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

Report Title: Interim Report – Adolescent 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 (study start); 15 October 2020 (adolescent)

Last Subject Last Visit: Not applicable

Data Cutoff Date: 02 September 2021

Serology Completion Dates: 29 October 2021

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): 29 in the United States for adolescent participants 12 through 15 years of age. Refer to Appendix 16.1.4.1 for a list of sites involved in this study.

Date of Current Version: 12 December 2021

Date(s) of Previous Report(s): 03 December 2021

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OBJECTIVES

Study Objectives and Endpoints:

Phase 1

Phase 1 results are not presented in this report.

Phase 2/3

The study objectives, estimands, and endpoints presented in Table S1 are from Protocol Amendment 18. Study objectives and endpoint analyses that were either previously reported, or will be reported at a later time, are indicated with gray shading and per the 'reference' column.

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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 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 – 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 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 the 6-month update interim CSR dated 29 April 2021. Efficacy data from 7 days after Dose 2 to the data cutoff date (13 March 2021) for participants 12 through 15 years of age only are reported in the adolescent interim CSR dated 14 April 2021.
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 the 6-month update interim CSR dated 29 April 2021. Efficacy data from 7 days after Dose 2 to the data cutoff date (13 March 2021) for participants 12 through 15 years of age only are reported in the adolescent interim CSR dated 14 April 2021.

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

Objectives[a]	Estimands	Endpoints	Reference
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.
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 cutoff date (13 March 2021) are reported in the 6-month update interim CSR dated 29 April 2021. Interim adolescent 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 data cutoff date (13 March 2021) are reported in the adolescent interim CSR dated 14 April 2021.

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

Objectives[a]	Estimands	Endpoints	Reference
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	Interim data are reported up to 1 month after Dose 2 and to the data cutoff date (13 March 2021) in the adolescent interim CSR dated 14 April 2021. Interim data for AEs and SAEs reported up to 6 months after Dose 2 and to the data cutoff date (02 September 2021) 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 the subset for evaluation of boostability and protection against emerging VOCs	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	Interim data for BNT162b2 given as a third dose to BNT162b2-experienced participants only are reported up to 1 month after Dose 3 and to the data cutoff date (17 June 2021) in the booster interim CSR dated 23 August 2021.
To describe the safety and tolerability profile of BNT162b2 given as a third dose at least 6 months after the second dose of BNT162b2 (or BNT162b2$_{SA}$) for participants who received a third dose as part of protocol amendment 18	In participants receiving at least 1 dose of study intervention, the percentage of participants reporting: • AEs from Dose 3 to 1 month after Dose 3 • SAEs from Dose 3 to 6 months after Dose 3	• AEs • SAEs	Interim data for BNT162b2 given as a third dose to BNT162b2-experienced participants only are reported up to 1 month after Dose 3 and to the data cutoff date (17 June 2021) in the booster interim CSR dated 23 August 2021.

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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 at 30 µg compared to after 2 doses of BNT162b2, in the same individuals	GMR of reference strain NT 1 month after the third dose of BNT162b2 at 30 µg 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 at 30 µg 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 at 30 µg) of past SARS-CoV-2 infection	Interim data for BNT162b2 given as a third dose to BNT162b2-experienced participants are reported up to 1 month after Dose 3 and to the data cutoff date (17 June 2021) in the booster interim CSR dated 23 August 2021.
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.
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.

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

Objectives[a]	Estimands	Endpoints	Reference
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 the 6-month update interim CSR dated 29 April 2021. 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 the adolescent interim CSR dated 14 April 2021.
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)	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

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

Objectives[a]	Estimands	Endpoints	Reference
	[ratio of active vaccine to placebo]		reported in the 6-month update interim CSR dated 29 April 2021. 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 the adolescent interim CSR dated 14 April 2021.
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 <u>without</u> 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 <u>with and without</u> 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 <u>without</u> 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 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.

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

Objectives[a]	Estimands	Endpoints	Reference
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 asymptomatic surveillance period) of past SARS-CoV-2 infection	Data will be reported at a later time.
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	Interim data are reported in the adolescent interim CSR dated 14 April 2021.
BNT162b2-experienced participants			
To demonstrate the noninferiority of the anti-SA immune response after a third dose of BNT162b2 at 30 µg 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 at 30 µg 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 at 30 µg 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 at 30 µg) 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.

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

Objectives[a]	Estimands	Endpoints	Reference
To descriptively compare the anti-SA immune response after 1 dose of BNT162b2$_{SA}$ and a third dose of BNT162b2 at 30 µg	GMR of SA NT 1 month after 1 dose of BNT162b2$_{SA}$ to 1 month after the third dose of BNT162b2 at 30 µg The difference in percentages of participants with seroresponse to the SA strain at 1 month after 1 dose of BNT162b2$_{SA}$ and 1 month after the third dose of BNT162b2 at 30 µg	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 at 30 µg) of past SARS-CoV-2 infection	Data will be reported at a later time.
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.

