2.7.4 SUMMARY OF CLINICAL SAFETY

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS AND TERMS

Abbreviation	Definition
ADR	adverse drug reaction
AE	adverse event
AESI	adverse events of special interest
BLA	Biologics License Application
BP	Blood pressure
CBER	(US Food and Drug Administration) Center for Biologics Evaluation and Research
CDC	Centers for Disease Control and Prevention
CDS	Core data sheet
CI	confidence interval
CIOMS	Council for International Organizations of Medical Sciences
COVID-19	Coronavirus Disease 2019
CRF	case report form
CSR	Clinical study report
DART	Developmental and Reproductive Toxicology
EMA	European Medicines Agency
EUA	Emergency Use Authorization
FDA	(US) Food and Drug Administration
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
IgG	Immunoglobulin Type G
IM	intramuscular(ly)
IRC	Internal Review Committee
IWR	interactive Web based response
MAA	Marketing Authorisation Application
MedDRA	Medical Dictionary for Regulatory Activities
MIS-C	multisystem inflammatory syndrome in children
NAAT	nucleic acid amplification testing
PCR	polymerase chain reaction
PT	Preferred Term
RNA	Ribonucleic acid

Abbreviation	Definition
RR	Respiratory rate
SAE	serious adverse event
SARS-CoV-2	SARS Coronavirus-2; virus causing the disease COVID-19
SCS	Summary of Clinical Safety
SmPC	Summary of Product Characteristics
SOC	System Organ Class
US	United States
TME	targeted medical events
VAED	vaccine-associated enhanced disease
VAERD	vaccine-associated enhanced respiratory disease

2.7.4. SUMMARY OF CLINICAL SAFETY

This Summary of Clinical Safety (SCS) presents the safety and tolerability data for a prophylactic, RNA-based SARS-CoV-2 vaccine, BNT162b2 (COMIRNATY), developed by BioNTech and Pfizer, in healthy children 5 to <12 years of age. BNT162b2 is administered intramuscularly (IM) as a primary series of two doses given 3 weeks apart.

A Marketing Authorization Application (MAA) was submitted to the European Medicines Agency (EMA) via a rolling review procedure that completed on 07 December 2020. Conditional marketing authorization was granted by the EMA on 21 December 2020 for individuals ≥16 years of age and was subsequently expanded on 28 May 2021 to include individuals ≥12 years of age.

A Biologics License Application (BLA) was submitted to the United States (US) Food and Drug Administration (FDA) on 18 May 2021. Licensure was granted by the FDA on 23 August 2021 for individuals ≥16 years of age.

Further details on regulatory approvals and authorizations can be found in Module 2.5 Clinical Overview (CO) Section 2.5.1.3.

This SCS provides Phase 1 dose finding (BNT162b2 10, 20, or 30 µg) and Phase 2/3 selected dose (BNT162b2 10 µg) data on safety and tolerability in children 5 to <12 years of age with at least 2 months of follow-up after receiving Dose 2 of BNT162b2 and through the data cutoff date (06 September 2021) in Study C4591007.

Nonclinical studies in this development program are summarized in the CO (Module 2.5 Section 2.5.1.2.3.1).

2.7.4.1. Exposure to BNT162b2 in Study C4591007

2.7.4.1.1. Overall Safety Evaluation Plan and Narratives of Safety Studies

2.7.4.1.1.1. Safety Objectives, Estimands, Endpoints

Study C4591007 includes Phase 1 and Phase 2/3 objectives and estimands for participants in protocol-defined age groups (5 to <12 years, 2 to <5 years, and 6 months to <2 years) as well as additional endpoints to analyze additional age groups and dose levels.

This SCS presents safety data for the group of participants 5 to <12 years of age, corresponding to safety objectives/endpoints for Phase 1 (data cutoff date: 16 July 2021) and for Phase 2/3 (data cutoff date: 06 September 2021), as shown in Table 1.

Table 1. Safety Objectives, Estimands, and Endpoints for Study C4591007

Objectives	Estimands	Endpoints
PHASE 1		
Primary Safety		
To describe the safety and tolerability profiles of prophylactic BNT162b2 at each dose level in each age group[a]	In participants receiving at least 1 dose of study intervention, the percentage of participants in each age group 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 Dose 2 • SAEs from Dose 1 to 6 months after Dose 2[c]	Participants 16 to <30[b], 12 to <16[b], 5 to <12, and 2 to <5[b] years of age: • 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
Exploratory		
To describe COVID-19 and severe COVID-19 cases with and without serological or virological evidence of past SARS-CoV-2 infection		• Confirmed COVID-19 cases • Confirmed severe COVID-19 cases
To describe MIS-C cases with and without evidence of past SARS-CoV-2 infection		• Confirmed cases as per CDC criteria

Table 1. Safety Objectives, Estimands, and Endpoints for Study C4591007

Objectives	Estimands	Endpoints
PHASE 2/3		
Primary Safety		
To define the safety profile of prophylactic BNT162b2 at the *selected-dose* level in all participants randomized in Phase 2/3 in each age group[a]	In participants receiving at least 1 dose of study intervention from each vaccine group, the percentage of participants in each age group 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 Dose 2 • SAEs from Dose 1 to 6 months after Dose 2[c]	Participants 16 to <30[b], 12 to <16[b], 5 to <12, and 2 to <5[b] years of age: • 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
Exploratory		
To describe COVID-19 and severe COVID-19 cases in participants in the *selected-dose* portion of the study with and without serological or virological evidence of past SARS-CoV-2 infection		• Confirmed COVID-19 cases • Confirmed COVID-19 cases resulting in hospitalization • Confirmed severe COVID-19 cases
To describe MIS-C cases with and without evidence of past SARS-CoV-2 infection in participants in the *selected-dose* portion of the study		• Confirmed cases as per CDC criteria

a. Results included in this SCS **only** for participants 5 to <12 years of age.
b. Results not included in this SCS
c. Results through data cutoff date included in this SCS.
Source: Module 5.3.5.1 C4591007 Protocol Section 3.

2.7.4.1.1.2. Overall Design

Study C4591007 is the ongoing, randomized, placebo-controlled, Phase 1/2/3 pediatric study in healthy children from 6 months to <12 years of age. The study was designed to evaluate BNT162b2 vaccination in an age de-escalation Phase 1 dose finding part and Phase 2/3 selected-dose part, in protocol-defined age groups:

- 5 to <12 years of age
- 2 to <5 years of age
- 6 months to <2 years of age

Initiation of the pediatric study with the oldest pediatric group (5 to <12 years of age) was based on acceptable safety and tolerability demonstrated in adolescents in Study C4591001.

Details of the study conduct and analyses are provided in C4591007 Protocol and Statistical Analysis Plan.

Phase 1

Phase 1 is the dose-finding portion of the study. Dose levels were tested in sentinel cohorts of children by age de-escalation, starting with the lowest dose level in the oldest age group. For each age group, the dose level identified as safe and tolerable and immunogenic in C4591007 Phase 1 was advanced for further evaluation in Phase 2/3.

Phase 1 of Study C4591007 was conducted in the US. Starting with the oldest age group (5 to <12 years of age), sentinel cohorts in that age group received the lowest dose level (N=16 per dose level) followed by either the progression to subsequent a higher dose level cohort or termination of a dose level based upon the safety evaluation by the IRC. The intent was to evaluate doses up to 30 µg in each age cohort if the safety was acceptable for all the lower doses. Terminated dose cohorts were not to be evaluated further in the age cohort that received the dose and in younger age cohorts. Progression to a subsequent younger age cohort occurred if a dose was judged safe in an older cohort, based upon the safety evaluation of the IRC.

Following this schema, the doses tested and selected in each age group during Phase 1 were:

- 5 to <12 years of age: dose levels 10, 20, 30 µg
- 2 to <5 years of age: dose levels 3 and 10 µg
- 6 to <2 years of age: dose level 3 µg

After the initial 4 participants in the 5 to <12 years of age group received the second dose of the highest dose level of BNT162b2 30 µg, the IRC recommended that a second dose 30 µg not be administered to the remaining participants due to reactogenicity after the second dose for these 4 participants. The remaining 12 participants in this group instead received a second dose of BNT162b2 at the 10-µg dose level based on the dose selected for Phase 2/3, and the 30-µg dose level was discontinued (ie, not administered to any further participants in any age group).

The Sponsor/agent study team was not blinded in Phase 1. Participants who enrolled in Phase 1 are followed for cases of COVID-19 but do not contribute to the efficacy assessment. Safety follow-up will continue for at least 2 years and/or end of study.

Based upon review of safety and immunogenicity from the Phase 1 part of the study, the final BNT162b2 dose levels selected were 10 µg for the 5 to <12 years and the 2 to <5 years of age groups, and 3 µg for the 6 months to <2 years of age group.

This SCS reports C4591007 Phase 1 dose finding data for the 5 to <12 years of age group only, in support of authorization of vaccination for this age group. Dose finding data for other age groups will be reported at a later time.

Phase 2/3

Phase 2/3 of Study C4591007 commenced with the selected vaccine dose for each age group, who were randomized 2:1 to receive vaccine or placebo.

Phase 2/3 is being conducted at sites in the US, Finland, Poland, and Spain. Phase 2/3 (which is ongoing) was planned to evaluate BNT162b2 at the selected dose levels for each age group for safety and tolerability, immunogenicity, and efficacy (depending on meeting success criteria for immunobridging and accrual of a sufficient number of COVID-19 cases). An immunobridging analysis was designed to compare SARS-CoV-2 neutralizing antibody responses in pediatric participants within each age group in Study C4591007 to a group of young adult participants 16 to 25 years of age in the C4591001 efficacy study. A supportive vaccine efficacy analysis was planned to be conducted when at least 22 confirmed cases of COVID-19 had accrued in the 5 to <12 years age group among participants without serological or virological evidence (prior 7 days after receipt of Dose 2) of past SARS-CoV-2 infection and if success criteria for immunobridging in this age group had first been met. Additional objectives were designed to explore lower dose levels and other vaccine immunogenicity evaluations subsets of participants.

Note that an additional 2250 participants 5 to <12 years of age are being enrolled and randomized 2:1 (1500 BNT162b2 at 10 µg and 750 placebo) at the selected dose level in the Phase 2/3 part of C4591007, to obtain a larger safety database to support licensure for this age group (but not included in this present submission). Enrollment for this expansion set of participants started in August 2021. Further, an additional 750 participants in this age group are being enrolled to collect samples for troponin I evaluation. Enrollment for this set of participants is anticipated to start in October 2021. Supportive safety data from these additional participants will be reported when available, in a future submission.

This SCS reports interim C4591007 Phase 2/3 dose finding data for the 5 to <12 years of age group only, in support of authorization of vaccination for this age group.

Unblinding Considerations

Sponsor and site personnel responsible for the ongoing conduct of Study C4591007 remain blinded to individual participants' randomization. Safety evaluation for such participants by the study team remains blinded until a decision is made to unblind the entire study.
A separate (from study conduct) unblinded submissions team is responsible for regulatory submissions including this SCS.

A participant in the 5 to <12 years of age group of C4591007 could be unblinded to treatment assignment per protocol, if he or she turned 12 years of age and became eligible to receive a COVID-19 vaccine available under conditional marketing authorization in their country/region. Unblinded recipients originally randomized to placebo will be offered BNT162b2 vaccination and thereafter followed in an open-label manner.

2.7.4.1.1.3. Study Population

The full eligibility criteria for Study C4591007 can be found in Module 5.3.5.1 C4591007 Protocol Section 5.

In Phase 1, the protocol-defined age groups were studied separately: 5 to <12 years of age, 2 to <5 years of age, and 6 months to <2 years of age. The study population includes male and female participants deemed healthy as determined by medical history, physical

examination, and clinical judgment of the investigator to be eligible for inclusion in the study. Exclusions included screened individuals with clinically important prior medical or psychiatric illness or laboratory abnormalities, past diagnosis of MIS-C, serological evidence of prior SARS-CoV-2 infection or current SARS-CoV-2 infection as measured by PCR.

In Phase 2/3, participants were enrolled into each protocol-defined age group to evaluate the dose level of BNT162b2 selected for that age group in the Phase 1 dose finding portion of the study. Eligibility in Phase 2/3 permitted enrollment of participants with medical conditions such as stable Type 1 diabetes or hypothyroidism; stable and controlled HIV, HCV, or HBV infection; and past serological or microbiological evidence of prior (not active) SARS-CoV-2 infection.

2.7.4.1.1.4. Safety Analysis Sets

Populations discussed in this SCS are shown in Table 2.

Table 2. Analysis Populations

Population	Description
Enrolled	All participants who had a signed ICD
Randomized	All participants who were assigned a randomization number in the IWR system
Safety	All participants who received at least 1 dose of the study intervention

2.7.4.1.1.5. Safety Assessments

Safety assessments for participant's 5 to <12 years of age in Study C4591007 were collected at planned timepoints as described in Module 5.3.5.1 C4591007 Protocol Section 1.3. Full details regarding safety assessments for Study C4591007 are found in Module 5.3.5.1 C4591007 Protocol Section 8. Key safety assessments are summarized below.

Safety assessments in Phase 1 were to support dose level selection to proceed to Phase 2/3 evaluation.

Reactogenicity

Phase 1 and Phase 2/3 participants or their parent/legal guardian were to monitor and record reactogenicity for 7 days after each dose. In the 5 to <12 years of age group events included:[1]

- Local reactions: pain, redness, swelling at the injection site
- Systemic events: fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, new or worsened joint pain

Antipyretic/pain medication usage was also to be recorded for 7 days after each dose. Reactogenicity and antipyretic use was to be recorded each evening for 7 days after each dose administration using prompts from an electronic diary (e-diary). This allowed recording only within a fixed time window to provide an accurate representation of the participant's experience. Grading scales used in this study to assess local reactions and systemic events were derived from the FDA CBER guidelines on toxicity grading scales for healthy adult and adolescent volunteers enrolled in preventive vaccine clinical trials.[2]

Adverse Events

For Phase 1 and Phase 2/3, AEs were collected from the Dose 1 to 1 month after Dose 2 and SAEs were collected from Dose 1 to 6 months after Dose 2. AEs were categorized by frequency, maximum severity, seriousness, and relationship to study intervention using SOC and PT according to MedDRA. Deaths are recorded to the end of study. Acute reactions within the first 30 minutes will be assessed and documented in the AE CRF.

Events of Special Interest

Myocarditis and pericarditis are designated in the C4591007 protocol as AESIs. For other events of specific clinical interest that were not designated as AESIs, Pfizer evaluates Targeted Medical Events (TMEs) during clinical safety data review and signal detection. TMEs are a dynamic list of MedDRA AE terms reviewed throughout the study; and are based on known pharmacology, toxicology findings, possible class effects, published literature, and potential signals arising from safety data assessments. TMEs include events of interest due to their association with COVID-19 and vaccines in general; taking into consideration the CDC list of AESIs for COVID-19 that include events potentially indicative of severe COVID-19 or autoimmune and neuroinflammatory disorders.

Other Safety Assessments

A clinical assessment, including medical history and physical examination, was performed on all participants at his/her first visit to establish a baseline. Significant medical history and observations from any physical examinations were documented in the CRF.

Prior SARS-CoV-2 infection was determined by virological testing via NAAT on anterior nares swab and serological testing for IgG to the SARS-CoV-2 N-antigen at baseline, and via NAAT at Dose 2. Participants were surveilled for potential COVID-19 illness from Visit 1 onwards.

Clinical safety laboratory assessments are not being collected in this study.

Phase 1 Stopping Rules

Stopping rules were in place for all Phase 1 participants, based on review of AE data and e-diary reactogenicity data, until the start of Phase 2/3 or 30 days after the administration of the second dose of study intervention in Phase 1, whichever was later. These data were monitored on an ongoing basis by the investigator (or medically qualified designee), Pfizer, and BioNTech personnel in order to promptly identify and flag any event that potentially contributes to a stopping rule.

Stopping Rule Criteria for Each BNT162b2 Dose Level:

1. If any participant vaccinated with the BNT162b2 candidate at any dose level developed an SAE that is assessed by the investigator as possibly related, or for which there was no alternative, plausible, attributable cause.

2. If any participant vaccinated with the BNT162b2 candidate at any dose level developed a Grade 4 local reaction or systemic event after vaccination that was assessed as possibly related by the investigator, or for which there was no alternative, plausible, attributable cause.

3. If any participant vaccinated with the BNT162b2 candidate at any dose level developed a fever >40.0°C (>104.0°F) for at least 1 daily measurement after vaccination that was assessed as possibly related by the investigator, or for which there was no alternative, plausible, attributable cause.

4. If any 2 participants vaccinated with the BNT162b2 candidate at any dose level within the 5 to <12 years of age group reported the same or similar severe (Grade 3) AE after vaccination, assessed as possibly related by the investigator, or for which there was no alternative, plausible, attributable cause.

5. If any participant died or required ICU admission due to SARS-CoV-2 infection; if this stopping rule was met, all available clinical and preclinical safety and immunogenicity data would be reviewed to evaluate for enhanced COVID-19.

2.7.4.1.1.6. Statistical Analysis Methods

Statistical methods are described in Module 5.3.5.1 C4591007 Protocol Section 9.4 and in Module 5.3.5.1 C4591007 Statistical Analysis Plan Section 6.1.1 and summarized below.

The primary safety objective was to be evaluated by descriptive summary statistics for local reactions, systemic events, and AEs/SAEs for each vaccine in the 5 to <12 years of age group. A 3-tier approach was used to summarize AEs in Phase 2/3 portion of the study. Under this approach, AEs were classified into 1 of 3 tiers:

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

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

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

Note that a total of 2250 additional participants, including 1500 participants receiving active vaccine and 750 participants receiving placebo, were added to the safety database in the age group of 5 to <12 years old for the Phase 2/3 part of Study C4591007 as a part of Protocol Amendment 2 (approval date: 06 August 2021), to obtain a larger safety database to support licensure. Further, per subsequent Protocol Amendment 3 (approval date: 10 September 2021), an additional 750 participants in this age group will be enrolled to collect samples for troponin I evaluation. Safety data analyses from these additional participants will be reported when available, in a future submission.

2.7.4.1.1.7. Subgroup Analyses

Phase 2/3 subgroup analyses based on demographics (sex, race, and ethnicity) and SARS-CoV-2 baseline status (positive or negative) were performed on primary safety endpoints as supplemental analyses.

2.7.4.1.1.8. Narratives

Narratives for safety events are located in Module 5.3.5.1 C4591007 Interim CSR (5 to <12 Years) Section 14 Narratives, and were prepared for participants if they had the following events:

- Deaths, vaccine-related SAEs, safety-related withdrawals
- COVID-19 cases for participants with severe and/or multiple episodes
- AEs of interest including those requested by FDA* (anaphylaxis, Bell's palsy, appendicitis, pregnancy exposures and outcomes, myocarditis/pericarditis, MIS-C cases).

* In lieu of individual narratives on lymphadenopathy, which typically are related AEs with little additional information, these cases are presented in tables summarizing incidence, timing relative to Dose 1 or 2, anatomical location, duration, severity, and event resolution.

