ratio of active vaccine to placebo]	Incidence of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on central laboratory–confirmed NAAT in participants with serological or virological evidence (up to the start of the	Data will be reported at a later time.

CLINICAL STUDY REPORT SYNOPSIS

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

Objectives[a]	Estimands	Endpoints	Reference
		asymptomatic surveillance period) of past SARS-CoV-2 infection	
To describe the serological responses to the BNT vaccine candidate and characterize the SARS-CoV-2 isolate in cases of: • Confirmed COVID-19 • Confirmed severe COVID-19 • SARS-CoV-2 infection without confirmed COVID-19		• Full S-binding or S1-binding IgG levels • SARS-CoV-2 neutralizing titers • Identification of SARS-CoV-2 variants(s)	Data will be reported at a later time.
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	Safety data only in participants with confirmed stable HIV disease are reported in this CSR.
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"		• AEs • SAEs • SARS-CoV-2 neutralizing titers	Data will be reported at a later time.
To describe the immune response to any variants of concern (VOCs) not already specified	Geometric mean NT for any VOCs not already specified, after any dose of BNT162b2$_{SA}$ or BNT162b2	• SARS-CoV-2 NTs for any VOCs not already specified	Data will be reported at a later time.
To describe the cell-mediated immune response, and additional humoral immune response parameters, to the reference strain and SA in a subset of participants: • 7 Days and 1 and 6 months after BNT162b2$_{SA}$ given as 1 or 2 doses to BNT162b2-experienced participants • 7 Days and 1 and 6 months after BNT162b2$_{SA}$ given as 2 doses to BNT162b2-naïve participants			Data will be reported at a later time.

CLINICAL STUDY REPORT SYNOPSIS

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

Objectives[a]	Estimands	Endpoints	Reference
• 7 Days and 1 and 6 months after BNT162b2 given as a third dose to BNT162b2-experienced participants			

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

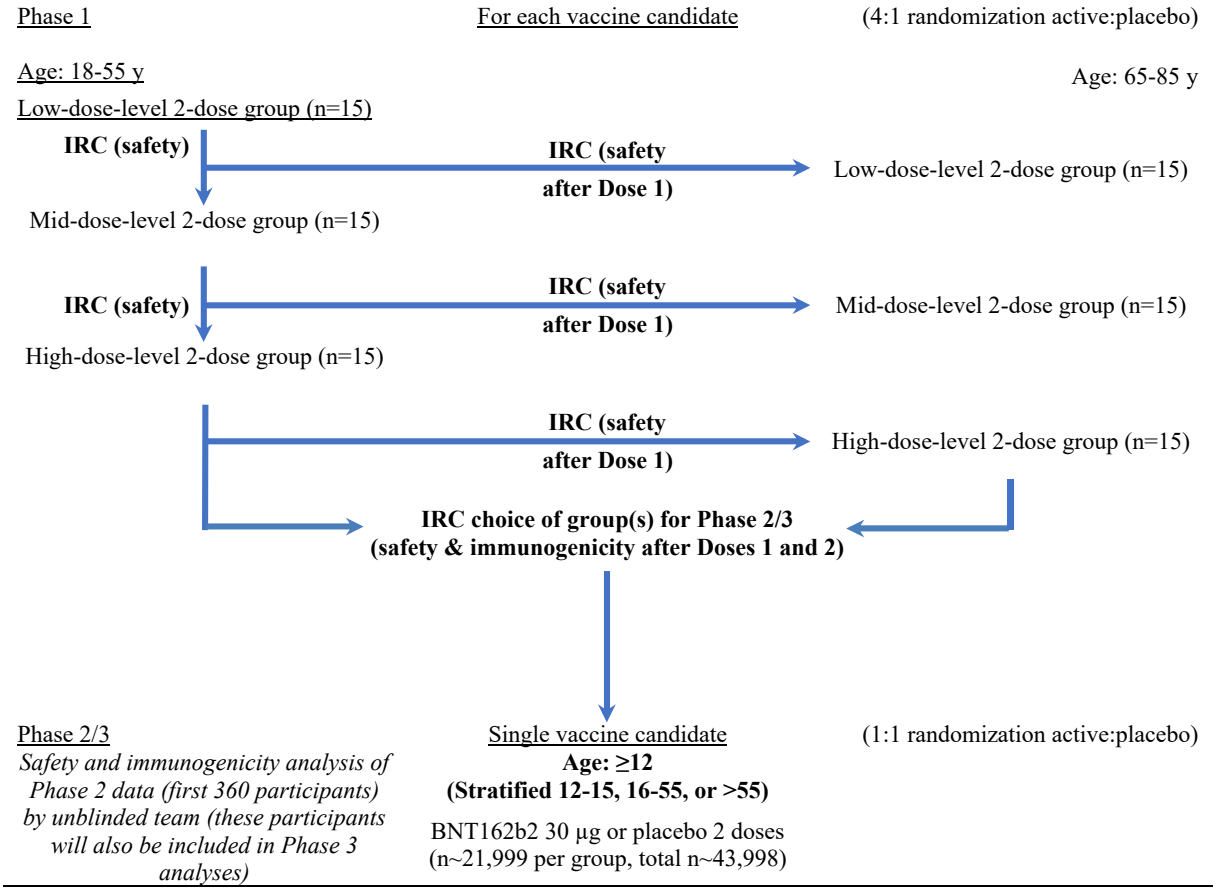
CLINICAL STUDY REPORT SYNOPSIS

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.

Figure S1. Study Schema



Abbreviation: IRC = internal review committee
Note: Participants ≥16 years of age who originally received placebo were offered the opportunity to receive BNT162b2 at defined points as part of the study

The study evaluated the safety, tolerability, and immunogenicity of 3 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;

CLINICAL STUDY REPORT SYNOPSIS

- At various dose levels in Phase 1;
- As a booster; (data will be reported at a later time)
- In various age groups:
  - Phase 1: 18 to 55 and 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).

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.

Planned Booster and Variant Strain Evaluation

Planned booster and VOC evaluation are not included in this report and will be reported at a later time.

Unblinding Considerations

The study was unblinded in stages once all ongoing participants either had been individually unblinded or had concluded their 6-month post–Dose 2 study visit, as follows:

- Phase 1 (after Visit 8).
- Phase 2/3, ≥16 years of age (after Visit 4).
- Phase 3, 12 through 15 years of age (after Visit 4).
- Original Phase 3 participants rerandomized to assess boostability and protection against emerging VOCs (after Visit 306) (data will be reported at a later time).

Participants ≥16 years of age who originally received placebo and became eligible for receipt of BNT162b2 according to recommendations detailed separately, and available in the electronic study reference portal, had the opportunity to receive BNT162b2 in a phased manner as part of the study. The investigator ensured the participant met at least 1 of the recommendation criteria.

Any Phase 1 placebo recipient who had not already been offered the opportunity to receive BNT162b2 was given this opportunity no later than at the approximate time participants in Phase 2/3 reached Visit 4. Any Phase 2/3 placebo recipient ≥16 years of age who had not

CLINICAL STUDY REPORT SYNOPSIS

already been offered the opportunity to receive BNT162b2 was given this opportunity no later than 6 months after Vaccination 2 (at the time of the originally planned Visit 4).

Any participant who originally received placebo but then went on to receive BNT162b2 was moved to a new visit schedule to receive both doses of BNT162b2 at each of 2 additional vaccination visits (Visits 101 and 102).

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.

