Clinical trial results:
A master phase 1/2/3 protocol to investigate the safety, tolerability, and immunogenicity of variant- adapted BNT162b2 RNA-based vaccine candidates(s) in healthy children

Summary

EudraCT number	2024-000001-33
Trial protocol	Outside EU/EEA
Global end of trial date	

Results information

Result version number	v1
This version publication date	06 March 2024
First version publication date	06 March 2024

Trial information

Trial identification

Sponsor protocol code	C4591048

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05543616
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BioNTech SE
Sponsor organisation address	An der Goldgrube 12, Mainz, Germany, 55131
Public contact	BioNTech SE, BioNTech clinical trials patient information, +49 6131 90840, patients@biontech.de
Scientific contact	BioNTech SE, BioNTech clinical trials patient information, +49 6131 90840, patients@biontech.de

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002861-PIP02-20
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	25 October 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

SSD: To describe the safety and tolerability profiles of prophylactic bivalent BNT162b2 given as a third or fourth dose in participants >=5 to <12 years of age. To descriptively compare the anti–Omicron BA.4/BA.5 immune response between participants >=5 to <12 years of age who received 3 prior doses of BNT162b2 10 microgram (µg) and received bivalent BNT162b2 as a fourth dose in Group 2 and Study C4591007 Phase 2/3 participants >=5 to <12 years of age who received 3 doses of BNT162b2 10 µg.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 September 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 134
Worldwide total number of subjects	134
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	134
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 136 participants were randomized in sub-study D(SSD) of which 2 participants were not vaccinated and 134 participants received at least 1 dose of vaccination.Data is reported at study completion date for SSD.PCD for SS A, B, C and E have not been reached and data collection is still ongoing,hence no data is reported for SS A, B, C and E.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: 2 prior doses of BNT162b2

Arm description:

Participants aged 5 to11 years who had received two prior doses of BNT162b2 10 microgram (mcg) 90 to 240 days before enrollment in the study were included. Participants received a single dose of BNT162b2 10 mcg via intramuscular route on Day 1 of the study.

Arm type	Experimental
Investigational medicinal product name	Bivalent BNT162b2 (original/Omicron BA.4/BA.5)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

10 micrograms (original BNT162b2 5 mcg and BNT162b2 Omicron [B.1.1.529 sublineage BA.4/BA.5] 5 mcg) administered intramuscularly.

Arm title	Group 2: 3 prior doses of BNT162b2

Arm description:

Participants aged 5 to11 years who had received three prior doses of BNT162b2 10 mcg 90 to 240 days before enrollment in the study were included. Participants received a single dose of BNT162b2 10 mcg via intramuscular route on Day 1 of the study.

Arm type	Experimental
Investigational medicinal product name	Bivalent BNT162b2 (original/Omicron BA.4/BA.5)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

10 micrograms (original BNT162b2 5 mcg and BNT162b2 Omicron [B.1.1.529 sublineage BA.4/BA.5] 5 mcg) administered intramuscularly.

Arm title	Group 3: Participants from study C4591007 Phase 1

Arm description:

Participants from C4591007 (NCT04816643) phase 1 trial, aged 5 to 11 years who had received three prior doses of BNT162b2 10 mcg at least 90 days before enrollment in the study were included. Participants received a single dose of BNT162b2 10 mcg via intramuscular route on Day 1 of the study.

Arm type	Experimental

Investigational medicinal product name	Bivalent BNT162b2 (original/Omicron BA.4/BA.5)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

10 micrograms (original BNT162b2 5 mcg and BNT162b2 Omicron [B.1.1.529 sublineage BA.4/BA.5] 5 mcg) administered intramuscularly.

Number of subjects in period 1	Group 1: 2 prior doses of BNT162b2	Group 2: 3 prior doses of BNT162b2	Group 3: Participants from study C4591007 Phase 1
Started	2	113	19
Completed	2	111	19
Not completed	0	2	0
Consent withdrawn by subject	-	1	-
Withdrawal by parents/guardian	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: 2 prior doses of BNT162b2
Reporting group description:	
Participants aged 5 to11 years who had received two prior doses of BNT162b2 10 microgram (mcg) 90 to 240 days before enrollment in the study were included. Participants received a single dose of BNT162b2 10 mcg via intramuscular route on Day 1 of the study.	
Reporting group title	Group 2: 3 prior doses of BNT162b2
Reporting group description:	
Participants aged 5 to11 years who had received three prior doses of BNT162b2 10 mcg 90 to 240 days before enrollment in the study were included. Participants received a single dose of BNT162b2 10 mcg via intramuscular route on Day 1 of the study.	
Reporting group title	Group 3: Participants from study C4591007 Phase 1
Reporting group description:	
Participants from C4591007 (NCT04816643) phase 1 trial, aged 5 to 11 years who had received three prior doses of BNT162b2 10 mcg at least 90 days before enrollment in the study were included. Participants received a single dose of BNT162b2 10 mcg via intramuscular route on Day 1 of the study.	