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

Objectives[a]	Estimands	Endpoints	Reference
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.
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 the 6-month update interim CSR dated 29 April 2021. Updated efficacy data from 7 days after Dose 2 through the blinded follow-up period for participants 12 through 15 years of age are provided in this CSR.
To describe the incidence of confirmed COVID-19 through the entire study follow-up period prior to receiving the third dose of BNT162b2 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 describe the incidence of confirmed COVID-19 after receiving the third dose of BNT162b2	In participants who received the third dose of BNT162b2: 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.

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

Objectives[a]	Estimands	Endpoints	Reference
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. 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 years of age are reported in the adolescent interim CSR dated 14 April 2021.
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.
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.

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

Objectives[a]	Estimands	Endpoints	Reference
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 the 6-month update interim CSR dated 29 April 2021.
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"[b]		• AEs • SAEs • SARS-CoV-2 neutralizing titers	Data will be reported at a later time.
To describe the immune response to any 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 immune response to a third dose of BNT162b2 (at 30 µg or a lower dose of 5 µg or 10 µg) or a third or fourth dose of BNT162b2$_{SA}$	• GMTs at Dose 3 and subsequent time points • GMFRs from Dose 3 to subsequent time points	• SARS-CoV-2 reference strain NTs	Interim data for BNT162b2 30 µg given as a third dose to BNT162b2-experienced participants are reported in the booster interim CSR dated 23 August 2021.
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.
b. See Appendix 16.1.1, Protocol Section 6.1.1 for a description of the manufacturing process.

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

Objectives[a]	Estimands	Endpoints	Reference

Source: Appendix 16.1.1, Protocol Section 3.2.

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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. 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;
- 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.

Boostability and Variant Strain Evaluations

Immunogenicity and safety evaluations of boostability were conducted in a subset of Phase 3 participants at selected sites in the US who received a third dose of BNT162b2 at 30 µg at least 6 months after their second dose, and restuls are reported in the booster interim CSR dated 23 August 2021. Evaluations of boostability in Phase 1 participants and a further subset of Phase 3 participants receiving a third, lower, dose of BNT162b2 at 5 or 10 µg will be reported at a later time.

Evaluations of VOC strains of SARS-CoV-2 (in participants who receive a SARS-CoV-2 variant encoding vaccine that encodes the Beta variant originally identified in South Africa

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[BNT162b2$_{SA}$] as a third dose) are not included in this report and will be reported at a later time.

Unblinding Considerations

The study was to be unblinded in stages once all ongoing participants either had been individually unblinded or had concluded their 6-month post–Dose 2 or post-Dose 3 study visit, in the following sequence:

- Phase 1 (after Visit 8 [6-month post-Dose 2 visit]).
- Phase 2/3, ≥16 years of age (after Visit 4 [6-month post-Dose 2 visit]).
- Phase 3, 12 through 15 years of age (after Visit 4 [6-month post-Dose 2 visit]).
- Original Phase 3 participants rerandomized to assess boostability and protection against emerging VOCs (after Visit 306) (data not included in this report).

Participants 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 based upon US recommendation.

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 who had not 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

Phase 1 safety follow-up is ongoing, and participants are expected to participate for up to a maximum of approximately 26 months.

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

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Dose 2 from these 360 Phase 2 participants. Enrollment continued during Phase 2 and these participants were 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 to 15 years of age 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 (CSR dated 03 December 2020), relatively few participants 12 to 15 years of age had enrolled in the study, and no COVID-19 cases in this age group accrued at that time. The adolescent interim CSR dated 14 April 2021 Noninferiority of immune response to prophylactic BNT162b2 in participants 12 to 15 years of age to response in participants 16 to 25 years of age was assessed based on the GMR of SARS-CoV-2 neutralizing titers using a 1.5-fold margin and reported in the adolescent interim CSR dated 14 April 2021 and in an EUA amendment, which supported issuance of the EUA for use in individuals 12 to 15 years of age. Additionally, the adolescent interim CSR dated 14 April 2021 presented updated descriptive efficacy analyses for participants 12 to 15 years of age, based on confirmed cases COVID-19 reported from at least 7 days after Dose 2 through the data cutoff date (13 March 2021), with an observed VE of 100% irrespective of evidence of prior infection with SARS-CoV-2. No severe COVID-19 cases were reported in this age group, based on either protocol definition (ie, per FDA criteria) or per CDC criteria for severity.

Updated efficacy analyses during the 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 and reported in the 6-month update interim CSR dated 29 April 2021, which presented 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 in the study for approximately 26 months from the time of enrollment.

Based on a data cutoff date of 02 September 2021, this interim report for adolescent participants 12 to 15 years of age summarizes updated descriptive efficacy analyses from 7 days after Dose 2 during blinded placebo-controlled follow-up and the following safety data, as ordered:

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- Blinded placebo-controlled follow-up period from Dose 1 to the date of unblinding for BNT162b2 and placebo participants, including new AEs that were reported after the EUA snapshot date (based on events on or after the data cutoff date of 13 March 2021)

- Open-label observational follow-up period of original BNT162b2 recipients from the date of unblinding to the data cutoff date

- Cumulative safety from Dose 1 to at least 6 months after Dose 2, inclusive of blinded data and open-label data for original BNT162b2 recipients, including new AEs that were reported after the EUA snapshot date

- Open-label observational follow-up period for original placebo recipients who then received BNT162b2 from the first dose of BNT162b2 to the data cutoff date

Inclusion/Exclusion Criteria:

Inclusion Criteria:

Participants were eligible to be included in the study only if all of the following criteria applied:

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.

