Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Walter EB, Talaat KR, Sabharwal C, et al. Evaluation of the BNT162b2 Covid-19 vaccine in children 5 to 11 years of age. N Engl J Med 2022;386:35-46. DOI: 10.1056/NEJMoa2116298

SUPPLEMENTARY APPENDIX

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Inclusion and Exclusion Criteria

The study included healthy participants with pre-existing stable disease (ie, disease not requiring a significant change in therapy or hospitalization for worsening disease in the 6 weeks before enrollment). In the phase 1 portion of the study, exclusion criteria included past clinical (based on COVID-19 symptoms/signs alone if a SARS-CoV-2 nucleic acid amplification test [NAAT] result was unavailable) or virologic (based on COVID-19 symptoms/signs and a positive SARS-CoV-2 NAAT result) COVID-19 diagnosis, as well as known HIV or hepatitis C or B virus infection. Exclusion criteria in the phase 1 and 2/3 portions of the study included receipt of COVID-19 preventative treatments, history of multisystem inflammatory syndrome in children (MIS-C) or of severe adverse reaction with a vaccine or any component of the study intervention, and immunodeficiency, autoimmune disease, or conditions associated with prolonged bleeding.

Ethical Conduct of the Study

Conduct of this study was in accordance with the study protocol and with consensus ethical principles derived from international guidelines including the Declaration of Helsinki, Council for International Organizations of Medical Sciences Ethical Guidelines, International Conference on Harmonisation Guidelines for Good Clinical Practice, and applicable laws and regulations, including applicable privacy laws. The study protocol and any amendments, informed consent documents, and other relevant documents were approved by institutional review board/ethics committees (IRB/EC) before study initiation. Before any study activity, written informed consent was obtained from the participants' parents/legal guardians, and affirmative agreement from the participant was subsequently obtained when in the capacity to provide assent, as determined by the IRB/EC.

Study Responsibilities

Pfizer was responsible for study design and conduct; data collection, analysis, and interpretation; and writing of this manuscript. Both Pfizer and BioNTech manufactured the vaccine and placebo. BioNTech was the regulatory sponsor of the study and contributed to data interpretation and writing of the manuscript. All data were available to the authors, who vouch for its accuracy and completeness and to adherence of the study to the protocol.

Phase 1 Review of Safety Data and Stopping Rules

An Internal Review Committee (IRC) reviewed safety and immunogenicity data to permit dose level finding in each age group, and to select the dose level to proceed to phase 2/3. Data supporting these selections included safety, binding antibody levels, and neutralizing titers.

Stopping rules were applied to all phase 1 participants based on review of adverse event (AE) and reactogenicity data, until the start of phase 2/3 or 30 days after the last vaccine dose in phase 1. These data were continuously monitored by the investigators and sponsor to allow prompt identification of any event contributing to the stopping rule.

The stopping rule criteria for each BNT162b2 dose level included: (1) if a participant developed a serious AE as assessed by the investigator as possibly related to the vaccine and for which there was no alternative, plausible, or attributable cause; (2) if a participant developed a grade 4 local reaction or systemic event; (3) if any participant developed a fever >40 ºC for ≥1 daily measurement after vaccination; (4) if 2 participants within the same age group reported the same or similar severe AEs after vaccination as assessed by the investigator as possibly related to the vaccine and for which there was no alternative, plausible, or attributable cause; and (5) if any participant died or required intensive care unit admission because of SARS-CoV-2 infection.

If a stopping rule was met, the IRC was to consider all data; randomization and vaccine administration for all dose levels in the affected age group were to be paused; and the Data Monitoring Committee was to review all appropriate data. All other routine study conduct activities were to continue for all vaccinated participants.

Calculation of Immunogenicity Parameters

The geometric mean titers (GMTs) were derived by exponentiating the mean, and geometric mean ratios were derived by exponentiating the mean of the differences (5–11-year-olds minus 16–25-year-olds), in logarithmically transformed neutralizing titer values. Associated 2-sided 95% CIs were based on the Student *t* distribution and then exponentiating results. Geometric mean fold rises (GMFRs) were calculated for participants with non-missing values both before and after each vaccination by exponentiating the mean of the difference of logarithmically transformed assay results. Associated 2-sided 95% CIs were obtained using the Student *t* distribution for the mean difference and exponentiating the confidence limits.

Determination of COVID-19 and MIS-C

Surveillance for potential cases of COVID-19 and MIS-C will occur throughout a participant's involvement in the study. If a participant developed an acute illness, the participant was considered to potentially have COVID-19 illness. In this circumstance, assessments were to include nasal (anterior nares) swab sample collection, which were tested at a central laboratory using the reverse transcription–polymerase chain reaction (RT-PCR) test (Cepheid) or other equivalent nucleic acid amplification–based test (NAAT), to detect SARS-CoV-2. In addition, clinical information and results from local standard-of-care tests were assessed. The central laboratory NAAT result was used for the case definition. If no result was available from the central laboratory, a local NAAT result could be used if it was obtained using either the Cepheid Xpert Xpress SARS-CoV-2, Roche Cobas SARS-CoV-2 Real-Time RT-PCR test, or the Abbott Molecular/RealTime SARS-CoV-2 assay.