Reporting group values	Group 1: 2 prior doses of BNT162b2	Group 2: 3 prior doses of BNT162b2	Group 3: Participants from study C4591007 Phase 1
Number of subjects	2	113	19
Age Categorical Units: Participants			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	2	113	19
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	5.0	8.6	8.4
standard deviation	± 0.00	± 1.65	± 2.19
Gender Categorical Units: Participants			
Female	0	56	11
Male	2	57	8
Race Units: Subjects			
White	2	66	12
Black or African American	0	9	2
Asian	0	13	2
Multiracial	0	22	3
Not reported	0	3	0

Native Hawaiian or other Pacific Islander	0	0	0
Ethinicity Units: Subjects			
Hispanic/Latino	0	23	0
Non-Hispanic/non-Latino	2	90	19

Reporting group values	Total		
Number of subjects	134		
Age Categorical Units: Participants			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	134		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical Units: Participants			
Female	67		
Male	67		
Race Units: Subjects			
White	80		
Black or African American	11		
Asian	15		
Multiracial	25		
Not reported	3		
Native Hawaiian or other Pacific Islander	0		
Ethinicity Units: Subjects			
Hispanic/Latino	23		
Non-Hispanic/non-Latino	111		

Subject analysis sets	
Subject analysis set title	Historical cohort: C4591007 BNT162b2 10 µg
Subject analysis set type	Per protocol

Subject analysis set description:

Participants aged >=5 to <12 years from study C4591007 (NCT04816643) who received 3 doses of original BNT162b2 10 mcg were included.

Reporting group values	Historical cohort: C4591007 BNT162b2 10 µg		
Number of subjects	113		
Age Categorical Units: Participants			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	113		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean	8.6		
standard deviation	± 1.65		
Gender Categorical Units: Participants			
Female	50		
Male	63		
Race Units: Subjects			
White	91		
Black or African American	4		
Asian	11		
Multiracial	4		
Not reported	1		
Native Hawaiian or other Pacific Islander	2		
Ethinicity Units: Subjects			
Hispanic/Latino	16		
Non-Hispanic/non-Latino	97		

End points

End points reporting groups

Reporting group title	Group 1: 2 prior doses of BNT162b2

Reporting group description:

Participants aged 5 to11 years who had received two prior doses of BNT162b2 10 microgram (mcg) 90 to 240 days before enrollment in the study were included. Participants received a single dose of BNT162b2 10 mcg via intramuscular route on Day 1 of the study.

Reporting group title	Group 2: 3 prior doses of BNT162b2

Reporting group description:

Participants aged 5 to11 years who had received three prior doses of BNT162b2 10 mcg 90 to 240 days before enrollment in the study were included. Participants received a single dose of BNT162b2 10 mcg via intramuscular route on Day 1 of the study.

Reporting group title	Group 3: Participants from study C4591007 Phase 1

Reporting group description:

Participants from C4591007 (NCT04816643) phase 1 trial, aged 5 to 11 years who had received three prior doses of BNT162b2 10 mcg at least 90 days before enrollment in the study were included. Participants received a single dose of BNT162b2 10 mcg via intramuscular route on Day 1 of the study.

Subject analysis set title	Historical cohort: C4591007 BNT162b2 10 µg
Subject analysis set type	Per protocol

Subject analysis set description:

Participants aged >=5 to <12 years from study C4591007 (NCT04816643) who received 3 doses of original BNT162b2 10 mcg were included.

Primary: SSD: Percentage of Participants With Local Reactions Within 7 Days After Study Vaccination

End point title	SSD: Percentage of Participants With Local Reactions Within 7 Days After Study Vaccination[1]

End point description:

Local reactions recorded by participants/parents/legal guardians in electronic diary(e-diary).Redness&swelling recorded in measuring device units(mdu)converted to centimeter(cm).1 mdu=0.5 cm&graded mild:(greater than[>]0.5 to 2.0cm),moderate:>2.0 to 7.0cm,severe:>7.0 cm,Grade 4(G4): necrosis/exfoliative dermatitis(redness)&necrosis(swelling).Pain at injection site graded mild:did not interfere with daily activity,moderate:interfered with daily activity,severe: prevented daily activity&G4:emergency room[ER]visit/hospitalisation.G4 classified by investigator/medically qualified person.Percentage of participants with local reactions within 7days after study vaccination and associated 2-sided 95% confidence interval(CI) based on Clopper and Pearson method.Safety population=all participants receiving at least 1dose of study intervention.Number of Participants Analysed(N)'= participants evaluable.99999=data could not be generated since it was not part of specified analysis in the protocol.