Planned Evaluations

- A third dose of BNT162b2 30 µg will be given to Phase 1 participants approximately 6 to 12 months after their second dose of BNT162b1 or BNT162b2 to evaluate safety and immunogenicity for boostability and potential heterologous protection against emerging VOCs.

Participants were expected to participate for up to a maximum of approximately 26 months.

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 through 55 years and >55 through 85 years] with approximately 50% in each age stratum) to assess

CLINICAL STUDY REPORT SYNOPSIS

safety data through 7 days after Dose 2 and immunogenicity data through 1 month after Dose 2 from these Phase 2 360 participants. 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 through 15, 16 through 55, or >55 years of age). The 12- through 15- year stratum comprised 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 either active vaccine or placebo.

Efficacy analyses for Phase 2/3 part of the study were event-driven. The prespecified interim analysis was conducted on an accrued 94 evaluable COVID-19 cases for the first primary efficacy endpoint (data cutoff date: 04 November 2020), and the final analysis was conducted on an accrued 170 evaluable COVID-19 cases for the first primary efficacy endpoint (data cutoff date: 14 November 2020). These data are reported in the final analysis interim CSR dated 03 December 2020 and included all study participants in the efficacy populations ≥12 years of age.

At the time of the final analysis of efficacy, relatively few participants 12 through 15 years of age had enrolled in the study, and no COVID-19 cases in this age group accrued at that time. Updated efficacy analyses during blinded placebo-controlled follow-up period were conducted on cases accrued up to the data cutoff date of 13 March 2021 to evaluate duration of protection. This report presents these analyses of all confirmed COVID-19 cases and any cases meeting protocol- and CDC-defined criteria for severe cases.

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

Planned Evaluations

Phase 2/3 (which is ongoing) includes additional planned analyses which are not included in this report and will be reported separately.

- In Phase 3, noninferiority of immune response to prophylactic BNT162b2 in participants 12 through 15 years of age to response in participants 16 through 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 through 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.

- Boostability and homologous/heterologous protection against emerging VOCs will allow the evaluation of safety and immunogenicity of BNT162b2$_{SA}$.

CLINICAL STUDY REPORT SYNOPSIS

- An intensive period of surveillance to evaluate the efficacy of BNT162b2 against asymptomatic SARS CoV-2 infection is being conducted at selected sites among Phase 2/3 participants.

Inclusion/Exclusion Criteria: Inclusion and exclusion criteria presented are reflected through Protocol Amendment 13 for this ongoing study. Updated inclusion and exclusion criteria of the subset of participants receiving the booster dose against emerging VOCs based on Protocol Amendment 14 are not analyzed in this report, and therefore, are not presented in this synopsis.

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.

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.

CLINICAL STUDY REPORT SYNOPSIS

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
    - 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).

CLINICAL STUDY REPORT SYNOPSIS

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.

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.

CLINICAL STUDY REPORT SYNOPSIS

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.

Vaccines Administered: The vaccine candidate selected for Phase 2/3 evaluation was BNT162b2 at a dose of 30 µg. This report evaluated a 2-dose (separated by 21 days) schedule of the following for active immunization against COVID-19 or saline placebo:

- BNT162b2 (BNT162 RNA-LNP vaccine containing modRNA that encodes P2 S): 30 µg
- Normal saline (0.9% sodium chloride solution for injection)

The final analysis interim C4591001 CSR dated 03 December 2020 for BNT162b1 and BNT162b2 presented other candidate dose levels previously evaluated.

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

CLINICAL STUDY REPORT SYNOPSIS

Table S3. Investigational Product Lot Numbers – Interim – 6 Month Update

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/P220395-0019L
			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

CLINICAL STUDY REPORT SYNOPSIS

Table S3. Investigational Product Lot Numbers – Interim – 6 Month Update

			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
			EE3813	NC2075485/P220395-0068L
			EE3813	NC2075485/P220395-0074L
			EE3813	NC2075485/P220395-0077L
			EJ0553Z	PA2085061/P220395-0070L
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/P220395-0034L
			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

CLINICAL STUDY REPORT SYNOPSIS

Table S3. Investigational Product Lot Numbers – Interim – 6 Month Update

	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 17Mar2021 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 – Interim – 6 Month Update, Final, Version 1.0, 18Mar2021.

Efficacy and Immunogenicity Evaluations: Efficacy was assessed for potential cases of COVID-19 and described in the final analysis interim C4591001 CSR dated 03 December 2020. The prespecified interim analysis was conducted on an accrued 94 evaluable COVID-19 cases (data cutoff date: 04 November 2020), and the final analysis was conducted on an accrued 170 evaluable COVID-19 cases for the first primary efficacy endpoint (data cutoff date: 14 November 2020). These analyses included data from all participants in Phase 3 age groups (12-15, 16-55, and >55 years of age) at the time of the analyses. Prespecified primary and secondary efficacy endpoint analyses were completed per protocol as of 14 November 2020, and no additional formal hypothesis testing of clinically confirmed COVID-19 cases is planned. At the time of the final analysis, there were relatively few participants 12-15 years of age enrolled in the study and no COVID-19 cases in this age group accrued at that time (14 November 2020). In this report, efficacy was assessed based on all cases in participants ≥12 years of age accrued in blinded follow-up to a data cutoff date of 13 March 2021.

Confirmed COVID-19: presence of at least 1 of the following symptoms and SARS-CoV-2 NAAT-positive during, or within 4 days before or after, the symptomatic period, either at the central laboratory or at a local testing facility (using an acceptable test):

- Fever;
- New or increased cough;
- New or increased shortness of breath;
- Chills;
- New or increased muscle pain;
- New loss of taste or smell;

- Sore throat;
- Diarrhea;
- Vomiting.

The second definition, which may be updated as more is learned about COVID-19, includes the following additional symptoms defined by the CDC (listed at https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html):

- Fatigue;
- Headache;
- Nasal congestion or runny nose;
- Nausea.

- 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, SpO_2 ≤93% on room air at sea level, or PaO_2/FiO_2 <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 intensive care unit (ICU);
  - Death.

In addition to the above specified definition of severe COVID-19, an efficacy analysis for any severe COVID-19 cases was conducted using the CDC definition of severe COVID-19 (hospitalization, admission to the ICU, intubation or mechanical ventilation, or death).

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 neutralization assay (reference strain and SA variant [data from SA variant will be reported at a later time])

CLINICAL STUDY REPORT SYNOPSIS

- Full length S-binding or S1-binding IgG levels (most relevant to BNT162b2 which encodes P2 S)

- RBD-binding IgG level assay (most relevant to BNT162b1, which encodes the RBD, Phase 1 only, and previously reported in the final analysis interim C4591001 CSR dated 03 December 2020))

Safety Evaluations:

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 through 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 were included in the reactogenicity subset. All other participants, including those who originally received placebo and then received BNT162b2 under Protocol Amendment 10 and onwards, did not complete an e-diary but had their local reactions and systemic events 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) 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.

CLINICAL STUDY REPORT SYNOPSIS

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).

Additionally, for those participants who originally received placebo but went on to receive BNT162b2 at Vaccinations 3 and 4, AEs were collected from the time the participant provided informed consent (for receipt of Vaccinations 3 and 4) through and including Visit 103. SAEs were collected from the time the participant provides informed consent (for receipt of Vaccinations 3 and 4) to approximately 6 months after the second dose of BNT162b2 (Visit 104).

