CLINICAL STUDY REPORT SYNOPSIS

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

Report Title: Interim Report – Adolescents: 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 Date: 22 March 2021 (Phase 2/3, Visit 3 [post-Dose 2 blood draw] assay completed for participants 12 through 25 years of age)

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 (US), 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.

Phase 3 participants ≥16 years of age were enrolled at sites in the US, Brazil, Argentina, Turkey, South Africa, and Germany. Participants 12-15 years of age were enrolled at sites in the US.

Date of Current Version: 14 April 2021

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

CLINICAL STUDY REPORT SYNOPSIS

OBJECTIVES

Study Objectives and Endpoints:

Phase 1

Phase 1 results are not presented in this report.

Phase 2/3

The study objective, estimands, and endpoints presented in Table S1 are from Protocol Amendment 14. Those previously reported in the final analysis interim C4591001 clinical study report (CSR) synopsis dated 03 December 2020, are based on Protocol Amendment 9.

Final efficacy analyses were completed and reported in the final analysis interim CSR dated 03 December 2020 along with safety and immunogenicity data available at that time (data cutoff date 14 November 2020). This prior CSR reported prespecified efficacy (event-driven) in participants ≥12 years of age and ongoing safety data in participants ≥16 years of age with a median of at least 2 months of follow-up after Dose 2 and up to the data cutoff date.

The current CSR presents safety, efficacy, and immunogenicity data for adolescents 12 through 15 years of age up to the data cutoff date (13 March 2021). Data are included from young adults 16 through 25 years of age for immunobridging analyses and descriptive safety analysis comparisons. Longer-term reference safety data are also presented from the adult 16 through 55 years of age stratum up to the date of participant unblinding. Note, these data are for comparative purposes and do not include a full independent safety evaluation.

This study is ongoing; results for objectives outside of the scope of this CSR, including full independent safety evaluation for participants ≥16 years of age, will be reported separately at a later time (Table S1).

CLINICAL STUDY REPORT SYNOPSIS

Table S1. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints	Reference
Primary Efficacy			
To evaluate the efficacy of prophylactic BNT162b2 against confirmed coronavirus disease 2019 (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 application test (NAAT) in participants with no serological or virological evidence (up to 7 days after receipt of the second dose) of past severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection	Prespecified complete efficacy data are reported in final analysis interim CSR dated 03 December 2020. Updated efficacy data for participants 12 through 15 years of age only 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 for participants 12 through 15 years of age only 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 • Adverse events (AEs) from Dose 1 to 7 days after the second dose • Serious adverse events (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 S1. 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. 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 Dose 2 and to the unblinding 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 from Dose 1 to 1 month after Dose 2 are reported in this CSR. 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 Dose 2 and to the cutoff date are reported in this CSR.
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 S1. 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	Geometric mean ratio (GMR) of reference strain 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 neutralizing titers (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 S1. 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 for participants 12 through 15 years of age only are reported in this CSR.

CLINICAL STUDY REPORT SYNOPSIS

Table S1. 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 for participants 12 through 15 years of age 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 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 binding (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 S1. 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 are reported in this CSR.
BNT162b2-experienced participants			
To demonstrate the noninferiority of the anti-South African variant (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 S1. 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 S1. 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	Data will be reported at a later time.
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	Geometric mean concentration (GMC)/geometric mean titer (GMT) and geometric mean fold rise (GMFR) at baseline and 1, 6, 12, and 24 months after completion of vaccination	• Full-length S-binding or S1-binding immunoglobulin G (IgG) levels • SARS-CoV-2 neutralizing titers	GMTs and GMFRs of SARS-CoV-2 neutralizing titers up to 1 month after Dose 2 in participants 12 through 15 and 16 through 25 are reported in this CSR.
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 asymptomatic surveillance period) of past SARS-CoV-2 infection	Data will be reported at a later time.

CLINICAL STUDY REPORT SYNOPSIS

Table S1. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints	Reference
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	Data will be reported at a later time.
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.