SARS-CoV-2–related cases, and SARS-CoV-2–related severe cases were documented (for both, the onset date of the case was the date that symptoms were first experienced by the participant; if new symptoms were reported within 4 days after resolution of all previous symptoms, they were considered as part of a single illness). The definition of confirmed COVID-19 included the presence of ≥1 symptom (ie, 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 [≥3 stools per day], vomiting) and being 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).

Diagnosis of severe COVID-19 included confirmed COVID-19 and the presence of ≥1 of the following:

(1) clinical signs at rest indicative of severe systemic illness (eg, respiratory rate and heart rate as shown in the following table, SpO_2 ≤92% on room air of >50% FiO_2 to maintain ≥92%, or PaO_2/FiO_2 <300 mmHg)

Participant age	Respiratory rate	Heart rate
4–6 years	>29	>131
6–<8 years	>27	>123
8–<12 years	>25	>115

(2) respiratory failure (ie, needing high-flow oxygen, including continuous positive airway pressure, bilevel positive airway pressure, noninvasive ventilation, mechanical ventilation, or extracorporeal membrane oxygenation)

(3) evidence of shock or cardiac failure (ie, systemic blood pressure <70 + (age in years × 2) for age up to 10 years, <90 for age ≥10 years; or requiring vasoactive drugs to maintain blood pressure in the normal range

(4) significant acute renal failure (ie, serum creatinine ≥2 × upper limit of normal [ULN] for age or 2-fold increase in baseline creatinine

(5) significant gastrointestinal/hepatic failure (ie, total bilirubin ≥4 mg/dL or ALT 2 × ULN for age)

(6) significant neurological dysfunction (ie, Glasgow Coma Scale score ≤11 or acute change in mental status with a decrease in Glasgow Coma Scale score ≥3 points from abnormal baseline)