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. Vaccine efficacy (VE) with respect to the first primary efficacy endpoint was assessed at the first interim analysis (at least 62 cases) at 94 cases (data cutoff date: 04 November 2020). At the final analysis, VE with respect to the first primary efficacy endpoint (at least 164 cases) was assessed on an accrued 170 evaluable COVID-19 cases (data cutoff date: 14 November 2020) and also included VE for the second primary and all secondary efficacy endpoints. No additional formal hypothesis testing of clinically confirmed COVID-19 cases is planned.

Assessment of VE of BNT162b2 was performed for confirmed COVID-19 cases observed at least 7 days after the receipt of Dose 2 onwards among participants without or with or 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.

Updated descriptive efficacy analyses during blinded placebo-controlled follow-up were conducted based on the data cutoff date of 13 March 2021 for the primary efficacy endpoints and for the secondary efficacy endpoint of severe disease, including subgroup analyses.

CLINICAL STUDY REPORT SYNOPSIS

The point estimate of VE in the blinded follow-up period and associated 2-sided 95% CI was derived using the Clopper Pearson method adjusted for surveillance time, and the posterior probability (ie, P[VE >30%|data]) was provided for the primary endpoints and secondary endpoints of severe disease. In addition to the protocol definition of severe COVID-19, supportive analyses using the CDC definition of severe COVID-19 was also performed.

COVID-19 cases and severe COVID-19 cases occurring after Dose 1 were also summarized descriptively and previously reported in the final analysis interim C4591001 CSR dated 03 December 2020. Updated COVID-19 and severe COVID-19 cases after Dose 1 were summarized descriptively based on the data cutoff date of 13 March 2021.

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.

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; reported in the final analysis interim C4591001 CSR dated 03 December 2020), 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.

CLINICAL STUDY REPORT SYNOPSIS

- 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 results for individuals with confirmed stable HIV disease were summarized descriptively. Furthermore, VE may be assessed if there is a sufficient number of COVID-19 cases in this group of participants.

AEs and SAEs reported during the open-label follow-up period were summarized separately for participants who were unblinded at the time of being eligible for receipt of BNT162b2 according to recommendations detailed separately, and available in the electronic study reference portal, or no later than at approximately Visit 4. To account for different durations of follow-up time due to unblinding in the study, AEs and SAEs during the blinded follow-up period and open label follow-up period were summarized as incidence rates adjusted by exposure time.

RESULTS – PHASE 1

Participant Disposition and Demography: All participants in each age group (18 through 55 and 65 through 85 years) randomized to the BNT162b2 group completed the visit at 6 months after Dose 2, with most of these visits occurring during the open-label follow-up period. All participants in each age group randomized to the placebo group received both doses of BNT162b2 (Dose 3 and Dose 4 in the study) during the open-label period and completed the visit at 1 month after Dose 4, as of the data cutoff date of 13 March 2021. No participants were withdrawn from the study up to the data cutoff date.

Demographics for Phase 1 healthy participants were previously reported in the final analysis interim C4591001 CSR dated 03 December 2020.

Immunogenicity Results:

Geometric Mean Titers (GMTs) and Geometric Mean Concentrations (GMCs)

Among participants who received the 30 µg dose level of BNT162b2, in both age groups, the observed SARS-CoV-2 serum 50% neutralizing GMTs declined from 1 month after Dose 2 (Day 52) to 6 months after Dose 2 (Day 202). In the younger age group, GMTs were 179.2 at 1 month after Dose 2 and 54.7 at 6 months after Dose 2; in the older age group GMTs declined from 151.6 to 29.0. Observed S1-binding IgG GMCs demonstrated similar declines.

Geometric Mean Fold Rises (GMFRs)

In the younger and older age groups, respectively, GMFRs of SARS-CoV-2 serum 50% neutralizing titers from before vaccination with BNT162b2 30 µg to each subsequent time point were 2.9 and 1.7 at Day 21 (before Dose 2); 17.9 and 15.2 at 1 month after Dose 2; 5.5

CLINICAL STUDY REPORT SYNOPSIS

and 2.9 at 6 months after Dose 2. Results for GMFRs of S1-binding IgG concentrations reflected similar trends.

Geometric Mean Ratios (GMRs)

At 6 months after Dose 2 of BNT162b2 30 µg, GMRs of SARS-CoV-2 50% neutralizing titers to S1-binding IgG levels were 0.057 in the younger age group and 0.052 in the older age group. These values are similar to those observed at Day 21.

Number (%) of Participants Achieving a ≥4-Fold Rise from Baseline

In the younger age group, the proportions of participants achieving a ≥4-fold rise in SARS-CoV-2 50% neutralizing titers from before vaccination to each time point were: 50.0% (6/12) at Day 21; 100.0% (11/11) at 1 month after Dose 2; and 60.0% (6/10) at 6 months after Dose 2 of BNT162b2 30 µg. In the older age group, these proportions were 9.1% (1/11) at Day 21; 81.8% (9/11) at 1 month after Dose 2; and 27.3% (3/11) at 6 months after Dose 2 of BNT162b2 30 µg.

With respect to S1-binding IgG concentrations, 100% of participants in both age groups had a ≥4-fold increase from baseline at each of these time points.

Immunogenicity Conclusions:

For Phase 1 participants who received BNT162b2 30 µg, at 6 months after Dose 2, SARS-CoV-2 serum neutralizing titers and serum S1-binding IgG concentrations had decreased relative to those observed at 1 month after Dose 2, but remained higher than values observed at prevaccination and compared with the placebo group.

Safety Results:

Local Reactions and Systemic Events

The majority of reactogenicity events were mild or moderate in severity. Local and systemic reactogenicity events after each dose for both BNT162b1 and BNT162b2 in older adults were milder and less frequent than those observed in younger adults. Reactogenicity was generally higher after Dose 2 than Dose 1.

Adverse Events

From Dose 1 of BNT162b2 30 µg to the unblinding date, 6 (50.0%) participants in the younger age group and 3 (25.0%) participants in the older age group reported at least 1 AE. Two (16.7%) participants in the BNT162b2 30 µg younger age group and 1 (8.3%) participant in the BNT162b2 30 µg older age group reported at least 1 severe AE. In the BNT162b2 30 µg younger age group, 3 (25.0%) participants reported at least 1 related AE and 1 (8.3%) participant reported 1 severe SAE.

CLINICAL STUDY REPORT SYNOPSIS

No AEs were reported in either the younger or older participants in the placebo group. No SAEs or related AEs were reported in the BNT162b2 30 µg older age group. No AEs leading to withdrawal, life-threatening AEs, or deaths were reported in either the younger or older participants in the BNT162b2 30 µg group.

From Dose 1 of BNT162b2 30 µg to the unblinding date, AEs were most commonly reported in the system organ class (SOC) of nervous system disorders (3 [25.0%] participants in the younger age group and 1 [8.3%] participant in the older age group), followed by musculoskeletal and connective tissue disorders (1 [8.3%] participant in each age group). All AEs by preferred term (PT) were reported by no more than 1 participant.

There were no Phase 1 participants randomized to BNT162b2 30 µg or corresponding placebo who died through the data cutoff date of 13 March 2021. From Dose 1 to the unblinding date, 1 participant in the BNT162b2 30 µg younger age group reported a severe SAE (neuritis) that was assessed by the investigator as not related to study intervention. No Phase 1 participants randomized to BNT162b2 30 µg or corresponding placebo reported any AEs leading to withdrawal from the study from Dose 1 to the unblinding date. AEs of special interest were not defined for Phase 1 of this study. Pregnancy was not reported in any Phase 1 participants through the data cutoff date of 13 March 2021.