For the boostability and protection-against-VOCs subset:

- Existing participants enrolled to receive a third dose of BNT162b2 at 30 µg or $BNT162b2_{SA}$; male or female participants between the ages of 18 and 55 years, inclusive, at rerandomization.

- Newly enrolled participants enrolled to receive 2 doses of $BNT162b2_{SA}$; male or female participants between the ages of 18 and 55 years, inclusive, at enrollment.

- Existing participants enrolled to receive a third dose of BNT162b2 at 5 or 10 µg; male or female participants ≥18 years at rerandomization.

Note that participants <18 years of age cannot be enrolled in the EU.

Type of Participant and Disease Characteristics:

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

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

Note: Healthy participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, could be included.

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

5. **Boostability and protection-against-VOCs existing participant subset only:** Participants who provided a serum sample at Visit 3, with Visit 3 occurring within the protocol-specified window.

Informed Consent:

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

Exclusion Criteria:

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

Medical Conditions:

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

2. **Phases 1 and 2 only:** Known infection with HIV, HCV, or 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.

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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
    - BMI >30 kg/m^2
    - Anticipating the need for immunosuppressive treatment within the next 6 months

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

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

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

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

11. Women who are pregnant or breastfeeding.

Prior/Concomitant Therapy:

12. Previous vaccination with any coronavirus vaccine.

13. Individuals who received treatment with immunosuppressive therapy, including cytotoxic agents or systemic corticosteroids, eg, for cancer or an autoimmune disease, or planned receipt throughout the study. If systemic corticosteroids were administered short term

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(<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 through and including 28 days after the last dose of study intervention, with the exception of non-Pfizer interventional studies for prevention of COVID 19, which are prohibited throughout 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 IgM and/or IgG antibodies at the screening visit.

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

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

20. **Phase 1 only:** Positive test for HIV, HBsAg, HBc Abs, or HCV Abs at the screening visit.

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

Other Exclusions:

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

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Vaccines Administered: The 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 the 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 respective lot numbers is provided in Table S2.

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Table S2. Investigational Product Lot Numbers – Interim – Adolescent 6-Month Update

Investigational Product	Manufacturer	Vendor Lot Number (Manufacturer)	Lot Number[a] (Pfizer)
BNT162b2 (30 µg)	BioNTech	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	PA2074300/P220395-0022L
		ED3938	PA2074300/P220395-0023L
		EE3813	NC2075485/P220395-0068L
		EE3813	NC2075485/P220395-0074L
		EE3813	NC2075485/P220395-0077L
		EE3813	PA2074838/P220395-0020L
		EE3813	PA2074838/P220395-0024L
		ER9449Z	PA2096794/P220395-0079L
		ER9449Z	PA2096794/P220395-0082L
		EE8493Y	PA2087473/P220395-0073L
		EJ0553Z	PA2085061/P220395-0070L
Placebo (normal saline 0.9% sodium chloride solution)	Pfizer	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/P220395-0055L
		DK2074;20-002221	PA2069407/P220395-0062L
		DK2074;20-002221	PA2069407/P220395-0065L
Diluent (normal saline 0.9% sodium chloride solution)	Pfizer	DK2074	20-002221
		DK1589	20-001776
		DK1589	20-001592

Note: C4591001 End of Study Information and Quality Control (QC) Record for Study Drug Appendix (Section D) dated 08Oct2021 was used to create this table.
a. Lot number assigned to the investigational product or diluent by Pfizer Global Clinical Supply.
Protocol C4591001 Investigational Product Lot Numbers Table – Interim – Adolescent 6-Month Update, Final, Version 1.0, 15Oct2021.

Efficacy and Immunogenicity Evaluations:

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 in the adolescent interm CSR, dated 14 April 2021.

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In this report, updated descriptive efficacy analyses for participants 12 through 15 years of age accrued during blinded placebo-controlled follow-up are summarized up to a data cutoff date of 02 September 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);

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- 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).

Immunogenicity evaluations in participants 12 through 15 years of age are not included in this interim report. The immune response to BNT162b2 30 µg in adolescents 12 through 15 years of age was previously reported to be noninferior (and in fact exceeded) the immune response in young adults 16 through 25 years of age (ie, successful immunobridging), as detailed in the adolescent interim report dated 14 April 2021.

Safety Evaluations:

Local Reactions and Systemic Events: There are no new e-diary data presented in this report (previously reported in the adolescent interim CSR, dated 14 April 2021).

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).

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 (1-month follow-up after Vaccination 4). SAEs were collected from the time the participant provided informed consent (for receipt of Vaccinations 3 and 4) to approximately 6 months after the second dose of BNT162b2 (Visit 104).

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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). 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.

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 (adolescent interim CSR, dated 14 April 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 were also performed.

In this report, 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 02 September 2021. In addition to the protocol definition of severe COVID-19, supportive analyses using the CDC definition of severe COVID-19 were also performed.

Immunogenicity Analysis: Immunogenicity evaluations in participants 12-15 years of age are not included in this interim report.