End point type	Primary

End point timeframe:

Day 1 up to Day 7 after study vaccination

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned for this endpoint.

End point values	Group 1: 2 prior doses of BNT162b2	Group 2: 3 prior doses of BNT162b2	Group 3: Participants from study C4591007 Phase 1	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	111	19	
Units: Percentage of participants				
number (confidence interval 95%)				

Redness: Any	0 (-99999 to 99999)	7.2 (3.2 to 13.7)	10.5 (1.3 to 33.1)	
Redness: Mild	0 (-99999 to 99999)	4.5 (1.5 to 10.2)	10.5 (1.3 to 33.1)	
Redness: Moderate	0 (-99999 to 99999)	2.7 (0.6 to 7.7)	0 (0.0 to 17.6)	
Redness: Severe	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
Redness: Grade 4	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
Swelling: Any	0 (-99999 to 99999)	4.5 (1.5 to 10.2)	10.5 (1.3 to 33.1)	
Swelling: Mild	0 (-99999 to 99999)	0.9 (0.0 to 4.9)	10.5 (1.3 to 33.1)	
Swelling: Moderate	0 (-99999 to 99999)	3.6 (1.0 to 9.0)	0 (0.0 to 17.6)	
Swelling: Severe	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
Swelling: Grade 4	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
Pain at the injection site: Any	0 (-99999 to 99999)	64.0 (54.3 to 72.9)	68.4 (43.4 to 87.4)	
Pain at the injection site: Mild	50.0 (-99999 to 99999)	45.0 (35.6 to 54.8)	52.6 (28.9 to 75.6)	
Pain at the injection site: Moderate	0 (-99999 to 99999)	18.9 (12.1 to 27.5)	15.8 (3.4 to 39.6)	
Pain at the injection site: Severe	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
Pain at the injection site: Grade 4	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	

Statistical analyses

No statistical analyses for this end point

Primary: SSD: Percentage of Participants With Systemic Events Within 7 Days After Study Vaccination

End point title	SSD: Percentage of Participants With Systemic Events Within 7 Days After Study Vaccination[2]

End point description:

Systemic events recorded by participants/parents/legal guardians in e-diary. Fever: oral temperature >= 38.0 degree Celsius(deg C)&categorised as >=38.0-38.4 deg C,>38.4-38.9 deg C,>38.9-40.0 deg C & >40.0 deg C.Fatigue,headache,chills,new/worsened muscle pain&new/worsened joint pain:mild:did not interfere with activity,moderate:some interference with activity&severe: prevented daily routine activity.Vomiting:mild: 1-2 times in 24hours(h),moderate:>2 times in 24h,severe:required intravenous hydration.Diarrhea:mild: 2-3 loose stools in 24h,moderate:4-5 loose stools in 24h&severe:6 or more loose stools in 24h.Except fever,G4=ER visit/hospitalisation.G4 events classified by investigator/medically qualified person. Exact 95% CI based on Clopper & Pearson method.Safety population=all participants receiving at least 1 dose of study intervention.N= participants evaluable for this endpoint.99999=data could not be generated since it was not part of specified analysis in the protocol.

End point type	Primary

End point timeframe:

Day 1 up to Day 7 after study vaccination

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned for this endpoint.

End point values	Group 1: 2 prior doses of BNT162b2	Group 2: 3 prior doses of BNT162b2	Group 3: Participants from study C4591007 Phase 1	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	111	19	
Units: Percentage of participants				
number (confidence interval 95%)				
Fever: Any	0 (-99999 to 99999)	4.5 (1.5 to 10.2)	10.5 (1.3 to 33.1)	
Fever: ≥38.0 to 38.4 deg C	0 (-99999 to 99999)	1.8 (0.2 to 6.4)	0 (0.0 to 17.6)	
Fever: >38.4 to 38.9 deg C	0 (-99999 to 99999)	0.9 (0.0 to 4.9)	5.3 (0.1 to 26.0)	
Fever: >38.9 to 40.0 deg C	0 (-99999 to 99999)	1.8 (0.2 to 6.4)	5.3 (0.1 to 26.0)	
Fever: >40.0 deg C	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
Fatigue: Any	0 (-99999 to 99999)	40.5 (31.3 to 50.3)	57.9 (33.5 to 79.7)	
Fatigue: Mild	0 (-99999 to 99999)	23.4 (15.9 to 32.4)	36.8 (16.3 to 61.6)	
Fatigue: Moderate	0 (-99999 to 99999)	16.2 (9.9 to 24.4)	15.8 (3.4 to 39.6)	
Fatigue: Severe	0 (-99999 to 99999)	0.9 (0.0 to 4.9)	5.3 (0.1 to 26.0)	
Fatigue: Grade 4	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
Headache: Any	0 (-99999 to 99999)	25.2 (17.5 to 34.4)	36.8 (16.3 to 61.6)	
Headache: Mild	0 (-99999 to 99999)	18.0 (11.4 to 26.4)	26.3 (9.1 to 51.2)	
Headache: Moderate	0 (-99999 to 99999)	6.3 (2.6 to 12.6)	10.5 (1.3 to 33.1)	
Headache: Severe	0 (-99999 to 99999)	0.9 (0.0 to 4.9)	0 (0.0 to 17.6)	
Headache: Grade 4	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
Chills: Any	0 (-99999 to 99999)	9.0 (4.4 to 15.9)	10.5 (1.3 to 33.1)	
Chills: Mild	0 (-99999 to 99999)	6.3 (2.6 to 12.6)	10.5 (1.3 to 33.1)	
Chills: Moderate	0 (-99999 to 99999)	2.7 (0.6 to 7.7)	0 (0.0 to 17.6)	
Chills: Severe	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
Chills: Grade 4	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
Vomiting: Any	0 (-99999 to 99999)	3.6 (1.0 to 9.0)	0 (0.0 to 17.6)	
Vomiting: Mild	0 (-99999 to 99999)	3.6 (1.0 to 9.0)	0 (0.0 to 17.6)	
Vomiting: Moderate	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
Vomiting: Severe	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
Vomiting: Grade 4	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
Diarrhea: Any	0 (-99999 to 99999)	3.6 (1.0 to 9.0)	0 (0.0 to 17.6)	