(7) intensive care unit admission

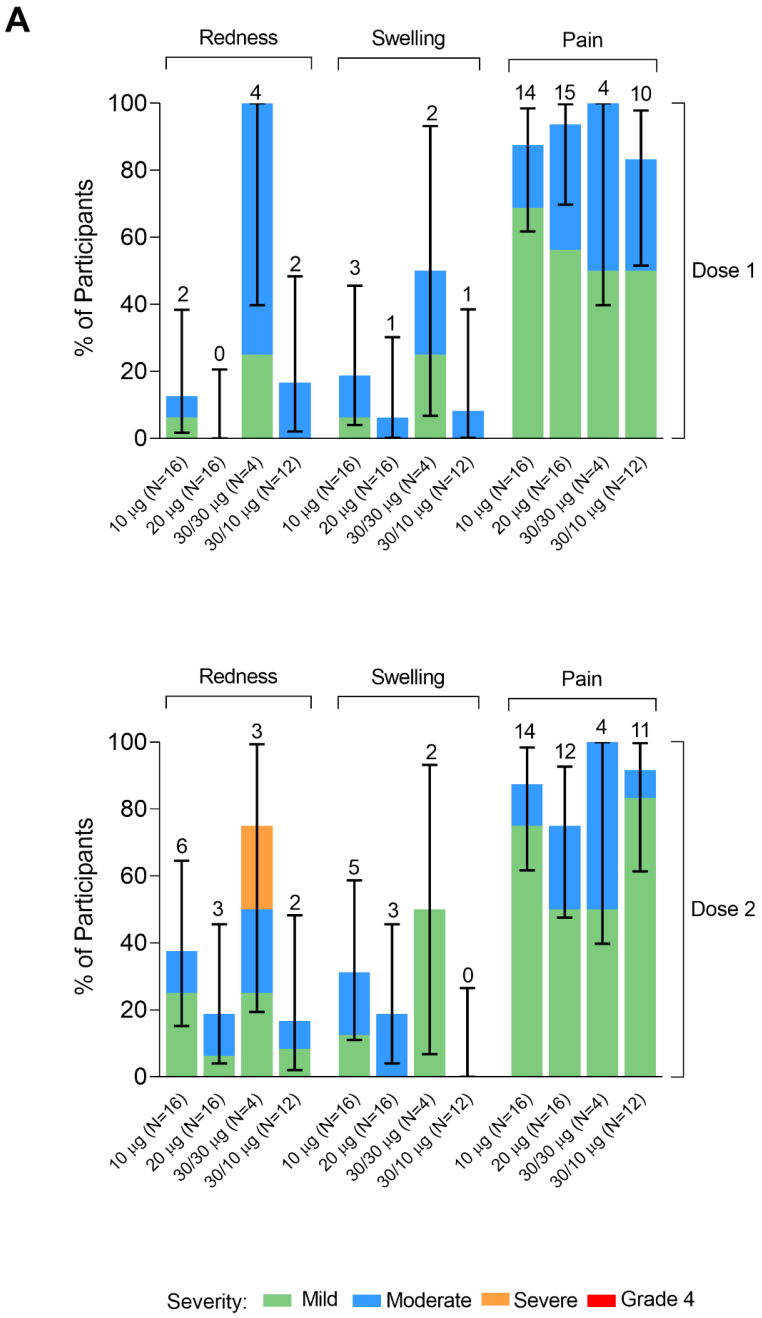
(8) death

Confirmed MIS-C was per the CDC MIS-C case definition (www.cdc.gov/mis-c/hcp/).

Figure S1. Local reactions (A) and systemic events (B) reported in the phase 1 study in participants 5–11 years old

Local reactions and systemic events were assessed within 7 days after administration of BNT162b2 at a 10-µg, 20-µg, or 30-µg dose level. Of 16 participants who received 30 µg BNT162b2 at dose 1, 4 received 30 µg BNT162b2 at dose 2, and 12 received 10 µg BNT162b2 at dose 2. Severity scales for reactogenicity events are summarized in **Table S5**. Fever categories are designated in the key. The numbers above the bars show the number of participants in each group with the specified local reaction or systemic event. Error bars are the 95% CIs.

10 µg=10 µg BNT162b2; 20 µg=20 µg BNT162b2; 30/30 µg=BNT162b2 administered at a 30-µg dose level at dose 1 and dose 2; 30/10 µg=BNT162b2 administered at a 30-µg dose level at dose 1 and at a 10-µg dose level at dose 2.