Clinical Laboratory Evaluation

Clinical laboratory evaluations, presented in final analysis interim C4591001 CSR dated 03 December 2020, 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.

Physical Examination Findings

Overall, there were fewer abnormalities noted during physical examinations after BNT162b2 than after BNT162b1 in both age groups. Full details of physical examinations are presented in the final analysis interim C4591001 CSR dated 03 December 2020.

Safety Conclusions:

BNT162b2 30 µg was safe and well tolerated at up to 6 months after Dose 2.

CLINICAL STUDY REPORT SYNOPSIS

RESULTS – PHASE 2/3

AE safety data are from either the blinded placebo-controlled follow-up period, the open-label observational follow-up period, or both. The time periods and safety analysis groups are presented below in Figure S2.

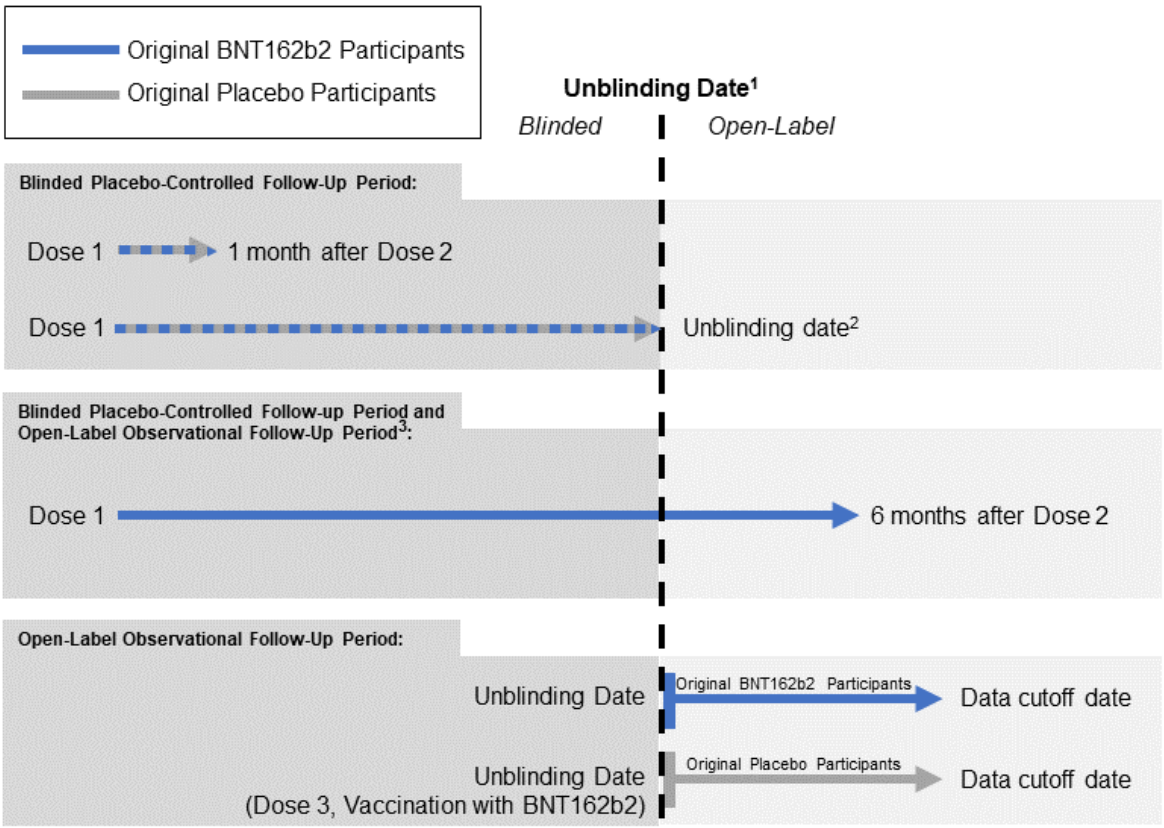
- Blinded placebo-controlled follow-up period from Dose 1 to 1 month after Dose 2 (frequencies)
- Blinded placebo-controlled follow-up period from Dose 1 to the unblinding date (IRs)
- Open-label follow-up period – original BNT162b2 participants (IRs)
- Blinded placebo-controlled and open-label follow-up periods from Dose 1 to 6 months after Dose 2 – original BNT162b2 participants (frequencies)
- Open-label follow-up period – original placebo participants who then received BNT162b2 (IRs)

For AE analyses beyond 1 month after Dose 2, and for AEs after unblinding, IRs per 100 Person-Years are reported (as opposed to frequencies) to account for the variable exposure since unblinding began for individual participants.

In this ongoing study, tables summarizing participant withdrawals may include some participants who were reported as withdrawn but remain in the study and are continuing to be evaluated. These participants are documented in the Errata.

CLINICAL STUDY REPORT SYNOPSIS

Figure S2. Phase 2/3 Safety Analyses: Time Periods and Analysis Groups



[1] Will vary by participant. Adverse event data analyzed from Dose 1 to unblinding date (on or after 14 December 2020), or from unblinding date to data cutoff date, are reported as incidence rates adjusted for exposure time.
[2] Up to ~6 months after Dose 2.
[3] Cumulative BNT162b2 follow-up to at least 6 months after Dose 2.

Participant Disposition and Demography:

During the blinded placebo-controlled follow-up period, 11253 (51.1%) participants in the BNT162b2 group and 11316 (51.4%) participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2. From Dose 2 to the cutoff date (blinded placebo-controlled and open-label follow-up periods, inclusive), 12006 (54.5%) participants in the BNT162b2 group had a total follow-up time of ≥6 months.

Disposition – Blinded Placebo-Controlled Follow-Up Period

During the blinded placebo-controlled follow-up period, most participants randomized received Dose 1 (99.8%) and Dose 2 (98.1%). There were 352 (1.6%) participants in the

CLINICAL STUDY REPORT SYNOPSIS

BNT162b2 group and 528 (2.4%) participants in the placebo group who discontinued from the vaccination period. Most participants completed the visit at 1 month post-Dose 2 (≥96.4%). Few participants in the BNT162b2 and placebo groups were withdrawn from the study (1.6% and 2.2%, respectively), and most were due to withdrawals by the participant, or they were lost to follow-up.

There were 7 participants with special data issues: 8 participant identification numbers from 4 participants who enrolled into the study more than once and 3 participants whose vaccine assignment was not confirmed in the interactive response technology (IRT) at the time of data cutoff.

- Three participants who were randomized and vaccinated, but actual vaccine assignment was not confirmed in the IRT at the time of data cutoff. Participants were vaccinated as per the case report form (CRF), but due to the inability to confirm consistency between the data in the CRF and IRT, these participants were not assigned to any actual dosing group.

- During the conduct of this study, 4 participants were each randomized twice with different participant identification numbers at 2 different sites. Because the significant misconduct of these participants compromised the integrity of the study data, results from these participants were excluded from all efficacy and safety analyses, including disposition and demographic tabulations.

Disposition – Open-Label Follow-Up Period

Individuals ≥16 years of age have been unblinded as they became locally eligible and wished to know their vaccine assignment to confirm prior vaccination with BNT162b2 (if randomized to this group), or to receive BNT162b2 (if randomized to placebo). Unblinded recipients originally randomized to BNT162b2 continue to be followed in an open-label manner. Unblinded recipients originally randomized to placebo are offered BNT162b2 vaccination (Doses 3 and 4 [first and second dose of BNT162b2 30 µg, respectively]) and thereafter followed in an open-label manner.