Safety Analysis: The primary safety objective was evaluated by descriptive summary statistics for local reactions, systemic events, and AEs/SAEs for each vaccine group. There are no new reactogenicity data in this report (previously reported in the adolescent interim CSR, dated 14 April 2021).

Other Analysis: AEs and SAEs reported during the open-label follow-up period were summarized separately for adolescent participants who were unblinded at the time of being eligible for receipt of BNT162b2 according to recommendations detailed separately, and

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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

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 and in Figure S1. AEs reported from Dose 1 to 1 month after Dose 2 during the blinded placebo-controlled follow-up period were previously reported in the adolescent interim CSR, dated 14 April 2021. For each time period, overall safety will be presented in addition to new AEs that were reported since the EUA snapshot occurred (based on a data cutoff date of 13 March 2021), in the following order:

- Blinded placebo-controlled follow-up period from Dose 1 to the unblinding date, including separate summaries for new AEs that were reported after the EUA snapshot date
- Open-label follow-up period – original BNT162b2 recipients
- Blinded placebo-controlled and open-label follow-up periods from Dose 1 to 6 months after Dose 2 – original BNT162b2 participants, including separate summaries for new AEs that were reported after the EUA snapshot date
- Open-label follow-up period – original placebo recipients who then received at least 1 dose of BNT162b2 after unblinding

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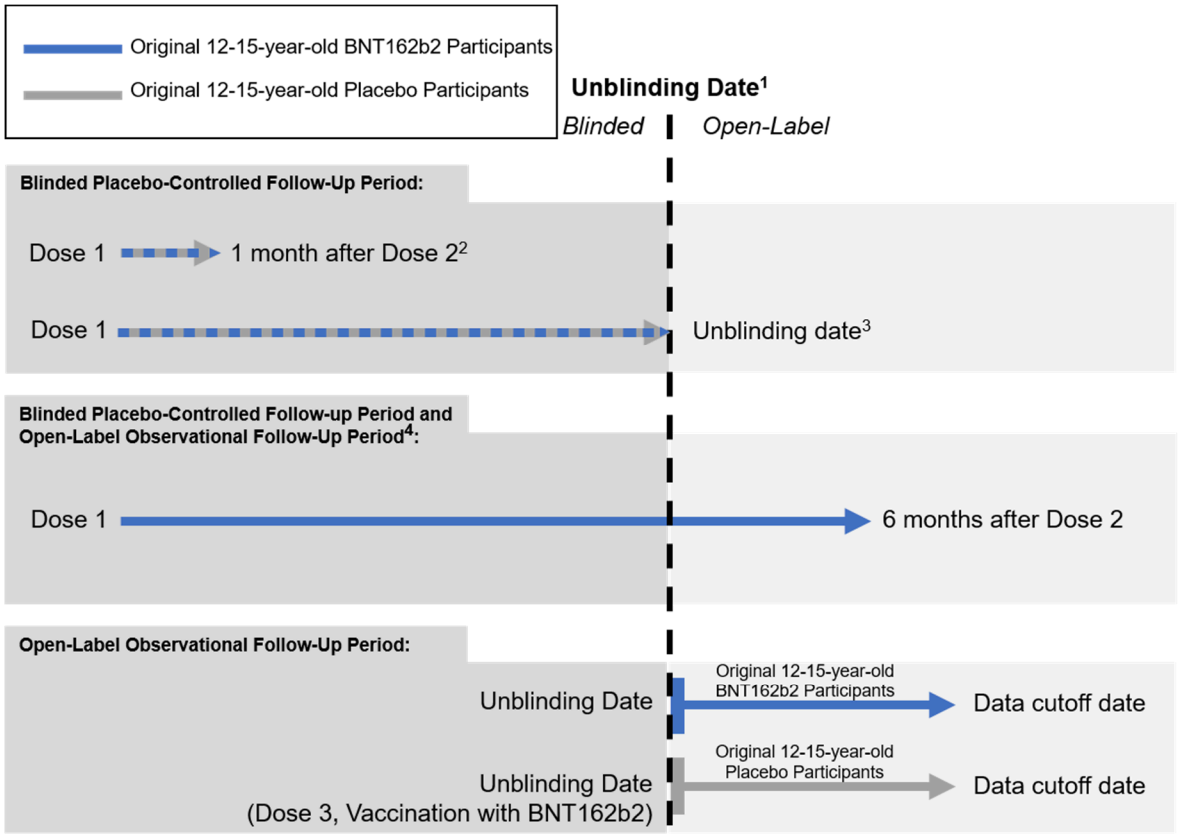
Figure S1 Phase 2/3 Safety Analyses of Adolescent Participants: Time Periods and Analysis Groups



[1] Will vary by participant. Adverse event data analyzed from Dose 1 to unblinding date or from unblinding date to data cutoff date are reported as incidence rates adjusted for exposure time.
[2] Data previously reported in the adolescent interim CSR dated 14 April 2021.
[3] Up to ~6 months after Dose 2.
[4] Cumulative BNT162b2 follow-up to at least 6 months after Dose 2.