CLINICAL STUDY REPORT SYNOPSIS

Table S1. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints	Reference
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 • 7 Days and 1 and 6 months after BNT162b2 given as a third dose to BNT162b2-experienced participants			Data will be reported at a later time.

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

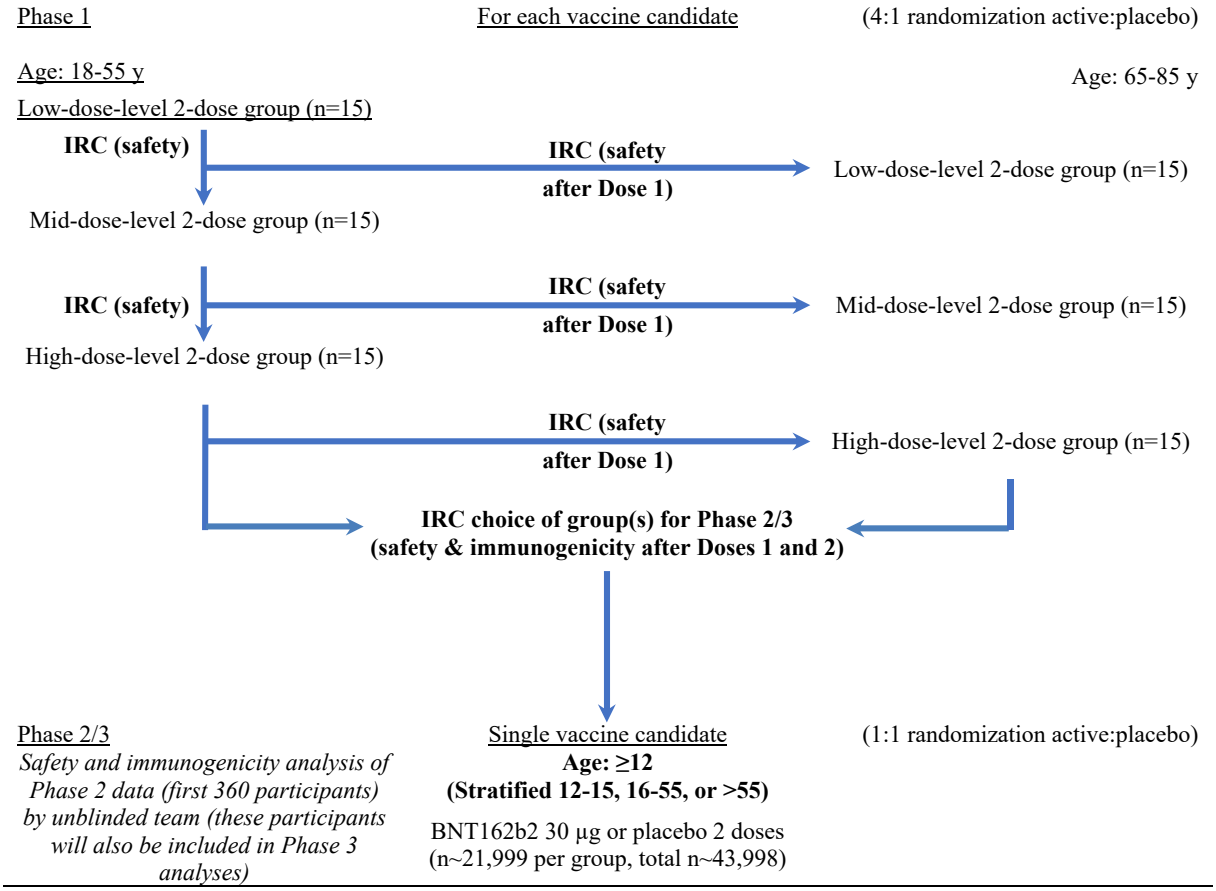
CLINICAL STUDY REPORT SYNOPSIS

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 ribonucleic acid (RNA) vaccine candidates against COVID-19 and the Phase 2/3 efficacy of 1 selected candidate based on Phase 1 results:

CLINICAL STUDY REPORT SYNOPSIS

As a 2-dose (separated by 21 days) schedule;

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.