Most participants in the BNT162b2 (96.8%) and placebo (96.4%) groups completed the 1 month post-Dose 2 visit before unblinding.

A total of 87 (0.4%) Phase 2/3 original BNT162b2 participants received Dose 1 of BNT162b2 during the blinded placebo-controlled follow-up period and then received Dose 2 of BNT162b2 30 µg during the open-label follow-up period (when they were unblinded). There were 105 (0.5%) participants withdrawn from the study, and most were due to withdrawals by the participant or because of a protocol deviation.

During the open-label follow-up period, most participants originally randomized in the placebo group received Doses 3 and 4 (88.8% and 72.4%, respectively) of BNT162b2. There

were few participants in this group (0.1%) who were withdrawn from the study, and most were due to withdrawals by the participant.

The disposition of HIV-positive participants is included in this summary but summarized separately in safety analyses.

Disposition of all participants ≥16 years of age randomized was similar by age group.

Demographics – Safety Population

Overall

Demographic characteristics for all Phase 2/3 participants ≥16 years of age were similar in the BNT162b2 and placebo groups. Overall, most participants were White (82.0%), with 9.6% Black or African American participants and 4.3% Asian participants, and all other racial groups were ≤2.5%. There were 25.9% Hispanic/Latino participants. Median age was 51.0 years and 50.9% of participants were male. Obesity was reported in 34.4% of participants in this safety population.

Baseline SARS-CoV-2 status was positive (defined as positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19) in 3.1% of participants in the BNT162b2 group and 3.3% of participants in the placebo group.

Demographic characteristics for participants with confirmed stable HIV disease were similar in the BNT162b2 and the placebo groups. Overall, 54.5% of participants were Black or African American, 40.5% of participants were White, and all other racial groups were ≤1.5%. There were 16.0% Hispanic/Latino participants. Median age was 49.5 years and 67.5% of participants were male. Obese participants made up 39.0% of this population.

Participants With At Least 6 Months Follow-Up Time – Original BNT162b2 Participants

Overall, most Phase 2/3 participants ≥16 years of age who originally received BNT162b2 and had at least 6 months of follow-up time after Dose 2 were White (86.4%), with 7.1% Black or African American participants and 3.8% Asian participants, and other racial groups were ≤1.6%. There were 27.8% Hispanic/Latino participants. Median age was 53.0 years and 50.3% of participants were male. Obese participants made up 34.2% of this safety population.

Original Placebo Participants Who Then Received BNT162b2

Overall, most participants who originally received placebo and received BNT162b2 later during the open-label follow-up period were White (83.1%), with 8.3% Black or African American participants and 4.3% Asian participants, and all other racial groups were ≤2.6%. There were 25.5% Hispanic/Latino participants. Median age was 51.0 years and 50.2% of participants were male. Obese participants made up 34.4% of this safety population.

CLINICAL STUDY REPORT SYNOPSIS

All Participants

Demographic characteristics for all participants (including adolescents) were similar in the BNT162b2 group and the placebo group.

Evaluable Efficacy *(7 Days) Population – Blinded Placebo-Controlled Follow-Up Period*

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

Efficacy Results:

Updated Analysis – Efficacy Against Confirmed COVID-19

- In the updated descriptive efficacy analysis (cutoff date 13 March 2021), among participants in the evaluable efficacy population without evidence of SARS-CoV-2 infection before and during the vaccination regimen, the estimated VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 91.3% (2-sided 95% CI: 89.0%, 93.2%), with 77 cases in the BNT162b2 group and 850 cases in the placebo group. Among participants with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen, the estimated VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 91.1% (2-sided 95% CI: 88.8%, 93.0%), with 81 and 873 cases in the BNT162b2 and placebo groups, respectively.

- All cases of confirmed COVID-19 are accounted for in the analyses of VE in the all-available (modified intention-to-treat) population (regardless of evidence of infection before or during the vaccination regimen). In this analysis, the estimated VE against all cases occurring at any time after Dose 1 was 87.8% (2-sided 95% CI: 85.3%, 89.9%), with 131 cases in the BNT162b2 group and 1034 cases in the placebo group.

- In this same all-available (modified intention-to-treat) population, the estimated VE against all cases occurring ≥7 days after Dose 2 was 91.2%. The estimated VE was 91.7% from ≥11 days after Dose 1 to before Dose 2, 96.2% for cases occurring from ≥7 days after Dose 2 to <2 months after Dose 2, 90.1% for the period from ≥2 months to <4 months after Dose 2, and 83.7% for the period ≥4 months after Dose 2.

Efficacy in Demographic and Risk Subgroups

Among participants without evidence of SARS-CoV-2 infection before and during the vaccination regimen (efficacy evaluable population), estimated VE against COVID-19 occurring at least 7 days after Dose 2 was evaluated for demographic and risk subgroups, with results as follows:

CLINICAL STUDY REPORT SYNOPSIS

- Estimated VE was ≥90% in most demographic subgroups, similar to the estimated 91.3% overall VE.

- High VE was observed across age subgroups, with an estimated VE of 100.0% in 12 to 15 year olds, 90.6% in 16 to 64 year olds, 94.5% in those ≥65 years, and 96.2% in those ≥75 years of age.

- The estimated VE was 86.5% in Argentina, 86.2% in Brazil, 92.6% in the United States, and 100.0% in South Africa, Germany, and Turkey.

- The estimated VE was similar for participants at risk (91.6%) and participants not at risk (91.0%). The estimated VE for participants ≥65 years of age and at risk was 91.8%, as compared with 98.1% for those ≥65 years of age and not at risk. The estimated VE was similar in obese (91.6%) and non-obese (91.1%) participants. When evaluated by type of comorbidity, the estimated VE was >85% for participants with each comorbidity evaluated, including any malignancy, cardiovascular disease, chronic pulmonary disease, diabetes, obesity, and hypertension.

Efficacy Against Severe Cases of COVID-19

- Among participants without evidence of SARS-CoV-2 infection before and during the vaccination regimen (evaluable efficacy population), the estimated VE against FDA-defined severe COVID-19 (protocol definition) occurring at least 7 days after Dose 2 was 95.3% (2-sided 95% CI: 71.0%, 99.9%), with 1 and 21 cases in the BNT162b2 and placebo groups, respectively. Similarly, the estimated VE was also 95.3% (2-sided 95% CI: 70.9%, 99.9%) among participants with or without evidence of SARS-CoV-2 infection, also with 1 and 21 cases in the BNT162b2 and placebo groups, respectively.
- Among participants without evidence of SARS-CoV-2 infection before and during the vaccination regimen (evaluable efficacy population), the estimated VE against CDC-defined severe COVID-19 occurring at least 7 days after Dose 2 was 100.0% (2-sided 95% CI: 88.1%, 100.0%), with 0 and 32 cases in the BNT162b2 and placebo groups, respectively. Similarly, the estimated VE was also 100.0% (2-sided 95% CI: 88.0%, 100.0%) among participants with or without evidence of SARS-CoV-2 infection, also with 0 and 32 cases in the BNT162b2 and placebo groups, respectively.
- Among participants in the Dose 1 all-available (modified intention-to-treat) population (regardless of evidence of infection before or during the vaccination regimen), the estimated VE against FDA-defined severe cases of COVID-19 occurring at any time after Dose 1 was 96.7% (2-sided 95% CI: 80.3%, 99.9%), with 1 case of severe COVID-19 in the BNT162b2 group compared to 30 cases in the placebo group.