B

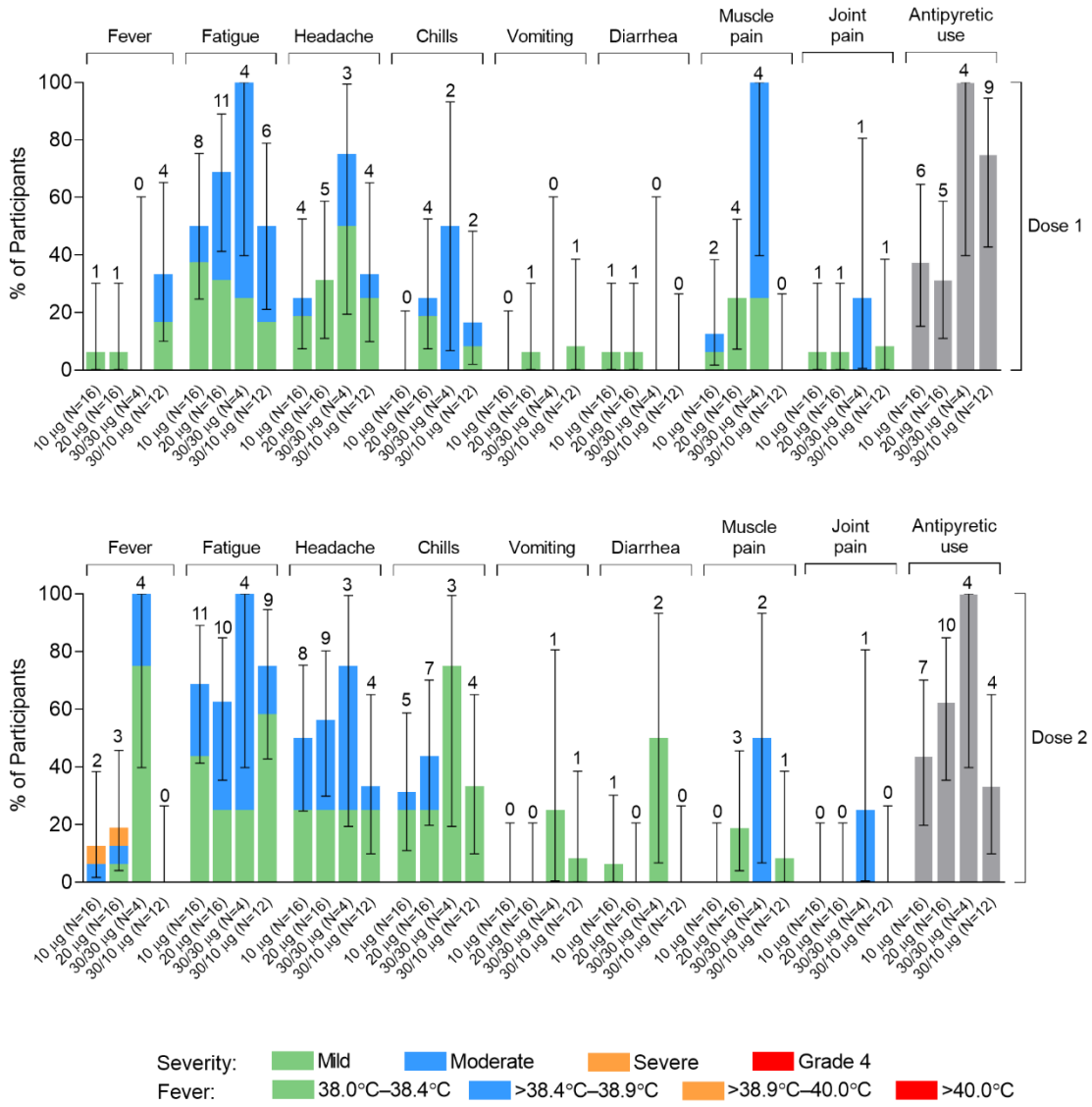

Fever
Fatigue
Headache
Chills
Vomiting
Diarrhea
Muscle pain
Joint pain
Antipyretic use
% of Participants
Dose 1
Dose 2
10 µg (N=16)
20 µg (N=16)
30/30 µg (N=4)
30/10 µg (N=12)
Severity:
Mild
Moderate
Severe
Grade 4
Fever:
38.0°C–38.4°C
>38.4°C–38.9°C
>38.9°C–40.0°C
>40.0°C

Figure S2. Immunogenicity of BNT162b2 at 7 days after dose 2 in the phase 1 study in participants 5–11 years old

Results are for participants in the evaluable immunogenicity population (**Table S1**) who had no serological or virological evidence of SARS-CoV-2 infection (before the 7-day post-dose 2 blood collection) and no medical history of COVID-19. Dots represent individual titers. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student *t* distribution). No assay results were below the lower limit of quantitation.

GMT=geometric mean titer; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

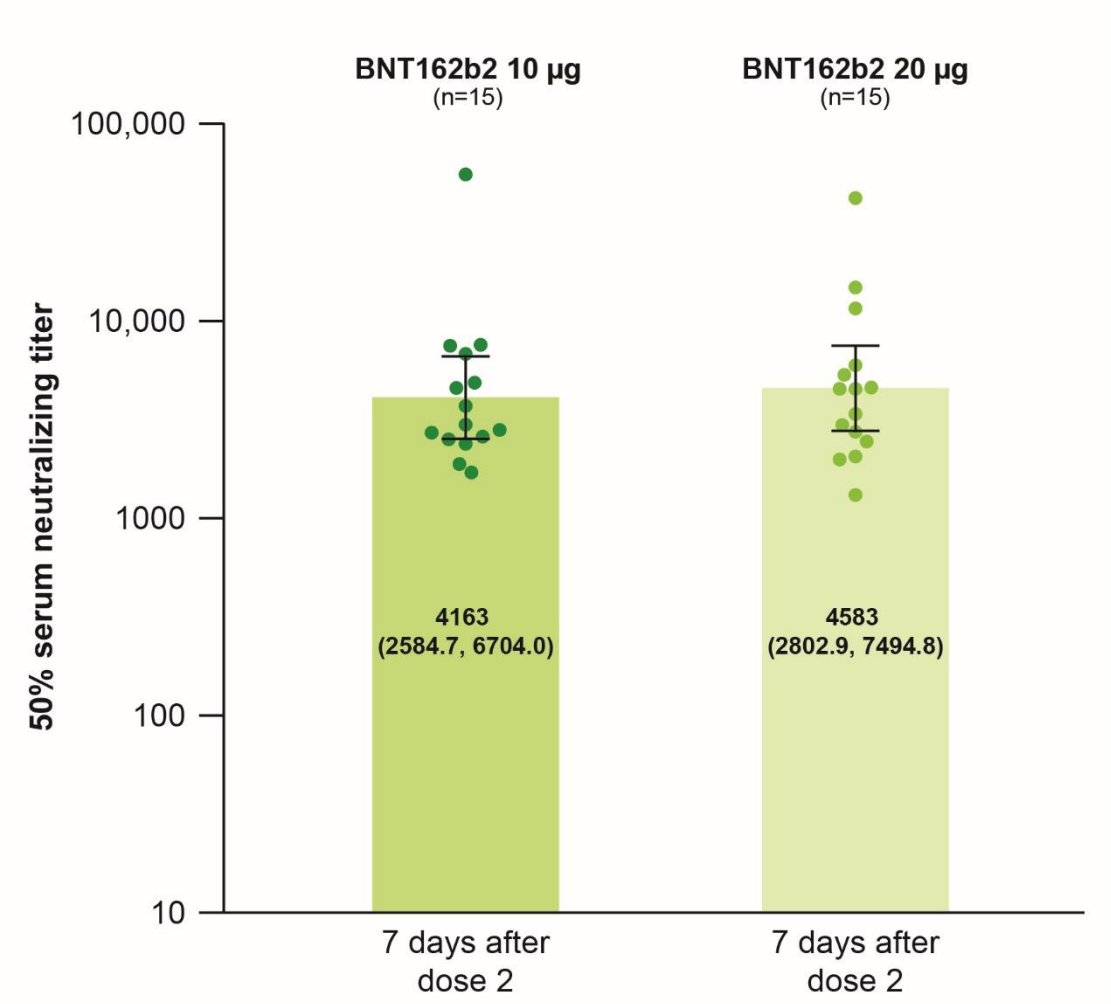


Figure S3. Geometric mean titers and geometric mean fold rises of SARS-CoV-2 neutralizing titers for participants 5–11 and 16–25 years old