In this report, interim data are presented up to 1 month after Dose 2 and up to the data cutoff date for blinded follow-up only (13 March 2021) and summarizes the following participant age groups:

- Adolescents (12 through 15 years of age): immunobridging and safety (median ≥2 months follow-up); descriptive efficacy analyses during blinded placebo-controlled follow-up period conducted on all confirmed COVID-19 cases accrued up to the data cutoff date of 13 March 2021
- Young adults (16 through 25 years of age): reference group for 12 through 15 years immunogenicity and descriptive safety analysis comparisons
- Adults (16 through 55 years of age): protocol specified 'younger adult' age stratum, to provide reference safety data from analyses of participants with longer-term follow-up. Note, these data are for comparative purposes and do not include a full independent safety evaluation.

A full independent safety evaluation of Phase 2/3 participants ≥16 years of age will be reported separately at a later time.

Planned Booster and Variant Strain Evaluation

Planned booster and variant of concern (VOC) vaccine evaluations are not included in this report and will be reported at a later time.

CLINICAL STUDY REPORT SYNOPSIS

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.

Adolescents 12 through 15 years of age remain blinded in this study, as BNT162b2 vaccination eligibility in all markets/regions is currently for 16 years of age and older. Note that a few participants in the 12 through 15 years of age group turned 16 years of age after study enrollment and thus became eligible for unblinding to treatment assignment and vaccination under the emergency use or conditional authorization in their country/region.

Phase 1

Phase 1 safety follow-up is ongoing, and participants were expected to participate for up to a maximum of approximately 26 months. This interim report only describes Phase 2/3 adolescents 12 through 15 years of age, with reference comparison to young adults 16 through 25 years of age and adults 16 through 55 years of age.

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 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.

CLINICAL STUDY REPORT SYNOPSIS

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 2200 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 (data cutoff date: 04 November 2020), and the final analysis was conducted on an accrued 170 evaluable COVID-19 cases (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, few participants 12 through 15 years of age had enrolled in the study, and no COVID-19 cases reported in this age group accrued at that time. Updated efficacy analyses during blinded placebo-controlled follow-up period were conducted on cases accrued in the 12 through 15 years of age group up to the data cutoff date of 13 March 2021. This report presents these analyses of all confirmed COVID-19 cases and any cases meeting protocol- and CDC-defined criteria for severe disease for participants 12 through 15 years of age.

Noninferiority (NI) of immune response to prophylactic BNT162b2 in participants 12 through 15 years of age to response in participants 16 through 25 years of age were assessed based on the GMR of SARS-CoV-2 neutralizing titers 1 month after Dose 2 using a 1.5-fold NI margin.

Safety data are included for adolescents 12 through 15 years of age through 1 month after Dose 2 and to the data cutoff date (13 March 2021) and include descriptive comparisons to participants (reactogenicity subset) in the group 16 through 25 years of age. Safety data from participants 16 through 55 years of age are included for comparative purposes, and a full independent safety evaluation of this age group along with participants >55 years of age will be reported separately at a later time.

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

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.

CLINICAL STUDY REPORT 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 European Union (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.

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.

CLINICAL STUDY REPORT SYNOPSIS

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).

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).

CLINICAL STUDY REPORT SYNOPSIS

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.

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.)

CLINICAL STUDY REPORT SYNOPSIS

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. The study evaluated a 2-dose (separated by 21 days) schedule of the following for active immunization against COVID-19 or saline placebo in participants 12 through 15 years of age and reference groups (16 through 25 and 16 through 55 years of age):

- BNT162b2 (BNT162 RNA-LNP vaccine containing modRNA that encodes SARS-CoV-2 full-length, P2 mutant, prefusion spike glycoprotein [P2 S]): 30 µg
- Normal saline (0.9% sodium chloride solution for injection)

A list of the study interventions administered in this study and their representative lot numbers is provided in Table S2.