CLINICAL STUDY REPORT SYNOPSIS

Safety Results:

Blinded Placebo-Controlled Follow-Up Period From Dose 1 to 1 Month After Dose 2

Local Reactions and Systemic Events

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 1 participant.

There were 177 BNT162b2 and 187 placebo participants with baseline positive SARS-CoV-2 status, and 4701 BNT162b2 and 4690 placebo participants with baseline negative SARS-CoV-2 status. Differences observed in local reactions and systemic events by baseline SARS-CoV-2 status were not clinically meaningful. Note that the baseline SARS-CoV-2 positive subgroup included far fewer participants the negative subgroup, so their results should be interpreted with caution.

Adverse Events

Most AEs from Dose 1 to 1 month after Dose 2 were mild or moderate in severity. The percentages of overall participants who reported at least 1 AE and at least 1 related AE were higher in the BNT162b2 group (30.2% and 23.9%, respectively) as compared with the placebo group (13.9% and 6.0%, respectively),which upon analysis, was attributed to reactogenicity events reported as AEs within 7 days after each dose. Severe AEs were reported by 1.2% and 0.7% in in the BNT162b2 and placebo groups respectively, and life-threatening AEs were similar (0.1% in both groups).

Most Tier 2 AEs were reactogenicity events and all were reported in 4 SOCs: general disorders and administration site conditions, musculoskeletal and connective tissue disorders, nervous system disorders, and gastrointestinal disorders. The proportions of participants reporting Tier 2 AEs were generally higher in the BNT162b2 group (N=21,926; ranging from 1.1% to 13.3%) than in the placebo group (N=21,921; ranging from 0.3% to 1.9%).

Most reported AEs were in SOCs with reactogenicity events. The most frequently reported AEs in the BNT162b2 group by PT overall were injection site pain, pyrexia, fatigue, chills, headache, and myalgia. During this time period from Dose 1 to 1 month after Dose 2, most of these AEs were reported during the e-diary 7-day reporting period. The frequency of AEs in the SOC of investigations was higher in the BNT162b2 group as compared with the placebo group (mainly due to the higher frequency of the PT Body temperature increased. A number

CLINICAL STUDY REPORT SYNOPSIS

of events were identified as occurring at a higher frequency than placebo within the 7-day period after either dose of BNT162b2 when reactogenicity is expected to be reported such as pain in extremity, decreased appetite, lethargy, asthenia, malaise, night sweats, and hyperhidrosis. These events are interpreted as attributable to the experience of local reactions and systemic events after vaccination with BNT162b2.

Nineteen study participants reported events in the Hepatobiliary Disorders SOC (14 BNT162b2 recipients and 5 placebo recipients). Of the 19 total participants, 3 participants had hepatic events: 1 in the BNT162b2 group (alcoholic cirrhosis) and 2 in the placebo group (hepatic cirrhosis and nonalcoholic fatty liver disease). The remaining 16 participants reported biliary events: 13 participants in the BNT162b2 group and 3 participants in the placebo group:

- In the BNT162b2 group, 8 participants reported cholelithiasis (1 reported an event each of cholelithiasis and cholecystitis), 1 participant reported cholecystitis acute, 2 participants reported biliary colic, and 1 participant each reported bile duct stone/biliary dyskinesia.

- In the placebo group, there were 3 participants who reported the following: 1 participant reported an event each of cholecystitis acute and cholelithiasis, 1 participant reported cholecystitis acute, and 1 participant reported cholelithiasis.

Most related AEs were reactogenicity events and in the SOC of general disorders and administration site conditions, reported by 4650 (21.2%) BNT162b2 recipients and 883 (4.0%) placebo recipients. Among the BNT162b2 participants who had AEs of lymphadenopathy, 62 of 83 participants had events assessed by the investigator as related to study intervention; the majority of lymphadenopathy events occurred in the arm and neck region and were reported within 1 to 4 days after vaccination.

SAEs were similar in the BNT162b2 (0.6%) and placebo (0.5%) groups. There were 3 SAEs reported in the BNT162b2 group that were assessed by the investigator as related to study intervention (lymphadenopathy; shoulder injury related to vaccine administration [SIRVA], erroneously administered into or near the shoulder joint capsule; and ventricular arrhythmia).

Few participants in the BNT162b2 group (0.1%) and placebo group (0.2%) were withdrawn because of AEs. There were 3 deaths in the BNT162b2 group (cardiac arrest, Shigella sepsis, and atherosclerosis) and 5 deaths in the placebo group (death [undetermined], myocardial infarction [2 participants], haemorrhagic stroke, and overdose); none were assessed as related to study intervention.

For the subset of HIV-positive participants, local reactions, systemic events, and AEs showed generally similar trends as the overall population.

CLINICAL STUDY REPORT SYNOPSIS

Blinded Placebo-Controlled Follow-Up Period From Dose 1 to the Unblinding Date

Adverse Events

Most AEs from Dose 1 to the unblinding date were mild or moderate in severity. The IR of at least 1 AE in the BNT162b2 group (83.2 per 100 person-years [PY]) was greater as compared with the placebo group (43.4 per 100 PY), which upon analysis, was attributed to reactogenicity events reported as AEs within 7 days after each dose. IRs of severe AEs, SAEs, and AEs leading to withdrawal were ≤4.3, ≤3.3, and ≤0.6 per 100 PY, respectively, in both groups. IRs for discontinuations because of related AEs were 0.2 per 100 PY in the BNT162b2 group and 0.1 per 100 PY in the placebo group. AEs with the highest IRs in the BNT162b2 group by PT overall were injection site pain, pyrexia, fatigue, chills, headache, and myalgia. The IR of AEs in the SOC of investigations was higher in the BNT162b2 group than in the placebo group mainly due to the higher IR of body temperature increased in the BNT162b2 group.

In the nervous systems disorder SOC, there were 4 participants who reported facial paralysis in the BNT162b2 group (compared to 1 in the placebo group). There is an additional case of facial paresis in the placebo group. Hence there are 4 cases of facial paralysis/paresis in the in the BNT162b2 group and 2 in the placebo group.

The IRs for hepatobiliary disorders was 0.3 per 100 PY and 0.2 per 100 PY in the BNT162b2 and placebo group, respectively. There were 24 participants in the BNT162b2 group who had AEs in the SOC of hepatobiliary disorders compared to 16 participants in the placebo group.

A total of 11 cases of reported PTs associated with deafness included: Deafness, Deafness unilateral , Deafness neurosensory, Hypoacusis, and Sudden hearing loss. Six participants were randomized to the BNT162b2 group (age range 43 to 65 years of age), and 5 participantswere randomized to placebo (age range 36 to 74 years of age). The toxicity grades were mostly mild or moderate, with one being severe (BNT162b2 group). In the BNT162b2 group, 2 events were deemed related to study vaccine by the investigator. None of the reported events were SAEs.

In addition to the 3 related SAEs reported from Dose 1 to 1 month after Dose 2, there were 2 additional related SAEs reported after 1 month post Dose 2 up to the unblinding date in the BNT162b2 group that were assessed by the investigator as related to study intervention: paraesthesia (BNT162b2 group) and psoriatic arthropathy (placebo).