Participant Disposition and Demography:

During the blinded placebo-controlled follow-up period, median follow-up time for adolescent participants was 4.4 months. There were 634 (56.1%) and 629 (55.7%) of participants in the BNT162b2 and placebo groups, respectively, who had follow-up time between ≥4 months to <6 months after Dose 2. From Dose 2 to the cutoff date, 740 (65.4%) of participants in the BNT162b2 group had a total follow-up time between ≥8 to <10 months, which was composed of blinded and unblinded exposure. There were few participants (18 total) with follow-up time of <6 months, as most adolescent participants 12-15 years of age should have had ≥6 months of follow-up by the data cutoff date (02 September 2021), and also corresponding with the number of participants who withdrew from the study.

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Disposition – Blinded Placebo-Controlled Follow-Up Period

During the blinded placebo-controlled follow-up period, there were 3 (0.3%) participants in the BNT162b2 group and 14 (1.2%) participants in the placebo group who discontinued from the vaccination period (Dose 1 to 1 month after Dose 2). Most participants completed the visit at 1 month after Dose 2 (≥97.0%). Few participants in the BNT162b2 and placebo groups were withdrawn from the study (0.4% and 1.2%, respectively), and all were because of withdrawal by the participant, withdrawal by parent/guardian, or they were lost to follow-up.

Disposition – Open-Label Follow-Up Period

Individuals 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). Participants who originally received BNT162b2 continued to be followed in an open-label manner. Participants who originally received placebo were 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 (98.1%) and placebo (97.0%) groups completed the 1 month post-Dose 2 visit before unblinding.

A total of 4 (0.4%) original BNT162b2 adolescent 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 45 (4.0%) participants withdrawn from the study, and most were because of other reasons (21 of 23 participants were enrolled into Study C4591031 to evaluate a booster dose of BNT162b2).

During the open-label follow-up period, most participants originally randomized to the placebo group received Doses 3 and 4 (89.4% and 87.8%, first and second dose of BNT162b2 30 µg, respectively). There were 47 (4.2%) participants who were withdrawn from the study after unblinding and before Dose 3. There were few participants in this group (who received at least the first dose of BNT162b2 30 µg) who were withdrawn from the study who (0.5%), and most were because of withdrawals by the participant, or they were lost to follow-up.

Demographics – Safety Population

Overall

Demographic characteristics for adolescents (12-15 years of age) were similar in the BNT162b2 and placebo groups in the safety population, and all adolescents were enrolled at sites in the United States. Most adolescent participants in the BNT162b2 group were White

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(85.8%), with 4.6% Black or African American participants and 6.4% Asian participants, and other racial groups were ≤2.1%. There were 11.7% Hispanic/Latino participants. The median age of adolescents in the BNT162b2 group was 14.0 years and 50.1% were male. Obese adolescents of this age group (based on age- and sex-specific BMI) made up 11.3% (placebo group) to 12.6% (BNT162b2 group).

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

Demographic characteristics for all original BNT162b2 adolescent participants who had at least 6 months of follow-up time after Dose 2 were similar to demographic characteristics in the BNT162b2 group overall.

Original Placebo Participants Who Then Received BNT162b2

Demographic characteristics for all original placebo adolescent participants who then received BNT162b2 later during the open-label follow-up period were similar to demographic characteristics in the placebo group overall.

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

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

Efficacy Results – Updated Analysis:

- In the updated descriptive efficacy analysis (data cutoff date 02 September 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 100% (2-sided 95% CI: 86.8%, 100%), with 0 cases in the BNT162b2 group and 28 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 100% (2-sided 95% CI: 87.5%, 100%), with 0 and 30 cases in the BNT162b2 and placebo groups, respectively.

- Among participants without and with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen (evaluable efficacy population), VE against COVID-19 occurring at least 7 days after Dose 2 was evaluated for demographic and risk subgroups, and the estimated VE was 100.0% for all subgroups.

- From the analysis of all cases of confirmed COVID-19 based on the all-available (modified intention-to-treat) population (regardless of evidence of infection before or during the vaccination regimen), the estimated VE against all cases occurring at any time

after Dose 1 was 94.0% (2-sided 95% CI: 81.3%, 98.8%), with 3 cases in the BNT162b2 group (all occurring within <11 days after Dose 1 and in participants who had baseline SARS-CoV-2 negative status) and 48 cases in the placebo group.

- No severe COVID-19 cases (per protocol definition or CDC criteria) were reported in participants 12-15 years of age as of the data cutoff date (02 September 2021).

- Most variants sequenced were neither VOI nor VOC except for the B.1.1.7 (Alpha) found in 23.3% of placebo participants. All of the cases in the efficacy analyses occurred between 02 November 2020 to 19 May 2021, which is before the Delta surge in the US.

Safety Results:

Blinded Placebo-Controlled Follow-Up Period From Dose 1 to the Unblinding Date – Participants 12 Through 15 Years of Age

Adverse Events

Total exposure time in 100 PY was similar in the BNT162b2 and placebo groups (4.6 vs 4.5 per 100 PY, respectively). Hence, frequencies are summarized in the safety results.