Table S2. Investigational Product Lot Numbers – Interim – Adolescents

Investigational Product	Phase	Manufacturer	Vendor Lot Number (Manufacturer)	Lot Number[a] (Pfizer)
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

CLINICAL STUDY REPORT SYNOPSIS

Table S2. Investigational Product Lot Numbers – Interim – Adolescents

				BCV40620-B	PA2071395/P220395-0016L
				BCV40620-B	PA2072396/P220395-0016L
				BCV40620-C	PA2071396/P220395-0047L
				BCV40620-C	PA2072439/P220395-0047L
				BCV40620-D	PA2072442/P220395-0042L
				BCV40620-D	PA2072765/P220395-0042L
				BCV40720-A	PA2074172/P220395-0053L
				BCV40720-A	PA2074998/P220395-0060L
				BCV40720-B	PA2074173/P220395-0051L
				BCV40720-C	PA2074071/P220395-0052L
				ED3938	PA2074300/P220395-0021L
				ED3938	EU2074330/E220395-0036L
				ED3938	PA2074300/P220395-0022L
				ED3938	PA2074300/P220395-0023L
				EE3813	PA2074838/P220395-0024L
				EE3813	PA2074838/P220395-0020L
				EE8493Z	PA2077905/P220395-0026L
				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

CLINICAL STUDY REPORT SYNOPSIS

Table S2. Investigational Product Lot Numbers – Interim – Adolescents

	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
	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 07Apr2021 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 – Adolescents, Final, Version 2.0, 09Apr2021.

Efficacy and Immunogenicity Evaluations: Efficacy (prespecified) 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 (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 few participants 12-15 years of age enrolled in the study and no COVID-19 cases reported in this age group accrued at that time (14 November 2020). In this report, efficacy was assessed based on all cases in participants 12 through 15 years of age accrued in blinded follow-up to a data cutoff date of 13 March 2021.

CLINICAL STUDY REPORT SYNOPSIS

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);

CLINICAL STUDY REPORT SYNOPSIS

- 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 participants 12 through 15 years of age: SARS-CoV-2 neutralization assay (reference strain).

Safety Evaluations:

Local Reactions and Systemic Events: All participants 12 through 15 years of age and a subset of participants 16 through 55 years of age (including the young adults 16 through 25 years of age) 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. All other participants 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 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 4 for Phase 2/3 participants).

Acute reactions (immediate AEs) were collected within the first 30 minutes after administration of the study intervention.

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) and met success criteria on the first primary endpoint. At the final analysis (at least 164 cases) vaccine efficacy with respect to all efficacy endpoints was assessed on an accrued 170 evaluable COVID-19 cases (data cutoff date: 14 November 2020) for both 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 either without or with or without serological or virological evidence before or during vaccination regimen (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 efficacy analyses during blinded placebo-controlled follow-up were conducted for participants 12 through 15 years of age based on the data cutoff date of 13 March 2021. 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. In addition to the protocol definition of severe COVID-19, supportive analyses using the CDC definition of severe COVID-19 was also performed.

Immunogenicity Analysis: For participants randomized to the BNT162b2 groups with no serological or virological evidence (up to 1 month after receipt of the second dose) of past SARS-CoV-2 infection, the GMR of SARS-CoV-2 50% neutralizing titers in participants 12 through 15 years of age to those in participants 16 through 25 years of age and 2-sided 95% CIs were provided at 1 month after Dose 2 for NI assessment. The GMR and its 2-sided 95% CI were derived by calculating differences in means and CIs on the natural log scale of

CLINICAL STUDY REPORT SYNOPSIS

the titers based on the Student's t-distribution and then exponentiating the results. The difference in means on the natural log scale were 12 through 15 years minus 16 through 25 years. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR was greater than 0.67, using 1.5-fold NI margin. In addition, the difference in percentages of participants (12 through 15 years – 16 through 25 years) achieving a ≥4-fold rise in SARS-CoV-2 neutralizing titers from before vaccination to 1 month after Dose 2 were provided. The associated 2-sided 95% CI for the difference in percentage was calculated using the Miettinen and Nurminen method.

For immunogenicity results of SARS-CoV-2 neutralizing titers, the GMT was computed along with associated 95% CIs. The GMT was 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 exact 95% CIs for binary endpoints were computed using the F distribution (Clopper-Pearson method).