IRs of participants withdrawn because of AEs were 0.5 per 100 PY in the BNT162b2 group and 0.6 per 100 PY in the placebo group. From Dose 1 to the unblinding date, there were a total of 15 deaths in the BNT162b2 group and 14 in the placebo group (which included 12 in the BNT162b2 group and 9 in the placebo group from 1 month post Dose 2 to the unblinding date); none of these deaths were assessed by the investigator as related to study intervention.

CLINICAL STUDY REPORT SYNOPSIS

For the subset of HIV-positive participants, IRs of AEs showed generally similar trends as the overall population.

Subgroup Analyses

For the subset of participants who were SARS-CoV-2 positive at baseline, IR of AEs followed similar trends found in the overall AE analysis. Given the differences in exposure (2.5 vs 80.4) by baseline SARS-CoV-2 positive and negative status, respectively, direct comparisons should be interpreted with caution. The overall rate of AEs is 70.7 per 100 PY (95% CI: 60.7, 81.9) (baseline positive) compared with 83.6 per 100 PY (95% CI: 81.7, 85.7) (baseline negative). For other SOCs, the IR were either numerically lower or similar for the baseline positive group compared to the baseline negative group. Overall, there is no evidence that individuals who are positive at baseline report AEs at a higher frequency than those who are negative at baseline.

In the BNT162b2 group, overall IRs for participants reporting at least 1 AE were highest for participants of all other races (120.1 per 100 PY) compared to White participants (83.1 per 100 PY), with Black or African American participants having the lowest IR (53.5 per 100 PY). The IR for nausea in the BNT162b2 group was higher in participants of all other races (4.7 per 100 PY BNT162b2 vs 1.6 per 100 PY placebo) and White participants (3.4 per 100 PY BNT162b2 vs 1.0 per 100 PY placebo) than in Black or African American participants where the IR was similar in both vaccine groups (1.3 per 100 PY BNT162b2 vs 1.2 per 100 PY placebo).

In the BNT162b2 group, the IR for participants reporting at least 1 AE was higher in non-Hispanic/non-Latino participants (85.4 per 100 PY BNT162b2 and 41.6 per 100 PY placebo) and Hispanic/Latino participants (78.4 per 100 PY BNT162b2 and 47.9 per 100 PY placebo) and lowest in the group where ethnicity was not reported (49.4 per 100 PY BNT162b2 and 43.3 per 100 PY placebo). IRs were higher for mainly reactogenicity events (chills, fatigue, myalgia, diarrhea, injection site reactions [pain, erythema, and swelling], pain, pyrexia, and headache) as well as lymphadenopathy, nausea, influenza like illness, malaise, increased body temperature, and pain in extremity.

Overall, females reported a higher IR of AEs (91.0 per 100 PY BNT162b2, 46.8 per 100 PY placebo) than males (76.0 per 100 PY BNT162b2, 40.1 per 100 PY placebo), with a greater difference in the BNT162b2 groups than in the placebo groups. The higher IRs in females were due to reactogenicity AEs (vomiting, chills, fatigue, pyrexia, myalgia, and headache) as well as other AEs (lymphadenopathy, nausea, pain, increased body temperature, and pain in extremity). There were sex appropriate differences as well, such as higher IRs in the SOC of cardiacdisorders in males (1.2 per 100 PY) versus females (0.9 per 100 PY) and lower IRs in the SOC of reproductive system and breast disorders in males (0.3 per 100 PY) versus females (0.9 per 100 PY).

CLINICAL STUDY REPORT SYNOPSIS

Overall, no clinically meaningful differences in IRs of SAEs were observed by baseline SARS-CoV-2 status, ethnicity, race, or sex subgroups. IRs were similar in the BNT162b2 and placebo groups for each of the subgroups.

Other Significant Adverse Events

Safety evaluations were conducted for AEs of clinical interest: anaphylaxis, Bell's Palsy, lymphadenopathy, and appendicitis based on feedback from the FDA. CDC-defined AESIs associated with COVID-19 vaccination were evaluated in the blinded placebo-controlled period of the study. Additional terms beyond those designated by the CDC as AESIs were evaluated in a medical review to assess potential imbalances between the BNT162b2 and placebo groups, and further characterized in the case of such an imbalance.

Lymphadenopathy was reported in 87 (1.0 per 100 PY) participants in the BNT162b2 group compared to 8 (0.1 per 100 PY) participants in the placebo group. The majority of events were mild to moderate; only 3 severe events of lymphadenopathy were reported (all in the BNT162b2 group). The median onset of lymphadenopathy after Dose 1 and before Dose 2 was 5.5 days in the BNT162b2 group and 5.0 days in the placebo group; median onset after Dose 2 was shorter in the BNT162b2 group versus the placebo group (2.0 days vs 7.0 days). The median duration of lymphadenopathy was 5.5 days in the BNT162b2 group and 4.0 days in the placebo group. As previously reported in the final analysis interim C4591001 CSR dated 03 December 2020, 1 was a related SAE.

There were 14 cases of appendicitis and 1 case of appendicitis perforated in the BNT162b2 group, and 9 cases of appendicitis, 2 cases of complicated appendicitis, and 1 appendicitis perforated in the placebo group. Appendicitis cases were all reported as SAEs, and none of the cases were considered related to study intervention.

Most AESIs are reported in higher numbers in the placebo group or were equal in the BNT162b2 and placebo groups. The allergic reaction evaluation did not identify anaphylaxis reactions associated with the vaccine. Note, there was an anaphylactoid reaction reported 2 days after receiving open-label BNT162b2 (Dose 3) in an originally placebo-randomized participant who was unblinded to receive BNT162b2, and who had a significant ongoing medical history of drug hypersensitivity and other allergies. For angioedema the frequencies were low and very similar in the BNT162b2 (0.14%) and placebo (0.13%) groups. For hypersensitivity reactions most of the reactions were due to rash, rash maculo-papular, and rash papular and were not reported within 7 days after either dose. Overall, the evaluation of cases reporting allergic reactions supports standard precautions for allergic reactions should be taken in the clinic when vaccinating.

There were 2 cases of optic neuritis reported in the BNT162b2 group that occurred 79 and 81 days after vaccination with BNT162b2. Both were considered not related to vaccine. Given the few number of events, non-proximity to vaccination and investigators judgement, there is not enough information to assess causality at this time.

CLINICAL STUDY REPORT SYNOPSIS

AESI evaluations were performed for blinded placebo-controlled follow-up. There were 4 cases of Bell's palsy reported in the BNT162b2 group (previously reported in the final analysis interim C4591001 CSR dated 03 December 2020). Since then there have been 2 additional cases in the placebo group during blinded placebo-controlled follow-up, and there have been 4 additional cases of Bells' palsy identified during the open-label follow-up period that are included for completeness: 3 cases in placebo participants who became unblinded and were then vaccinated with BNT162b2, and 1 participant who was originally randomized to BNT162b2, was unblinded, and developed Bell's palsy 154 days after the second dose of BNT162b2.

There were 2 cases of encephalopathy in the vaccine group and none in the placebo. Both cases had clear etiologic causes (uremia and toxic encephalopathy after a fall with hypotension, diverticulum, and a urinary tract infection) and hence are not associated with the vaccine.