2.7.4.1.2. Overall Extent of Exposure, Disposition, and Study Population Characteristics

2.7.4.1.2.1. Phase 1

Study results for pediatric participants 5 to <12 years of age in the Phase 1 dose-finding portion of Study C4591007 are presented through the data cutoff date of 16 July 2021.

Details and outputs regarding disposition, exposure, data sets, demographics, and diary compliance for Phase 1 of Study C4591007 are in Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Section 10.

2.7.4.1.2.1.1. Disposition (Phase 1)

A total of 48 (98.0%) participants assigned to the 10-µg, 20-µg, and 30-µg dose level groups (N=16 each) received two doses of BNT162b2 and completed the 1-month post-Dose 2 visit. One (1) additional participant assigned to the 20-µg dose level group did not receive BNT162b2. No participants were withdrawn from Phase 1 of the study.

Due to observed reactogenicity in the initial 4/16 participants of the assigned 30-µg dose level group after receiving both doses, an IRC decision was made for the remaining 12/16 participants in the dose level group to receive the same dose that was to be selected for Phase 2/3 (10-µg) at Dose 2, and the 30-µg dose level was discontinued in the study (see details in Section 2.7.4.2.1.1).

All participants assigned to the 30-µg dose level are included in safety analyses, but safety results are reported separately for those who received different dose levels at Dose 2 (ie, those who received 30/30 µg and those who received 30/10 µg).

2.7.4.1.2.1.2. Exposure (Phase 1)

For Phase 1 pediatric participants 5 to <12 years of age, almost all participants were administered study intervention as assigned. Except for 1 participant assigned to the 20-µg dose level group who did not receive BNT162b2, 48 (98.0%) of participants received Dose 1 and Dose 2. As noted in Section 2.7.4.1.2.1.1, due to observed reactogenicity in the initial 4/16 participants who received 30 µg for both doses as assigned, 12/16 participants who received a 30 µg dose at Dose 1 received the 10-µg dose level at Dose 2 (based on 10-µg dose level being selected for Phase 2/3 progression in this age group).

The majority of participants received Dose 2 between 19 to 23 days after Dose 1 in the 10 µg and 20 µg dose level groups (100.0% and 82.4%, respectively). In the 30 µg dose level group, the 4 (25.0%) participants who received 30/30 µg dosing received Dose 2 between 19 to 23 days after Dose 1; the 12 (75.0%) participants who received a 30/10 µg dosing received Dose 2 at >23 days after Dose 1.

2.7.4.1.2.1.3. Safety Datasets Analyzed (Phase 1)

Of the 49 participants 5 to <12 years of age assigned to receive BNT162b2 in Phase 1, 48 were included in the safety population. One (1) participant assigned to the 20-µg dose level group did not receive BNT162b2 and was excluded from the safety population.

As described in Section 2.7.4.1.2.1.1, due to observed reactogenicity in the initial 4/16 participants who received a 30 µg for both doses (30/30 µg), 12/16 participants who received a 30 µg dose at Dose 1 received the 10 µg dose level at Dose 2 (30/10 µg).

2.7.4.1.2.1.4. Demographic and Other Characteristics of Study Population (Phase 1)

Overall, most Phase 1 participants 5 to <12 years of age in the safety population were White (79.2%), with 6.3% Black or African American participants and 10.4% Asian participants, and other racial groups were <5%. There were 8.3% Hispanic/Latino participants. The median age was 8.0 years and 50.0% of participants were male.

Participants in the Phase 1 safety population had a medical history profile consistent with that of individuals in the general population in the same age group. Psychiatric disorders (8 [16.7%]), immune system disorders (6 [12.5%]), and infections and infestations (4 [8.3%]) were the 3 most frequently reported SOCs. The psychiatric disorders included attention deficit hyperactive disorder (5), anxiety (2), and insomnia (1). There were no participants with a history of any cardiac disorder.

No Phase 1 participants 5 to <12 years of age received concomitant vaccines after Dose 1.

2.7.4.1.2.1.5. E-Diary Compliance (Phase 1)

For Phase 1 pediatric participants 5 to <12 years of age, transmission of e-diary data for each day during the 7 days after Dose 1 of BNT162b2 ranged from 85.4% to 100%. After Dose 2 of BNT162b2, transmission of e-diary data ranged from 81.3% to 97.9% for Day 1 through Day 7.

2.7.4.1.2.2. Phase 2/3

Study results for pediatric participants 5 to <12 years of age in the Phase 2/3 portion of Study C4591007 are presented through the data cutoff date of 06 September 2021.

Details and outputs regarding disposition, exposure, data sets, demographics, and diary compliance for Phase 1 of Study C4591007 are in Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Section 10.

2.7.4.1.2.2.1. Disposition (Phase 2/3)

The disposition of Phase 2/3 pediatric participants 5 to <12 years of age is summarized in Table 7 in Appendix B. In total, 1528 participants were randomized to receive BNT162b2 10 µg and 757 participants were randomized to placebo, reflecting the 2:1 randomization ratio. Most participants randomized to either group (≥98.7%) received Dose 1 and Dose 2.

Two (2) participants (0.1%) in the BNT162b2 group and 2 participants (0.3%) in the placebo group discontinued from the vaccination period and are continuing in the study for safety follow-up. Most participants across both groups completed the visit at 1 month after Dose 2 (≥98.5%). Among participants who discontinued from the vaccination period but continued in the study up to the 1-month post-Dose 2 visit, none of the discontinuations were reported as due to an AE.

Two (2) participants (0.1%) in the BNT162b2 group and 2 participants (0.3%) in the placebo group withdrew from the study before the 1-month post-Dose 2 visit. None of these withdrawals were reported as due to an AE.

During the course of the study, 3 participants in the 5 to <12 years of age group turned 12 years of age and became eligible to receive a COVID-19 vaccine outside of the study (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Listing 16.2.1.3). These participants were unblinded to their treatment assignment per protocol to seek vaccination with a COVID-19 vaccine (eg, BNT162b2 30 µg) that is authorized for individuals ≥12 years of age under conditional approval. Of these, 2 participants received both doses of BNT162b2 10 µg prior to being unblinded, and 1 participant received both doses of placebo before being unblinded and withdrew to receive a COVID-19 vaccine outside of the study. Data from these participants are included in endpoint analyses up to the point at which they were unblinded.

2.7.4.1.2.2.2. Exposure (Phase 2/3)

Among all randomized Phase 2/3 pediatric participants 5 to <12 years of age, almost all participants (>99%) were administered study intervention as randomized (Table 8 in Appendix B). Altogether, 99.3% and 99.2% received Dose 1 of BNT162b2 and placebo, respectively, and 99.1% and 98.7% received Dose 2 of BNT162b2 and placebo, respectively. One (1) participant, who was randomized to the placebo group, received vaccination not as randomized (ie, received 2 doses of BNT162b2 10 µg; Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Listing 16.2.5.1).

The majority of participants received Dose 2 in the protocol-defined window of 19 to 23 days after Dose 1 in the BNT162b2 (94.4%) and placebo (94.5%) groups (Table 9 in Appendix B). Second doses administered outside of the protocol specified window included 0.7% and 0.4% of the BNT162b2 and placebo groups, respectively, who received Dose 2 at <19 days after Dose 1 and 4.0% and 3.8% of the BNT162b2 and placebo groups, respectively, who received Dose 2 at >23 days after Dose 1.

Longer time intervals reported for Dose 2 administration after Dose 1 were balanced for the BNT162b2 and placebo groups (Table 9 in Appendix B). The total range for timing of Dose 2 administration after Dose 1 of BNT162b2 was 14 days to >55 days. For placebo, the total range for timing of Dose 2 administration after Dose 1 was 14 to 55 days.

2.7.4.1.2.2.3. Safety Datasets Analyzed (Phase 2/3)

The safety population for Phase 2/3 pediatric participants 5 to <12 years of age reflected the 2:1 randomization in the BNT162b2 (N=1518) and placebo (N=750) groups (Table 10 in Appendix B). The only exclusions from the safety population were due to 17 participants (0.7%) not receiving study vaccine. No participants 5 to <12 years of age included in the safety population were HIV+.

The duration of follow-up for Phase 2/3 pediatric participants 5 to <12 years of age was at least 2 months after Dose 2 for most participants (Table 11 in Appendix B). Almost all (95.1%) of the participants had 2 to <3 months of follow-up after Dose 2.

2.7.4.1.2.2.4. Demographic and Other Characteristics of Study Population (Phase 2/3)

Demographic characteristics for Phase 2/3 pediatric participants 5 to <12 years of age were similar in BNT162b2 and placebo groups in the safety population Table 12 in Appendix B). Overall, most participants were White (78.9%), with 6.5% Black or African American participants and 6.0% Asian participants, 7.0% multiracial participants, and other racial groups <1%. There were 21.1% Hispanic/Latino participants. The median age was 8.0 years and 52.1% of participants were male.

Obese children (based on age- and sex-specific body mass index) made up 11.5% (BNT162b2 group to 12.3% (placebo group of this age group in the safety population (Table 12 in Appendix B). Comorbidities present at baseline that increase the risk of severe COVID-19 disease[3] (which include obesity) were present in similar proportions of participants in the BNT162b2 group (20.6%) and placebo group (20.3%). The most common of these comorbidities reported in participants at study baseline were (Table 13 in Appendix B):

- asthma (7.8% in BNT162b2 and 8.3% in placebo)
- neurologic disorders (1.3% in BNT162b2 and 0.4% in placebo)
- congenital heart disease (1.0% in BNT162b2 and 0.7% in placebo).

One (1) participant, who was in the BNT162b2 group, had an immunocompromised condition reported at baseline (acute lymphocytic leukemia) (Table 13 in Appendix B).

In the safety population, similar proportions of participants in the BNT162b2 group (8.8%) and placebo group (8.7%) had baseline SARS-CoV-2 positive status (Table 12).

The safety population included children with a medical history profile consistent with the general population (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.14). The most frequently reported SOCs in either group were:

- *immune system disorders* (22.8% in BNT162b2 and 22.7% in placebo) mostly consisting of a variety of non-drug allergies, also including drug hypersensitivity (2.8% in BNT162b2 and 3.2% in placebo) and anaphylactic reaction (0.2% in BNT162b2 and 0.1% in placebo)

- *respiratory, thoracic, and mediastinal disorders* (11.7% in BNT162b2 and 13.2% in placebo) mostly consisting of asthma and respiratory illnesses commonly seen in this age group

- *psychiatric disorders* (10.3% in BNT162b2 and 10.1% in placebo) including attention deficit hyperactivity disorder (6.7% in BNT162b2 and 6.5% in placebo) and a variety of behavioral disorders commonly seen in this age group

- *infections and infestations* (6.9% in BNT162b2 and 9.5% in placebo) including a variety of ear, nose, and throat infections commonly seen in this age group

- *nervous system disorders* (3.6% in BNT162b2 and 2.8% in placebo) including various types of epilepsy, headaches, and sensory disorders commonly seen in this age group

- *cardiac disorders* in 9 participants (0.6%), all in the BNT162b2 group, that included arrhythmias, congestive cardiomyopathy, and Wolff-Parkinson-White syndrome. Additionally, congenital cardiac conditions were reported in both the BNT162b2 and placebo groups including atrial septal defect (0.3% in BNT162b2 and 0.1% in placebo), ventricular septal defect (0.2% in BNT162b2 and 0.3% in placebo), bicuspid aortic valve (0.2% in BNT162b2 and 0,1% in placebo), and coarctation of the aorta (0.1% in BNT162b2 and none in placebo). Cardiac murmurs were reported for 11 participants (0.7%) in the BNT162b2 group and 4 participants (0.5%) in the placebo group.

A small percentage of Phase 2/3 pediatric participants 5 to <12 years of age in either group (≤0.8%) received any concomitant vaccine after Dose 1, and most concomitant vaccines received were routine pediatric immunizations (ie, diphtheria, pertussis, tetanus vaccine; human papilloma virus vaccine; and meningococcal vaccine) (Table 14 in Appendix B).

2.7.4.1.2.2.5. E-Diary Compliance (Phase 2/3)

For Phase 2/3 pediatric participants 5 to <12 years of age, transmission of e-diary data for each day during the 7 days after Dose 1 of BNT162b2 ranged from 89.7% to 95.5% (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim Table 14.20). After Dose 2 of BNT162b2, transmission of e-diary data ranged from 80.6% to 91.7% for Day 1 through Day 7.

2.7.4.2. Safety Results for BNT162b2 in Children 5 to <12 Years of Age

Safety methods are described in Section 2.7.4.1.1 with more details provided in Module 5.3.5.1 C4591007 Protocol Section 8.2.

This SCS includes results for participants 5 to <12 years of age for the Phase 1 dose-finding portion and Phase 2/3 portion as follows:

Phase 1 safety and tolerability up to 1 month after Dose 2 and to the Phase 1 data cutoff date (16 July 2021) which represents follow-up of approximately 3 months after Dose 2;
Phase 2/3 safety and tolerability up to the data cutoff date (06 September 2021) which represents follow-up of 2 months after Dose 2.

2.7.4.2.1. Phase 1

2.7.4.2.1.1. Reactogenicity (Phase 1)

Reactogenicity (local reactions and systemic events) was assessed via e-diary in participants for 7 days after each dose. Details and outputs regarding reactogenicity for Phase 1 of Study C4591007 are in Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Section 12.1.

2.7.4.2.1.1.1. Local Reactions (Phase 1)

Frequency and Severity of Local Reactions

Overall, reactogenicity in the 5 to <12 years of age group tended to increase in a dose level- and dose number-dependent manner with regard to incidence and/or severity of local reactions at 10, 20, and 30 µg dose levels (Figure 3 in Appendix A). Local reactions were mostly mild to moderate and short-lived.

For 10 and 20 µg groups, pain at the injection site was the most commonly reported local reaction within 7 days after any dose (range: 87.5% to 93.8%) with the highest frequency in the 20 µg dose level after Dose 1. Redness and swelling were reported in the 10 and 20 µg dose level groups without a clear dose level or dose number effect for incidence or severity.

In the 4/16 participants who received both doses in the 30-µg dose level group as assigned, pain at the injection site was reported in all 4 participants after Doses 1 and 2. Redness was reported in all 4 participants after Dose 1 and 3/4 participants after Dose 2 with 1 participant reporting severe redness. Swelling was reported in 2/4 participants after each dose and was mild to moderate. The high frequency of local reactions for these first 4 sentinel participants at Dose 2 contributed to the IRC decision to discontinue the 30-µg dose level for Dose 2 in the remaining of the 30-µg group.

The remaining 12/16 participants who received 10 µg for Dose 2 (the 30/10-µg dose regimen) had a local reaction profile similar to groups that received 10 or 20 µg as assigned.

All local reactions were mild or moderate in severity, except for 1 severe event of redness within 7 days after Dose 2 in the 30/30 µg dose regimen.

Onset and Duration

Median onset day for most local reactions was within 1 to 2 days after Dose 1 or Dose 2, and the majority of events resolved within 1 or 2 days of onset.

2.7.4.2.1.1.2. Systemic Events (Phase 1)

Frequency and Severity of Systemic Events

Overall, reactogenicity generally increased in an increasing dose level- and dose number-dependent manner with regard to incidence and/or severity of systemic events at 10, 20, and 30 µg dose levels (Figure 4 in Appendix A). Systemic events were mostly mild to moderate and short-lived.

For 10 and 20 µg groups, fatigue was the most commonly reported systemic event within 7 days after any dose (87.5% and 81.3%, respectively) which did not show a clear dose number effect for incidence or severity. Headache, muscle pain, and chills were reported in the 10 and 20 µg dose level groups with increasing incidence and/or severity associated with dose number and dose level. Vomiting, diarrhea, and joint pain were uncommon or absent after any dose in these dose level groups.

In the 4 participants who received both doses in the 30-µg group as assigned 4/4 developed fevers up to 38.9 °C after the second dose of vaccine. These 4 participants also reported, mild to moderate fatigue and muscle pain after Dose 1; after Dose 2 fatigue was reported in all 4 participants while muscle pain became moderate in severity in 2/4 participants. Headache was mild to moderate in 3/4 participants after Dose 1 and Dose 2. Diarrhea and vomiting were absent after Dose 1 but were reported in 1 to 2 participants after Dose 2. This systemic event profile, particularly occurrence of fevers, in these first 4 sentinel participants contributed to the IRC decision to discontinue the 30-µg dose level.

The remaining 12/16 participants assigned to the 30 µg group who received the 30/10-µg dose regimen had a systemic event profile similar to groups that received 10 or 20 µg as assigned, with the exception of fever which was reported with greater incidence and severity after Dose 1 of 30 µg (33.3%, up to 38.9 °C) compared to the 10 or 20 µg dose level groups (6.3% each, up to 38.4 °C). The reverse was observed after Dose 2, with no fevers reported in the 30/10-µg group after receipt of 10 µg compared with the 10-µg as assigned dose level (12.5%; n=1, up to 38.9 °C and n=1, >38.9 to 40.0 °C) and the 20-µg as assigned dose level (18.8%; n=2, up to 38.9 °C and n=1, >38.9 to 40.0 °C).

Antipyretic or pain medication use was dose number dependent, reported by 31.3% to 37.5% participants after Dose 1 and 43.8% to 62.5% after Dose 2 in 10 and 20 µg groups. The 4/16 participants who received both doses in the 30-µg group as assigned all reported medication use after both doses; the remaining 12/16 participants who received the 30/10-µg dose regimen reported medication use in 75.0% after Dose 1 (30 µg) and 33.3% after Dose 2 (10 µg).

All systemic events were mild or moderate in severity within 7 days after Dose 1 and Dose 2, with the exception of fevers >38.9 °C to 40.0 °C reported in 1 participant each in the 10 and

20 µg groups, occurring after Dose 2. The participant in the 10-µg group had a high temperature of 39.0 °C on Day 2 that fell to <38.0 °C and resolved by Day 3. The participant in the 20-µg group had a high temperature of 39.7 °C on Day 2 that fell to <38.0 °C and resolved by Day 3. No Grade 4 events were reported at any levels.

Onset and Duration

Median onset day for most systemic events was 1 to 2 days after Dose 1 or Dose 2, and the majority of events resolved within 1 day of onset.

2.7.4.2.1.2. Summary of Adverse Events (Phase 1)

This section summarizes AEs reported up to 1 month after Dose 2 for BNT162b2 (all dose levels) for participants 5 to <12 years of age. Supplemental AE data are included up to the data cutoff date (16 July 2021), which represents up to approximately 3 months of follow-up after Dose 2.

From Dose 1 to 1 month after Dose 2, AEs were reported by 7 participants (43.8%) who received BNT162b2 at 10 µg and 5 participants (31.3%) who received 20 µg. Of these, the AEs were considered related to study intervention for 4 (25.0%) and 2 (12.5%) participants in the 10 µg and 20 µg dose groups, respectively.

In 4/16 participants who received both doses in the 30-µg group as assigned, AEs were reported by 2 participants with both considered by the investigator as related to study intervention (lymphadenopathy and arthralgia, n=1 each; these cases are described in Section 2.7.4.2.1.4.4). In the remaining 12/16 participants who received the 30/10-µg dose regimen, 3 participants reported 4 AEs (injection site pain, n=2; injection site erythema and vomiting, n=1). Of these, the 3 AEs localized to the injection site were considered related to study intervention.