Results are for participants in the immunobridging subset of the evaluable immunogenicity population **(Table S1)** who had no serological or virological evidence of SARS-CoV-2 infection before the 1-month post-dose 2 blood sample collection, and who had no COVID-19 medical history. GMTs, GMFRs, and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers or fold rises and the corresponding CIs (based on the Student *t* distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

GMFR=geometric mean fold rise; GMT=geometric mean titer; LLOQ=lower limit of quantitation; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

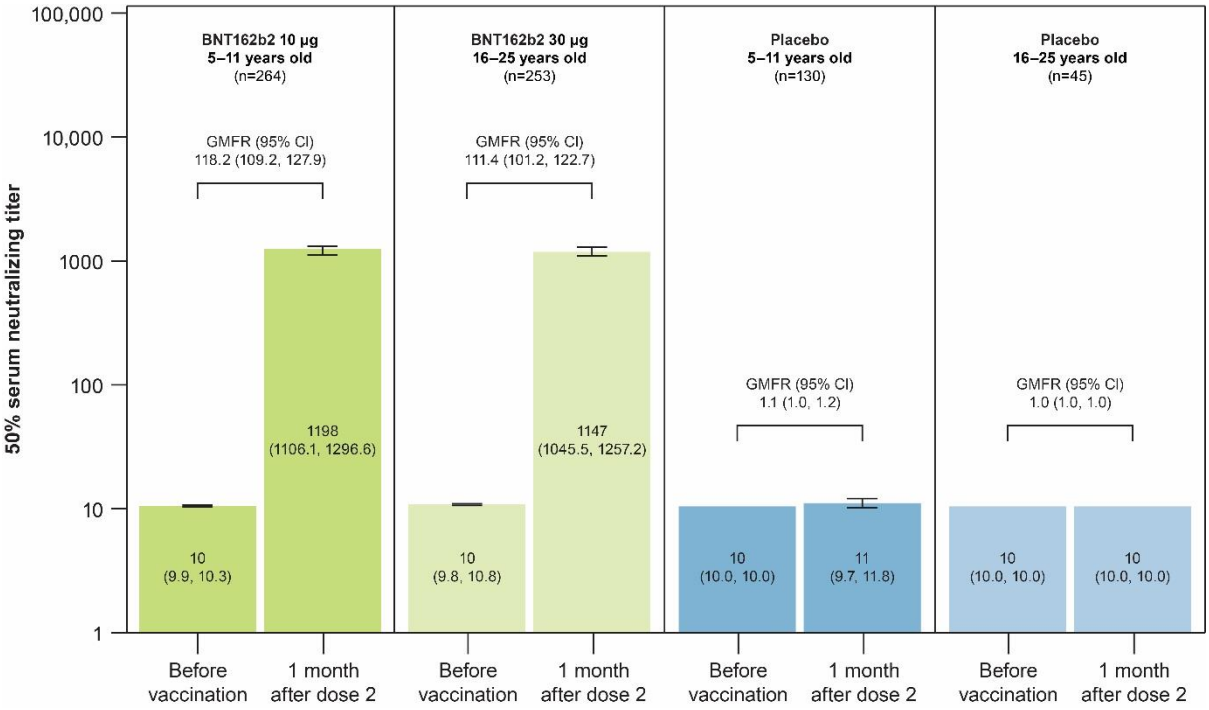


Table S1. Study populations

Population	Description
Enrolled	All participants who provided informed consent
Randomized	All participants who were assigned a randomization number
Immunobridging subset	A subset of participants 5–11 years old from this study (approximately the first 6 participants from every site) and randomly selected participants 16–25 years old from the ongoing pivotal study selected for immunogenicity analyses.
Evaluable immunogenicity	All eligible randomized participants who received 2 vaccine doses to which they were randomized (with dose 2 received within the predefined window), had ≥1 valid and determinate immunogenicity result from the blood sample collected within an appropriate window, and had no important protocol deviations as determined by the clinician
All-available immunogenicity	All randomized participants who received ≥1 dose of the study intervention and had ≥1 valid and determinate immunogenicity result after vaccination
Safety	All randomized participants who received ≥1 dose of the study intervention
Evaluable efficacy	All eligible randomized participants who received 2 vaccine doses to which they were randomized within the predefined window, and who had no other important protocol deviations as determined by the investigator
All-available efficacy	Dose 1: all randomized participants who received at least 1 dose Dose 2: all randomized participants who received both doses