Open-Label Follow-Up Period – Original BNT162b2 Participants

During open-label follow-up for the original BNT162b2 group from unblinding date through the data cutoff date, most AEs were mild or moderate in severity. The IRs for any AE, at least 1 related AE, and severe AE were 8.8 per 100 PY, 0.7 per 100 PY, and 1.6 per 100 PY, respectively, which is markedly reduced relative to those from Dose 1 to the unblinding date (83.2, 62.9, 4.3 respectively. The IR of life-threatening AEs is 0.4 per 100 PY (95% CI: 0.2, 0.8), which is similar to the IR from Dose 1 to the unblinding date, 0.6 per 100 PY (95% CI: 0.4, 0.8). Overall, the rates in all SOCs after the unblinding date decreased or remained similar to those in the blinded placebo-controlled period. The IR for the SOC of injury, poisoning and procedural complications was 1.4 per 100 PY, with the PT fall having the highest IR (0.4 per 100 PY). The IR for the SOC of vascular disorders was 0.8 per 100 PY, with the PT hypertension having the highest IR (0.6 per 100 PY).

The IRs of related AEs were highest for reactogenicity events and in the SOC of general disorders and administration site conditions reflecting AEs from their initial vaccinations. One participant in the younger age group had 1 SAE of myocardial infarction assessed by the investigator as related to study intervention.

The IR of participants withdrawn because of AEs was 0.1 per 100 PY. There were 3 additional deaths (road traffic accident, lung metastases, and myocardial infarction); none of these deaths were assessed by the investigator as related to study intervention.

Blinded Placebo-Controlled and Open-Label Follow-Up Periods to 6 Months After Dose 2 – Original BNT162b2 Participants

For the 12,006 participants with at least 6 months of follow-up time, most AEs were mild or moderate in severity from Dose 1 to 6 months after Dose 2. There were 28.8% of participants who reported at least 1 AE, and 18.7% of participants reported at least 1 related AE. The most frequently reported AEs in the BNT162b2 group were reactogenicity events. Severe

CLINICAL STUDY REPORT SYNOPSIS

AEs and SAEs were reported by 2.1% and 1.6%, respectively. One participant discontinued because of an AE (not related).

Most related AEs were reactogenicity events and in the SOC of general disorders and administration site conditions. The AE of lymphadenopathy in 29 (0.2%) participants was assessed by the investigator as related to study intervention

The number of participants with SAEs increased from 0.5% (Dose 1 to 1 month after the Dose 2) to 1.1% (1 month after Dose 2 to 6 months after Dose 2). However, the number of related SAEs remained low. There were 2 participants with related SAEs reported: SIRVA, erroneously administered into or near the shoulder joint capsule reported from Dose 1 to 1 month after Dose 2; and paraesthesia, reported from 1 month after Dose 2 to 6 months after Dose 2.

There were no deaths.

AE frequencies decreased over time from 1 month after the second dose to 6 months after the second dose without an increase by SOC.

Overall, BNT162b2 at 30 μg was well tolerated with at least 6 months of follow-up after Dose 2.

Open-Label Follow-Up Period – Original Placebo Participants Who Then Received BNT162b2

For the 19,525 original placebo participants who then received BNT162b2 after unblinding, most AEs were mild or moderate in severity from Dose 3 through the data cutoff date. The IR of at least 1 AE was 205.4 per 100 PY, which was greater than the IR in original BNT162b2 participants (83.2 per 100 PY), due to the shorter exposure time in original placebo participants compared with original BNT162b2 participants (23.8 per 100 PY vs 83.4 per 100 PY). However, the IRs for life-threatening AE, SAE, AEs leading to withdrawal and deaths were similar (0.5 per 100 PY, 2.7 per 100 PY, 0.8 per 100 PY, 0.1 per 100 PY vs 0.6 per 100 PY, 3.2 per 100 PY, 0.5 per 100 PY, 0.2 per 100 PY, respectively). The IR of related AEs was 189.5 per 100 PY and IRs of related AEs were highest for reactogenicity events and in the SOC of general disorders and administration site conditions. Immediate AEs were low in frequency (0.6%) and most were in the SOC of general disorders and administration site conditions, primarily injection site reactions, with injection site pain (0.4%) most frequently reported. From Dose 3 (first Dose of BNT162b2) to the data cutoff date, the severe AE IR was 6.0 per 100 PY in original placebo participants.

One participant had 1 SAE of anaphylactoid reaction 2 days after receiving BNT162b2 that was assessed as related to study intervention.

CLINICAL STUDY REPORT SYNOPSIS

The IR of participants withdrawn because of AEs was 0.8 per 100 PY. There were 2 deaths (cardiorespiratory arrest and completed suicide); none of these deaths were assessed by the investigator as related to study intervention.

Overall, AEs after receipt of BNT162b2 in placebo participants showed a similar safety profile as that observed in the participants originally randomized to BNT162b2.

Open-Label Follow-Up Period – Original Placebo Participants, had COVID-19 Occurrence After Dose 1, and Then Received BNT162b2

For original placebo participants who had COVID-19 occurrence after Dose 1 and then received BNT162b2, IRs for any AE and at least 1 related AE were 256.8 per 100 PY and 240.9 per 100 PY, respectively. Most AEs reported from Dose 3 (the first dose of BNT162b2) to the data cutoff date were in SOCs with reactogenicity events. IRs of severe AEs, SAEs, and AEs leading to withdrawal were 4.6 per 100 PY, 3.4 per 100 PY, and 3.4 per 100 PY. The IR for discontinuations because of related AEs was 3.4 per 100 PY, and no participants died.

SAE rates were similar in these participants (3.4 per 100 PY; 95% CI: 0.7, 10.0) compared to those originally randomized to BNT162b2 (3.2 per 100 PY; 95% CI: 2.8, 3.6). None of the SAEs in the original placebo participants who developed COVID-19 and subsequently were vaccinated with BNT162b2 were related to BNT162b2. There were 3 participants with AEs leading to withdrawal that were assessed as related to BNT162b2: 1 participant with an AE of allergy to vaccine, 1 participant with an AE of pain, and 1 participant with 5 AEs (chills, injection site pain, myalgia, headache, and diarrhea). No deaths were reported in placebo participants who developed COVID-19 and subsequently were vaccinated with BNT162b2.

Overall, a similar safety profile was observed for this population compared to those originally randomized to BNT162b2.

Pregnancy

At the time of the data cutoff date (13 March 2021), a total of 50 participants who had received BNT162b2 had reported pregnancies, including 42 participants originally randomized to the BNT162b2 group and 8 participants originally randomized to the placebo group who then received BNT162b2. In total, 12 participants (n=6 each in the randomized BNT162b2 and placebo groups) withdrew from the blinded placebo-controlled vaccination period of the study due to pregnancy, and 4 participants originally randomized to placebo who then received BNT162b2 withdrew from the open-label vaccination period due to pregnancy. These participants continue to be followed for pregnancy outcomes.

CLINICAL STUDY REPORT SYNOPSIS

Overall Conclusion(s):

- In Phase 1, BNT162b2 at 30 µg induced a robust immune response 1 month after Dose 2 which decreased relative to those observed at 1 month after Dose 2, but remained higher than values observed at prevaccination and compared with the placebo group. The safety profile was satisfactory in both younger and older adults up to the unblinding date (approximately 6 months after Dose 2).

- In Phase 2/3, updated efficacy analysis continued to show that BNT162b2 at 30 µg provided a high level of protection against COVID-19. This was shown in participants irrespective of evidence of prior infection with SARS-CoV-2 and across various demographic subgroups. Severe cases were observed predominantly in the placebo group.

- The tolerability and safety profile of BNT162b2 30 µg in participants ≥16 years of age at up to 6 months after Dose 2 was acceptable throughout the follow-up period (to the data cutoff date) and consistent with results previously reported.