Diarrhea: Mild	0 (-99999 to 99999)	3.6 (1.0 to 9.0)	0 (0.0 to 17.6)	
Diarrhea: Moderate	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
Diarrhea: Severe	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
Diarrhea: Grade 4	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
New or worsened muscle pain: Any	0 (-99999 to 99999)	13.5 (7.8 to 21.3)	21.1 (6.1 to 45.6)	
New or worsened muscle pain: Mild	0 (-99999 to 99999)	7.2 (3.2 to 13.7)	10.5 (1.3 to 33.1)	
New or worsened muscle pain: Moderate	0 (-99999 to 99999)	6.3 (2.6 to 12.6)	10.5 (1.3 to 33.1)	
New or worsened muscle pain: Severe	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
New or worsened muscle pain: Grade 4	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
New or worsened joint pain: Any	0 (-99999 to 99999)	9.0 (4.4 to 15.9)	10.5 (1.3 to 33.1)	
New or worsened joint pain: Mild	0 (-99999 to 99999)	7.2 (3.2 to 13.7)	5.3 (0.1 to 26.0)	
New or worsened joint pain: Moderate	0 (-99999 to 99999)	1.8 (0.2 to 6.4)	5.3 (0.1 to 26.0)	
New or worsened joint pain: Severe	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	
New or worsened joint pain: Grade 4	0 (-99999 to 99999)	0 (0.0 to 3.3)	0 (0.0 to 17.6)	

Statistical analyses

No statistical analyses for this end point

Primary: SSD: Percentage of Participants Reporting Adverse Events (AEs) 1 Month After Study Vaccination

End point title	SSD: Percentage of Participants Reporting Adverse Events (AEs) 1 Month After Study Vaccination[3]

End point description:

An AE was defined as any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Percentage of participants reporting AEs within 1 month after study vaccination were reported in this endpoint. Exact 2-sided CI was calculated using the Clopper and Pearson method. Only AEs collected by non-systematic assessment (i.e., excluding local reactions and systemic events) were reported in this endpoint. Safety population included all participants who received at least 1 dose of the study intervention. 99999= data could not be generated since it was not part of specified analysis in the protocol.

End point type	Primary

End point timeframe:

From study vaccination on Day 1 up to 1 month after study vaccination

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned for this endpoint.

End point values	Group 1: 2 prior doses of BNT162b2	Group 2: 3 prior doses of BNT162b2	Group 3: Participants from study C4591007 Phase 1	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	113	19	
Units: Percentage of participants				
number (confidence interval 95%)	0.0 (-99999 to 99999)	3.5 (1.0 to 8.8)	15.8 (3.4 to 39.6)	

Statistical analyses

No statistical analyses for this end point

Primary: SSD: Percentage of Participants Reporting Serious Adverse Events (SAEs) Within 6 Months After Study Vaccination

End point title	SSD: Percentage of Participants Reporting Serious Adverse Events (SAEs) Within 6 Months After Study Vaccination[4]

End point description:

An SAE was defined as any untoward medical occurrence that at any dose resulted in death, was life-threatening; resulted in persistent disability/incapacity; constituted a congenital anomaly/birth defect; was important medical event; required inpatient hospitalisation or prolongation of existing hospitalisation. Safety population included all participants who received at least 1 dose of the study intervention.