No SAEs, deaths, or AEs leading to withdrawal were reported in Phase 1 participants 5 to <12 years of age as of the data cutoff date.

No change in AE profile was reported in any dose level group up to the data cutoff date.

2.7.4.2.1.3. Analysis of Adverse Events (Phase 1)

Details and outputs regarding analysis of AEs for Phase 1 of Study C4591007 are in Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Section 12.1.3.

All AEs through the data cutoff date were mild to moderate, with the exception of 1 severe AE (Grade 3 pyrexia) reported in the 20-µg group on Day 1 post-Dose 2 (also recorded as a systemic event; see Section 2.7.4.2.1.1.2). This participant had a high temperature of 39.7 °C on Day 2 that fell to <38 °C and resolved by Day 3. The investigator considered the event related to study intervention.

Immediate AEs (reported within 30 minutes post-dose) after Dose 1 included injection site discomfort and presyncope in 1 participant each in the 10-µg group and injection site pain in

2 participants in the 30/10-µg dose regimen group. After Dose 2, 1 participant in the 10-µg group reported immediate injection site pain.

2.7.4.2.1.4. Deaths, Serious Adverse Events, Safety-Related Participant Withdrawals, and Other Significant Adverse Events (Phase 1)

Details and outputs regarding deaths, SAEs, safety-related participant withdrawals, and other significant AEs for Phase 1 of Study C4591007 are in Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Section 12.1.

2.7.4.2.1.4.1. Deaths (Phase 1)

No deaths were reported in the 5 to <12 years of age group evaluated in safety analyses up to the data cutoff date.

2.7.4.2.1.4.2. Serious Adverse Events (Phase 1)

No SAEs were reported in the 5 to <12 years of age group evaluated in safety analyses up to the data cutoff date.

2.7.4.2.1.4.3. Safety-Related Participant Withdrawals (Phase 1)

No AEs leading to withdrawal were reported in the 5 to <12 years of age group evaluated in safety analyses up to the data cutoff date.

2.7.4.2.1.4.4. Other Significant Adverse Events (Phase 1)

Adverse Events of Clinical Interest

No Phase 1 participants 5 to <12 years of age had any cases reported of anaphylaxis, appendicitis, Bell's palsy, myocarditis/pericarditis, or MIS-C.

One (1) participant who received two doses of BNT162b2 30 µg as assigned had an AE of Grade 2 arthralgia (right hip pain) that was judged by the investigator as related to study intervention. This participant was a [PPD] years of age with no relevant medical history or concomitant vaccinations. The event was reported with an onset of 7 days after Dose 1, and was reported as involving no limitation in movement of the extremity, no accompanying fever, no injection site abnormality, and no other symptoms; the event resolved the same day after administration of ibuprofen.

Lymphadenopathy

Two (2) participants 5 to <12 years of age had cases of lymphadenopathy up to the data cutoff date; refer to the narratives in Section 2.7.4.2.1.6 for further details.

- 1 [PPD] years of age in the 20-µg group had Grade 1 bilateral cervical and inguinal lymphadenopathy with onset at 21 days post-Dose 2 and reported as ongoing at the time of the data cutoff. This event was considered by the investigator as not related to study intervention.

- 1 [redacted] PPD [redacted] years of age in the 30-µg group as assigned (ie, received both doses of 30 µg), had Grade 1 left axillary lymphadenopathy with onset at 3 days post-Dose 2 and reported as resolved 17 days after onset. This event was considered by the investigator to be related to study intervention.

2.7.4.2.1.5. Physical Examination Findings (Phase 1)

There were no participants 5 to <12 years of age with abnormal findings from physical examinations performed after Dose 1.

2.7.4.2.1.6. Narratives (Phase 1)

Narratives for the participants who reported other significant adverse events, including AEs of specific clinical interest, as of the data cutoff date are provided in Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Section 14 Narratives.

2.7.4.2.1.7. Safety Conclusions (Phase 1)

High frequencies of reactogenicity to the 20 and 30 µg dose levels in participants 5 to <12 years of age contributed to the decision to select a lower dose of 10 µg as the final dose level of BNT162b2 to proceed to Phase 2/3 for this age group. The dose level selection decision for this age group was confirmed on the basis of Phase 1 safety and immunogenicity results. BNT162b2 at 10 µg was well tolerated in participants 5 to <12 years of age based on available Phase 1 safety results representing follow-up to approximately 3 months after Dose 2.

2.7.4.2.2. Phase 2/3

Phase 2/3 safety results are summarized below for participants 5 to <12 years of age randomized 2:1 to receive the selected dose of BNT162b2 (10 µg) or placebo.

2.7.4.2.2.1. Reactogenicity (Phase 2/3)

Reactogenicity (local reactions and systemic events) was assessed via e-diary in participants for 7 days after each dose. Details and outputs regarding local reactions for Phase 2/3 of Study C4591007 are in Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Section 12.2.

2.7.4.2.2.1.1. Local Reactions (Phase 2/3)

Frequency and Severity of Local Reactions

In the BNT162b2 group, pain at the injection site was most frequently reported in pediatric participants 5 to <12 years of age, and frequency was similar after Dose 1 and after Dose 2 of BNT162b2 (74.1% vs 71.0%) (Figure 1; Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.43). In the placebo group, pain at the injection site after Doses 1 and 2 was less frequently reported compared to the BNT162b2 group and was similar after each dose (31.3% vs 29.5%).

In the BNT162b2 group, frequencies of redness and swelling were similar after Doses 1 and 2. Frequencies of redness showed a modest increase from after Dose 1 compared to after Dose 2 of BNT162b2 (14.7% vs 18.5%). Frequencies of swelling also showed a modest increase after Dose 1 compared with Dose 2 of BNT162b2 (10.5% vs 15.3%). In the placebo

group, redness was less frequently reported compared to the BNT162b2 group and was similar after each dose (5.7% vs 5.4%), and swelling was infrequent (2.7%) after both Dose 1 and Dose 2.

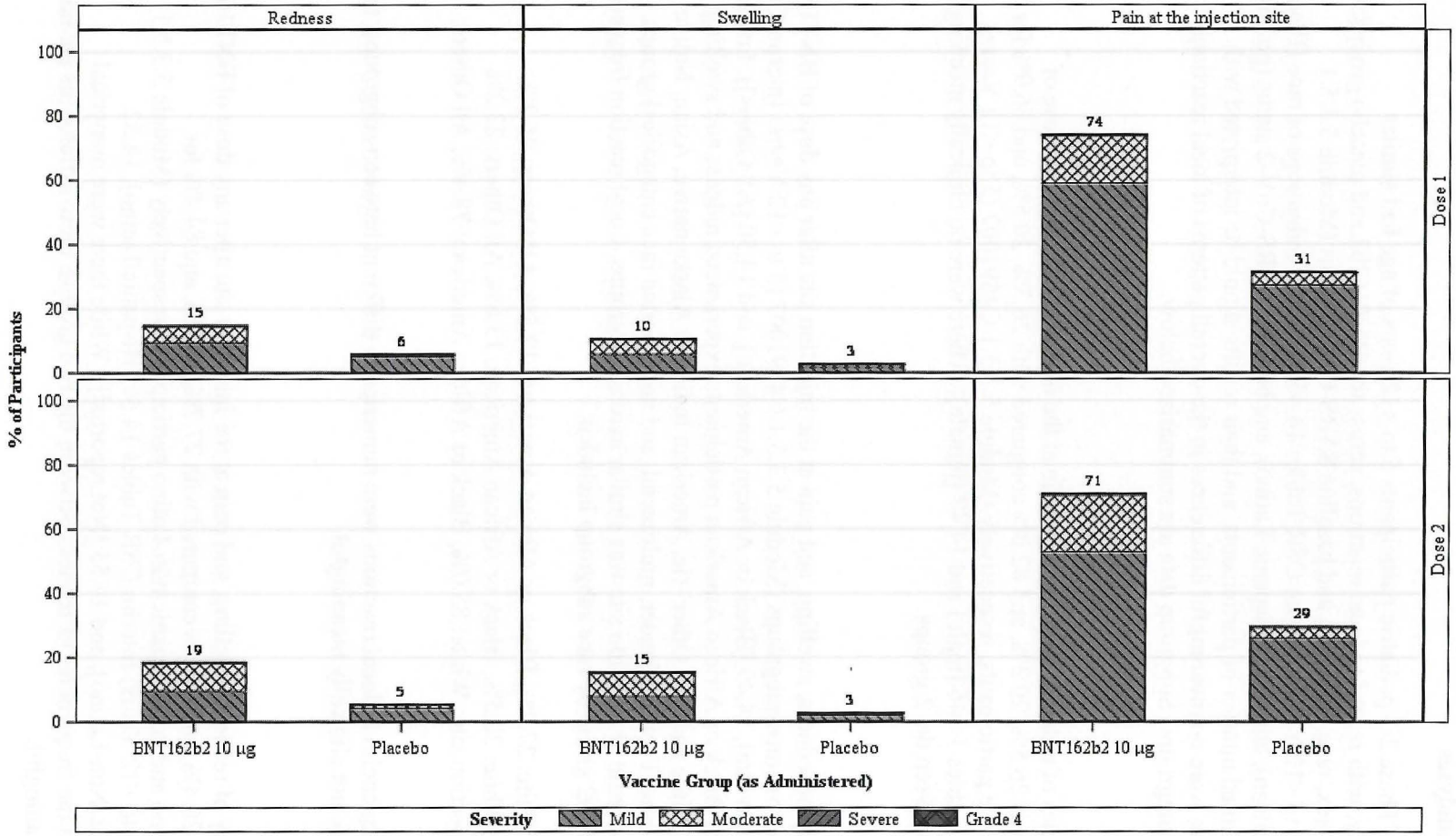
After the first and second dose, most local reactions were mild or moderate in severity. Severe local reactions were reported infrequently (≤0.3%) across the BNT162b2 and placebo groups after either dose. No Grade 4 local reactions were reported in either group (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Appendix 16.2.7.2.3).

Onset and Duration

Across groups, median onset for all local reactions after receiving BNT162b2 was 1 to 2 days after Dose 1 or Dose 2 (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.44), and all events resolved with a median duration of 1 to 2 days (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.45).

Overall, the pattern of local reactions reported in children 5 to <12 years of age after each dose was generally similar to that observed in prior analyses of Phase 2/3 participants ≥12 years of age in Study C4591001 with regard to pain at the injection site, but children had slightly higher frequencies of swelling and redness at the injection site (still within tolerable limits) (as reported in C4591001 Final Analysis Interim CSR, dated 03 December 2020; C4591001 6-Month Update Interim CSR, dated 29 April 2021 and C4591001 Adolescent Interim CSR, dated 14 April 2021).

Figure 1. Participants Reporting Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Phase 2/3 - 5 to <12 Years of Age - Safety Population



Note: The number above each bar denotes the percentage of participants reporting the reaction with any severity.
PFIZER CONFIDENTIAL SDTM Creation: 13SEP2021 (17:18) Source Data: adfacevd
Table Generation: 15SEP2021 (23:02) (Cutoff Date: 06SEP2021, Snapshot Date: 13SEP2021) Output File: /nda2_ubped/C4591007_P23_EUA/adce_f001_lr_p2_12

Subgroup Analyses

Subgroups of Phase 2/3 pediatric participants 5 to <12 years of age had similar reactogenicity, with regard to local reactions, across the BNT162b2 and placebo groups when evaluated by sex, race, ethnicity, and baseline SARS-CoV-2 status (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.46 to 14.55). Subgroups of race (Black or African American), ethnicity (Hispanic/Latino), and baseline SARS-CoV-2 status (positive) included a limited number of participants, and their results should be interpreted with caution. There were no meaningful differences in the overall patterns of local reactions across these subgroups. Subgroup data are summarized below.

Sex

The frequencies of redness, swelling, and pain at the injection site after any dose of BNT162b2 was 26.5%, 20.3%, and 82.0% compared with 26.3%, 20.5%, and 86.9% for male and female participants, respectively (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.46 [male] and 14.47 [female]). There were no clinically meaningful differences between the 2 groups.

Race

The frequency of redness, swelling, and pain at the injection site after any dose of BNT162b2 was similar across race subgroups (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.48 [White], 14.49 [Black or African American], and 14.50 [All Others]). Lower proportions of Black or African American participants experienced redness and swelling compared to White and 'All Other' (ie, American Indian or Alaska native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories) groups. Frequencies of pain at injection site was similar across the groups. Local reaction frequencies in the BNT162b2 group by race subgroup included:

- redness: White: 27.7%, Black or African American: 12.5%, All Others: 25.3%
- swelling: White: 20.5%, Black or African American: 13.6%, All Others: 22.2%
- pain at injection site: White: 85.0%, Black or African American: 78.4%, All Others: 82.7%

While the frequencies of local reactions were numerically different between subgroups, these differences are not clinically meaningful.

Ethnicity

The frequency of redness, swelling, and pain at the injection site after any dose of BNT162b2 were 21.7%, 20.4%, and 84.0% compared with 27.7%, 20.4%, and 84.4% for Hispanic/Latino and non-Hispanic/non-Latino participants, respectively (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.51 [Hispanic/Latino], 14.52 [Non-Hispanic/Non-Latino], and 14.53 [Not reported]). While there were numerical differences in the frequencies of redness between the two groups, these differences are not clinically meaningful.

SARS-CoV-2 Baseline Status

There were 133 BNT162b2 and 65 placebo participants with baseline positive SARS-CoV-2 status, and 1378 BNT162b2 and 684 placebo participants with baseline negative SARS-CoV-2 status) (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.54 [Positive] and 14.55 [Negative]). The frequencies of redness, swelling, and pain at the injection site after any dose of BNT162b2 was 20.3%, 12.8%, and 82.7% compared with 27.0%, 21.1%, and 84.5% for those positive and negative at baseline, respectively. The frequencies between individuals positive or negative at baseline were similar although numerically lower in those positive at baseline. Note that the baseline SARS-CoV-2 positive subgroup included far fewer participants than the negative subgroup, so their results should be interpreted with caution.

2.7.4.2.2.1.2. Systemic Events (Phase 2/3)

Frequency and Severity of Systemic Events

In the population of Phase 2/3 pediatric participants 5 to <12 years of age, systemic events showed increased frequencies and severity for Dose 2 compared to Dose 1 for most events, with the exceptions of vomiting and diarrhea which were reported infrequently and at similar incidences after each dose and across both groups (Figure 2). Systemic events in the BNT162b2 group, in decreasing order of frequency after Dose 1 versus after Dose 2, were (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.56):

- fatigue: 33.6% vs 39.4%
- headache: 22.4% vs 28.0%
- muscle pain: 9.1% vs 11.7%
- chills: 4.6% vs 9.8%
- joint pain: 3.3% vs 5.2%
- fever: 2.5% vs 6.5%
- diarrhea: 5.9% vs 5.3%
- vomiting: 2.2% vs 1.9%

Most systemic events were reported less frequently in the placebo group compared to the BNT162b2 group.

In the BNT162b2 group the use of antipyretic/pain medication was modestly increased from after Dose 1 compared to after Dose 2 (14.4% and 19.7%). Use of antipyretic/pain medication was less frequent in the placebo group than in the BNT162b2 group and was similar after both Dose 1 and Dose 2 (8.3% and 8.1%).

After the first and second dose, most systemic events were mild or moderate in severity. Severe systemic events were infrequent, reported at low incidences (≤0.7%) across BNT162b2 and placebo groups after either dose. In the BNT162b2 group, highest frequencies of severe systemic events reported after Dose 1 and Dose 2 were fatigue (0.3% and 0.7%) and fever (0.2% and 0.5%).

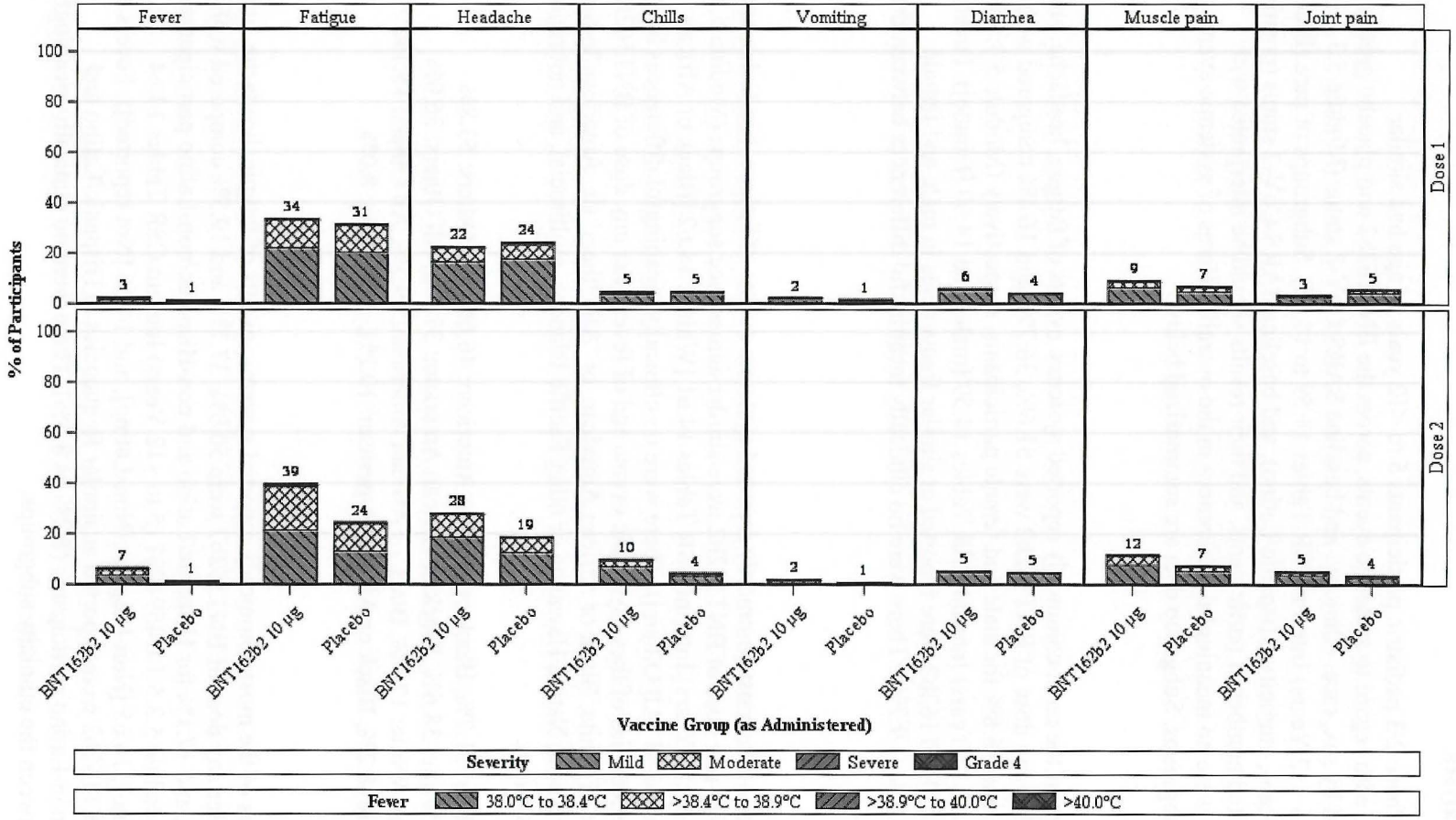
One (1) participant, who was in the BNT162b2 group, had a fever >40 °C (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Listings 16.2.7.3 and 16.2.7.4). This participant reported a fever of 40.0°C at 2 days after Dose 2 which returned to normal body temperature (36.7°C) the next day. This participant had no concurrent AEs (including infections, or injuries, or other illnesses) reported at this time or during the study.

Onset and Duration

Across groups, median onset or all systemic events after receiving BNT162b2 was 1 to 4 days after Dose 1 or Dose 2 (most had a median of 2 days post-dose) (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.57), and all events resolved with a median duration of 1 day (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.58).

Overall, the pattern of systemic events reported in children 5 to <12 years of age after each dose was generally comparable to, or less than, that observed in prior analyses of Phase 2/3 participants ≥12 years of age in Study C4591001 (as reported in: C4591001 Final Analysis Interim CSR, dated 03 December 2020; C4591001 6-Month Update Interim CSR, dated 29 April 2021; C4591001 Adolescent Interim CSR, dated 14 April 2021).

Figure 2. Participants Reporting Systemic Events, by Maximum Severity, Within 7 Days After Each Dose - Phase 2/3 - 5 to <12 Years of Age - Safety Population



Note: Severity was not collected for use of antipyretic or pain medication.
Note: The number above each bar denotes the percentage of participants reporting the event with any severity.
PFIZER CONFIDENTIAL SDTM Creation: 13SEP2021 (17:18) Source Data: adfacevd
Table Generation: 15SEP2021 (23:02) (Cutoff Date: 06SEP2021, Snapshot Date: 13SEP2021) Output File: ./nda2_ubped/C4591007_P23_EUA/adce_f001_se_p2_12

Subgroup Analyses

Subgroups of Phase 2/3 pediatric participants 5 to <12 years of age had similar reactogenicity, with regard to systemic events, across the BNT162b2 and placebo groups when evaluated by sex, race, ethnicity, and baseline SARS-CoV-2 status (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.59 to 14.68). Subgroups of race (Black or African American), ethnicity (Hispanic/Latino), and baseline SARS-CoV-2 status (positive) included a limited number of participants, and their results should be interpreted with caution. There were no meaningful differences in the overall patterns of systemic events across these subgroups. Subgroup data are summarized below.

Sex

The frequencies of the most commonly reported systemic events of fatigue, headache, and muscle pain after any dose of BNT162b2 were 51.6%, 36.7%, and 16.4% compared with 51.9%, 39.8%, and 18.8% for male and female participants, respectively (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.59 [male] and 14.60 [female]). Fevers after any dose of BNT162b2 were reported at similar frequencies in male and female participants (7.0% vs 9.7%). There were no clinically meaningful differences between the sex subgroups.

Race

The frequencies of the most commonly reported systemic events of fatigue, headache, and muscle pain after any dose of BNT162b2 were similar across race subgroups (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.61 [White], 14.62 [Black or African American], and 14.63 [All Others]). There were no clinically meaningful differences between the groups. Frequencies of these systemic events and of fever after any dose of BNT162b2 by race subgroups of White, Black or African American, or 'All Others' (ie, American Indian or Alaska native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories) were:

- fatigue: White: 51.7%, Black or African American: 46.6%, All Others: 53.8%
- headache: White: 38.6%, Black or African American: 37.5%, All Others: 36.0%
- muscle pain: White: 17.9%, Black or African American: 19.3%, All Others: 15.1%
- fever: White: 8.2%, Black or African American: 10.2%, All Others: 8.0%

Ethnicity

The frequencies of the most commonly reported systemic events of fatigue, headache, and muscle pain after any dose of BNT162b2 were 50.0%, 37.7%, and 19.5% compared with 52.3%, 38.4%, and 17.1% for Hispanic/Latino and non-Hispanic/non-Latino participants, respectively (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.64 [Hispanic/Latino], 14.65 [Non-Hispanic/Non-Latino], and 14.66 [Not reported]). Fevers after any dose of BNT162b2 were reported at similar frequencies in Hispanic/Latino and non-Hispanic/non-Latino participants (8.2% vs 8.4%). There were no clinically meaningful differences between the ethnicity subgroups.

SARS-CoV-2 Baseline Status

There were 133 BNT162b2 and 65 placebo participants with baseline positive SARS-CoV-2 status, and 1384 BNT162b2 and 685 placebo participants with baseline negative SARS-CoV-2 status (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.67 [Positive] and 14.68 [Negative]). The frequencies of the most commonly reported systemic events of fatigue, headache, and muscle pain after any dose of BNT162b2 was generally similar, or numerically lower among those positive at baseline: fatigue, headache and muscle pain frequencies were 40.6%, 39.1% and 15.8% compared with 52.8%, 38.1%, and 17.7% for those positive and negative for SARS-CoV-2 at baseline, respectively. Fevers after any dose of BNT162b2 were reported at a slightly lower frequency in baseline positive compared to baseline negative participants (6.0% vs 8.5%). Note that the baseline SARS-CoV-2 positive subgroup included far fewer participants than the negative subgroup, so their results should be interpreted with caution.

2.7.4.2.2.2. Summary of Adverse Events (Phase 2/3)

AE summaries for Phase 2/3 pediatric participants 5 to <12 years of age are reported from Dose 1 to 1 month after Dose 2 (Section 2.7.4.2.2.2.1) and from Dose 1 until the data cutoff date (06 September 2021) (Section 2.7.4.2.2.2.2).

Details and outputs regarding adverse events for Phase 2/3 of Study C4591007 are in Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Section 12.2.

2.7.4.2.2.2.1. Adverse Events From Dose 1 to 1 Month After Dose 2 (Phase 2/3)

An overview of AEs from Dose 1 to 1 month after Dose 2 is shown in Table 3. The proportions of participants with any AE were similar in the BNT162b2 (10.9%) and placebo (9.2%) groups.

Any related AEs, any severe AEs, and any SAEs were reported across the BNT162b2 and placebo groups by ≤3.0%, 0.1%, and 0.1% (reported in the placebo group only), respectively. One (1) participant in the placebo group had SAEs (pancreatitis and abdominal pain) that were considered by the investigator as not related to study intervention (see Section 2.7.4.2.2.4.2 for details).

No withdrawals due to AEs were reported. No study participants died.

Analysis of specific AEs reported from Dose 1 to 1 month after Dose 2 is presented in Section 2.7.4.2.2.3.1.1.

Table 3. Number (%) of Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2 – Phase 2/3 – 5 to <12 Years of Age – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 10 µg (N^a=1518)	Placebo (N^a=750)
Adverse Event	n^b (%)	n^b (%)
Any adverse event	166 (10.9)	69 (9.2)
Related[c]	46 (3.0)	16 (2.1)
Severe	2 (0.1)	1 (0.1)
Life-threatening	0	0
Any serious adverse event	0	1 (0.1)
Related[c]	0	0
Severe	0	1 (0.1)
Life-threatening	0	0
Any nonserious adverse event	166 (10.9)	68 (9.1)
Related[c]	46 (3.0)	16 (2.1)
Severe	2 (0.1)	0
Life-threatening	0	0
Any adverse event leading to withdrawal	0	0
Related[c]	0	0
Serious	0	0
Severe	0	0
Life-threatening	0	0
Death	0	0

a. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of participants reporting at least 1 occurrence of the specified event category. For "any adverse event," n = the number of participants reporting at least 1 occurrence of any adverse event.
c. Assessed by the investigator as related to investigational product.
PFIZER CONFIDENTIAL SDTM Creation: 13SEP2021 (17:16) Source Data: adae Table Generation: 15SEP2021 (17:46)
(Cutoff Date: 06SEP2021, Snapshot Date: 13SEP2021) Output File: ./nda2_ubped/C4591007_P23_EUA/adae_s130_1md2_p2_12

Subgroup Analyses

Subgroups of Phase 2/3 pediatric participants 5 to <12 years of age had similar AE profiles from Dose 1 to 1 month after Dose 2, overall and categorically (ie, related or severe events) across the BNT162b2 and placebo groups when evaluated by sex, race, ethnicity, and baseline SARS-CoV-2 status (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.69 to 14.78). Subgroups of race (Black or African American), ethnicity (Hispanic/Latino) and baseline SARS-CoV-2 status (positive) included a limited number of participants, and their results should be interpreted with caution. No life-threatening AEs or

any AEs leading to withdrawal were reported in the study. There were no meaningful differences in the overall patterns of AEs by category across these subgroups. These subgroups are summarized below.

Sex

In the BNT162b2 group, overall incidences of participants reporting at least 1 AE were 11.1% for male participants and 10.7% for female participants (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.69 [male] and 14.70 [female]). Any related AEs were reported in 3.3% of male participants and 2.8% of female participants. Any severe AEs were reported by 0.3% of male participants and no female participants. Two (2) SAEs were reported for 1 participant within 1 month after Dose 2 (details provided in Section 2.7.4.2.2.4.2):

- 1 female participant in the placebo group reported SAEs of pancreatitis and abdominal pain (reported as occurring 'post-injury') that occurred up to 1 month after Dose 2, considered by the investigator as not related to study intervention

There were no clinically meaningful differences between the 2 sex subgroups.

Race

In the BNT162b2 group, overall incidences of participants reporting at least 1 AE were similar (range: 9.0% to 12.0%) across race subgroups of White, Black or African American, and 'All Others' (ie, American Indian or Alaska native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories) (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.71 [White], 14.72 [Black or African American], and 14.73 [All Others]). Any related AEs were reported in 2.8% to 4.0% of participants across race subgroups. Any severe AEs were reported by 0.2% of participants across race subgroups. The participant who had SAEs (refer to Section 2.7.4.2.2.4.2), that were both considered as not related to study intervention, was White. While the frequency of AEs was numerically different, these differences between race subgroups are not clinically meaningful.

Ethnicity

In the BNT162b2 group, overall incidences of participants reporting at least 1 AE were 11.3% for Hispanic/Latino participants and 10.9% for non-Hispanic/non-Latino participants (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.74 [Hispanic/Latino], 14.75 [Non-Hispanic/Non-Latino], and 14.76 [Not reported]). Any related AEs were reported in 2.8% of Hispanic/Latino participants and 3.1% of non-Hispanic/non-Latino participants. Any severe AEs were reported by 0% of Hispanic/Latino participants and 0.2% of non-Hispanic/non-Latino participants. The participant who had SAEs (refer to Section 2.7.4.2.2.4.2), that were both considered as not related to study intervention, was non-Hispanic/non-Latino. There were no clinically meaningful differences between the 2 ethnicity groups.

SARS-CoV-2 Baseline Status

There were 133 BNT162b2 and 65 placebo participants with baseline positive SARS-CoV-2 status, and 1385 BNT162b2 and 685 placebo participants with baseline negative SARS-CoV-2 status (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.77 [Positive] and 14.78 [Negative]). In the BNT162b2 group, overall incidences of participants reporting at least 1 AE were 8.3% for baseline positive participants and 11.2% for baseline negative participants. Any related AEs were reported in 1.5% of baseline positive participants and 3.2% of baseline negative participants. Any severe AEs were reported by none of the baseline positive participants and 0.1% of baseline negative participants. The participant who had reported SAEs (refer to Section 2.7.4.2.2.4.2), both considered as not related to study intervention, did not have a determinant baseline status (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Listing 16.2.6). While the frequencies of AEs were numerically different, these differences are not clinically meaningful. Note that the baseline SARS-CoV-2 positive subgroup included far fewer participants than the negative subgroup, so their results should be interpreted with caution.

2.7.4.2.2.2. Adverse Events From Dose 1 to Data Cutoff Date (Phase 2/3)

From Dose 1 to the data cutoff date, which represents up to 2 months of follow-up after Dose 2, the proportions of Phase 2/3 pediatric participants 5 to <12 years of age with any event was similar in the BNT162b2 (11.6%) and placebo (9.6%) groups (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.79).

Few additional AEs were reported between 1 month after Dose 2 to the data cutoff date (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.79). Any related AEs, any severe AEs, and any SAEs were reported across the BNT162b2 and placebo groups by ≤3.0%, ≤0.2%, and 0.1%, respectively, up to the data cutoff date. From 1 month after Dose 2 up to the data cutoff date, 1 SAE (limb fracture) was reported in a participant in the BNT162b2 group that was considered by the investigator as not related to study intervention (see Section 2.7.4.2.2.4.2 for details).

No withdrawals due to AEs were reported. As of the data cutoff date, no study participants died.

Analysis of specific AEs reported from Dose 1 to the data cutoff date is presented in Section 2.7.4.2.2.3.1.2.

2.7.4.2.2.3. Analysis of Adverse Events (Phase 2/3)

Details and outputs regarding adverse events for Phase 2/3 of Study C4591007 are in Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Section 12.2.

2.7.4.2.2.3.1. Adverse Events by System Organ Class and Preferred Term (Phase 2/3)

2.7.4.2.2.3.1.1. Adverse Events From Dose 1 to 1 Month After Dose 2

AEs reported from Dose 1 to 1 month after Dose 2 for Phase 2/3 participants 5 to <12 years of age who were randomized 2:1 to receive BNT162b2 10 µg or placebo are presented in Table 4. Overall, frequencies of any AEs reported after Dose 1 up to 1 month after Dose 2 were similar in the BNT162b2 and placebo groups (10.9% vs 9.2%). Many of the AEs were reflective of reactogenicity events that were reported as AEs (ie, headache, vomiting, and injection site pain). AE frequencies in these reactogenicity SOCs (BNT162b2 vs placebo) were:

- general disorders and administration site conditions: 1.6% vs 1.7%
- gastrointestinal disorders: 1.6% vs 1.7%
- nervous system disorders: 0.7% vs 0.5%
- musculoskeletal and connective tissue disorders: 0.5% vs 0.7%.

Overall, many AEs reported up to 1 month after Dose 2 were attributable to vaccine reactogenicity events. This observation provides a reasonable explanation for the greater rates of some AEs observed in the BNT162b2 group compared with the placebo group. In this regard, the pattern of AEs reported in children 5 to <12 years of age was generally consistent with that observed in prior analyses of Phase 2/3 participants ≥12 years of age in Study C4591001 (as reported in: C4591001 Final Analysis Interim CSR, dated 03 December 2020; C4591001 6-Month Update Interim CSR, dated 29 April 2021; C4591001 Adolescent Interim CSR, dated 14 April 2021). Of note, the frequencies of some of these events were not differentiated between the BNT162b2 and placebo group in children 5 to <12 years of age, which may be a function of the similarity of overall AE frequencies reported between the groups up to 1 month post-Dose 2.

Aside from SOCs that reflect events consistent with reactogenicity, other categories of events are discussed below by SOC and PT (Table 4; Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR, Listings 16.2.7.1 and 16.2.7.4). Many of the other commonly reported AEs are consistent with events that would be expected in a general population of healthy children in this age group and/or showed no imbalance between the vaccine and placebo groups.

- *Infections and infestations* were reported in 1.9% of participants in the BNT162b2 group and 2.0% of participants in the placebo group. The events reported in this SOC are typical for this age group, including ear infections, conjunctivitis, and terms consistent with common colds and infections. There was no imbalance in reported infections between the BNT162b2 and placebo groups.

- *Injury, poisoning and procedural complications* were reported in 1.7% of participants in the BNT162b2 group and 0.7% of participants in the placebo group. The events reported in this SOC are typical for this age group, such as fractures and sprains, sunburns, and insect bites. The overall numerical difference between BNT162b2 and placebo groups is primarily due to unrelated events of insect bites, sunburns, and a variety of concurrent events (ie, fall and contusion) reported in a limited number of participants in the

BNT162b2 group, which is a larger group of participants due to the 2:1 randomization of BNT162b2: placebo.

- *Psychiatric disorders* were reported in 0.3% of participants in the BNT162b2 group and 0.4% of participants in the placebo group. The events reported in this SOC include several terms typical for this age group, such as attention deficit hyperactivity disorder, as well as several that may be part of the constellation of reactogenicity such as irritability and poor quality sleep. One participant in the BNT162b2 group had a Grade 3 event of tic that was considered by the investigator as related to study intervention (later determined by neurology consultation to be unrelated); this event is discussed further in AEs of clinical interest in Section 2.7.4.2.2.4.4. There was no imbalance in reported psychiatric disorders between the BNT162b2 and placebo groups.

Blood and lymphatic system disorders were reported in 0.9% of participants in the BNT162b2 group and 0.1% of participants in the placebo group, which included lymphadenopathy and lymph node pain. Lymphadenopathy is discussed as an AE of clinical interest in Section 2.7.4.2.2.4.4. Note that this incidence of lymphadenopathy in children 5 to <12 years of age is slightly higher than that previously reported in Phase 2/3 participants ≥12 years of age after receiving the 2-dose primary series of BNT162b2 30 µg in Study C4591001.

- *Skin and subcutaneous disorders* were reported in 1.4% of participants in the BNT162b2 group and 0.8% of participants in the placebo group, and included rashes, urticaria, eczema, and pruritis that were overall reported more frequently in the BNT162b2 group than in the placebo group. Events in this SOC, including rash and urticaria, are discussed further with AEs of clinical interest in Section 2.7.4.2.2.4.4.

- *Immune system disorders* were reported in 0.1% of participants in the BNT162b2 group and 0.1% of participants in the placebo group and included hypersensitivity (n=1 in the placebo group) and other non-drug allergies. Hypersensitivity is an AE of clinical interest and is discussed in Section 2.7.4.2.2.4.4.

- *Cardiac disorders* were reported in 1 participant in the BNT162b2 group.
  One (1) non-serious Grade 1 event of angina pectoris was considered by the investigator as related to study intervention; the episode was characterized as mild, transient chest pain that lasted 1 minute and was reported 2 days after receiving Dose 2, then resolved with no sequalae. No additional investigations were warranted as determined by the investigator. This event is discussed further in AEs of clinical interest in Section 2.7.4.2.2.4.4.

Table 4. Number (%) of Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Phase 2/3 – 5 to <12 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 10 µg (N[a]=1518)		Placebo (N[a]=750)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any adverse event	166 (10.9)	(9.4, 12.6)	69 (9.2)	(7.2, 11.5)
Blood and lymphatic system disorders	14 (0.9)	(0.5, 1.5)	1 (0.1)	(0.0, 0.7)
Lymphadenopathy	13 (0.9)	(0.5, 1.5)	1 (0.1)	(0.0, 0.7)
Lymph node pain	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Cardiac disorders	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Angina pectoris	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Congenital, familial and genetic disorders	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Phimosis	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Ear and labyrinth disorders	4 (0.3)	(0.1, 0.7)	2 (0.3)	(0.0, 1.0)
Ear pain	2 (0.1)	(0.0, 0.5)	2 (0.3)	(0.0, 1.0)
Cerumen impaction	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Otorrhoea	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Eye disorders	3 (0.2)	(0.0, 0.6)	2 (0.3)	(0.0, 1.0)
Conjunctivitis allergic	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Dry eye	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Hypermetropia	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Periorbital oedema	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Vision blurred	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Gastrointestinal disorders	25 (1.6)	(1.1, 2.4)	13 (1.7)	(0.9, 2.9)
Nausea	6 (0.4)	(0.1, 0.9)	2 (0.3)	(0.0, 1.0)
Vomiting	6 (0.4)	(0.1, 0.9)	2 (0.3)	(0.0, 1.0)
Abdominal pain	4 (0.3)	(0.1, 0.7)	2 (0.3)	(0.0, 1.0)
Diarrhoea	5 (0.3)	(0.1, 0.8)	1 (0.1)	(0.0, 0.7)
Abdominal pain upper	0	(0.0, 0.2)	2 (0.3)	(0.0, 1.0)
Toothache	0	(0.0, 0.2)	2 (0.3)	(0.0, 1.0)
Aphthous ulcer	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Flatulence	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Gastrooesophageal reflux disease	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Odynophagia	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Oral pain	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Pancreatitis	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Rectal haemorrhage	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
General disorders and administration site conditions	25 (1.6)	(1.1, 2.4)	13 (1.7)	(0.9, 2.9)

Table 4. Number (%) of Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Phase 2/3 – 5 to <12 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 10 µg (N[a]=1518)		Placebo (N[a]=750)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Injection site pain	11 (0.7)	(0.4, 1.3)	3 (0.4)	(0.1, 1.2)
Pyrexia	3 (0.2)	(0.0, 0.6)	6 (0.8)	(0.3, 1.7)
Fatigue	1 (0.1)	(0.0, 0.4)	3 (0.4)	(0.1, 1.2)
Injection site erythema	3 (0.2)	(0.0, 0.6)	0	(0.0, 0.5)
Axillary pain	2 (0.1)	(0.0, 0.5)	0	(0.0, 0.5)
Malaise	2 (0.1)	(0.0, 0.5)	0	(0.0, 0.5)
Non-cardiac chest pain	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Injection site haemorrhage	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Injection site induration	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Injection site rash	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Peripheral swelling	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Swelling	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Swelling face	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Thirst	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Immune system disorders	2 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.7)
Seasonal allergy	2 (0.1)	(0.0, 0.5)	0	(0.0, 0.5)
Allergy to animal	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Hypersensitivity	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Mite allergy	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Infections and infestations	29 (1.9)	(1.3, 2.7)	15 (2.0)	(1.1, 3.3)
Otitis externa	7 (0.5)	(0.2, 0.9)	6 (0.8)	(0.3, 1.7)
Nasopharyngitis	3 (0.2)	(0.0, 0.6)	1 (0.1)	(0.0, 0.7)
Hordeolum	3 (0.2)	(0.0, 0.6)	0	(0.0, 0.5)
Cellulitis	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Impetigo	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Upper respiratory tract infection	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Conjunctivitis	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Ear infection	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
External ear cellulitis	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Folliculitis	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Gastroenteritis viral	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Herpes zoster	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Molluscum contagiosum	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Onychomycosis	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)

Table 4. Number (%) of Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Phase 2/3 – 5 to <12 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 10 µg (N[a]=1518)		Placebo (N[a]=750)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Oral candidiasis	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Otitis media	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Paronychia	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Parotitis	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Pharyngitis	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Rhinitis	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Tonsillitis	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Tooth abscess	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Urinary tract infection	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Viral infection	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Vulvovaginal mycotic infection	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Injury, poisoning and procedural complications	26 (1.7)	(1.1, 2.5)	5 (0.7)	(0.2, 1.5)
Fall	5 (0.3)	(0.1, 0.8)	1 (0.1)	(0.0, 0.7)
Arthropod bite	5 (0.3)	(0.1, 0.8)	0	(0.0, 0.5)
Contusion	3 (0.2)	(0.0, 0.6)	0	(0.0, 0.5)
Skin laceration	3 (0.2)	(0.0, 0.6)	0	(0.0, 0.5)
Sunburn	2 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.7)
Ligament sprain	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Upper limb fracture	2 (0.1)	(0.0, 0.5)	0	(0.0, 0.5)
Accident	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Arthropod sting	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Back injury	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Burns first degree	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Concussion	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Foreign body	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Hand fracture	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Head injury	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Heavy exposure to ultraviolet light	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Joint dislocation	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Joint injury	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Limb fracture	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Limb injury	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Muscle strain	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Radius fracture	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)

Table 4. Number (%) of Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Phase 2/3 – 5 to <12 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 10 µg (N[a]=1518)		Placebo (N[a]=750)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Investigations	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Body temperature increased	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Serum ferritin decreased	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Metabolism and nutrition disorders	1 (0.1)	(0.0, 0.4)	2 (0.3)	(0.0, 1.0)
Decreased appetite	1 (0.1)	(0.0, 0.4)	2 (0.3)	(0.0, 1.0)
Musculoskeletal and connective tissue disorders	7 (0.5)	(0.2, 0.9)	5 (0.7)	(0.2, 1.5)
Pain in extremity	3 (0.2)	(0.0, 0.6)	2 (0.3)	(0.0, 1.0)
Musculoskeletal chest pain	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Arthralgia	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Muscle mass	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Myalgia	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Osteitis	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Synovitis	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Pyogenic granuloma	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Nervous system disorders	10 (0.7)	(0.3, 1.2)	4 (0.5)	(0.1, 1.4)
Headache	6 (0.4)	(0.1, 0.9)	2 (0.3)	(0.0, 1.0)
Disturbance in attention	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Dizziness	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Dyslexia	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Migraine	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Paraesthesia	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Somnolence	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Psychiatric disorders	4 (0.3)	(0.1, 0.7)	3 (0.4)	(0.1, 1.2)
Attention deficit hyperactivity disorder	1 (0.1)	(0.0, 0.4)	2 (0.3)	(0.0, 1.0)
Irritability	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Poor quality sleep	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Tic	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Renal and urinary disorders	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Dysuria	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Reproductive system and breast disorders	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Balanoposthitis	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)

Table 4. Number (%) of Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Phase 2/3 – 5 to <12 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 10 µg (N[a]=1518)		Placebo (N[a]=750)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Respiratory, thoracic and mediastinal disorders	22 (1.4)	(0.9, 2.2)	9 (1.2)	(0.6, 2.3)
Nasal congestion	5 (0.3)	(0.1, 0.8)	4 (0.5)	(0.1, 1.4)
Cough	5 (0.3)	(0.1, 0.8)	2 (0.3)	(0.0, 1.0)
Oropharyngeal pain	5 (0.3)	(0.1, 0.8)	1 (0.1)	(0.0, 0.7)
Epistaxis	3 (0.2)	(0.0, 0.6)	0	(0.0, 0.5)
Rhinorrhoea	2 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.7)
Asthma	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Sneezing	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Throat irritation	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Tonsillolith	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Skin and subcutaneous tissue disorders	22 (1.4)	(0.9, 2.2)	6 (0.8)	(0.3, 1.7)
Urticaria	3 (0.2)	(0.0, 0.6)	3 (0.4)	(0.1, 1.2)
Rash	5 (0.3)	(0.1, 0.8)	0	(0.0, 0.5)
Dermatitis contact	3 (0.2)	(0.0, 0.6)	0	(0.0, 0.5)
Erythema	2 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.7)
Rash papular	3 (0.2)	(0.0, 0.6)	0	(0.0, 0.5)
Eczema	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Cold sweat	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Dermatitis	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Dermatitis allergic	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Macule	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Mechanical urticaria	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Pruritus	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Rash erythematous	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Rash macular	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Rash pruritic	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Surgical and medical procedures	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Suture insertion	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Tooth extraction	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)

Table 4. Number (%) of Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Phase 2/3 – 5 to <12 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 10 µg (N[a]=1518)		Placebo (N[a]=750)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of participants reporting at least 1 occurrence of the specified event. For "any adverse event," n = number of participants reporting at least 1 occurrence of any adverse event.
c. Exact 2-sided CI based on the Clopper and Pearson method.
PFIZER CONFIDENTIAL SDTM Creation: 13SEP2021 (17:16) Source Data: adae Table Generation: 15SEP2021 (12:20)
(Cutoff Date: 06SEP2021, Snapshot Date: 13SEP2021) Output File: ./nda2_ubped/C4591007_P23_EUA/adae_s150_1md2_soc_p2_12

Tier 2 AEs

In participants 5 to <12 years of age, from Dose 1 to 1 month after Dose 2 there were no AEs considered per protocol as Tier 2 events (ie, "relatively common" AEs with an incidence rate ≥1.0% in any vaccine group at the PT level).

Subgroup Analyses

Subgroups of Phase 2/3 pediatric participants 5 to <12 years of age had similar AE profiles from Dose 1 to 1 month after Dose 2 with regard to most frequently reported events by SOC and PT across the BNT162b2 and placebo groups when evaluated by sex, race, ethnicity, and baseline SARS-CoV-2 status (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.80 to 14.89). Subgroups of race (Black or African American), ethnicity (Hispanic/Latino) and baseline SARS-CoV-2 status (positive) included a limited number of participants, and their results should be interpreted with caution. There were no meaningful differences in the AEs profiles across these subgroups. These subgroups are summarized below.

Sex

In the BNT162b2 group, overall incidences of participants reporting at least 1 AE were 11.1% for male participants and 10.7% for female participants (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.80 [male] and 14.81 [female]). Consistent with the overall safety population, most commonly reported AEs were in the reactogenicity SOCs (male vs female):

- general disorders and administration site conditions: 1.8% vs 1.5%
- gastrointestinal disorders: 1.9% vs 1.4%
- nervous system disorders: 0.4% vs 1.0%
- musculoskeletal and connective tissue disorders: 0.6% vs 0.3%.

Notably, in the BNT162b2 group, lymphadenopathy and/or lymph node pain were reported by more male participants (10 [1.3%]) than in female participants (4 [0.6%]). Skin and subcutaneous tissue disorders were reported at a higher frequency in male participants (18 [2.3%]) than in female participants (4 [0.6%]), mostly due to more events of rash reported in males (refer to Section 2.7.4.2.2.4.4 or additional detail on rashes analyzed as of AEs of clinical interest).

The few observed numerical differences in AE frequencies were not associated with clinically meaningful differences between the sex subgroups.

Race

In the BNT162b2 group, overall incidences of participants reporting at least 1 AE were similar (range: 9.0% to 12.0%) across race subgroups (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.82 [White], 14.83 [Black or African American], and 14.84 [All Others]). Frequencies of the most commonly reported AEs in the reactogenicity SOCs in the BNT162b2 group by race subgroups for White versus Black or African American versus 'All Others' (ie, American Indian or Alaska native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories) were:

- general disorders and administration site conditions: 1.7% vs 1.1% vs 1.8%
- gastrointestinal disorders: 1.5% vs 2.2% vs 2.2%
- nervous system disorders: 0.7% vs 0% vs 0.9%
- musculoskeletal and connective tissue disorders: 0.4% vs 0% vs 0.9%.

Lymphadenopathy and/or lymph node pain were reported by more White or Black or African American participants (1.0% and 1.1%) than in the 'All Other' race subgroup (0.4%). Skin and subcutaneous tissue disorders were reported in 1.3%, 0%, and 2.7% of White, Black or African American, and All Other race subgroups, respectively.

The few observed numerical differences in AE frequencies were not associated with clinically meaningful differences between the race subgroups. Due to limited number of participants in the Black or African American subgroup, these results should be interpreted with caution.

Ethnicity

In the BNT162b2 group, overall incidences of participants reporting at least 1 AE were 11.3% for Hispanic/Latino participants and 10.9% for non-Hispanic/non-Latino participants (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.85 [Hispanic/Latino], 14.86 [Non-Hispanic/Non-Latino], and 14.87 [Not reported]). The frequencies of the most commonly reported AEs were similar across ethnic subgroups. Frequencies of the most

commonly reported AEs in the reactogenicity SOCs in the BNT162b2 group by ethnic subgroups were (Hispanic/Latino vs Non-Hispanic/Non-Latino) were:

- general disorders and administration site conditions: 1.3% vs 1.8%
- gastrointestinal disorders: 2.5% vs 1.4%
- nervous system disorders: 1.3% vs 0.5%
- musculoskeletal and connective tissue disorders: 0.6% vs 0.4%

The frequency of lymphadenopathy and/or lymph node pain was similar (0.9% each) in the Hispanic/Latino and Non-Hispanic/Non-Latino subgroups. Skin and subcutaneous tissue disorders were similar between the Hispanic/Latino and non-Hispanic/non-Latino subgroups (1.9% vs 1.3%).

While the frequency of AEs was generally numerically higher in the Hispanic/Latino subgroup, due to limited number of participants, these results should be interpreted with caution.

SARS-CoV-2 Baseline Status

There were 133 BNT162b2 and 65 placebo participants with baseline positive SARS-CoV-2 status, and 1385 BNT162b2 and 685 placebo participants with baseline negative SARS-CoV-2 status (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Tables 14.88 [Positive] and 14.89 [Negative]). In the BNT162b2 group, overall incidences of participants reporting at least 1 AE were 8.3% for baseline positive participants and 11.2% for baseline negative participants. The most commonly reported AEs in the reactogenicity SOCs in the BNT162b2 group by baseline SARS-CoV-2 status (positive vs negative) were:

- general disorders and administration site conditions: 0.8% vs 1.7%
- gastrointestinal disorders: 3.0% vs 1.5%
- nervous system disorders: 0.8% vs 0.6%
- musculoskeletal and connective tissue disorders: 0.8% vs 0.4%

The frequency of lymphadenopathy and/or lymph node pain was similar (0.8% vs 0.9%) in the baseline positive and negative subgroups. Skin and subcutaneous tissue disorders were reported at a lower incidence in the SARS-CoV-2 baseline positive subgroup compared to the baseline negative subgroup (0.8% vs 1.5%).

While there were numerical differences in the frequencies of AEs between the SARS-CoV-2 baseline subgroup, due to limited number of participants in the baseline positive subgroup, these results should be interpreted with caution.

2.7.4.2.2.3.1.1.1. Related Adverse Events by System Organ Class and Preferred Term (Phase 2/3)

From Dose 1 to 1 month after Dose 2, AEs assessed as related by the investigator were reported at a slightly higher frequency in the BNT162b2 group (3.0%) than in the placebo group (2.1%) (Table 5). Most related AEs were reactogenicity events and in the SOC of general disorders and administration site conditions, reported by 1.1% of participants in the

BNT162b2 group compared with 0.9% of participants in the placebo group (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.90). Other notable related events reported from Dose 1 to 1 month after Dose 2 are summarized below (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.90, Listings 16.1.7.1, 16.2.7.1 and 16.2.7.4); refer to AEs of clinical interest in Section 2.7.4.2.2.4.4 for more details for each.

- Non-serious, non-severe, related events of lymphadenopathy were reported in 0.7% of participants in the BNT162b2 group and none in the placebo group All cases were considered mild.
- Non-serious related events of rash, urticaria, and other skin and subcutaneous tissue disorders were reported in 0.4% participants in the BNT162b2 group and 0.5% of participants in the placebo group.
- One (1) non-serious, non-severe event of angina pectoris considered by the investigator as related to study intervention was reported by a participant in the BNT162b2 group. This event lasted 1 minute in duration, with onset at 2 days after Dose 2, and resolved with no sequalae or further investigation deemed warranted by the investigator.
- One (1) related non-serious, Grade 3 event of tic was reported in a participant in the BNT162b2 group (later determined by neurology consultation to be unrelated).
- One (1) non-serious, immediate (post-Dose 1) event of Grade 1 periorbital edema considered by the investigator as related to study intervention was reported in a participant in the placebo group. This same participant reported other non-serious, Grade 1 AEs of hypersensitivity, erythema, and urticaria considered by the investigator as related to study intervention; all of these events occurred on the same day the participant received the first dose of placebo (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Listing 16.2.4), all were reported as resolved the same day, and the participant later received the second dose of placebo without any AEs reported post-Dose 2.

Table 5. Number (%) of Participants Reporting at Least 1 Related Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Phase 2/3 – 5 to <12 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 10 µg (N^a=1518)		Placebo (N^a=750)	
System Organ Class Preferred Term	n^b (%)	(95% CI[c])	n^b (%)	(95% CI[c])
Any adverse event	46 (3.0)	(2.2, 4.0)	16 (2.1)	(1.2, 3.4)
Blood and lymphatic system disorders	11 (0.7)	(0.4, 1.3)	0	(0.0, 0.5)
Lymphadenopathy	10 (0.7)	(0.3, 1.2)	0	(0.0, 0.5)

Table 5. Number (%) of Participants Reporting at Least 1 Related Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Phase 2/3 – 5 to <12 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 10 µg (N[a]=1518)		Placebo (N[a]=750)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Lymph node pain	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Cardiac disorders	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Angina pectoris	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Eye disorders	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Periorbital oedema	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Gastrointestinal disorders	6 (0.4)	(0.1, 0.9)	4 (0.5)	(0.1, 1.4)
Nausea	5 (0.3)	(0.1, 0.8)	1 (0.1)	(0.0, 0.7)
Abdominal pain	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Abdominal pain upper	0	(0.0, 0.2)	2 (0.3)	(0.0, 1.0)
General disorders and administration site conditions	17 (1.1)	(0.7, 1.8)	7 (0.9)	(0.4, 1.9)
Injection site pain	11 (0.7)	(0.4, 1.3)	3 (0.4)	(0.1, 1.2)
Fatigue	1 (0.1)	(0.0, 0.4)	2 (0.3)	(0.0, 1.0)
Axillary pain	2 (0.1)	(0.0, 0.5)	0	(0.0, 0.5)
Injection site erythema	2 (0.1)	(0.0, 0.5)	0	(0.0, 0.5)
Pyrexia	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Injection site haemorrhage	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Injection site induration	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Injection site rash	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Non-cardiac chest pain	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Thirst	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Immune system disorders	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Hypersensitivity	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Metabolism and nutrition disorders	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Decreased appetite	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Musculoskeletal and connective tissue disorders	2 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.7)
Arthralgia	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Musculoskeletal chest pain	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Pain in extremity	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Nervous system disorders	2 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.7)
Headache	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Paraesthesia	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Somnolence	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Psychiatric disorders	2 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.7)

Table 5. Number (%) of Participants Reporting at Least 1 Related Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Phase 2/3 – 5 to <12 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 10 µg (N[a]=1518)		Placebo (N[a]=750)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Irritability	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Tic	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Respiratory, thoracic and mediastinal disorders	2 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.7)
Nasal congestion	2 (0.1)	(0.0, 0.5)	0	(0.0, 0.5)
Oropharyngeal pain	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Throat irritation	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Skin and subcutaneous tissue disorders	6 (0.4)	(0.1, 0.9)	4 (0.5)	(0.1, 1.4)
Urticaria	1 (0.1)	(0.0, 0.4)	3 (0.4)	(0.1, 1.2)
Eczema	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Erythema	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Macule	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Pruritus	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Rash	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Rash macular	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Rash pruritic	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of participants reporting at least 1 occurrence of the specified event. For "any adverse event," n = number of participants reporting at least 1 occurrence of any adverse event.
c. Exact 2-sided CI based on the Clopper and Pearson method.
PFIZER CONFIDENTIAL SDTM Creation: 13SEP2021 (17:16) Source Data: adae Table Generation: 15SEP2021 (12:20)
(Cutoff Date: 06SEP2021, Snapshot Date: 13SEP2021) Output File: ./nda2_ubped/C4591007_P23_EUA/adae_s150_1md2_rel_p2_12

2.7.4.2.2.3.1.1.2. Immediate Adverse Events (Phase 2/3)

After Dose 1, immediate AEs (reported within 30 minutes of the first vaccination) were low in frequency (≤0.4%) in the BNT162b2 and placebo groups (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.91). Immediate AEs reported after Dose 1 in the BNT162b2 versus placebo groups were predominantly injection site pain, reported in 3 participants (0.2%) in the BNT162b2 group and 2 participants (0.3%) in the placebo group. No other immediate AEs post-Dose 1 were reported in the BNT162b2 group. Immediate AEs post-Dose 1 reported in the placebo group (n=1 each) were fatigue, hypersensitivity, erythema, urticaria, and periorbital edema.

After Dose 2, immediate AEs (reported within 30 minutes of the second vaccination) were low in frequency (0.3%) in the BNT162b2 and placebo groups (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.92). Immediate AEs reported after Dose 2 in the BNT162b2 versus placebo groups were predominantly injection site pain, reported in 1 participant (0.1%) in the BNT162b2 group and 2 participants (0.3%) in the placebo group. Other immediate AEs reported post-Dose 2 in the BNT162b2 group (n=1 each) were injection site erythema, erythema and nausea.

Refer to AEs of clinical interest in Section 2.7.4.2.2.4.4 for details on hypersensitivity and rashes.

No allergic AEs were reported after either dose of BNT162b2 within 30 minutes after vaccination.

2.7.4.2.2.3.1.1.3. Severe or Life-Threatening Adverse Events (Phase 2/3)

From Dose 1 to 1 month after Dose 2, severe AEs were low in frequency (0.1%) in both the BNT162b2 and placebo groups (Table 3; Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.93). Severe events reported included Grade 3 events of abdominal pain and pancreatitis (noted as occurring 'post-injury') both reported in 1 participant in the placebo group that were reported as SAEs considered not related to study intervention (refer to Section 2.7.4.2.2.4.2).

A non-serious Grade 3 AE of tic considered by the investigator as related to study intervention (later determined by neurology consultation to be unrelated) was reported in 1 participant in the BNT162b2 group; refer to AEs of clinical interest in Section 2.7.4.2.2.4.4 for details. A Grade 3 rash (bilateral pleomorphic light eruption on arms) was reported by a participant in the BNT162b2 group, considered by the investigator as not related to study intervention and noted as possibly due to a reaction to sunscreen, and this same participant had an unrelated Grade 2 AE of leg (flank, hip, thigh) folliculitis after Dose 2 due to 'exposure in hot tub' at 24 days post-Dose 2 that resolved after 7 days of onset. Refer to AEs of clinical interest in Section 2.7.4.2.2.4.4 for details on rashes.

No life-threatening (ie, Grade 4) AEs were reported from Dose 1 to 1 month after Dose 2 (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.93, Listing 16.2.7.4).

2.7.4.2.2.3.1.2. Adverse Events From Dose 1 to Data Cutoff Date

AEs reported in Phase 2/3 pediatric participants 5 to <12 years of age through the data cutoff date (06 September 2021), which represented at least 2 months of follow-up after Dose 2, were reported at similar frequencies in the BNT162b2 group (11.6%) and placebo group (9.6%) (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.94). In addition to the AEs reported up to 1 month after Dose 2 (Table 4), the most frequently reported AEs in the BNT162b2 group through the data cutoff date were reactogenicity events. Overall, few additional AEs were reported from after 1 month post-Dose 2 to the cutoff date, and no additional AEs of clinical interest were identified.

2.7.4.2.2.4. Deaths, Serious Adverse Events, Safety-Related Participant Withdrawals, and Other Significant Adverse Events (Phase 2/3)

Details and outputs regarding Phase 2/3 deaths, SAEs, and safety-related participant withdrawals, and other significant AEs for children 5 to <12 years of age are in Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Section 12.2.4.

2.7.4.2.2.4.1. Deaths (Phase 2/3)

No deaths were reported in the Phase 2/3 pediatric population of children 5 to <12 years of age up to the data cutoff date (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Appendix 16.2.7.7).

2.7.4.2.2.4.2. Serious Adverse Events (Phase 2/3)

SAEs were reported from Dose 1 through the data cutoff date, which represents at least 2 months of follow-up after Dose 2 (Table 6). Overall, 1 participant (0.1%) in each group reported any SAE after receiving BNT162b2 or placebo through the data cutoff date. These SAEs were all assessed by the investigator as not related to study intervention.

As of the data cutoff date, a total of 3 SAEs were reported by 2 participants (n=1 each in the BNT162b2 and placebo groups), as summarized below (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Listings 16.2.7.4, 16.2.7.5, 16.2.4, 16.1.7.1).

- The participant in the BNT162b2 group was a [redacted PPD] years of age who had a non-serious Grade 3 AE of fall reported 45 days after receiving Dose 2; this was concurrent with a reported Grade 3 SAE of upper limb fracture (elbow) identified the same day (45 days post-Dose 2) as being due to a '[redacted PPD]' ([redacted PPD]). The fracture was reported as recovering/resolving at the time of the data cutoff. The SAE was considered by the investigator as not related to study intervention.

- The participant in the placebo group was a [redacted PPD] [redacted] years of age who reported an SAE of Grade 3 pancreatitis (noted as occurring 'post-injury') with onset at 4 days post-Dose 2 and reported as resolved within 7 days of onset with concomitant drug treatment. This same participant reported a second Grade 3 SAE of abdominal pain with onset at 11 days post-Dose 2 and reported as resolved within 6 days after onset. Both SAEs were considered by the investigator as not related to study intervention. This participant had no reported medical history and received no prohibited concomitant treatments or nonstudy vaccines.

Table 6. Number (%) of Participants Reporting at Least 1 Serious Adverse Event From Dose 1 Through Cutoff Date (06SEP2021), by System Organ Class and Preferred Term – Phase 2/3 – 5 to <12 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 10 µg (N[a]=1518)		Placebo (N[a]=750)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any adverse event	1 (0.1)	(0.0, 0.4)	1 (0.1)	(0.0, 0.7)
Gastrointestinal disorders	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Abdominal pain	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Pancreatitis	0	(0.0, 0.2)	1 (0.1)	(0.0, 0.7)
Injury, poisoning and procedural complications	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)
Upper limb fracture	1 (0.1)	(0.0, 0.4)	0	(0.0, 0.5)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of participants reporting at least 1 occurrence of the specified event. For "any adverse event," n = number of participants reporting at least 1 occurrence of any adverse event.
c. Exact 2-sided CI based on the Clopper and Pearson method.
PFIZER CONFIDENTIAL SDTM Creation: 13SEP2021 (17:16) Source Data: adae Table Generation: 15SEP2021 (12:21)
(Cutoff Date: 06SEP2021, Snapshot Date: 13SEP2021) Output File: ./nda2_ubped/C4591007_P23_EUA/adae_s150_1md2_sae_p2_12

2.7.4.2.2.4.3. Safety-Related Participant Withdrawals (Phase 2/3)

No AEs leading to withdrawal were reported in the Phase 2/3 pediatric population of children 5 to <12 years of age up to the data cutoff date (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Appendix 16.2.7.6).

2.7.4.2.2.4.4. Other Significant Adverse Events (Phase 2/3)

Adverse Events of Clinical Interest

Adverse events of specific clinical interest, such as those in the CDC list of AESIs for COVID-19, were reviewed based on AEs reported up to the cutoff date (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.94). Narratives were prepared if such events were reported. Information on events of clinical interest included terms requested by the FDA included: anaphylaxis, appendicitis, Bell's palsy, and lymphadenopathy. The protocol-defined AESI of myocarditis/pericarditis was also considered in the safety review. These cases are summarized below for reported events up to the data cutoff date (06 September 2021), which represents at least 2 months of follow-up after Dose 2.

Among the FDA-requested AEs of clinical interest, no cases were reported in the 5 to <12 years of age group up to the data cutoff date of anaphylaxis, myocarditis/pericarditis, Bell's palsy (or facial paralysis/paresis), or appendicitis. Other events of potential clinical interest that were reported in the study safety database are summarized below.

Anaphylaxis/Hypersensitivity

No cases of anaphylaxis or anaphylactic/anaphylactoid reaction were reported in the study (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Listing 16.2.7.4).

No cases of hypersensitivity were reported in the BNT162b2 group (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Listing 16.2.7.4). One (1) participant in the placebo group reported hypersensitivity and several additional AEs considered by the investigator as related to study intervention following the first dose of placebo, as summarized below (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Listings 16.2.7.4, 16.2.7.5, 16.2.4, 16.1.7.1).

- 1 [redacted] years of age in the placebo group had concurrent AEs of Grade 1 hypersensitivity, erythema, urticaria ([redacted]), and periorbital edema (which was reported as an immediate AE, occurring within 30 minutes after the first dose) all occurring on the day of receiving Dose 1 of placebo, all considered by the investigator as related to study intervention, and all reported as resolved on the same day as onset. This participant received the second dose of placebo without any AEs reported post-Dose 2. This participant had a reported medical history including past [redacted] reported no other AEs or any severe reactogenicity events, and received no prohibited concomitant treatments or nonstudy vaccines.

A further safety review was conducted using SMQs of angioedema/hypersensitivity reported from Dose 1 to 1 month after Dose 2. Among approximately 2250 participants 5 to <12 years of age randomized 2:1 to receive BNT162b2 or placebo, 18 participants (1.2%) in the BNT162b2 group and 6 participants (0.8%) in the placebo group had events in angioedema/hypersensitivity SMQs (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.95).

Events in the SMQ of angioedema reported in the BNT162b2 group included face swelling (caused by an insect bite and considered by the investigator as not related to study intervention) (n=1) and urticaria (n=3) (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.95). Urticaria was also reported in the placebo group in the same number of participants (n=3), therefore there was no imbalance between the groups.

Events in the SMQ of hypersensitivity more commonly reported in the BNT162b2 group than the placebo group were dermatitis (including contact and allergic dermatitis, n=5 in the BNT162b2 group vs none in the placebo group) of which all cases were deemed as not related to vaccine; and rash (including pruritic, macular, injection site rash, n=8 in the BNT162b2 group vs n=1 in the placebo group (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.95, Listing 16.2.7.4). Of the rashes in the BNT162b2 group, 4 were considered by the investigator as related to study intervention: all of these were Grade 1, typically had an onset 7 days or more post vaccination; only 1 injection site rash was reported with earlier onset at 3 days post-Dose 2. All but 1 event (rash on torso with onset at 11 days post-Dose 2) were reported as resolved. These related rashes were observed on the arm, torso, face and/or body with no clear pattern, and 2 participants had other skin reactions in the same anatomical location a short time before or after the reported SMQ event (ie, prior erythema reaction to Tegaderm patch on arm, or subsequent rash on face due to bee sting).

Allergic conjunctivitis and eczema were also reported, at the same frequencies in BNT162b2 and placebo groups (n=1 each) (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.95).

All angioedema/hypersensitivity SMQ events were mild or moderate, with the exception of 1 participant in the BNT162b2 group who had a Grade 3 rash (bilateral pleomorphic light eruption on arms) with onset at 3 days post-Dose 1 and reported as resolved 6 days later, not related to study intervention, and noted as possibly due to a reaction to sunscreen (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.95, Listing 16.2.7.4).

Rash is considered an adverse reaction to vaccine and is noted as such in the current product labeling. Overall, the pattern of events in the hypersensitivity SMQ within the skin and subcutaneous tissue disorders SOC (including rashes) reported in children 5 to <12 years of age in Study C4591007 was consistent with that observed in prior analyses of Phase 2/3 participants ≥12 years of age in Study C4591001.

Lymphadenopathy

Lymphadenopathy is considered an adverse reaction to vaccine and is noted as such in the current product labeling. Among approximately 2250 children 5 to <12 years of age randomized 2:1 to receive BNT162b2 or placebo, as of the data cutoff date (06 September 2021), 13 participants (0.9%) in the BNT162b2 group and 1 participant (0.1%) in the placebo group had events of lymphadenopathy (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.96).

In the BNT162b2 group, the mean time to onset after Dose 1 was 6.2 days (median 3 days), and after Dose 2 was 2.6 days (median 2 days). The mean duration of the events was 4.7 days

(median 3.5 days, range 1 to 14 days). The single event in the placebo group had an onset at 22 days post-Dose 1 with a duration of 2 days. All reported cases of lymphadenopathy in either group were mild (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.96).

Overall, the pattern of lymphadenopathy cases reported in children 5 to <12 years of age was generally similar to that observed in prior analyses of Phase 2/3 participants ≥12 years of age in Study C4591001 (as reported in: C4591001 Final Analysis Interim CSR, dated 03 December 2020; C4591001 6-Month Update Interim CSR, dated 29 April 2021; C4591001 Adolescent Interim CSR, dated 14 April 2021).

Other Adverse Events of Clinical Interest

In addition to the FDA-requested AEs of clinical interest, 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): thrombocytopenic events, thromboembolic or intravascular coagulation events, autoimmune or demyelination events, meningitis, encephalitis, neuritis, Kawasaki disease, MIS-C, or acute respiratory distress syndrome.

Additional AEs of clinical interest, regardless of inclusion on the CDC AESI list, were evaluated based on sponsor safety data review. These AEs were identified from the C4591007 study database as of the data cutoff date (06 September 2021) and are summarized below (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Listings 16.2.7.5, 16.2.7.2, 16.2.7.3, 16.2.7.4, 16.1.7.1).

Arthralgia

In the BNT162b2 group, an event of arthralgia was reported in 1 participant:

[redacted] years of age in the BNT162b2 group had an AE of Grade 1 arthralgia (right elbow joint pain) with an onset the same day as Dose 2 (administered in the left deltoid muscle), that was reported as resolved the next day. The AE was considered by the investigator as related to study intervention. This participant had a medical history including [redacted] reported one other unrelated AE of vomiting (attributed to 'car sickness'), and reported no severe reactogenicity events. He received no prohibited concomitant treatments or nonstudy vaccines. A narrative is provided for this Phase 2/3 participant in Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Listings Section 14.

Paresthesia

In the BNT162b2 group, an event of paresthesia was reported in 1 participant:

- 1 [redacted] years of age in the BNT162b2 group had an AE of Grade 2 paresthesia (bilateral lower extremity tingling) with onset at 1 day post-Dose 2 and reported as recovered/resolved 3 days after onset. The AE was considered by the investigator as related to study intervention. This participant had a medical history including [redacted] reported no other

AEs or any severe reactogenicity events, and received no prohibited concomitant treatments or nonstudy vaccines.

Tic

In the BNT162b2 group, a psychiatric disorder event of tic was reported in 1 participant:

- 1 [redacted] years of age in the BNT162b2 group had an AE of Grade 3 tic with onset at 7 days post-Dose 2 and reported as recovering/resolving at the time of the data cutoff. The AE was considered by the investigator as related to study intervention. This participant reported no medical history, no other AEs or any severe reactogenicity events, and received no prohibited concomitant treatments or nonstudy vaccines. Within approximately 1 week after onset of the tic, the participant was evaluated by [redacted] primary care physician; approximately 1 week later [redacted] had an MRI which showed no pathology. A pediatric neurologist was consulted, which did not result in a specific diagnosis, included a recommendation of lifestyle change, and the neurologist was not able to relate the new tic to vaccine. As of the cutoff date, the child was reported as continuing in [redacted] regular daily routine.

Chest Pain

In the BNT162b2 group, an event of angina pectoris was reported in 1 participant, and in the placebo group, an event of non-cardiac chest pain was reported in 1 participant:

- 1 [redacted] years of age in the BNT162b2 group had an AE of Grade 1 angina pectoris with onset at 2 days post-Dose 2; the episode was characterized as mild, transient chest pain lasting 1 minute in duration, and reported as resolved with no sequalae. Further investigation into the chest pain was not clinically indicated per the investigator. The AE was considered by the investigator as related to study intervention. This participant had a medical history of [redacted]. This participant reported no other AEs or any severe reactogenicity events and received no prohibited concomitant treatments or nonstudy vaccines. Other mild to moderate reactogenicity events reported by this participant during the time period when the AE was reported after Dose 2 were pain at injection site (Day 2 post-Dose 2) and fatigue and headache (Days 2-4 post-Dose 2).
- 1 [redacted] years of age in the placebo group had an AE of Grade 1 non-cardiac chest pain with onset at 6 days post-Dose 2 and resolved 3 days after onset. The event was characterized as transient in nature, with no cardiac involvement. Further investigation into the non-cardiac chest pain was not clinically indicated per the investigator. [redacted] previously had reported an AE of Grade 1 pain in extremity ('whole left arm pain') with onset at 2 days post-Dose 2 that resolved 8 days after onset. Both events were considered by the investigator as related to study intervention. This participant had a medical history of [redacted] This participant reported no other AEs or any severe reactogenicity events and received no

prohibited concomitant treatments or nonstudy vaccines. Other mild or moderate reactogenicity events reported by this participant during the time period when the AE of non-cardiac chest pain was reported after Dose 2 included pain at injection site (Days 2-7 post-Dose 2), headache (Days 2-3 post-Dose 2), fatigue (Days 2-4 and Days 6-7 post-Dose 2), and new or worsened muscle pain (Days 4-5 post-Dose 2).

2.7.4.2.2.4.5. Analysis of Adverse Events by Organ System or Syndrome (Phase 2/3)

Adverse reactions (ADRs), defined as AEs for which there is reason to conclude that the vaccine caused the event, have been identified from clinical study safety data and are specified in the current product labeling.

Safety data from Phase 2/3 of Study C4591007 were reviewed to determine if any ADRs should be identified for the 5 to <12 year old age group. The review included AE data, as well as local reactions and systemic events collected systematically by e-diaries. ADRs are included in BNT162b2 product labeling.

The CIOMS frequency categories for adverse reactions are as follows:

- Very common: ≥10%
- Common: ≥1% and <10%
- Uncommon: ≥0.1% and <1%
- Rare: ≥0.01% and <0.1%
- Very rare: <0.01%

Reactogenicity ADRs that occurred with a very common frequency, based on any dose in the BNT162b2 group in individuals 5 to <12 years of age, from the reactogenicity subset of data as of 06 September 2021, are:

- Injection site pain: 1279/1517 (84.3%)
- Fatigue: 785/1517 (51.7%)
- Headache: 579/1517 (38.2%)
- Injection site redness: 401/1517 (26.4%)
- Injection site swelling: 309/1517 (20.4%)
- Muscle pain: 266/1517 (17.5%)
- Chills: 188/1517 (12.4%)

Reactogenicity ADRs that occurred with a common frequency, based on any dose in the BNT162b2 group in individuals 5 to <12 years of age, from the reactogenicity subset of data as of 06 September 2021, are:

- Diarrhea: 146/1517 (9.6%)
- Vomiting: 60/1517 (4.0%)
- Joint pain: 115/1517 (7.6%)
- Fever: 126/1517 (8.3%)

No new ADRs were identified from safety data associated with administration of BNT162b2 10 µg to children 5 to <12 years of age in Study C4591007.

2.7.4.2.2.4.6. Other Safety Assessments (Phase 2/3)

2.7.4.2.2.4.6.1. Severe COVID-19 and MIS-C Illness

As of the data cutoff date, no severe COVID-19 or MIS-C cases were reported in Phase 2/3 pediatric participants 5 to <12 years of age in Study C4591007 in the safety database (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Listing 16.2.7.4).

Prior analyses of efficacy for all C4591001 Phase 2/3 participants ≥12 years of age showed confinement of severe cases predominantly to the placebo group. Together, these data continue to suggest no evidence for VAED, including VAERD.

2.7.4.2.2.4.6.2. Pregnancies

No pregnancies were reported in Study C4591007 as of the data cutoff date (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Listing 16.2.7.4).

2.7.4.2.2.5. Physical Examination Findings (Phase 2/3)

Details and outputs regarding physical examination findings for Phase 2/3 of Study C4591007 are in Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Section 12.2.5.

In Phase 2/3 participants 5 to <12 years of age, there were no clinically important findings from physical examinations.

The proportions of participants noted to have any abnormality during baseline physical examinations were similar in the BNT162b2 (1.8%) and placebo (1.9%) groups (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.97, Listing 16.2.5.4).

After vaccination, the proportions of participants with any abnormality observed at 19 to 23 days after Dose 1 were similar in the BNT162b2 (0.9%) and placebo (0.8%) groups (Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Table 14.98, Listing 16.2.5.4). Abnormalities were balanced across the BNT162b2 and placebo groups for lymph nodes (0.6% vs 0.5%), heart (0.2% vs 0.3%), and lungs (0.1% vs 0%).

2.7.4.2.2.6. Narratives (Phase 2/3)

Narratives for Phase 2/3 participants (adverse events of clinical interest) are provided in Module 5.3.5.1 C4591007 (5 to <12 Years) Interim CSR Section 14 Narratives.

2.7.4.2.2.7. Safety Conclusions (Phase 2/3)

Phase 2/3 data from approximately 2250 children 5 to <12 years of age with a follow-up time of at least 2 months after Dose 2 showed BNT162b2 at 10 µg was safe and well-tolerated.

Reactogenicity in children 5 to <12 years of age was mostly mild to moderate and short-lived, with median onset of 1 to 4 days after dosing (most within a median of 2 days post-dose), and resolution within 1 to 2 days after onset. Local reactions presented predominantly as injection

site pain with no effect of dose number, which was similar to what was previously reported in Study C4591001 participants ≥12 years of age; however mild to moderate redness and swelling occurred at higher frequencies in children than previously reported in C4591001. Systemic events most commonly included fatigue, headache, and muscle pain, and generally increased in frequency and/or severity with increasing dose number; these were typically milder and less frequent than previously reported in Study C4591001.

The observed AE profile in this study did not suggest any new safety concerns for BNT162b2 vaccination in children 5 to <12 years of age. Most reported AEs occurred from Dose 1 to 1 month after Dose 2 and reflected reactogenicity events occurring post-vaccination with BNT162b2, or other unrelated infections or injuries that are expected to be observed in a pediatric general population with similar frequencies in the BNT162b2 and placebo groups.

A total of 3 unrelated SAEs were reported in 2 participants (1 participant in the BNT162b2 group had an unrelated SAE of limb fracture, and 1 participant in the placebo group had 2 unrelated SAEs of pancreatitis and abdominal pain noted as occurring 'post-injury'), and no deaths or withdrawals due to AEs were reported as of the data cutoff date (06 September 2021), which represents at least 2 months of follow-up after Dose 2.

As of the data cutoff date, there were very few AEs of clinical interest reported in children 5 to <12 years of age, and no cases of myocarditis/pericarditis were reported. Lymphadenopathy has been identified as related to BNT162b2 in study participants ≥12 years of age and is also observed in children 5 to <12 years of age, with all events reported as mild. Rashes were more frequent in the BNT162b2 group than the placebo group, but very few (n=4) were considered as related to vaccination and these were characterized as mild and self-limited.

Overall, the safety and tolerability profile of BNT162b2 10 µg when administered as a 2-dose primary series 3 weeks apart to approximately 1500 children 5 to <12 years of age, who had at least 2 months of follow-up since receiving their second dose, reflects age-appropriate events that are consistent with a pediatric general population and the known reactogenicity profile of BNT162b2. Subgroup analyses of safety endpoints suggested no meaningful differences in safety profile based on participant demographics or baseline SARS-CoV-2 status.

2.7.4.3. Safety in Special Groups and Situations

2.7.4.3.1. Intrinsic Factors

2.7.4.3.1.1. Geriatric Use

Clinical studies of BNT162b2 (30 µg) include participants ≥65 years of age whose data contribute to overall assessment of safety and efficacy. The clinical data have demonstrated a predominantly mild reactogenicity profile in older adults, overall and compared with younger adults. This is coupled with evidence of robust immune response following the 2-dose vaccination regimen, and overwhelming efficacy comparable to younger adults (>90%).

2.7.4.3.1.2. Pediatric Use

Further study of pediatric use of the vaccine and/or immunobridging study will be undertaken to characterize the vaccine response in children <5 years of age.

2.7.4.3.1.3. Use in Immunocompromised Individuals

Individuals who are immunocompromised or taking immunosuppressive therapy at the time of vaccine administration may have diminished response to immunization. Study C4591001 included enrollment of individuals with medical history of immunocompromised condition or immunosuppressive therapy. There are limited data on the safety of the vaccine in this patient population at the time of this application.

A third dose of BNT162b2 30 μg may be given to individuals ≥12 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

2.7.4.3.2. Extrinsic Factors

Not applicable.

2.7.4.3.3. Drug Interactions

Refer to Module 5.3.5.1 C4591007 Protocol Section 6.5 for information regarding prior and concomitant vaccines, medications, and procedures that were allowed or prohibited.

2.7.4.3.4. Use in Pregnancy and Lactation

Individuals who were pregnant or breastfeeding were not eligible to participate in Study C4591007 or Study C4591001.

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In a DART study, no vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for vaccination with BNT162b2 and any potential adverse effects on the breastfed child from BNT162b2 or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

2.7.4.3.5. Overdose

In Study C4591007, any dose of study intervention greater than 1 dose of study intervention within a 24-hour time period was considered an overdose. No overdoses of BNT162b2 were reported in participants 5 to <12 years of age in Study C4591007.

2.7.4.3.6. Drug Abuse

Not applicable.

2.7.4.3.7. Withdrawal and Rebound

Not applicable.

2.7.4.3.8. Effects on Ability to Drive or Operate Machinery or Impairment of Mental Ability

BNT162b2 has no or negligible influence on the ability to drive and use machines.

2.7.4.4. Post-Marketing Data

Post-authorization safety data are continually monitored by Pfizer and BioNTech for pharmacovigilance and risk management purposes, including weekly reviews of the Safety database. Pfizer's safety database contains AEs reported spontaneously to Pfizer, cases reported by the health authorities, cases published in the medical literature, cases from Pfizer-sponsored marketing programs, non-interventional studies, and cases of SAEs reported from clinical studies regardless of causality assessment.

Post-authorization safety data are communicated in the following contexts:

- The first Periodic Safety Update Report covering the period of 19 December 2020 through 18 June 2021 that evaluated safety data and signal detection, and concluded:

  "Risks have been evaluated in the context of the benefits of the vaccine. Based on the available safety and efficacy/effectiveness data from the reporting interval for BNT162b2, the benefit-risk profile of BNT162b2 remains favourable."

- Post-authorization Summary Monthly Safety Reports (SMSRs) that include safety events reported from countries in which BNT162b2 is authorized or conditionally approved and are submitted monthly to regulatory authorities. These monthly reports provide information on safety signals and risks determined from signal detection activity.

Myocarditis/pericarditis is considered an important identified risk of the vaccine in the US Pharmacovigilance Plan and the EU Risk Management Plan; however, the low incidence and favorable prognosis of these events compared to the known risks of COVID-19, including COVID-19 associated myocarditis, support a positive benefit/risk profile for this vaccine in the 5 to <12 years of age group.

Overall, review of the post-authorization safety data has continued to confirm the overall favorable risk-benefit assessment of the vaccine for individuals ≥12 years of age.

2.7.4.5. Overall Conclusions

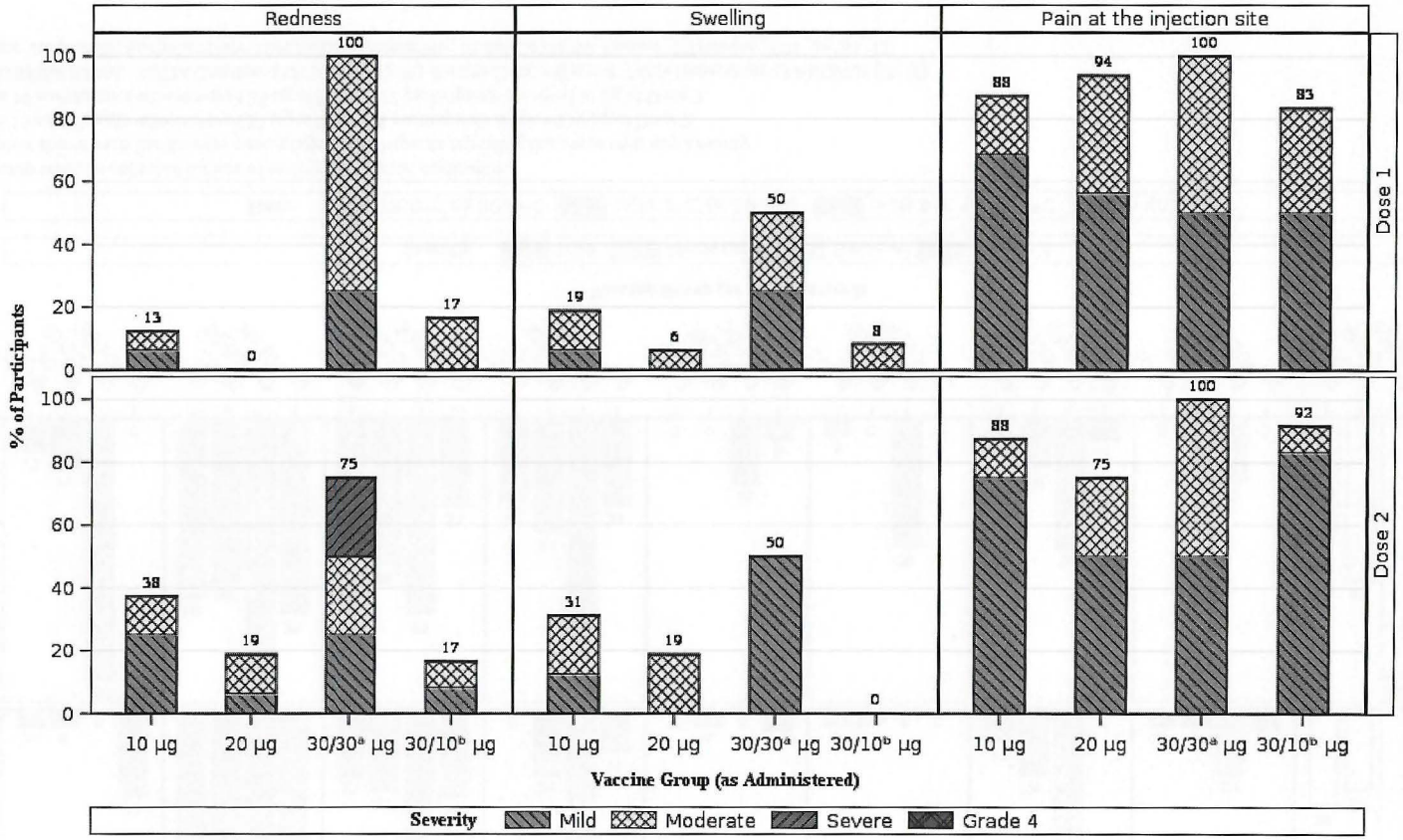
Phase 1 safety and immunogenicity across BNT162b2 dose levels of 10, 20, and 30 µg led to selection of the 10-µg dose level for Phase 2/3 evaluation in children 5 to <12 years of age, based on increased incidence of reactogenicity observed with increasing dose level and comparably high immunogenicity observed at both (10 and 20 µg) dose levels. In approximately 1500 children 5 to <12 years of age who received BNT162b2 10-µg, the 2-dose regimen was safe and well-tolerated and highly immunogenic.

2.7.4.6. APPENDICES

2.7.4.6.1. Appendix A: Phase 1 Study C4591007, Post-text Figures

2.7.4.6.1.1. Reactogenicity (Phase 1 Study C4591007, Post-text Figures)

Figure 3. Participants Reporting Local Reactions, by Maximum Severity, Within 7 Days After Each Dose - Phase 1 - 5 to <12 Years of Age - Safety Population



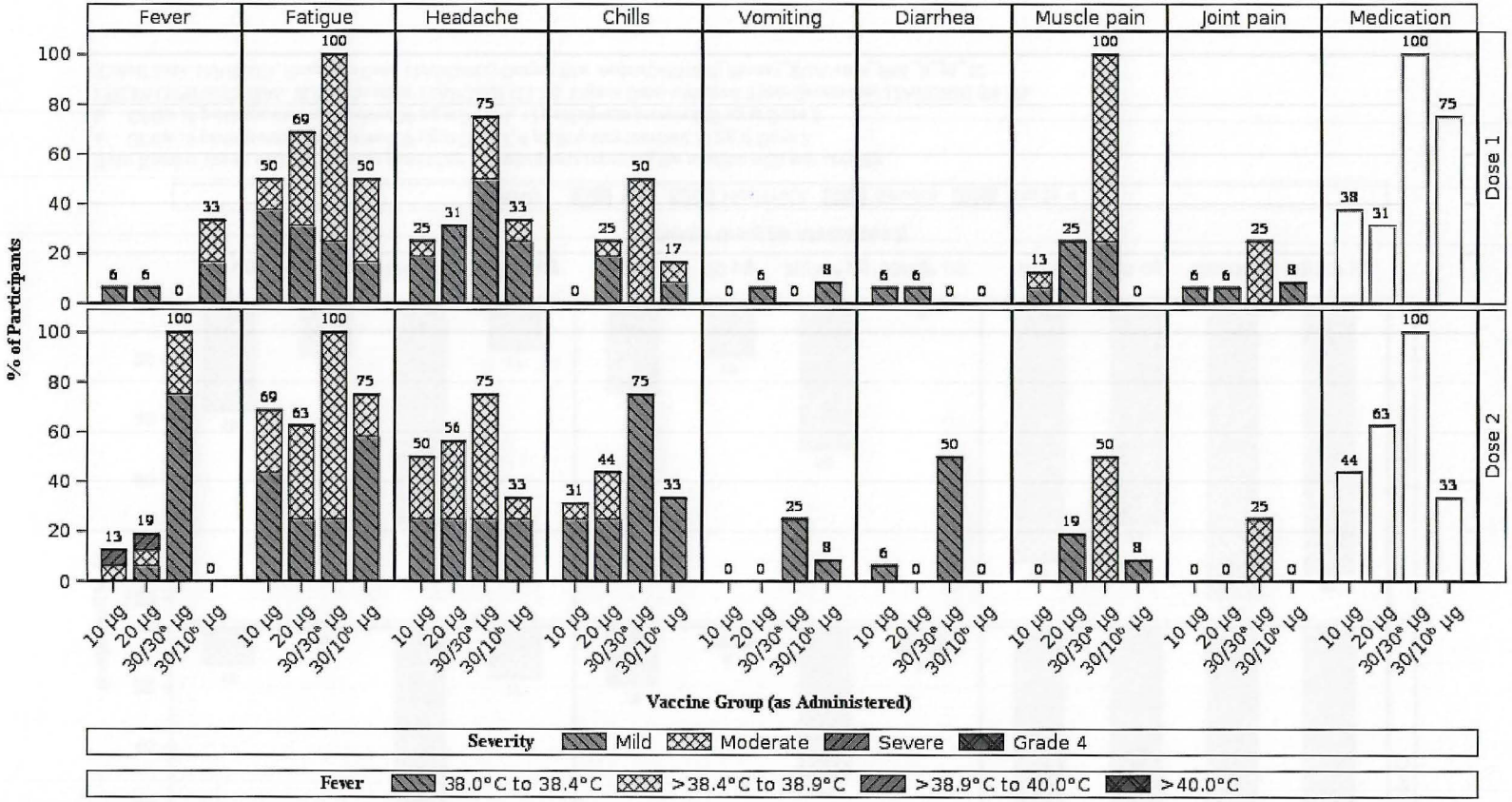
Note: Number above each bar denotes percentage of participants reporting the reaction with any severity.

a. Of the 16 participants who received 30 µg at Dose 1, 4 participants received 30 µg at Dose 2.

b. Of the 16 participants who received 30 µg at Dose 1, 12 participants received 10 µg at Dose 2.

PFIZER CONFIDENTIAL SDTM Creation: 11AUG2021 (13:36) Source Data: adfacevd Table Generation: 17AUG2021 (06:18)
(Cutoff Date: 16JUL2021, Snapshot Date: 11AUG2021) Output File: /nda3/C4591007_Phase1_EUA/adce_f001_lr_p1_12

Figure 4. Participants Reporting Systemic Events, by Maximum Severity, Within 7 Days After Each Dose - Phase 1 - 5 to <12 Years of Age - Safety Population



Note: Severity was not collected for use of antipyretic or pain medication.
Note: Number above each bar denotes percentage of participants reporting the event with any severity.
a. Of the 16 participants who received 30 µg at Dose 1, 4 participants received 30 µg at Dose 2.
b. Of the 16 participants who received 30 µg at Dose 1, 12 participants received 10 µg at Dose 2.
PFIZER CONFIDENTIAL SDTM Creation: 11AUG2021 (13:36) Source Data: adfacevd Table Generation: 17AUG2021 (06:18)
(Cutoff Date: 16JUL2021, Snapshot Date: 11AUG2021) Output File: /nda3/C4591007_Phase1_EUA/adce_f001_se_p1_12

2.7.4.6.2. Appendix B: Phase 2/3 Study C4591007, Post-text Tables and Figures

2.7.4.6.2.1. Disposition, Exposure, Safety Datasets Analyzed and Study Population Characteristics (Phase 2/3 Study C4591007, Post-text Tables)

Table 7. Disposition of All Randomized Participants – Phase 2/3 – 5 to <12 Years of Age

	Vaccine Group (as Randomized)		
	BNT162b2 10 µg (N^a=1528) n^b (%)	Placebo (N^a=757) n^b (%)	Total (N^a=2285) n^b (%)
Randomized	1528 (100.0)	757 (100.0)	2285 (100.0)
Not vaccinated	11 (0.7)	6 (0.8)	17 (0.7)
Vaccinated	1517 (99.3)	751 (99.2)	2268 (99.3)
Dose 1	1517 (99.3)	751 (99.2)	2268 (99.3)
Dose 2	1514 (99.1)	747 (98.7)	2261 (98.9)
Completed 1-month post–Dose 2 visit (vaccination period)	1510 (98.8)	746 (98.5)	2256 (98.7)
Discontinued from vaccination period but continued in the study	2 (0.1)	2 (0.3)	4 (0.2)
Discontinued after Dose 1 and before Dose 2	2 (0.1)	2 (0.3)	4 (0.2)
Discontinued after Dose 2 and before 1-month post–Dose 2 visit	0	0	0
Reason for discontinuation from vaccination period			
Withdrawal by participant	1 (0.1)	2 (0.3)	3 (0.1)
Withdrawal by parent/guardian	1 (0.1)	0	1 (0.0)
Withdrawn from the study	5 (0.3)	6 (0.8)	11 (0.5)
Withdrawn after Dose 1 and before Dose 2	1 (0.1)	2 (0.3)	3 (0.1)
Withdrawn after Dose 2 and before 1-month post–Dose 2 visit	2 (0.1)	2 (0.3)	4 (0.2)
Withdrawn after 1-month post–Dose 2 visit	2 (0.1)	2 (0.3)	4 (0.2)
Reason for withdrawal from the study			
Other	1 (0.1)	0	1 (0.0)
Withdrawal by participant	0	2 (0.3)	2 (0.1)
Withdrawal by parent/guardian	4 (0.3)	4 (0.5)	8 (0.4)

a. N = number of randomized participants in the specified group, or the total sample. This value is the denominator for the percentage calculations.
b. n = Number of participants with the specified characteristic.
PFIZER CONFIDENTIAL SDTM Creation: 13SEP2021 (17:17) Source Data: adds Table Generation: 15SEP2021 (11:59)
(Cutoff Date: 06SEP2021, Snapshot Date: 13SEP2021) Output File: ./nda2_ubped/C4591007_P23_EUA/adds_s002_disp_p2_12

Table 8. Vaccine as Administered – Phase 2/3 – 5 to <12 Years of Age – All Randomized Participants

	Vaccine Group (as Randomized)	
Vaccine (as Administered)	BNT162b2 10 µg (N[a]=1528) n[b] (%)	Placebo (N[a]=757) n[b] (%)
Vaccinated	1517 (99.3)	751 (99.2)
Not vaccinated	11 (0.7)	6 (0.8)
Dose 1		
BNT162b2 10 µg	1517 (99.3)	1 (0.1)
Placebo	0	750 (99.1)
Dose 2		
BNT162b2 10 µg	1514 (99.1)	1 (0.1)
Placebo	0	746 (98.5)

a. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of participants with the specified characteristic.
PFIZER CONFIDENTIAL SDTM Creation: 13SEP2021 (23:25) Source Data: adsl Table Generation: 16SEP2021 (06:59) (Cutoff Date: 06SEP2021, Snapshot Date: 13SEP2021) Output File: ./nda2 ubped/C4591007 P23 EUA/advx s002 adm p2 12

Table 9. Vaccine Administration Timing – Phase 2/3 – 5 to <12 Years of Age – All Randomized Participants

	Vaccine Group (as Randomized)	
	BNT162b2 10 µg (N[a]=1528) n[b] (%)	Placebo (N[a]=757) n[b] (%)
Randomized	1528 (100.0)	757 (100.0)
Not vaccinated	11 (0.7)	6 (0.8)
Dose 1	1517 (99.3)	751 (99.2)
Dose 2[c]	1514 (99.1)	747 (98.7)
Protocol defined window		
<19 Days	10 (0.7)	3 (0.4)
19-23 Days[d]	1443 (94.4)	715 (94.5)
>23 Days	61 (4.0)	29 (3.8)
Weekly intervals		

Table 9. Vaccine Administration Timing – Phase 2/3 – 5 to <12 Years of Age – All Randomized Participants

	Vaccine Group (as Randomized)	
	BNT162b2 10 µg (N[a]=1528) n[b] (%)	Placebo (N[a]=757) n[b] (%)
<14 Days	0	0
14-20 Days	349 (22.8)	186 (24.6)
21-27 Days	1124 (73.6)	540 (71.3)
28-34 Days	26 (1.7)	12 (1.6)
35-41 Days	8 (0.5)	5 (0.7)
42-48 Days	2 (0.1)	1 (0.1)
49-55 Days	3 (0.2)	3 (0.4)
>55 Days	2 (0.1)	0

a. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of participants with the specified characteristic.
c. Days calculated since Dose 1.
d. Protocol-specified time frame.
PFIZER CONFIDENTIAL SDTM Creation: 13SEP2021 (23:25) Source Data: adsl Table Generation: 15SEP2021 (11:51) (Cutoff Date: 06SEP2021, Snapshot Date: 13SEP2021) Output File: ./nda2 ubped/C4591007 P23 EUA/advx s002 time p2 12

Table 10. Safety Population – Phase 2/3 – 5 to <12 Years of Age

	Vaccine Group (as Administered)		
	BNT162b2 10 µg n[a]	Placebo n[a]	Total n[a] (%)
Randomized[b]			2285
Vaccinated	1518	750	2268 (99.3)
Safety population	1518	750	2268 (99.3)
HIV-positive	0	0	0
Excluded from safety population			17 (0.7)
Reason for exclusion			
Participant did not receive study vaccine			17 (0.7)

Table 10. Safety Population – Phase 2/3 – 5 to <12 Years of Age

	Vaccine Group (as Administered)		
	BNT162b2 10 µg n[a]	Placebo n[a]	Total n[a] (%)

Abbreviation: HIV = human immunodeficiency virus.
a. n = Number of participants with the specified characteristic, or the total sample.
b. This value is the denominator for the percentage calculations.
PFIZER CONFIDENTIAL SDTM Creation: 13SEP2021 (23:25) Source Data: adsl Table Generation: 16SEP2021 (06:12) (Cutoff Date: 06SEP2021, Snapshot Date: 13SEP2021) Output File: ./nda2_ubped/C4591007_P23_EUA/adsl_s008_saf_pop_p2_12

Table 11. Follow-up Time After Dose 2 - Phase 2/3 - 5 to <12 Years of Age - Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 10 µg (N[a]=1518) n[b] (%)	Placebo (N[a]=750) n[b] (%)	Total (N[a]=2268) n[b] (%)
Time from Dose 2 to cutoff date			
<1 Month	7 (0.5)	4 (0.5)	11 (0.5)
≥1 Month to <2 months	67 (4.4)	32 (4.3)	99 (4.4)
≥2 Months to <3 months	1444 (95.1)	714 (95.2)	2158 (95.1)
≥3 Months	0	0	0

Note: Follow-up time was calculated from Dose 2 to the cutoff date or withdrawal date or the date of unblinding (per protocol), whichever date was earlier.
a. N = number of participants in the specified group, or the total sample. This value is the denominator for the percentage calculations.
b. n = Number of participants with the specified characteristic.
PFIZER CONFIDENTIAL SDTM Creation: 13SEP2021 (23:25) Source Data: adsl Table Generation: 15SEP2021 (11:51) (Cutoff Date: 06SEP2021, Snapshot Date: 13SEP2021) Output File: ./nda2_ubped/C4591007_P23_EUA/adsl_s005_fup_time_12

Table 12. Demographic Characteristics – Phase 2/3 – 5 to <12 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 10 µg (N[a]=1518) n[b] (%)	Placebo (N[a]=750) n[b] (%)	Total (N[a]=2268) n[b] (%)
Sex			
Male	799 (52.6)	383 (51.1)	1182 (52.1)
Female	719 (47.4)	367 (48.9)	1086 (47.9)
Race			
White	1204 (79.3)	586 (78.1)	1790 (78.9)
Black or African American	89 (5.9)	58 (7.7)	147 (6.5)
American Indian or Alaska Native	12 (0.8)	3 (0.4)	15 (0.7)
Asian	90 (5.9)	47 (6.3)	137 (6.0)
Native Hawaiian or other Pacific Islander	5 (0.3)	0	5 (0.2)
Multiracial	109 (7.2)	49 (6.5)	158 (7.0)
Not reported	9 (0.6)	7 (0.9)	16 (0.7)
Ethnicity			
Hispanic/Latino	319 (21.0)	159 (21.2)	478 (21.1)
Non-Hispanic/Non-Latino	1196 (78.8)	591 (78.8)	1787 (78.8)
Not reported	3 (0.2)	0	3 (0.1)
Age at vaccination (years)			
Mean (SD)	8.2 (1.93)	8.1 (1.97)	8.2 (1.94)
Median	8.0	8.0	8.0
Min, max	(5, 11)	(5, 11)	(5, 11)
Obese[c]			
Yes	174 (11.5)	92 (12.3)	266 (11.7)
No	1343 (88.5)	658 (87.7)	2001 (88.2)
Missing	1 (0.1)	0	1 (0.0)
Baseline SARS-CoV-2 status			
Positive[d]	133 (8.8)	65 (8.7)	198 (8.7)
Negative[e]	1385 (91.2)	685 (91.3)	2070 (91.3)
Comorbidities[f]			
Yes	312 (20.6)	152 (20.3)	464 (20.5)
No	1206 (79.4)	598 (79.7)	1804 (79.5)

Table 12. Demographic Characteristics – Phase 2/3 – 5 to <12 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 10 µg (N[a]=1518) n[b] (%)	Placebo (N[a]=750) n[b] (%)	Total (N[a]=2268) n[b] (%)

Abbreviations: BMI = body mass index; COVID-19 = coronavirus disease 2019; MMWR = Morbidity and Mortality Weekly Report; NAAT = nucleic acid amplification test; N-binding = SARS-CoV-2 nucleoprotein-binding; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
a. N = number of participants in the specified group, or the total sample. This value is the denominator for the percentage calculations.
b. n = Number of participants with the specified characteristic.
c. Obese is defined as a body mass index (BMI) at or above the 95th percentile according to the growth chart. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev htm.
d. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
e. Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19
f. Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as participants who had at least one of the prespecified comorbidities based on MMWR 69(32);1081-1088 and/or obesity (BMI ≥ 95th percentile).
PFIZER CONFIDENTIAL SDTM Creation: 13SEP2021 (23:25) Source Data: adsl Table Generation: 15SEP2021 (11:51) (Cutoff Date: 06SEP2021, Snapshot Date: 13SEP2021) Output File: ./nda2_ubped/C4591007_P23_EUA/adsl_s005_demo_p2_12

Table 13. Baseline MMWR Comorbidities – Phase 2/3 – 5 to <12 Years of Age – Safety Population

Comorbidity Category Preferred Term	Vaccine Group (as Administered)	
	BNT162b2 10 µg (N[a]=1518) n[b] (%)	Placebo (N[a]=750) n[b] (%)
Participants with any baseline MMWR comorbidity[c]	168 (11.1)	71 (9.5)
Asthma	119 (7.8)	62 (8.3)
Asthma	101 (6.7)	52 (6.9)
Asthma exercise induced	4 (0.3)	2 (0.3)
Bronchial hyperreactivity	11 (0.7)	8 (1.1)

Table 13. Baseline MMWR Comorbidities – Phase 2/3 – 5 to <12 Years of Age – Safety Population

Comorbidity Category Preferred Term	Vaccine Group (as Administered) BNT162b2 10 µg (N[a]=1518) n[b] (%)	Vaccine Group (as Administered) Placebo (N[a]=750) n[b] (%)
Bronchospasm	0	1 (0.1)
Childhood asthma	1 (0.1)	1 (0.1)
Wheezing	2 (0.1)	1 (0.1)
Blood disorders	1 (0.1)	1 (0.1)
Thalassaemia alpha	1 (0.1)	1 (0.1)
Cardiovascular disease	8 (0.5)	0
Aortic valve incompetence	1 (0.1)	0
Atrioventricular block first degree	1 (0.1)	0
Congestive cardiomyopathy	1 (0.1)	0
Mitral valve incompetence	1 (0.1)	0
Pulmonary valve disease	1 (0.1)	0
Pulmonary valve stenosis	1 (0.1)	0
Supraventricular extrasystoles	1 (0.1)	0
Supraventricular tachycardia	1 (0.1)	0
Tricuspid valve incompetence	1 (0.1)	0
Wolff-Parkinson-White syndrome	1 (0.1)	0
Chronic lung disease	1 (0.1)	1 (0.1)
Cystic fibrosis	1 (0.1)	0
Primary ciliary dyskinesia	0	1 (0.1)
Chronic metabolic disease	2 (0.1)	0
Hypercholesterolaemia	1 (0.1)	0
Insulin resistance	1 (0.1)	0
Congenital heart disease	15 (1.0)	5 (0.7)
Atrial septal defect	4 (0.3)	1 (0.1)
Bicuspid aortic valve	3 (0.2)	1 (0.1)
Coarctation of the aorta	1 (0.1)	0
Congenital pulmonary valve atresia	1 (0.1)	0
Patent ductus arteriosus	3 (0.2)	0
Pulmonary valve stenosis congenital	0	1 (0.1)
Transposition of the great vessels	1 (0.1)	0
Ventricular septal defect	3 (0.2)	2 (0.3)

Table 13. Baseline MMWR Comorbidities – Phase 2/3 – 5 to <12 Years of Age – Safety Population

Comorbidity Category Preferred Term	Vaccine Group (as Administered) BNT162b2 10 µg (N[a]=1518) n[b] (%)	Vaccine Group (as Administered) Placebo (N[a]=750) n[b] (%)
Diabetes mellitus	2 (0.1)	1 (0.1)
Diabetic ketoacidosis	1 (0.1)	0
Type 1 diabetes mellitus	2 (0.1)	1 (0.1)
Feeding tube dependent	2 (0.1)	0
Gastrostomy	2 (0.1)	0
Immunocompromised condition	1 (0.1)	0
Acute lymphocytic leukaemia	1 (0.1)	0
Neurologic disorder	19 (1.3)	3 (0.4)
Benign rolandic epilepsy	1 (0.1)	0
Cerebral cyst	1 (0.1)	0
Cerebral palsy	1 (0.1)	0
Craniocerebral injury	1 (0.1)	0
Epilepsy	5 (0.3)	0
Febrile convulsion	7 (0.5)	1 (0.1)
Frontal lobe epilepsy	1 (0.1)	0
Partial seizures	1 (0.1)	0
Petit mal epilepsy	0	1 (0.1)
Seizure	3 (0.2)	0
Spinal cord lipoma	0	1 (0.1)
Tethered cord syndrome	1 (0.1)	0
Sickle cell disease	1 (0.1)	0
Sickle cell disease	1 (0.1)	0

Table 13. Baseline MMWR Comorbidities – Phase 2/3 – 5 to <12 Years of Age – Safety Population

Comorbidity Category Preferred Term	Vaccine Group (as Administered) BNT162b2 10 µg (N[a]=1518) n[b] (%)	Vaccine Group (as Administered) Placebo (N[a]=750) n[b] (%)

Abbreviations: COVID-19 = coronavirus disease 2019; MMWR = Morbidity and Mortality Weekly Report.
Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of participants with the specified characteristic. Participants with multiple occurrences of the same preferred term are counted only once. For "Participants with any baseline MMWR comorbidity," n = number of participants reporting at least 1 occurrence of any baseline comorbidity.
c. Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as participants who had at least one of the prespecified comorbidities based on MMWR 69(32);1081-1088.
PFIZER CONFIDENTIAL SDTM Creation: 13SEP2021 (17:20) Source Data: admh Table Generation: 15SEP2021 (11:46)
(Cutoff Date: 06SEP2021, Snapshot Date: 13SEP2021) Output File:
./nda2 ubped/C4591007 P23 EUA/admh s002 com p2 12

Table 14. Concomitant Vaccines Received After Dose 1 – Phase 2/3 – 5 to <12 Years of Age – Safety Population

Vaccine[b]	Vaccine Group (as Administered) BNT162b2 10 µg (N[a]=1518) n[c] (%)	Vaccine Group (as Administered) Placebo (N[a]=750) n[c] (%)	Total (N[a]=2268) n[c] (%)
Any concomitant vaccine	10 (0.7)	6 (0.8)	16 (0.7)
DIPHTHERIA VACCINE TOXOID;PERTUSSIS VACCINE ACELLULAR 5-COMPONENT;TETANUS VACCINE TOXOID	0	1 (0.1)	1 (0.0)
DIPHTHERIA VACCINE TOXOID;PERTUSSIS VACCINE ACELLULAR;TETANUS VACCINE TOXOID	5 (0.3)	3 (0.4)	8 (0.4)
DIPHTHERIA VACCINE TOXOID;TETANUS VACCINE TOXOID	0	1 (0.1)	1 (0.0)
HPV VACCINE	3 (0.2)	4 (0.5)	7 (0.3)
HPV VACCINE VLP RL1 4V (YEAST)	1 (0.1)	1 (0.1)	2 (0.1)
MENINGOCOCCAL VACCINE	2 (0.1)	0	2 (0.1)
MENINGOCOCCAL VACCINE A/C/Y/W	1 (0.1)	2 (0.3)	3 (0.1)
MENINGOCOCCAL VACCINE A/C/Y/W CONJ (DIP TOX)	1 (0.1)	0	1 (0.0)

Table 14. Concomitant Vaccines Received After Dose 1 – Phase 2/3 – 5 to <12 Years of Age – Safety Population

Vaccine[b]	Vaccine Group (as Administered)		
	BNT162b2 10 µg (N[a]=1518) n[c] (%)	Placebo (N[a]=750) n[c] (%)	Total (N[a]=2268) n[c] (%)
TICK-BORNE ENCEPHALITIS VACCINE	1 (0.1)	0	1 (0.0)
TICK-BORNE ENCEPHALITIS VACCINE INACT (K23)	2 (0.1)	0	2 (0.1)

Note: WHODDG B3 v202103 coding dictionary applied.
a. N = number of participants in the specified group, or the total sample. This value is the denominator for the percentage calculations.
b. Participants are counted only once for each preferred term.
c. n = Number of participants with the specified characteristic. For "any concomitant vaccine," n = number of participants received at least one concomitant vaccine.
PFIZER CONFIDENTIAL SDTM Creation: 13SEP2021 (17:17) Source Data: adcm Table Generation: 15SEP2021 (11:46)
(Cutoff Date: 06SEP2021, Snapshot Date: 13SEP2021) Output File:
./nda2 ubped/C4591007 P23 EUA/adcm s001 p2 12

2.7.4.7. REFERENCES

1 Food and Drug Administration (FDA). Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trial. Guidance for Industry. Sept 2007. Available at: https://www.fda.gov/media/73679/download.

2 Agresti A. Introduction: distributions and inference for categorical data. In: Agresti A, ed. Categorical data analysis. 2nd ed. Hoboken, NJ: John Wiley & Sons; 2002:1-35.

3 Kim L, Whitaker M, O'Halloran A, et al. Hospitalization Rates and Characteristics of Children Aged <18 Years Hospitalized with Laboratory-Confirmed COVID-19 - COVID-NET, 14 States, March 1-July 25, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(32):1081-88.

Document Approval Record

Document Name:	COVID-19 Vaccine 2.7.4 SCS MAA Extension - Pediatric (5 to <12 years) Oct 2021
Document Title:	COVID-19 Vaccine 2.7.4 SCS MAA Extension - Pediatric (5 to <12 years) Oct 2021

Signed By:	Date(GMT)	Signing Capacity
PPD	05-Oct-2021 13:34:21	Business Line Approver