The percentage of adolescent participants with any AE was similar in the BNT162b2 and placebo groups (8.4% and 10.0%, respectively). Severe AEs, SAEs, and AEs leading to withdrawal were reported by ≤1.1%, ≤0.9%, and ≤0.1%, respectively, in both groups. All reported SAEs were assessed by the investigator as not related to study intervention. Withdrawals due to related AEs were reported in 1 adolescent participant in the BNT162b2 group (pyrexia occurring 1 day after Dose 1; previously reported in adolescent interim CSR dated 14 April 2021), and none in the placebo group. There were no deaths.

The most frequently reported AEs in the BNT162b2 group included lymphadenopathy (9 [0.8%]), injection site pain (8 [0.7%]), fatigue (8 [0.7%]), pyrexia (6 [0.5%]), depression (6 [0.5%]), nausea (5 [0.4%]), and headache (5 [0.4%]). Most of these AEs were previously reported in the adolescent interim CSR, dated 14 April 2021.

The number of participants with psychiatric disorder AEs were comparable in the 2 groups, (17 [1.5%] in BNT162b2 group vs. 13 [1.2%] in placebo group). There were 4 participants who were hospitalized with the event of suicidal ideation (3 of these were new after the EUA snapshot). All participants were in the BNT162b2 group and had an ongoing past medical history of depression and/or anxiety (3 diagnosed within 2020 and 1 since 2018). Of these 4 participants, 3 had been taking selective serotonin reuptake inhibitors (fluoxetine or sertraline) for their ongoing condition. The fourth participant had their concomitant medication for attention deficit hyperactivity disorder changed from methylphenidate hydrochloride to demethylphenidate hydrochloride approximately 22 days before the event of suicidal ideation occurred.

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A total of 9 participants reported depression: 6 [0.5%] in the BNT162b2 group and 3 [0.3%] in the placebo group, (6 of these were new after the EUA snapshot; 4 in the BNT162b2 group and 2 in the placebo group. Of the 6 participants in the BNT162b2 group 3 participants had a known past medical history of ongoing depression, and of the 4 newly diagnosed cases in the BNT162b2 group, 3 participants had an ongoing past medical history of attention deficit hyperactivity disorder and the depression for the remaining participant in this group was reported to be due to social events. Within the placebo group, 2 of the 3 participants were newly diagnosed with depression.

The event of conversion disorder (BNT162b2 group) has been previously reported in the adolescent interim CSR dated 14 April 2021, as an SAE of neuralgia and had been extensively investigated. Further follow-up since the adolescent interim CSR; the participant was continuing with physical therapy and had undergone further neurological examination and investigations including an MRI brain scan with and without contrast that was normal. There has been little change in her symptoms, and she continues to require treatment.

The 1 participant in the BNT162b2 group who reported a tic had an exacerbation of their known tic disorder (diagnosed since 2019) and was considered to be due to life stressors (as determined by the principal investigator). This event was previously reported in the adolescent interim CSR dated 14 April 2021.

Subgroup Analyses

For the baseline SARS-CoV-2 positive and negative subgroups, AEs by SOC and PT were similar to those in the overall safety population. Considering that the positive subgroup (N=46) had fewer participants than the negative subgroup (N=1083) in the BNT162b2 group, differences in SOCs were considered not clinically meaningful, and there is no evidence that individuals who are positive at baseline report AEs at a higher frequency than those who are negative at baseline.

For the ethnicity subgroups, AEs by SOC and PT were similar to those in the overall safety population for Hispanic/Latino and non-Hispanic/non-Latino participants. Considering that the Hispanic/Latino subgroup (N=132) had fewer participants than non-Hispanic/non-Latino subgroup (N=997) in the BNT162b2 group, differences in AEs by SOC and PT in these subgroups were not clinically meaningful.

For race subgroups, AEs by SOC and PT were similar to those in the overall safety population. Considering that some race subgroups had fewer participants than others (within the BNT162b2 groups: White N=970, Black or African American N=52, and 'All Others' N=109), differences in AEs by SOC and PT in these subgroups were not clinically meaningful.

For sex subgroups, AEs by SOC and PT were similar to those in the overall safety population. There was a slightly higher frequency of any event reported in the BNT162b2 group in female participants compared to males (53 [9.4%], 42 [7.4%] respectively), and of

any SAEs 7 (1.2%) females, 3 (0.5%) males. Within the placebo group there were 2 (0.3%) SAEs reported in male participants and none in the females. In the BNT162b2 group, lymphadenopathy was reported in 8 (1.4%) male participants and in 1 (0.2%) female participant. AEs in the psychiatric disorders SOC were reported in 12 (2.1%) female participants compared to 5 (0.9%) male participants. Depression was the most frequently reported event in both sexes (4 [0.7%] females and 2 [0.4%] males). Anxiety was reported in 4 (0.7%) females and no males. Suicidal ideation was the next most frequently reported event: in females, 3 [0.5%], 1 (0.2%) in males.

New Adverse Events After the EUA Snapshot

The frequency of adolescent participants in the BNT162b2 group with any new AE after the EUA snapshot from Dose 1 to the unblinding date was 2.6%, which was less than the frequency in the placebo group (4.2%). There were 6 (0.5%) participants in the BNT162b2 group with SAEs, and all events were assessed by the investigator as not related to study intervention. No SAEs were reported in the placebo group. There were no withdrawals because of any AEs or deaths.