End point type	Primary

End point timeframe:

From study vaccination on Day 1 up to 6 months after study vaccination

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned for this endpoint.

End point values	Group 1: 2 prior doses of BNT162b2	Group 2: 3 prior doses of BNT162b2	Group 3: Participants from study C4591007 Phase 1	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	113	19	
Units: Percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: SSD:Geometric Mean Ratio(GMR)Based on Geometric Mean Titers of Severe Acute Respiratory Syndrome Coronavirus 2(SARSCoV2)Omicron(BA.4/BA.5)-Neutralizing Titers at 1 Month After Dose 4 for Group 2 and C4591007 Phase 2/3 Participants(1 Month After Dose 3)

End point title	SSD:Geometric Mean Ratio(GMR)Based on Geometric Mean

	Titers of Severe Acute Respiratory Syndrome Coronavirus 2(SARSCoV2)Omicron(BA.4/BA.5)-Neutralizing Titers at 1 Month After Dose 4 for Group 2 and C4591007 Phase 2/3 Participants(1 Month After Dose 3)[5]

End point description:

GMTs and the corresponding 2-sided CIs were calculated by exponentiating the least square means and the corresponding CIs based on analysis of log-transformed assay results using a linear regression model with baseline log-transformed neutralizing titers, postbaseline infection status, and vaccine group as covariates. Evaluable immunogenicity population included all eligible randomised participants who received the study intervention to which they were randomised, had a valid and determinate immunogenicity result within 28-42 days after the study vaccination, and had no other important protocol deviations as determined by the clinician. Results include those from a comparator group of C4591007 (NCT04816643) Phase 2/3 participants of the same age who received 3 doses of original BNT162b2 10 µg as of the data cutoff date of 27 May 2022.Participants with or without evidence of prior infection were included in the analysis.'N'=participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

1 month after Dose 4 for Group 2 and 1 month after Dose 3 for C4591007 control arm

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Group 2: 3 prior doses of BNT162b2	Historical cohort: C4591007 BNT162b2 10 µg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	101	112		
Units: Titers				
geometric mean (confidence interval 95%)	1836.1 (1593.8 to 2115.2)	1632.5 (1427.5 to 1867.0)		

Statistical analyses

Statistical analysis title	Group 2 and Historical cohort from C4591007

Statistical analysis description:

GMRs and 2-sided CIs were calculated by exponentiating the difference of LSMeans for the assay and the corresponding CIs based on a linear regression model with baseline log-transformed neutralizing titers, postbaseline infection status, and vaccine group as covariates.

Comparison groups	Group 2: 3 prior doses of BNT162b2 v Historical cohort: C4591007 BNT162b2 10 µg
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric Mean Ratio
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.37

Primary: SSD: Percentages of Participants With Seroresponse to the Omicron (BA.4/BA.5)– Neutralizing Titers at 1 Month After Dose 4 for Group 2 and C4591007 Phase 2/3 Participants (1 Month After Dose 3)

End point title	SSD: Percentages of Participants With Seroresponse to the Omicron (BA.4/BA.5)– Neutralizing Titers at 1 Month After Dose 4 for Group 2 and C4591007 Phase 2/3 Participants (1 Month After Dose 3)[6]

End point description:

Seroresponse was defined as achieving >= 4-fold rise from baseline (before Dose 4 for C4591048 Substudy D Group 2 and before Dose 3 for C4591007). If the baseline measurement was below the lower limit of quantification (LLOQ), the postvaccination assay result of >= 4 × LLOQ was considered a seroresponse. Exact 2-sided 95% CI was based on the Clopper and Pearson method. Percentage of participants achieving seroresponse at 1 month after study vaccination was reported in this endpoint. Evaluable immunogenicity population was analyzed. Results include those from a comparator group of C4591007 (NCT04816643) Phase 2/3 participants of the same age who received 3 doses of original BNT162b2 10 µg as of the data cutoff date of 27 May 2022.Participants with or without evidence of prior infection were included in the analysis.'N'=participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

1 month after Dose 4 for Group 2 and 1 month after Dose 3 for C4591007 control arm

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Group 2: 3 prior doses of BNT162b2	Historical cohort: C4591007 BNT162b2 10 µg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	101	112		
Units: Percentage of participants				
number (confidence interval 95%)	53.5 (43.3 to 63.5)	52.7 (43.0 to 62.2)		

Statistical analyses

Statistical analysis title	Group 2 and Historical cohort from C4591007

Statistical analysis description:

Adjusted difference in proportions based on the Miettinen and Nurminen method stratified by baseline neutralizing titer category (< median, ≥ median), expressed as a percentage (bivalent BNT162b2 [original/Omi BA.4/BA.5] 10 µg - BNT162b2 10 µg). 2-Sided CI, based on the Miettinen and Nurminen method for the difference in proportions stratified by baseline neutralizing titer category (< median,>= median), expressed as a percentage.