Titers 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, and AEs/SAEs for each vaccine group. A 3-tier approach was used to summarize AEs in Phase 2/3. Under this approach, AEs were classified into 1 of 3 tiers:

Tier 1 events are prespecified events of clinical importance and are identified in a list in the product's Safety Review Plan; there are no Tier 1 AEs identified for this program.

Tier 2 events were those that were not Tier 1 but were considered "relatively common"; a MedDRA preferred term is defined as a Tier 2 event if there are at least 1% of participants with the AE term in at least 1 vaccine group.

Tier 3 events were those that were neither Tier 1 nor Tier 2.

CLINICAL STUDY REPORT SYNOPSIS

RESULTS

Participant Disposition and Demography:

Participants 12 Through 15 Years of Age:

Study population characteristics are provided for adolescents 12 to 15 years of age, and those of young adults 16 through 25 years of age are included for comparison. Note that for safety endpoint analyses of adolescents that included comparative data from young adults, the young adult group analyzed was the reactogenicity subset (ie, those participants in the young adult group who completed an e-diary for reactogenicity in addition to AE reporting).

The disposition of adolescents (12 through 15 years of age) and young adults (16 through 25 years of age) was similar in BNT162b2 and placebo groups through 1 month after Dose 2. Most participants randomized in both age groups (≥97.4%) received Dose 1 and Dose 2. Among adolescents, 7 participants (0.6%) in the BNT162b2 group and 17 participants (1.5%) in the placebo group discontinued from the vaccination period and are continuing in the study for safety follow-up. Most participants across age groups completed the visit at 1 month after Dose 2 (≥94.5%). Among adolescents who discontinued from vaccination period but continued in the study up to the 1 month post Dose 2 visit, 2 participants discontinued due to AEs, both in the BNT162b2 group (pyrexia considered by the investigator as related to study intervention, and unrelated anxiety/depression) and none in the placebo group.

No adolescents in the BNT162b2 and 2 participants in the placebo group withdrew from the study before the 1 month post Dose 2 visit.

The median duration of follow-up for adolescents was >2 months after Dose 2. Almost all (98.3%) of adolescent participants had at least 1 month of follow-up after Dose 2, and 1308 out of 2260 enrolled adolescents (57.9%) had at least 2 months of follow-up after Dose 2.

A total of 49 adolescent participants withdrew from the vaccination period when they turned 16 years of age after entering the study and became eligible to be unblinded to receive BNT162b2 vaccination; of these, 19/49 received Dose 3 and Dose 4 (BNT162b2). Participants originally randomized to placebo who received Dose 3 of BNT162b2 (per protocol) continued in open-label follow-up in the study, but their data were censored at the time of unblinding with regard to analyses in this submission. Information for these participants are provided for SAEs or other significant AEs.

Demographic characteristics for adolescents (12 through 15 years of age) and young adults (16 through 25 years of age) were similar in the corresponding BNT162b2 and placebo groups in the safety population. Overall, most adolescent participants in the BNT162b2 group were White (85.9%), with 4.6% Black participants and 6.4% Asian participants, and other racial groups were <3.0%. There were 11.7% Hispanic/Latino participants. The median age in the BNT162b2 group was 14.0 years and 50.1% were male. Obese adolescents (based

on age- and sex-specific body mass index) made up 11.3% (placebo group) to 12.6% (BNT162b2 group) of this age group in the safety population.

Demographic characteristics for the adolescents and young adults in the reactogenicity subset were similar to those in the safety population.

Participants 16 Through 55 Years of Age:

The disposition of randomized adult participants (16 through 55 years of age) was similar in the BNT162b2 and placebo groups during the blinded follow-up period. Most participants randomized (97.7%) received Dose 1 and Dose 2. There were 278 (2.1%) participants in the BNT162b2 group and 388 (3.0%) participants in the placebo group who discontinued from the vaccination period. Most participants (95.8%) completed the 1 month post Dose 2 visit and 25.5% of the BNT162b2 group participants completed the 6 months post Dose 2 (25.5%) visit as of the data cutoff date. There were 608 participants in the BNT162b2 and placebo groups who were withdrawn from the study (2.0% and 2.7%, respectively), mostly due to lost to follow-up (1.2%) or withdrawn by subject (0.9%).

Duration of follow-up was ≥4 months after Dose 2 for 57.8% of adult participants (16 through 55 years of age) during the blinded placebo-controlled follow-up period. As of the data cutoff date (13 March 2021), the proportion of participants in this age group with blinded follow-up to at least 6 months after Dose 2 included 10.4% in the BNT162b2 group and 8.2% in the placebo group. When total exposure time from Dose 2 to the data cutoff date is considered, 6666 participants in this age group (51.0%) had ≥6 months of follow-up time.

Demographic characteristics for Phase 2/3 adults in the 16 through 55 years of age group were similar in the BNT162b2 and placebo groups. Overall, most adult participants were White (78.2%), with 11.0% Black participants and 5.4% Asian participants, and other racial groups were <6.0%. There were 30.8% Hispanic/Latino participants. The median age was 40.0 years and 49.9% of participants were male. Obese adults made up 33.7% of this safety population.

Efficacy Results:

Participants 12 Through 15 Years of Age:

Descriptive efficacy analyses were conducted for the adolescent group on cases accrued during blinded follow-up period through the data cutoff date of 13 March 2021.

In the adolescent group, in the efficacy analyses in the evaluable efficacy population based on cases reported from at least 7 days after Dose 2 through the data cutoff date, the observed VE was 100% (0 and 16 cases in the BNT162b2 and placebo group, respectively, with 2-sided 95% CI: 75.3%, 100%) for individuals without evidence of prior SARS-CoV-2 infection before and during vaccination regimen, and 100% (0 and 18 cases in the BNT162b2

and placebo group respectively with 2-sided 95% CI: 78.1%, 100%) for those with or without evidence of prior SARS-CoV-2 infection before and during vaccination regimen.

The efficacy analysis for the Dose 1 all-available (modified intention-to-treat) population included 3 cases in the BNT162b2 group and 35 cases in the placebo group, with an observed VE of 91.6% (2-sided 95% CI: 73.5%, 98.4%), with no cases reported in the BNT162b2 group starting from ≥11 days after Dose 1.

No severe cases were reported in the 12-15 years of age group as of the date cutoff date.

Overall, these efficacy data strongly support BNT162b2 use in adolescents 12-15 years of age.

Immunogenicity Results – Participants 12 Through 15 Years of Age:

Noninferiority of Immune Response to Prophylactic BNT162b2 in Participants 12 Through 15 Years Compared with Participants 16 Through 25 Years of Age:

Geometric Mean Ratio (GMR) in Neutralization Titers

The immune response to BNT162b2 in adolescents 12 through 15 years of age was noninferior to that observed in young adults 16 through 25 years of age, based on SARS-CoV-2 50% neutralizing titers at 1 month after Dose 2, in participants without prior evidence of SARS-COV-2 infection, and in fact greatly exceeded the response observed in young adults. The GMT ratio of adolescents to young adults was 1.76 (2-sided 95% CI: 1.47, 2.10), meeting the 1.5-fold noninferiority (NI) criterion (ie, lower bound of the 2-sided 95% CI for GMR >0.67). Of note, the lower bound of the 2-sided 95% CI for the GMR is >1 which indicates a statistically greater response in the adolescents than that of young adults.

Seroresponse

Among participants without prior evidence of SARS-CoV-2 infection up to 1 month after Dose 2 of BNT162b2, high proportions (97.9% of adolescents and 100.0% of young adults) had a ≥4-fold rise (seroresponse) in SARS-CoV-2 50% neutralizing titers from before vaccination to 1 month after Dose 2. The difference in proportions of participants who had a ≥4-fold rise between the two age groups (adolescents – young adults) was -2.1% (2-sided 95% CI: -6.0%, 0.9%).

Geometric Mean Titers (GMTs):

At 1 month after Dose 2 (Day 52) of BNT162b2, substantial increases above baseline in SARS-CoV-2 50% neutralizing GMTs were observed in both age groups, with a greater magnitude of increase in the adolescent group compared with the young adult group. The neutralizing GMT in adolescents at 1 month after Dose 2 was approximately 1.76-fold

that of the young adult group. As expected, the neutralizing GMTs were low in both placebo groups.

Geometric Mean Titers (GMTs) by Baseline SARS-CoV-2 Status

Vaccination with BNT162b2 induced an increased immune response (GMTs) at 1 month after Dose 2 for all participants, regardless of baseline SARS-CoV-2 positive or negative status. Adolescents who were baseline SARS-CoV-2 positive had SARS-CoV-2 50% neutralizing GMTs approximately 1.89-fold that of adolescents who were baseline negative. A similar pattern was observed for baseline SARS-CoV-2 positive versus negative young adults.

Geometric Mean Fold Rises (GMFRs):

The GMFRs of SARS-CoV-2 50% serum neutralizing titers from before vaccination to 1 month after Dose 2 of BNT162b2 were robust, with a greater magnitude of rise in the adolescent group (118.3) compared with the young adult group (71.2).

GMFR in Titers by Baseline SARS-CoV-2 Status

The GMFRs were higher in the adolescent compared to young adult group 1 month after the second dose. Given the limited sample size for those positive at baseline, the GMFRs were numerically higher in those who were negative at baseline.

Seroresponse Rate

Proportions of participants with a ≥4-fold rise in SARS-CoV-2 50% neutralizing titers from before vaccination to 1 month after Dose 2 of BNT162b2 (seroresponse rate) were 98.1% in adolescents and 99.3% in young adults. As expected, very few placebo participants reached a ≥4-fold rise in SARS-CoV-2 neutralizing titers from before to 1 month after Dose 2.

Seroresponse Rate by Baseline SARS-CoV-2 Status

Adolescents who were baseline SARS-CoV-2 positive or negative had similar seroresponse rates (100.0% vs 97.9%).

Safety Results:

Participants 12 Through 15 Years of Age:

Phase 3 data from approximately 2200 adolescents 12 through 15 years of age with a median follow-up time of at least 2 months after Dose 2 showed BNT162b2 at 30 µg was safe and well-tolerated. Safety in young adults 16 through 25 years of age (reactogenicity subset) were evaluated for descriptive comparison.

CLINICAL STUDY REPORT SYNOPSIS

Local Reactions and Systemic Events

Reactogenicity in adolescents 12 through 15 years of age was mostly mild to moderate and short-lived after dosing (ie, median onset mostly between 1 to 3 days after dosing and resolution within 1 to 3 days after onset), similar to the reactogenicity data in the young adults 16 through 25 years of age. Local reactions presented predominantly as injection site pain with minimal effect of dose number, and systemic events generally increased in frequency and/or severity with increasing dose number; also similar to findings in the 16 through 25 years of age group. Adolescents tended to have less severe local reactions and systemic events after each vaccine dose compared with young adults. The rate of fever was somewhat higher in the adolescent group compared to the young adult group (10.1% vs 7.3% after Dose 1, respectively), especially after the second dose (19.6% vs 17.2%, respectively), but fevers were mostly mild to moderate in severity.

The observed AE profile did not suggest any serious safety concerns for BNT162b2 vaccination of adolescents 12 through 15 years of age. Overall, AEs reported in the study for adolescents and young adults reflect age-appropriate events consistent with the general population.

AEs From Dose 1 to 1 Month After Dose 2

From Dose 1 to 1 month after Dose 2, severe AEs, SAEs, and AEs leading to withdrawal were reported by ≤1.7%, ≤0.4%, and ≤0.4%, respectively, in both groups. No reported SAEs were considered by the investigator as related to study intervention. Most of the AEs were reactogenicity events reported as AEs (ie, headache, nausea, and diarrhea) in both age groups and were frequently reported in the reactogenicity SOCs of general disorders and administration site conditions, musculoskeletal and connective tissue disorders, nervous system disorders, and gastrointestinal disorders. Similarly, most related AEs were also reactogenicity events and in the SOC of general disorders and administration site conditions. Immediate AEs were reported in the BNT162b2 groups after Dose 2 only, were low in frequency (≤0.4%), and most were in the SOC of general disorders and administration site conditions.

AEs From Dose 1 to the Data Cutoff Date

Safety data up to the cutoff date (13 March 2021) were summarized for adolescents 12 through 15 years of age; due to variable unblinding dates among participants 16 through 25 years of age, young adult data could not be compared with blinded adolescent data up to the cutoff date.

From Dose 1 to the data cutoff date, the number of adolescents with any AE was similar in the BNT162b2 and placebo groups. Severe AEs, SAEs, and AEs leading to withdrawal were reported by ≤0.8%, ≤0.4%, and ≤0.2%, respectively, in both groups. No reported SAEs among adolescents were considered by the investigator as related to study intervention. The most frequently reported AEs included lymphadenopathy (0.8%), injection site pain (0.6%), fatigue (0.6%), pyrexia (0.4%), nausea (0.4%), and headache (0.4%).

CLINICAL STUDY REPORT SYNOPSIS

As of the data cutoff date (13 March 2021), there were very few AEs of clinical interest corresponding to the CDC list of AESIs reported in adolescents. Lymphadenopathy has been identified as related to BNT162b2 in study participants ≥16 years of age and is also identified as related to BNT162b2 in the 12-15 year old adolescent group. No cases of Bell's palsy/facial paralysis were reported in adolescents as of the data cutoff date (13 March 2021). No AEs of appendicitis were considered as related to the study intervention.

The incidence of SAEs was low in the context of the number of adolescent participants enrolled and comparable between BNT162b2 (≤0.4% from Dose 1 to 1 month after Dose 2 and to the data cutoff date) and placebo (≤0.4%, from Dose 1 to 1 month after Dose 2, and ≤0.2% from Dose 1 to the data cutoff date). The incidence of withdrawals due to AEs was also low and similar between BNT162b2 and placebo groups.

No deaths were reported in adolescents 12 through 15 years of age or in young adults 16 through 25 years of age included in the safety analyses.

Participants 16 Through 55 Years of Age:

The adult (16-25 years of age and 16-55 years of age) safety data included for reference purposes in the context of this report are from approximately 26,000 adults 16 through 55 years of age, among whom a majority in the BNT162b2 group had at least 6 months of blinded follow-up after Dose 2 in Phase 2/3 of this study. These data show BNT162b2 at 30 µg was safe and well-tolerated in this adult age group. Reactogenicity was mostly mild to moderate and short-lived after dosing (ie, median onset between 1 to 2 days after dosing and resolution within 1 to 2 days after onset), with local reactions presenting predominantly as injection site pain with minimal effect of dose number, and systemic events generally increasing in frequency and/or severity with increasing dose number.

Review of AEs and SAEs in the adult (16 through 55 years of age) population presented in this report did not suggest new safety concerns to date. A full and independent safety evaluation of the adult population is being conducted and will be included in a full clinical study report in support of licensing/marketing application submissions including a BLA planned in second quarter of 2021.

Comparing adolescents (12 through 15 years of age) to young adults (16 through 25 years of age) and adults (16 through 55 years of age) identifies very similar reactogenicity profiles. Reactogenicity after each dose was observed in all groups with similar patterns after Dose 1 and Dose 2. Fever was highest for the adolescent group compared to the young adult group but was still within tolerable limits. Arthralgia and muscle pain were higher in the young adult group than the adolescent group for both doses of BNT162b2. Overall, the differences in reported AEs were age-appropriate and not related to vaccination.

CLINICAL STUDY REPORT SYNOPSIS

Overall Conclusion(s):

In Phase 2/3, BNT162b2 at 30 µg provided protection against COVID-19 in adolescents 12 through 15 years of age irrespective of evidence of prior infection with SARS-CoV-2 (100% VE), with no severe cases observed in this age group. The immune responses in adolescent participants were noninferior to the immune responses in young adults, and in fact were statistically greater than that observed in young adults. The tolerability and safety profile was acceptable and supports BNT162b2 at 30 µg administered as a 2-dose regimen (21 days apart) to adolescents 12 through 15 years of age for the prevention of COVID-19.