The most frequently reported AEs in adolescents were in the psychiatric disorders SOC (11 [1.0%] and 9 [0.8%] adolescent participants in the BNT162b2 and placebo groups, respectively).

No new safety signals or concerns were for new AEs reported after the EUA snapshot.

Open-Label Follow-Up Period From the Unblinding Date to the Data Cutoff Date– Original BNT162b2 Recipients 12 Through 15 Years of Age

There were 18 (1.6%) participants who experienced any AE, including 0.4%, 0.3%, and 0% who experienced related, severe, and life-threatening events, respectively. This is markedly reduced relative to AEs from Dose 1 to the unblinding date (8.4% of BNT162b2 participants experienced any AE, including 3.2%, 1.1%, and 0.2% who experienced related, severe, and life-threatening events, respectively). The frequencies of SAEs and AEs leading to withdrawal during the open-label follow-up period (0.4% and 0%, respectively) were similar to those from Dose 1 to the unblinding date (0.9% and 0.1%, respectively). There were no adolescent deaths in the study.

Overall, the rates in all SOCs after the unblinding date were lower or remained similar to those in the blinded placebo-controlled period.

The frequency for the SOC of nervous system disorders was 6 (0.5%), including the PTs dizziness (2), headache (2), presyncope (2), and syncope (1). The frequency for the SOC of general disorders and administration site conditions was 4 (0.4%), with injection site pain (3) as the most frequently reported PT.

CLINICAL STUDY REPORT SYNOPSIS

Blinded Placebo-Controlled and Open-Label Follow-Up Periods to 6 Months After Dose 2 – Original BNT162b2 Recipients 12 Through 15 Years of Age

Adverse Events

There were 1113 adolescent participants who originally received BNT162b2 and had at least 6 months of follow-up time after Dose 2 for the blinded placebo-controlled and open-label follow-up periods. There were 98 (8.8%) participants who reported at least 1 AE, and 34 (3.1%) participants reported at least 1 related AE. Severe AEs and SAEs were reported by 13 (1.2%) and 10 (0.9%) participants, respectively. There were no AEs leading to withdrawal, and there were no deaths.

The frequencies of any AEs and related AEs are 70 (6.3%) and 34 (3.1%) through 1 month after Dose 2 compared with 35 (3.1%) and no related AEs from 1 month after Dose 2 to 6 months after Dose 2, respectively. From Dose 1 to 1 month after Dose 2, 3 (0.3%) adolescent participants reported SAEs. From 1 month to 6 months after Dose 2, 9 (0.8%) participants reported SAEs. All SAEs were assessed by the investigator as not related to study intervention. There were no AEs leading to withdrawal, and there were no deaths.

Frequently reported AEs included reactogenicity events in the following SOCs:

- general disorders and administration site conditions (16 [1.4%])
- musculoskeletal and connective tissue disorders (8 [0.7%])
- nervous system disorders (16 [1.4%])
- gastrointestinal disorders (16 [1.4%])

AEs were reported by 15 (1.3%) participants in the injury, poisoning, and procedural complications SOC; 10 (0.9%) participants in the infections and infestations SOC, and 16 (1.4%) participants in the psychiatric disorders SOC.

All lymphadenopathy events were reported from Dose 1 to 1 month after Dose 2, and none were reported from 1 month to 6 months after Dose 2.

AEs in the pyschiatric disorders SOC were reported by 7 (0.6%) participants from Dose 1 to 1 month after Dose 2 and in 11 (1.0%) participants from 1 month to 6 months after Dose 2.

Overall, AEs reported after 1 month post Dose-2 reflect age-appropriate events consistent with the general population.

New Adverse Events After the EUA Snapshot

From the time after the EUA snapshot for adolescent participants who had at least 6 months of follow-up time after Dose 2 during the blinded placebo-controlled and open-label follow-up periods, there were 36 (3.2%) participants who reported at least 1 AE, and

3 (0.3%) participants reported at least 1 related AE. Severe AEs and SAEs were reported by 6 (0.5%) and 7 (0.6%) participants, respectively. There were no AEs leading to withdrawal, and there were no deaths.

When frequencies of new AEs for participants with at least 6 months of follow-up time are examined by time since the second dose, the frequency of any AEs and related AEs is 6 (0.5%) and 3 (0.3%) through 1 month after Dose 2 compared with 32 (2.9%) and no related AEs from 1 month after Dose 2 to 6 months after Dose 2. At 1 month after Dose 2, no adolescent participants reported severe AEs or SAEs. From 1 month to 6 months after Dose 2, the number of participants with severe AEs and SAEs was 6 (0.5%) and 7 (0.6%), respectively. All new SAEs and all AEs reported from 1 month after Dose 2 to 6 months after Dose 2 were assessed by the investigator as not related to study intervention.

Most of the new AEs reported after the EUA snapshot in adolescent participants with at least 6 months of follow-up time after Dose 2 were in the psychiatric disorders SOC (11 [1.0%]).

When AEs are compared from Dose 1 to 1 month after Dose 2 and from 1 month after Dose 2 to 6 months after Dose 2, AEs reported in the psychiatric disorders SOC was 1 (0.1%) and 10 (0.9%) participants, respectively. All AEs in this SOC were assessed by the investigator as not related to study intervention.

Open-Label Follow-Up Period – Original Placebo Recipients 12 Through 15 Years of Age Who Then Received BNT162b2 After Unblinding

For the 1,010 original placebo recipients who then received BNT162b2 after unblinding, the total exposure time is shorter than those who originally received BNT162b2 (2.9 per 100 PY vs 4.6 per 100 PY, respectively.

After participants who originally received placebo were unblinded and then received BNT162b2 after unblinding, events related to reactogenicity were not reported using an e-diary but were instead reported as AEs. Because an e-diary was not used after original placebo recipients received open-label BNT162b2, in comparison to participants randomized to BNT162b2 from Dose 1 to the unblinding date, the frequencies for any AE and at least 1 related AE for participants who originally received placebo and then received BNT162b2 are greater (26.2% and 24.0%) than the frequencies (8.4% and 3.2%) for participants who originally received BNT162b2, respectively. However, the frequencies for severe, life-threatening AE, SAE, AEs leading to withdrawal and deaths were similar (1.2%, 0%, 0.6%, 0%, 0% versus 1.1%, 0.2%, 0.9%, 0.1%, 0%, respectively). There was 1 related SAE of appendicitis for a placebo recipient who was vaccinated with BNT162b2.

Most AEs reported from Dose 3 (first dose of BNT162b2) to the data cutoff date were in SOCs with reactogenicity events.

- general disorders and administration site conditions (225 [22.3%])
- nervous system disorders (75 [7.4%])

- musculoskeletal and connective tissue disorders (48 [4.8%])
- gastrointestinal disorders (20 [2.0%])

The most frequently reported AEs overall were injection site pain (15.5%), fatigue (10.3%), headache (7.0%), pyrexia (6.3%), chills (4.5%), myalgia (3.8%), pain (3.5%), nausea (1.2%), pain in extremity (0.9%), vomiting (0.7%), malaise (0.7%), and injection site erythema (0.5%).

Other Significant Adverse Events

Adverse events of clinical interest include AESIs, such as those in the CDC list of AESIs for COVID-19 that include events potentially indicative of severe COVID-19 or autoimmune and neuroinflammatory disorders, were considered, in addition to program-defined TMEs, in the review of reported events for the adolescent group.

No cases of anaphylaxis, hypersensitivity, Bell's palsy, or vaccine-related appendicitis were reported as of the data cutoff date (02 September 2021) during the blinded placebo-controlled period.

FDA-Requested Adverse Events of Clinical Interest

Lymphadenopathy

Lymphadenopathy is identified as an adverse reaction for BNT162b2 vaccine.

During the blinded placebo-controlled follow-up period, 9 and 2 participants in the BNT162b2 and placebo groups reported AEs of lymphadenopathy, respectively. All events were mild or moderate in severity (only 1 moderate AE in the BNT162b2 group).

Appendicitis

During the blinded placebo-controlled follow-up period, 2 participants in the placebo group each had an SAE of appendicitis, and both events were assessed by the investigator as not related to study intervention.

During the open-label follow-up period:

- Two original BNT162b2 recipients each had an SAE of appendicitis long after vaccination from Dose 2 (Day 148 and Day 177), and both events were assessed by the investigator as not related to study intervention.

- One original placebo recipient had an SAE of appendicitis that was assessed by the investigator as related to study intervention.

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Myocarditis/pericarditis

One original placebo participant had an SAE of myocarditis (previously reported to CBER and discussed by ACIP) on Day 3 after Dose 4 (second dose of BNT162b2 30 µg), which was assessed by the investigator as not related to study intervention (Pfizer assessed event as related to study intervention).

Other Adverse Events of Clinical Interest

Additional AEs of clinical interest, including those on the CDC AESI list, were evaluated based on sponsor agent safety data review. These AEs were identified from the C4591001 study database as of the data cutoff date (02 September 2021). From this analysis, notable pertinent negatives (ie, no cases reported in this population as of the data cutoff for this submission) with regard to the CDC list of AESIs included (but were not limited to): thromboembolic or intravascular coagulation events, autoimmune or demyelination events, meningitis, encephalitis, optic neuritis, Kawasaki disease, MIS-C, or acute respiratory distress syndrome.

An analysis of AEs of clinical interest for potential numerical imbalance (based on risk difference >0) between BNT162b2 and placebo SOC and PT showed no numerical difference for most PTs in the BNT162b2 and placebo groups. SOCs which did include PTs more frequently reported after BNT162b2 compared to placebo, or otherwise considered of particular clinical interest, are summarized below.

There was a numerical difference for events of pyrexia, which was reported by 6 participants in the BNT162b2 group and none in the placebo group. These are recognized as reactogenicity events known to be associated with BNT162b2 vaccination.

There was no imbalance of arthralgia being reported more frequently in the BNT162b2 group.

Overall Conclusion(s):

- In Phase 2/3, updated descriptive efficacy analysis continues to show that BNT162b2 at 30 µg provided a high level of protection against COVID-19 in participants 12 through 15 years of age with or without evidence of infection with SARS-CoV-2 (100% VE), with no severe cases overall observed in this age group.

- The tolerability and safety profile of BNT162b2 30 µg in participants 12 through 15 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.