Comparison groups	Group 2: 3 prior doses of BNT162b2 v Historical cohort: C4591007 BNT162b2 10 µg

Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	8.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.47
upper limit	19.99

Secondary: SSD: Geometric Mean Titers (GMT) of SARS-CoV-2 Omicron BA.4/BA.5–Neutralizing Titers at Baseline and 1 Month After Dose 4 for Group 2 and C4591007 Phase 2/3 Participants (1 Month After Dose 3)

End point title	SSD: Geometric Mean Titers (GMT) of SARS-CoV-2 Omicron BA.4/BA.5–Neutralizing Titers at Baseline and 1 Month After Dose 4 for Group 2 and C4591007 Phase 2/3 Participants (1 Month After Dose 3)[7]

End point description:

GMT of SARS-CoV-2 Omicron strain–neutralizing titers at 1 month after the study vaccination was reported in this endpoint. GMTs and the corresponding 2-sided CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on Student's t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ. Evaluable immunogenicity population was analyzed. Results include those from a comparator group of C4591007 (NCT04816643) Phase 2/3 participants of the same age who received 3 doses of original BNT162b2 10 µg as of the data cutoff date of 27 May 2022.Participants with or without evidence of prior infection were included in the analysis.'N'=participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Group 2: Baseline and 1 month after Dose 4; C4591007 control arm: Baseline and 1 month after Dose 3

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Group 2: 3 prior doses of BNT162b2	Historical cohort: C4591007 BNT162b2 10 µg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	102	113		
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline (n=102,112)	488.3 (361.9 to 658.8)	248.3 (187.2 to 329.5)		
1 Month (n=102,113)	2189.9 (1742.8 to 2751.7)	1393.6 (1175.8 to 1651.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: SSD: Geometric Mean Titers (GMT) of SARS-CoV-2 Reference-Strain–Neutralizing Titers at Baseline and 1 Month After Dose 4 for Group 2 and C4591007 Phase 2/3 Participants (1 Month After Dose 3)

End point title	SSD: Geometric Mean Titers (GMT) of SARS-CoV-2 Reference-Strain–Neutralizing Titers at Baseline and 1 Month After Dose 4 for Group 2 and C4591007 Phase 2/3 Participants (1 Month After Dose 3)[8]

End point description:

GMT of SARS-CoV-2 reference-strain-neutralizing titers before vaccination to 1 month after study vaccination was reported in this endpoint.GMTs and the corresponding 2-sided CIs were calculated by exponentiating the mean logarithm of the titers & the corresponding CIs(based on Student's t distribution).Assay results below the LLOQ were set to 0.5 × LLOQ.Evaluable immunogenicity population was analyzed. Results include those from a comparator group of C4591007(NCT04816643) Phase 2/3 participants of the same age who received 3 doses of original BNT162b2 10 µg as of the data cutoff date of 27 May 2022.Participants with or without evidence of prior infection were included in the analysis.'N'=participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Group 2: Baseline and 1 month after Dose 4; C4591007 control arm: Baseline and 1 month after Dose 3

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Group 2: 3 prior doses of BNT162b2	Historical cohort: C4591007 BNT162b2 10 µg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	102	113		
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline	2904.0 (2372.6 to 3554.5)	1323.1 (1055.7 to 1658.2)		
1 Month	8245.9 (7108.9 to 9564.9)	7235.1 (6331.5 to 8267.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: SSD: Geometric Mean Fold Rise (GMFR) of SARS-CoV-2 Omicron BA.4/BA.5–Neutralizing Titers at 1 Month After Dose 4 for Group 2 and C4591007 Phase 2/3 Participants (1 Month After Dose 3)

End point title	SSD: Geometric Mean Fold Rise (GMFR) of SARS-CoV-2 Omicron BA.4/BA.5–Neutralizing Titers at 1 Month After Dose 4 for Group 2 and C4591007 Phase 2/3 Participants (1 Month After Dose 3)[9]

End point description:

GMFR of SARS-CoV-2 omicron BA.4/BA.5-neutralizing titers at 1 month after study vaccination was

reported in this endpoint. GMFRs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis. Evaluable immunogenicity population was analyzed. Results include those from a comparator group of C4591007 (NCT04816643) Phase 2/3 participants of the same age who received 3 doses of original BNT162b2 10 µg as of the data cutoff date of 27 May 2022.Participants with or without evidence of prior infection were included in the analysis.'N'=participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

1 month after Dose 4 for Group 2 and 1 month after Dose 3 for C4591007 control arm