Table S2. Demographic characteristics of phase 1 participants 5–11 years old*

Characteristic	BNT162b2 10 µg (N=16)	BNT162b2 20 µg (N=16)	BNT162b2 30/30 µg† (N=4)	BNT162b2 30/10 µg† (N=12)	Total (N=48)
Male, n (%)	5 (31.3)	10 (62.5)	3 (75.0)	6 (50.0)	24 (50.0)
Race, n (%)‡					
White	11 (68.8)	13 (81.3)	4 (100.0)	10 (83.3)	38 (79.2)
Black or African American	3 (18.8)	0	0	0	3 (6.3)
Asian	2 (12.5)	2 (12.5)	0	1 (8.3)	5 (10.4)
Multiracial, American Indian or Alaska Native	0	1 (6.3)	0	1 (8.3)	2 (4.2)
Ethnicity, n (%)‡					
Hispanic/Latinx	2 (12.5)	0	2 (50.0)	0	4 (8.3)
Non-Hispanic/non-Latinx	14 (87.5)	16 (100.0)	2 (50.0)	12 (100.0)	44 (91.7)
Age, years					
Mean, ± standard deviation	7.9±1.89	8.0±1.97	6.8±2.36	8.3±1.76	7.9±1.90
Median (range)	8.5 (5–11)	8.5 (5–10)	6.0 (5–10)	8.5 (5–10)	8.0 (5–11)
Country, n (%)					
United States	16 (100.0)	16 (100.0)	4 (100.0)	12 (100.0)	48 (100.0)

* Results are for the safety population **(Table S1)**.

† Of 16 participants who received 30 µg at dose 1, 4 received 30 µg at dose 2 and 12 received 10 µg at dose 2.

Percentages may not total 100 because of rounding.

‡ Race and ethnic group were reported by the participants or their parents/guardians.

Table S3. Demographic characteristics of phase 2/3 participants 5–11 and 16–25 years old*

Characteristic	BNT162b2 10 µg	BNT162b2 30 µg	Placebo	
	5–11 years old (N=311)	16–25 years old† (N=286)	5–11 years old (N=156)	16–25 years old† (N=49)
Male, n (%)	161 (51.8)	141 (49.3)	89 (57.1)	18 (36.7)
Race, n (%)§				
White	247 (79.4)	217 (75.9)	127 (81.4)	31 (63.3)
Black or African American	20 (6.4)	33 (11.5)	6 (3.8)	12 (24.5)
Asian	23 (7.4)	17 (5.9)	15 (9.6)	3 (6.1)
Multiracial	17 (5.5)	12 (4.2)	6 (3.8)	1 (2.0)
Other/not reported	4 (1.3)	7 (2.4)	2 (1.3)	2 (4.1)
Ethnicity, n (%)§				
Hispanic/Latinx	55 (17.7)	102 (35.7)	27 (17.3)	14 (28.6)
Age at vaccination, years				
Mean, ± standard deviation	8.3±1.88	20.9±3.03	8.2±2.06	20.8±3.05
Median (range)	8.0 (5–11)	21.0 (16–25)	9.0 (5–11)	22.0 (16–25)
Obese, n (%)§	30 (9.6)	48 (16.8)	20 (12.8)	15 (30.6)
Baseline SARS-CoV-2 status**				
Positive	24 (7.7)	14 (4.9)	14 (9.0)	1 (2.0)
Negative	287 (92.3)	271 (94.8)	142 (91.0)	48 (98.0)
Missing	0	1 (0.3)	0	0

* Results are for the all-available immunogenicity population of the immunobridging subset (**Table S1**).

† Randomly selected from participants in all countries in the ongoing pivotal trial.

‡ Race and ethnic group were reported by the participants or their parents/guardians.

§ Body mass index ≥95th percentile according to the growth chart (https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm) for 5–11-year-olds, or ≥30 kg/m² for 16–25-year-olds.

** A positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) status required a positive N-binding antibody result at vaccination visit 1, a positive nucleic acid amplification test result at vaccination visit 1, or a medical history of coronavirus disease 2019.