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Group 2: 3 prior doses of BNT162b2	Historical cohort: C4591007 BNT162b2 10 µg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	101	112		
Units: Fold rise				
geometric mean (confidence interval 95%)	4.5 (3.8 to 5.4)	5.6 (4.5 to 6.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: SSD: GMFR of SARS-CoV-2 Reference-Strain–Neutralizing Titers at 1 Month After Dose 4 for Group 2 and C4591007 Phase 2/3 Participants (1 Month After Dose 3)

End point title	SSD: GMFR of SARS-CoV-2 Reference-Strain–Neutralizing Titers at 1 Month After Dose 4 for Group 2 and C4591007 Phase 2/3 Participants (1 Month After Dose 3)[10]

End point description:

GMFR of SARS-CoV-2 reference-strain-neutralizing titers before vaccination to 1 month after study vaccination was reported in this endpoint. GMFRs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.Evaluable immunogenicity population was analyzed. Results include those from a comparator group of C4591007 (NCT04816643) Phase 2/3 participants of the same age who received 3 doses of original BNT162b2 10 µg as of the data cutoff date of 27 May 2022.Participants with or without evidence of prior infection were included in the analysis.'N'=participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

1 month after Dose 4 for Group 2 and 1 month after Dose 3 for C4591007 control arm

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Group 2: 3 prior doses of BNT162b2	Historical cohort: C4591007 BNT162b2 10 µg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	101	113		
Units: Fold rise				
geometric mean (confidence interval 95%)	2.8 (2.5 to 3.3)	5.5 (4.5 to 6.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: SSD: Percentages of Participants With Seroresponse to SARS-CoV-2 Omicron BA.4/BA.5–Neutralizing Titers at 1 Month After Dose 4 for Group 2 and C4591007 Phase 2/3 Participants (1 Month After Dose 3)

End point title	SSD: Percentages of Participants With Seroresponse to SARS-CoV-2 Omicron BA.4/BA.5–Neutralizing Titers at 1 Month After Dose 4 for Group 2 and C4591007 Phase 2/3 Participants (1 Month After Dose 3)[11]

End point description:

Seroresponse was defined as achieving >= 4-fold rise from baseline (before Dose 4 for C4591048 Substudy D Group 2 and before Dose 3 for C4591007). If the baseline measurement was below the lower limit of quantification (LLOQ), the postvaccination assay result of >= 4 ×* LLOQ was considered a seroresponse. Exact 2-sided 95% CI, based on the Clopper and Pearson method. Percentage of participants achieving seroresponse at 1 month after study vaccination was reported in this endpoint. Evaluable immunogenicity population was analyzed. Results include those from a comparator group of C4591007 (NCT04816643) Phase 2/3 participants of the same age who received 3 doses of original BNT162b2 10 µg as of the data cutoff date of 27 May 2022.Participants with or without evidence of prior infection were included in the analysis.'N'=participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

1 month after Dose 4 for Group 2 and 1 month after Dose 3 for C4591007 control arm

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Group 2: 3 prior doses of BNT162b2	Historical cohort: C4591007 BNT162b2 10 µg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	101	112		
Units: Percentage of participants				
number (confidence interval 95%)	53.5 (43.3 to 63.5)	52.7 (43.0 to 62.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: SSD: Percentages of Participants With Seroresponse to Reference-Strain-Neutralizing Titers at 1 Month After Dose 4 for Group 2 and C4591007 Phase 2/3 Participants (1 Month After Dose 3)

End point title	SSD: Percentages of Participants With Seroresponse to Reference-Strain-Neutralizing Titers at 1 Month After Dose 4 for Group 2 and C4591007 Phase 2/3 Participants (1 Month After Dose 3)[12]

End point description:

Seroresponse was defined as achieving >= 4-fold rise from baseline (before Dose 4 for C4591048 Substudy D Group 2 and before Dose 3 for C4591007). If the baseline measurement was below the lower limit of quantification (LLOQ), the postvaccination assay result of >= 4 ×* LLOQ was considered a seroresponse. Exact 2-sided 95% CI, based on the Clopper and Pearson method. Percentage of participants achieving seroresponse at 1 month after study vaccination was reported in this endpoint.Results include those from a comparator group of C4591007 (NCT04816643) Phase 2/3 participants of the same age who received 3 doses of original BNT162b2 10 µg as of the data cutoff date of 27 May 2022.Participants with or without evidence of prior infection were included in the analysis.' N'=participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

1 month after Dose 4 for Group 2 and 1 month after Dose 3 for C4591007 control arm

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Group 2: 3 prior doses of BNT162b2	Historical cohort: C4591007 BNT162b2 10 µg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	101	113		
Units: Percentage of participants				
number (confidence interval 95%)	30.7 (21.9 to 40.7)	54.9 (45.2 to 64.2)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Local reactions/systemic events(systematic assessment): up to Day 7 after vaccination. Non-SAEs (non-systematic assessment):From Day 1 up to 1 month after study vaccination.For SAE (non-systematic assessment)from Day 1 to 6 month after study vaccination.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Group 1: 2 prior doses of BNT162b2

Reporting group description:

Participants aged 5 to 11 years who had received two prior doses of BNT162b2 10 microgram (mcg) 90 to 240 days before enrollment in the study were included. Participants received a single dose of BNT162b2 10 mcg via intramuscular route on Day 1 of the study.