Table S4. Duration from first to last day of local reactions and systemic events

Phase 1				
Local reaction or systemic event	**BNT162b2 10 µg**	**BNT162b2 20 µg**	**BNT162b2 30/30 µg***	**BNT162b2 30/10 µg***
Dose 1, median (range), days [n]				
Redness	3.5 (2, 5) [2]	NE [0]	2.0 (1, 4) [4]	3.5 (3, 4) [2]
Swelling	1.0 (1, 1) [3]	1.0 (1, 1) [1]	1.0 (1, 1) [2]	2.0 (2, 2) [1]
Injection site pain	2.0 (1, 5) [14]	2.0 (1, 6) [15]	3.0 (2, 5) [4]	2.0 (1, 5) [10]
Fever	1.0 (1, 1) [1]	1.0 (1, 1) [1]	NE [0]	1.0 (1, 1) [4]
Fatigue	2.0 (1, 6) [8]	2.0 (1, 6) [11]	1.0 (1, 5) [4]	1.5 (1, 3) [6]
Headache	1.5 (1, 5) [4]	2.0 (1, 5) [5]	2.0 (2, 5) [3]	1.0 (1, 1) [4]
Chills	NE [0]	1.0 (1, 5) [4]	2.5 (1, 4) [2]	1.0 (1, 1) [2]
Vomiting	NE [0]	1.0 (1, 1) [1]	NE [0]	1.0 (1, 1) [1]
Diarrhea	1.0 (1, 1) [1]	1.0 (1, 1) [1]	NE [0]	NE [0]
Muscle pain	1.5 (1, 2) [2]	1.0 (1, 3) [4]	1.0 (1, 4) [4]	NE [0]
Joint pain	1.0 (1, 1) [1]	1.0 (1, 1) [1]	3.0 (3, 3) [1]	1.0 (1, 1) [1]
Dose 2, median (range), days [n]				
Redness	1.0 (1, 2) [6]	1.0 (1, 1) [3]	3.0 (2, 3) [3]	1.0 (1, 1) [2]
Swelling	2.0 (1, 3) [5]	1.0 (1, 5) [3]	1.0 (1, 1) [2]	NE [0]
Injection site pain	2.0 (1, 5) [14]	2.0 (1, 6) [12]	2.5 (2, 4) [4]	2.0 (1, 3) [11]
Fever	1.0 (1, 1) [2]	1.0 (1, 1) [3]	1.0 (1, 1) [4]	NE [0]
Fatigue	1.0 (1, 6) [11]	1.0 (1, 5) [10]	1.0 (1, 9) [4]	1.0 (1, 4) [9]
Headache	1.0 (1, 5) [8]	2.0 (1, 6) [9]	1.0 (1, 4) [3]	1.0 (1, 1) [4]
Chills	1.0 (1, 4) [5]	1.0 (1, 3) [7]	1.0 (1, 2) [3]	1.0 (1, 1) [4]
Vomiting	NE [0]	NE [0]	1.0 (1, 1) [1]	1.0 (1, 1) [1]
Diarrhea	1.0 (1, 1) [1]	NE [0]	1.0 (1, 1) [2]	NE [0]
Muscle pain	NE [0]	1.0 (1, 6) [3]	5.0 (1, 9) [2]	1.0 (1, 1) [1]
Joint pain	NE [0]	NE [0]	9.0 (9, 9) [1]	NE [0]

Phase 2/3		
Dose 1, median (range), days [n†]	**BNT162b2 10 µg**	**Placebo**
Redness	1.0 (1, 8) [176]	1.0 (1, 10) [89]
Swelling	1.0 (1, 9) [125]	1.0 (1, 6) [53]
Injection site pain	2.0 (1, 10) [915]	2.0 (1, 10) [437]
Fever	1.0 (1, 3) [29]	1.0 (1, 3) [19]
Fatigue	1.0 (1, 21) [501]	1.0 (1, 10) [241]
Headache	1.0 (1, 22) [359]	1.0 (1, 19) [160]
Chills	1.0 (1, 9) [77]	1.0 (1, 10) [28]
Vomiting	1.0 (1, 3) [26]	1.0 (1, 5) [18]
Diarrhea	1.0 (1, 6) [85]	1.0 (1, 8) [35]
Muscle pain	1.0 (1, 8) [133]	1.0 (1, 9) [55]
Joint pain	1.0 (1, 7) [60]	1.0 (1, 5) [31]

Dose 2, median (range), days [n†]		
Redness	2.0 (1, 11) [211]	1.0 (1, 8) [105]
Swelling	2.0 (1, 12) [164]	2.0 (1, 8) [83]
Injection site pain	2.0 (1, 12) [849]	2.0 (1, 9) [431]
Fever	1.0 (1, 5) [79]	1.0 (1, 3) [28]
Fatigue	1.0 (1, 12) [527]	1.0 (1, 14) [243]
Headache	1.0 (1, 51) [379]	1.0 (1, 9) [179]
Chills	1.0 (1, 8) [131]	1.0 (1, 8) [48]
Vomiting	1.0 (1, 5) [17]	1.0 (1, 2) [17]
Diarrhea	1.0 (1, 28) [88]	1.0 (1, 9) [26]
Muscle pain	1.0 (1, 9) [155]	1.0 (1, 8) [75]
Joint pain	1.0 (1, 7) [73]	1.0 (1, 18) [33]

n=number of participants reporting the specified reaction or event on any of the 7 days after dose 1 or dose 2; NE=not estimable.

Results are for the safety population **(Table S1)**.

Duration was calculated in days as the difference from the start of the first reported reaction or event to the resolution of the last reported reaction or event, inclusive. For symptoms that were ongoing at the time of the next dose, the stop date was computed as the next dose date. Reactions and events were recorded in the electronic diary and unscheduled clinical assessments from Day 1 through Day 7 after each dose. The resolution date for reactions lasting longer than 7 days was recorded on the participant's case report form.

* Of 16 participants who received 30 μg at dose 1, 4 received 30 μg at dose 2 and 12 received 10 μg at dose 2.

† Includes participants with reactions or events of unknown duration.

Table S5. Severity scale for local reactions and systemic events

	Mild	Moderate	Severe	Grade 4
Local reaction				
Pain	Does not interfere with activity	Interferes with activity	Prevents daily activity	ER visit or hospitalization
Redness	1–4 caliper units (0.5–2.0 cm)	5–14 caliper units (>2.0–7.0 cm)	>14 caliper units (>7.0 cm)	Necrosis or exfoliative dermatitis
Swelling	1–4 caliper units (0.5–2.0 cm)	5–14 caliper units (>2.0–7.0 cm)	>14 caliper units (>7.0 cm)	Necrosis
Systemic event				
Vomiting	1–2 times/24 hours	>2 times/24 hours	Requiring IV hydration	ER visit or hospitalization
Diarrhea	2–3 loose stools/24 hours	4–5 loose stools/24 hours	≥6 loose stools/24 hours	ER visit or hospitalization
Headache	Does not interfere with activity	Some interference with activity	Prevents daily routine activity	ER visit or hospitalization
Fatigue	Does not interfere with activity	Some interference with activity	Prevents daily routine activity	ER visit or hospitalization
Chills	Does not interfere with activity	Some interference with activity	Prevents daily routine activity	ER visit or hospitalization
Muscle pain	Does not interfere with activity	Some interference with activity	Prevents daily routine activity	ER visit or hospitalization
Joint pain	Does not interfere with activity	Some interference with activity	Prevents daily routine activity	ER visit or hospitalization

ER=emergency room; IV=intravenous.

For the fever scale, refer to the legend and scale of **Figure 2B** and **Figure S1B**.

Table S6. Phase 1 participants 5–11 years old reporting at least 1 adverse event

Adverse event	BNT162b2 10 µg (N†=16) n‡ (%)	BNT162b2 20 µg (N†=16) n‡ (%)	BNT162b2 30/30 µg* (N†=4) n‡ (%)	BNT162b2 30/10 µg* (N†=12) n‡ (%)
Any event (from dose 1 to 1 month after dose 2)	7 (43.8)	5 (31.3)	2 (50.0)	3 (25.0)
Related§	4 (25.0)	2 (12.5)	2 (50.0)	3 (25.0)
Severe	0	1 (6.3)	0	0
Life-threatening	0	0	0	0
Any serious adverse event (from dose 1 through data cutoff)	0	0	0	0
Any adverse event leading to discontinuation (from dose 1 through data cutoff)	0	0	0	0
Death (from dose 1 through data cutoff)	0	0	0	0

Results are for the safety population **(Table S1)**.

The data cutoff date was July 16, 2021.

* Of 16 participants who received 30 µg at dose 1, 4 received 30 µg at dose 2 and 12 received 10 µg at dose 2.

† Number of participants in the specified group. This value is the denominator for the percentage calculations.

‡ Number of participants reporting ≥1 occurrence of the specified event category. For 'any event', n=the number of participants reporting ≥1 occurrence of any event.

§ Assessed by the investigator as related to the investigational product.

Table S7. Phase 2/3 participants 5–11 years old reporting at least 1 adverse event

Adverse event	BNT162b2 10 µg (N*=1518) n† (%)	Placebo (N*=750) n† (%)
Any adverse event (from dose 1 to 1 month after dose 2)	166 (10.9)	69 (9.2)
Related‡	46 (3.0)	16 (2.1)
Severe	2 (0.1)	1 (0.1)
Life-threatening	0	0
Any serious adverse event (from dose 1 through data cutoff)	1 (0.1)	1 (0.1)
Related‡	0	0
Severe	1 (0.1)	1 (0.1)
Life-threatening	0	0
Any adverse event leading to discontinuation (from dose 1 through data cutoff)	0	0
Death (from dose 1 through data cutoff)	0	0

Results are for the safety population **(Table S1)**.

The data cutoff date was September 6, 2021.

* Number of participants in the specified group. This value is the denominator for the percentage calculations.

† Number of participants reporting ≥1 occurrence of the specified event category. For 'any event', n=the number of participants reporting ≥1 occurrence of any event.

‡ Assessed by the investigator as related to the investigational product.