Reporting group title	Group 3: Participants from study C4591007 Phase 1

Reporting group description:

Participants from C4591007 phase 1 trial, aged 5 to 11 years who had received three prior doses of BNT162b2 10 mcg at least 90 days before enrollment in the study were included. Participants received a single dose of BNT162b2 10 mcg via intramuscular route on Day 1 of the study.

Reporting group title	Group 2: 3 prior doses of BNT162b2

Reporting group description:

Participants aged 5 to 11 years who had received three prior doses of BNT162b2 10 mcg 90 to 240 days before enrollment in the study were included. Participants received a single dose of BNT162b2 10 mcg via intramuscular route on Day 1 of the study.

Serious adverse events	Group 1: 2 prior doses of BNT162b2	Group 3: Participants from study C4591007 Phase 1	Group 2: 3 prior doses of BNT162b2
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 19 (0.00%)	0 / 113 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Group 1: 2 prior doses of BNT162b2	Group 3: Participants from study C4591007 Phase 1	Group 2: 3 prior doses of BNT162b2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	16 / 19 (84.21%)	88 / 113 (77.88%)
Injury, poisoning and procedural complications			

Animal bite			
subjects affected / exposed	0 / 2 (0.00%)	1 / 19 (5.26%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 2 (0.00%)	7 / 19 (36.84%)	28 / 113 (24.78%)
occurrences (all)	0	7	28
General disorders and administration site conditions			
Injection site haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	1 / 19 (5.26%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 2 (0.00%)	2 / 19 (10.53%)	8 / 113 (7.08%)
occurrences (all)	0	2	8
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 2 (0.00%)	11 / 19 (57.89%)	45 / 113 (39.82%)
occurrences (all)	0	11	45
Chills			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 2 (0.00%)	2 / 19 (10.53%)	10 / 113 (8.85%)
occurrences (all)	0	2	10
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 2 (0.00%)	2 / 19 (10.53%)	5 / 113 (4.42%)
occurrences (all)	0	2	5
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 2 (50.00%)	13 / 19 (68.42%)	71 / 113 (62.83%)
occurrences (all)	1	13	71
Injection site swelling			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 2 (0.00%)	2 / 19 (10.53%)	5 / 113 (4.42%)
occurrences (all)	0	2	5
Gastrointestinal disorders			
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 2 (0.00%)	0 / 19 (0.00%)	4 / 113 (3.54%)
occurrences (all)	0	0	4
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 2 (0.00%)	0 / 19 (0.00%)	4 / 113 (3.54%)
occurrences (all)	0	0	4
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 2 (0.00%)	1 / 19 (5.26%)	0 / 113 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 2 (0.00%)	4 / 19 (21.05%)	15 / 113 (13.27%)
occurrences (all)	0	4	15
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 2 (0.00%)	2 / 19 (10.53%)	10 / 113 (8.85%)
occurrences (all)	0	2	10
Infections and infestations			
Upper respiratory tract infections			
subjects affected / exposed	0 / 2 (0.00%)	1 / 19 (5.26%)	0 / 113 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 October 2022	Amendment 1: Updated section 1.1 :Decreased the number of days since last dose prior to enrollment in Group 3 to 90 days. Updated Sections 10.7.5.2, 10.8.5.2, 10.9.5.2, 10.10.5.2 Exclusion Criteria Substudy A, B,C, D: Added radiotherapy, within 60 days before enrollment. Updated section 10.10.3 Clarified that the primary immunogenicity comparison would be between the SSD Group 1 to C4591007 Phase 2/3 participants and made editorial change to the estimands. Updated section 10.10.9.3.2: Clarified that the primary immunogenicity comparison would be between the SSD Group 2 to C4591007 Phase 2/3 participants and made editorial changes to the estimands and analysis. Updated section 10.10.1.2: Removed 1-month postdose blood draw group 3 only. Updated section 10.10.1.3.2: Added the group numbers to rows specific to blood sample collection. Updated section 10.10.1.3.2: Added row specific to Group 3 blood draw to be collected at baseline only.
01 August 2023	Amendment 3: Updated section: 10.10.3: Added "at 1 month after Dose 4" to the second primary immunogenicity objective.
01 September 2023	Amendment 4: Updated section 10.10.3 and 10.10.9.3.2: Removed objectives for immunogenicity comparisons and descriptive summaries related to Group 1.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported