Vaccines and Related Biological Products Advisory Committee Meeting

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Vaccines and Related Biological Products Advisory Committee Meeting

FDA Review of Effectiveness and Safety of COMIRNATY (COVID-19 Vaccine, mRNA) Booster Dose *Biologics License Application Supplement*

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September 17, 2021

Outline

- Background
- Booster Study Design
- Immunogenicity Results
- Safety Results
- Summary of Data

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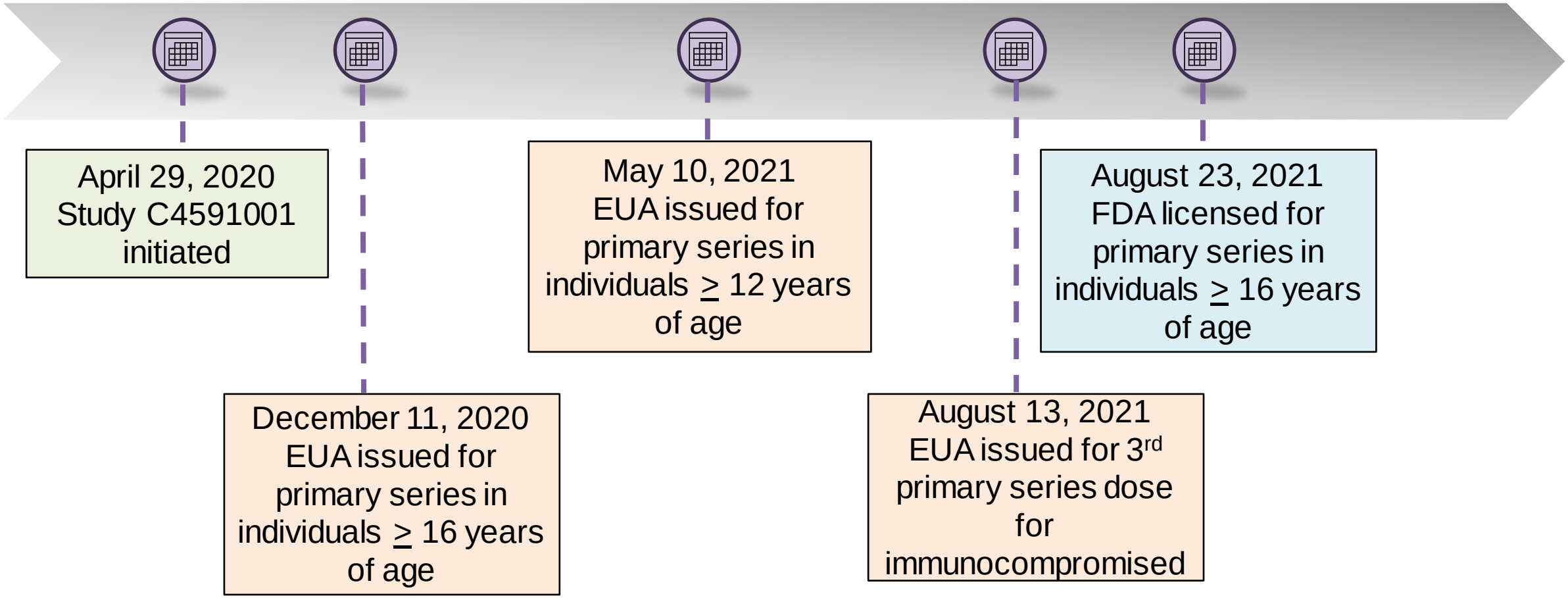
COMIRNATY (COVID-19 vaccine, mRNA)

Vaccine composition	Dosing Regimen
• Based on the SARS-CoV-2 spike glycoprotein (S) antigen encoded by RNA • Formulated in lipid particles • Based on Wuhan strain	Intramuscular 2-dose series (primary series), administered 3 weeks apart; 30 µg mRNA each dose

- On August 23, 2021, FDA approved the BNT162b2 vaccine under the proprietary name COMIRNATY for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.
- COMIRNATY is the only vaccine or medical product that is FDA approved for prevention of COVID-19.
- **The supplemental BLA is intended to support approval for booster administration of COMIRNATY approximately 6 months following the primary series.**

Regulatory background



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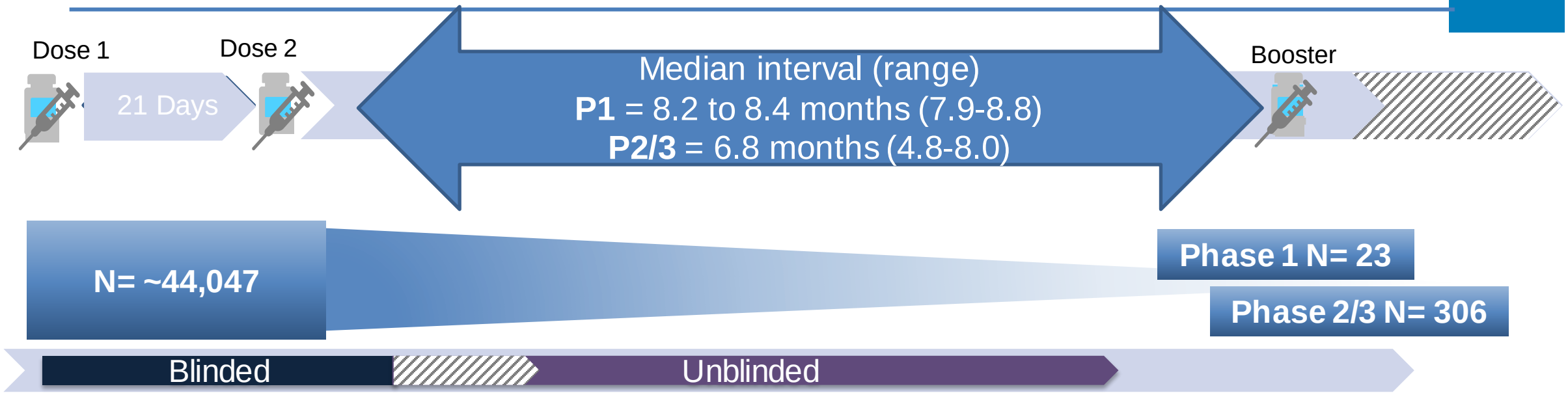
C4591001: Study Overview



Adverse event collection after each dose

- Solicited x 7 days*
- Unsolicited x 28 days
- Serious x 6 months
- Deaths and related SAEs for duration of study — 2 Years Post Dose 2

*Reactogenicity data collected from a subset after Doses 1 (N= 2899) and 2 (N= 2862) and from all participants after booster dose

Booster Study Design

Base Study **(C4591001)**
Phase 1/2/3 study in individuals ≥12 years old

Booster Dose Sub-Study

Phase 1: Participants 18-55 (n= 11) and 65-85 years of age (n= 12) who received a primary series of 30 µg BNT162b2 and a booster dose of 30 µg BNT162b2 approximately 8 months after dose 2 of BNT162b2 (started early 2021)

Phase 2/3: Participants 18-55 years of age (N= 306) who received a primary series of 30 µg BNT162b2 and a booster dose of 30 µg BNT162b2 approximately 6 months after dose 2 of BNT162b2 (started March 2021)

Demographics for Booster Dose Participants

Characteristic	Phase 1 18-55 Years N=11 n (%)	Phase 1 65-85 Years N=12 n (%)	Phase 2/3 18-55 Years N=306 n (%)
Sex: Female	9 (81.8)	6 (50)	166 (54.2)
Sex: Male	2 (18.2)	6 (50)	140 (45.8)
Age: Mean (years)	38.3	69.3	41.2
Age: Median (years)	39.0	69.0	42.0
Age: Min, max (years)	24, 55	65, 75	19, 55
Race: American Indian or Alaska Native	0 (0)	0 (0)	2 (0.7)
Race: Asian	2 (18.2)	0 (0)	16 (5.2)
Race: Black or African American	1 (9.1)	0 (0)	28 (9.2)
Race: Native Hawaiian or other Pacific Islander	0 (0)	0 (0)	1 (0.3)
Race: White	8 (72.7)	12 (100.0)	249 (81.4)
Race: Multiracial	0 (0)	0 (0)	4 (1.3)
Race: Not reported	0 (0)	0 (0)	6 (2.0)
Ethnicity: Hispanic or Latino	0	0	85 (27.8)
Ethnicity: Not Hispanic or Latino	11 (100.0)	12 (100.0)	219 (71.6)
Ethnicity: Not reported	0 (0)	0 (0)	2 (0.7)
History of SARS-CoV-2 exposure pre-Dose 1	0 (0)	0 (0)	11 (3.6)
Comorbidities[a]: Yes	0 (0)	0 (0)	56 (18.3)
Obese[b]	0 (0)	0 (0)	122 (39.9)

a Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease defined as patients who had at least one of the Charlson comorbidity index category. ***Phase 1: Co-morbidities that constituted risk factors for severe COVID-19 were exclusion criteria.***

b Defined as BMI greater than 30 kg/m²

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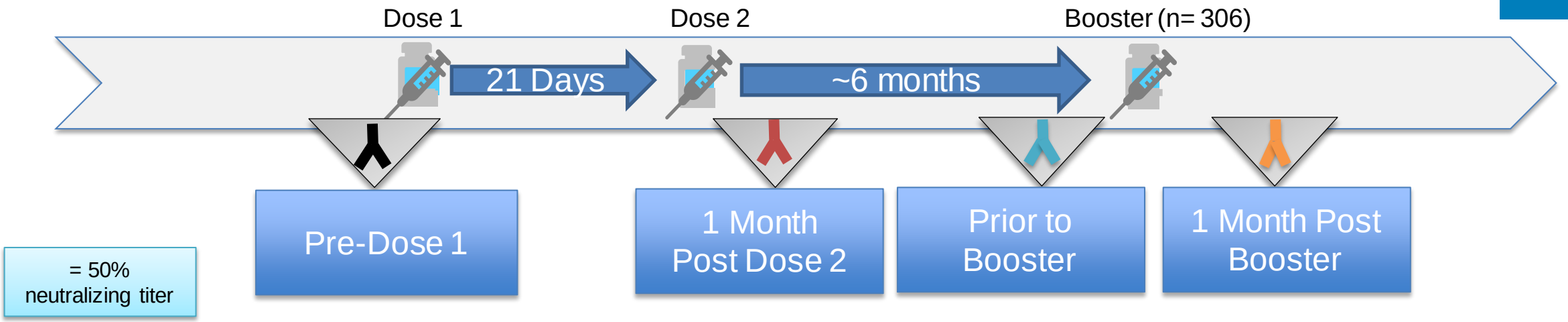
Booster Dose Immunogenicity Assessments



Primary immunogenicity objective: Demonstrate noninferiority of neutralizing antibody geometric mean titers (GMTs) against the reference SARS-CoV-2 strain (USA_WA1/2020), measured after a booster dose of BNT162b2 (30 µg), compared to after the 2-dose primary series of BNT162b2 (30 µg) in the same individuals

A validated SARS-CoV-2 mNeonGreen virus microneutralization assay (SARS-CoV-2 mNG NT) was used for evaluations of the homologous booster dose

Booster Dose Immunogenicity Endpoints

Endpoint

Geometric mean titer (GMT) ratio of SARS-CoV-2 neutralizing titers

$$\frac{\text{GMT 1 month Post Booster Dose}}{\text{GMT 1 month Post Dose 2}}$$

Non-inferiority declared if:

- lower bound of the 2-sided 97.5% CI for GMT ratio >0.67
- point estimate of GMT ratio ≥0.8

Booster Dose Immunogenicity Endpoints

Endpoint

Percentage difference of seroresponse at 1 month post Booster Dose and at 1 month post Dose 2

Seroresponse= ≥4-fold rise; for baseline measurement <LLOQ, postvaccination measure ≥4 × LLOQ is considered seroresponse

% with 4-fold rise from pre-Dose 1 to 1 month post Booster Dose

MINUS

% with 4-fold rise from pre-Dose 1 to 1 month post Dose 2

Noninferiority declared if the lower limit of the 97.5% CI for the difference in % of participants with seroresponse > -10%

Immunogenicity Analysis Populations

Phase 2/3 participants who received booster dose of BNT162b2 at 30 µg

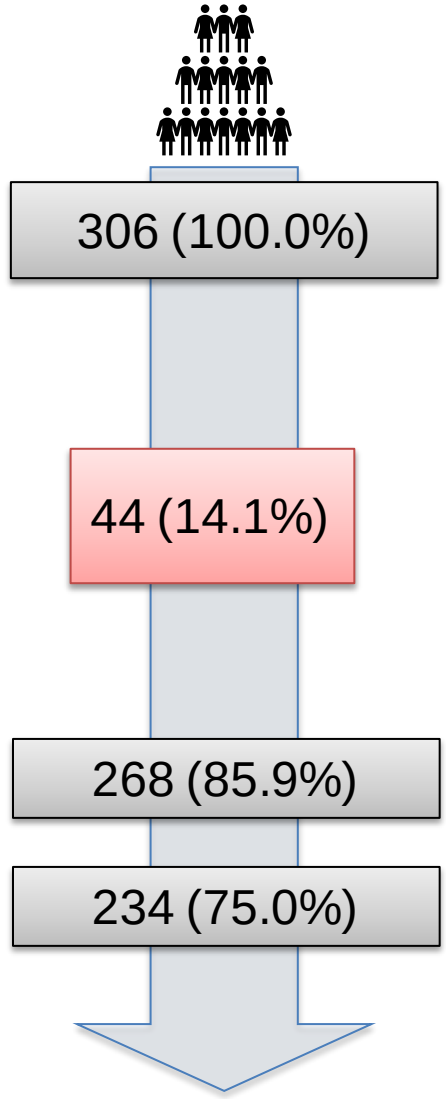
All available immunogenicity population

Excluded participants
- Dose 2 out of window (n= 1)
- No valid and determinate immunogenicity result 28-42 days after booster vaccination (n= 15)
- Important protocol deviation (n= 30)

*participants may have been excluded for more than 1 reason

Evaluable immunogenicity population

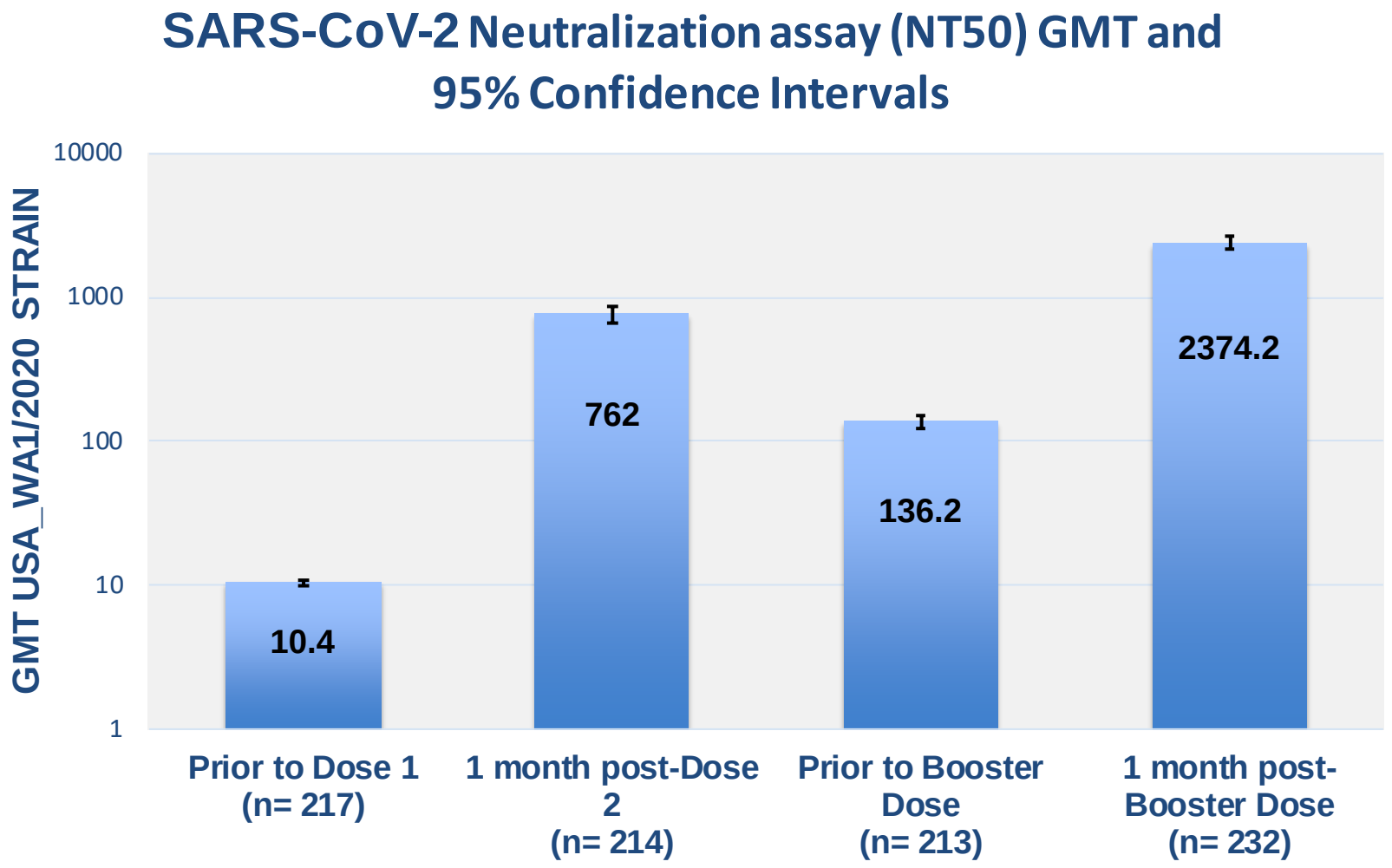
Without evidence of infection* from Dose 1 to 1 month after booster dose



*Subjects who had no serological or virological evidence of past SARS-CoV-2 infection (i.e., N-binding antibody negative, NAAT negative by nasal swab prior to each vaccine dose and negative NAAT (nasal swab) at any unscheduled visit up to 1 month after booster vaccination).

Immunogenicity results: GMTs (USA_WA1/2020 Strain)

Dose 3 Booster Evaluable Immunogenicity Population without evidence of infection



Immunogenicity Results: Non-inferiority analysis based on GMT ratios (USA_WA1/2020 Strain)

		GMT 1 Month After Dose 3 (95% CI)	GMT 1 Month After Dose 2 (95% CI)	GMT post-Dose 3/ GMT post-Dose 2 Ratio (97.5% CI)
Analysis population	N	Point estimate	Point estimate (95% CI)	Point estimate (95% CI)
Evaluable Immunogenicity, no evidence of infection	210	2476.4 (2210.1, 2774.9)	753.7 (658.2, 863.1)	**3.29** (**2.76**, 3.91)
All Available Immunogenicity, no evidence of infection	236	2382.4 (2140.8, 2651.3)	764.9 (670.4, 872.6)	**3.11** (**2.63**, 3.68)

Non-inferiority declared as the lower bound of the 2-sided 97.5% CI for the GMR was >0.67 and the point estimate of the GMR was ≥0.8.

Immunogenicity Results: Pre-specified non-inferiority analysis based on seroresponse (USA_WA1/2020 Strain)

		≥ 4-fold rise from pre-Dose 1 to 1 month after Dose 2	≥ 4-fold rise from pre-Dose 1 to 1 month after Booster	Difference in seroresponse between 1 Month After Booster and 1 Month After Dose 2
Analysis population	N	n (%) (95% CI)	n (%) (95% CI)	% Difference (95% CI)
Evaluable Immunogenicity, no evidence of infection	198	194 (98.0)	197 (99.5)	1.5 (-0.7, 3.7)
All Available Immunogenicity, no evidence of infection	224	220 (98.2)	223 (99.6)	1.3 (-0.6, 3.3)

Non-inferiority declared as the lower limit of the 97.5% CI for the difference in percentages of participants with seroresponse was greater than -10%.

Immunogenicity Results: Post-hoc non-inferiority analysis based on seroresponse (USA_WA1/2020 Strain)

		≥ 4-fold rise from pre-Dose 1 to 1 month after Dose 2	≥ 4-fold rise from pre-Booster to 1 month after Booster	Difference in seroresponse between 1 Month After Booster and 1 Month After Dose 2
Analysis population	N	n (%) (95% CI)	n (%) (95% CI)	% Difference (95% CI)
Evaluable Immunogenicity, no evidence of infection	179	175 (97.8) (94.4, 99.4)	168 (93.9) (89.3, 96.9)	**-3.9** (-8.2, 0.4)
All Available Immunogenicity, no evidence of infection	200	196 (98.0) (95.0, 99.5)	188 (94.0) (89.8, 96.9)	**-4.0** (-7.9, 0.0)

Exploratory Phase 1 Analysis (USA_WA1/2020 Strain and Delta Variant)

- A 50% plaque-reduction neutralization test (PRNT) was used to determine neutralizing titers in **23 participants** against the reference USA_WA1/2020 strain and Delta variant (B.1.617.2)
- PRNT titers were assessed in sera 1 month after BNT162b2 Dose 2 and 1 month after Dose 3

The PRNT assay is a non-validated assay and was used in Phase I for exploratory purposes; the relative sensitivity for the two viruses is not known

Reference USA-WA1/2020 strain was based on the clinical strain isolated in Washington in January 2020

Delta variant was generated from the recombinant USA-WA1/2020 with the full spike gene replaced with the Delta variant spike gene

Immunogenicity Results: Phase 1 Exploratory Analysis (Delta Variant and USA_WA1/2020 Strain)

		18 – 55 Years* P1 n=11	65 – 85 Years* P1 n=12
Assay Target	**Time point**	**GMT** (95% CI)	**GMT** (95% CI)
USA_WA1/2020	1 Month post-Dose 2	**310.1** (203.3, 473.0)	**195.8** (114.7, 334.4)
	1 Month post-Booster Dose	**1546.4** (896.9, 2666.0)	**1612.7** (875.5, 2970.8)
Delta variant	1 Month post-Dose 2	**241.0** (180.1, 322.4)	**123.4** (70.2, 216.9)
	1 Month post-Booster Dose	**1321.0** (698.5, 2498.3)	**1478.9** (734.9, 2975.8)

*Booster all-available immunogenicity population

Post-hoc analysis of efficacy: Delta surge

Protocol-specified COVID-19 cases accrued during the current delta variant surge
01 July 2021 through 31 August 2021
Participants ≥16 years of age

Participants who completed the 2-dose vaccination series **early in the study** (i.e., those who were originally randomized to BNT162b2; n= 18727)

Incidence **70.3 cases per 1,000 person years** (3 severe cases)
Mean of **9.8 months post-Dose 2** at the beginning of the analysis period

Participants who completed the 2-dose vaccination series **later in the study** (i.e., those who were originally randomized to placebo and then crossed over to BNT162b2; n= 17748)

Incidence **51.6 cases per 1,000 person years** (no severe cases)
Mean of **4.7 months post-Dose 2** at the beginning of the analysis period

Post-hoc analysis of efficacy: Translating relative breakthrough rates to efficacy

1

Calculate the incidence rate (IR) ratio between late group (placebo crossover) and the early group (original vaccine group)

$$\textbf{0.73} = \frac{\text{IR late (51.6)}}{\text{IR early (70.3)}}$$

2

For each assumed efficacy value, calculate the corresponding efficacy =

$$1 - \frac{(1 - \text{assumed efficacy})}{\text{IR ratio (0.73)}}$$

Assumed efficacy in placebo crossover group (vaccinated ~4.7 months before observation)	Corresponding efficacy in originally vaccinated group (vaccinated ~9.8 months before observation)
98%	97%
95%	93%
90%	86%
85%	80%

Post-hoc analysis of efficacy: Delta surge

- During the blinded, placebo-controlled follow-up period of the study with data cutoff of March 13, 2021 (prior to the Delta variant surge), the incidence of COVID-19 among BNT162b2 recipients in the Evaluable Efficacy Population (nearly 60% of whom had 4 months or more of blinded follow-up post-Dose 2) was **12.6 cases per 1,000 person-years.**

- Among study participants who completed the primary series <4 months prior to the start of the analysis period, the incidence of COVID-19 was **43.4 cases per 1,000 person-years**.

Limitations of the analysis

- C4591001 not designed to assess relative VE of the crossover group versus the original BNT162b2 group and the post-hoc analysis is exploratory in nature.
- Open label nature may have introduced confounding factors (e.g., behavioral) that biased the results. In addition, other unknown confounding factors may bias the results.

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- **Safety Results**
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Length of Safety Follow-up in Booster Recipients

	Phase 1 18-55 Years N=11 n (%)	Phase 1 65-85 Years N=12 n (%)	Phase 2/3 18-55 Years N=306 n (%)
Booster dose to cutoff date*			
<2 Months	0	0	1 (0.3)
≥2 - <4 Months	11 (100.0)	12 (100.0)	305 (99.7)
Mean	2.7	2.7	2.7
Median	2.6	2.6	2.6
Min, max	2.1, 2.9	2.6, 2.8	1.1, 2.8

N = number of participants in the specified group. This value is the denominator for the percentage calculations.
n = Number of participants with the specified characteristic.
** Phase 1 cutoff date: 13 May 2021; Phase 2/3 cutoff date: 27 June 2021*

Safety: Local Reactogenicity (7 Days After Each Dose)

	Dose 1 Phase 2/3 16-55 years N=2899* n (%)	Dose 2 Phase 2/3 16-55 years N=2682* n (%)	Booster Phase 2/3 18-55 years N=289 n (%)	Booster Phase 1 65-85 years N= 12 n (%)
Any Injection Site Pain[a]	**2426 (83.7)**	**2101 (78.3)**	**240 (83.0)**	**8 (66.7)**
Severe	39 (1.3)	39 (1.5)	1 (0.3)	0 (0)
Any Swelling[b]	**184 (6.3)**	**183 (6.8)**	**23 (8.0)**	**0 (0)**
Severe	6 (0.2)	7 (0.3)	1 (0.3)	0 (0)
Any Redness[b]	**156 (5.4)**	**151 (5.6)**	**17 (5.9)**	**0 (0)**
Severe	7 (0.2)	11 (0.4)	0 (0)	0 (0)

**= Reactogenicity subset; N= number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. n = Number of participants with the specified characteristic*

a. *Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity*
b. *Mild: >2.0 to 5.0 cm; moderate: >5.0 to 10.0 cm; severe: >10.0 cm; Grade 4: necrosis (redness and swelling categories) or exfoliative dermatitis (redness category only)*

Safety: Systemic Reactogenicity (7 Days After Each Dose)

	Phase 2/3 Dose 1 16-55 Years N=2899* n (%)	Phase 2/3 Dose 2 16-55 Years N=2682* n (%)	Phase 2/3 Booster 18-55 Years N=289[d] n (%)
Any Fatigue[a]	1431 (49.4)	1649 (61.5)	185 (63.8)
Severe	41 (1.4)	142 (5.3)	13 (4.5)
Any Headache[a]	1262 (43.5)	1448 (54.0)	140 (48.4)
Severe	33 (1.1)	91 (3.4)	3 (1.0)
Any New or worsened muscle pain[a]	664 (22.9)	1055 (39.3)	113 (39.1)
Severe	15 (0.5)	62 (2.3)	4 (1.4)
Any New or worsened joint pain[a]	342 (11.8)	638 (23.8)	73 (25.3)
Severe	5 (0.2)	27 (1.0)	1 (0.3)
Any Chills[a]	479 (16.5)	1015 (37.8)	84 (29.1)
Severe	15 (0.5)	69 (2.6)	3 (1.0)
Any Diarrhea[b]	309 (10.7)	269 (10.0)	25 (8.7)
Severe	3 (0.1)	6 (0.2)	0 (0)
Any Vomiting[c]	34 (1.2)	58 (2.2)	5 (1.7)
Severe	0 (0)	4 (0.1)	0 (0)
Fever			
≥38.0°C	119 (4.1)	440 (16.4)	25 (8.7)
>38.9 to 40.0°C	8 (0.3)	39 (1.5)	1 (0.3)
> 40.0°C	0 (0)	1 (0)	0 (0)
Use of antipyretic or pain medication	805 (27.8)	1213 (45.2)	135 (46.7)

**= Reactogenicity subset*

N= number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.

n = Number of participants with the specified characteristic

a. *Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity*
b. *Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours*
c. *Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration*
d. *N= 290 for fatigue and N= 289 for all other events*

Safety: Systemic Reactogenicity 7 Days Post-Booster by Age Strata

	Phase 2/3 Booster 18-55 Years N=289 n (%)	Phase 1 Booster 65-85 years N= 12[d] n (%)
Any Fatigue[a]	185 (63.8)	5 (41.7)
Severe	13 (4.5)	0 (0)
Any Headache[a]	140 (48.4)	5 (41.7)
Severe	3 (1.0)	0 (0)
Any New or worsened muscle pain[a]	113 (39.1)	4 (33.3)
Severe	4 (1.4)	0 (0)
Any New or worsened joint pain[a]	73 (25.3)	2 (16.7)
Severe	1 (0.3)	0 (0)
Any Chills[a]	84 (29.1)	2 (16.7)
Severe	3 (1.0)	0 (0)
Any Diarrhea[b]	25 (8.7)	0 (0)
Severe	0 (0)	0 (0)
Any Vomiting[c]	5 (1.7)	0 (0)
Severe	0 (0)	0 (0)
Fever		
≥38.0°C	25 (8.7)	0 (0)
>38.9 to 40.0°C	1 (0.3)	0 (0)
> 40.0°C	0 (0)	0 (0)
Use of antipyretic or pain medication	135 (46.7)	4 (33.3)

N= number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.

n = Number of participants with the specified characteristic

a. *Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity*
b. *Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours*
c. *Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration*
d. *N= 290 for fatigue and N= 289 for all other events*

Safety: Unsolicited Adverse Events (1 Month after Booster)

Most common unsolicited adverse events (reported by ≥ 2 participants) from Booster Dose to 1 Month after Booster Dose, by System Organ Class and Preferred Term – Phase 3 Booster Safety Population (N=306)

	n (%)
Blood and lymphatic system disorders	**16 (5.2)**
Lymphadenopathy	16 (5.2)
Gastrointestinal disorders	**4 (1.3)**
Nausea	2 (0.7)
General disorders and administration site conditions	**8 (2.6)**
Injection site pain	2 (0.7)
Pain	2 (0.7)
Musculoskeletal and connective tissue disorders	**7 (2.3)**
Back pain	2 (0.7)
Neck pain	2 (0.7)
Nervous system disorders	**5 (1.6)**
Headache	2 (0.7)
Psychiatric disorders	**2 (0.7)**
Anxiety	2 (0.7)
Skin and subcutaneous tissue disorders	**3 (1.0)**
Dermatitis contact	2 (0.7)

N = number of subjects in the specified group. This value is the denominator for the percentage calculations. n = Number of subjects reporting at least 1 occurrence of the specified event.

- One **severe** event of lymphadenopathy was reported by 1 participant (onset of 2 days post-booster, recovered/resolved 5 days from onset
- Booster Dose to the data cutoff date (at least 2 months of post-Dose 3 follow-up):
  - One additional AE of acute myocardial infarction, reported as an unrelated **serious adverse event** on Day 62 post-Booster Dose that was recovered/resolved with sequelae.
  - No participants were withdrawn due to AEs.
  - No cases of anaphylaxis, hypersensitivity, Bell's palsy, appendicitis, or myocarditis/pericarditis were reported.
- Among the 23 Phase 1 booster recipients, no reported AEs 1 month after booster

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Summary of data

Immunogenicity

- Immunobridging success criteria for the USA_WA1/2020 strain were met for both pre-specified co-primary immunogenicity endpoints of GMT ratio and difference in seroresponse rates among study participants with no evidence of SARS-CoV-2 infection prior to 1 month after the booster dose
- Immunogenicity data to support effectiveness of the booster dose against the Delta variant are limited to exploratory analyses in a small number of participants using non-validated assays

Safety

- Safety data from 306 Phase 2/3 booster recipients do not show evidence of increased reactogenicity relative to Dose 2
- Difficult to reach conclusions about relative reactogenicity by age as only 12 participants ages 65-75 years received the booster dose
- Lymphadenopathy observed more frequently following the booster dose than after primary series doses (5.2% compared to 0.4%)
- No deaths, vaccine-related SAEs, or events of myocarditis, pericarditis, anaphylaxis, appendicitis, or Bell's palsy were reported among the 329 study participants who received the BNT162b2 booster dose

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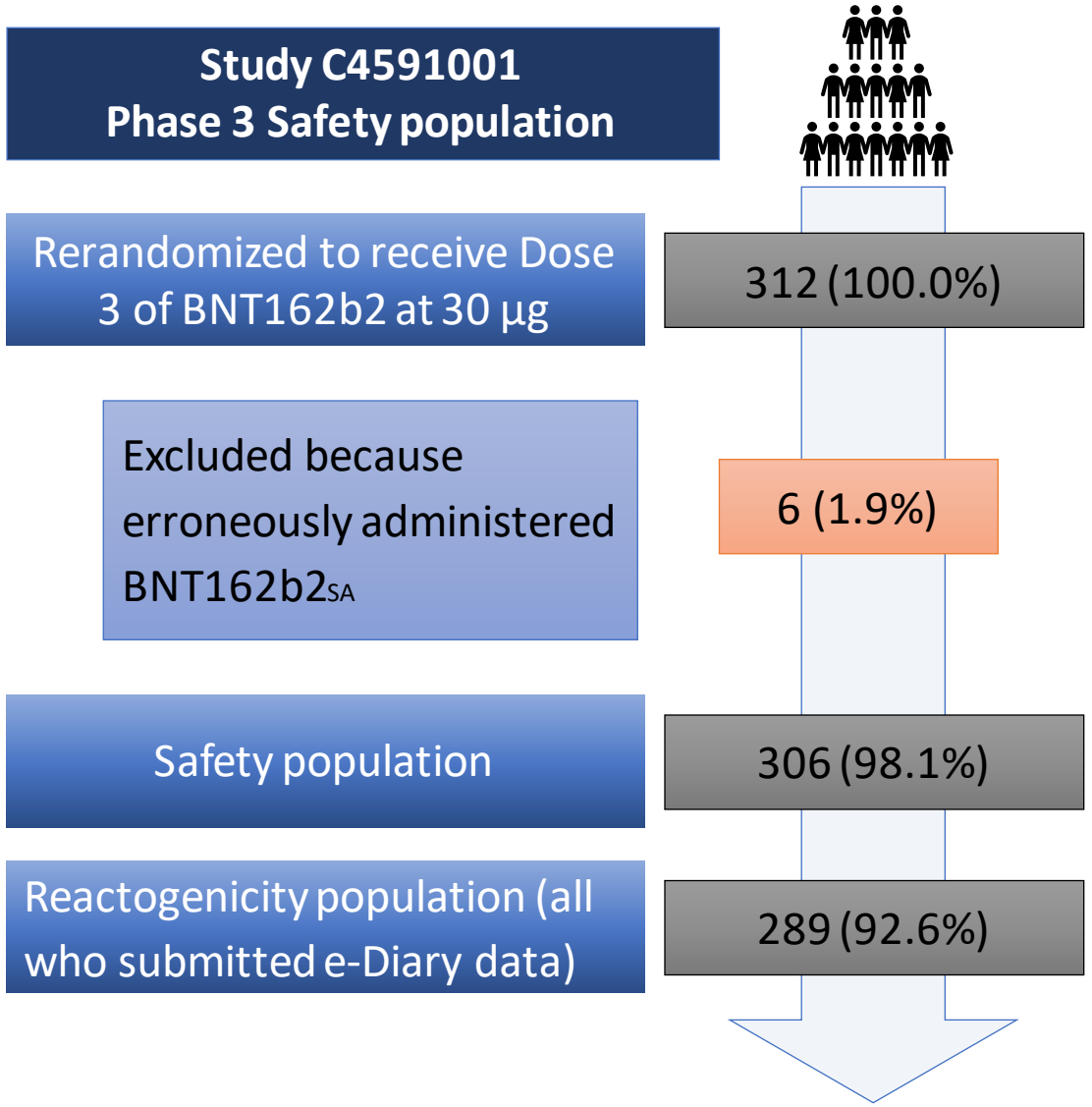
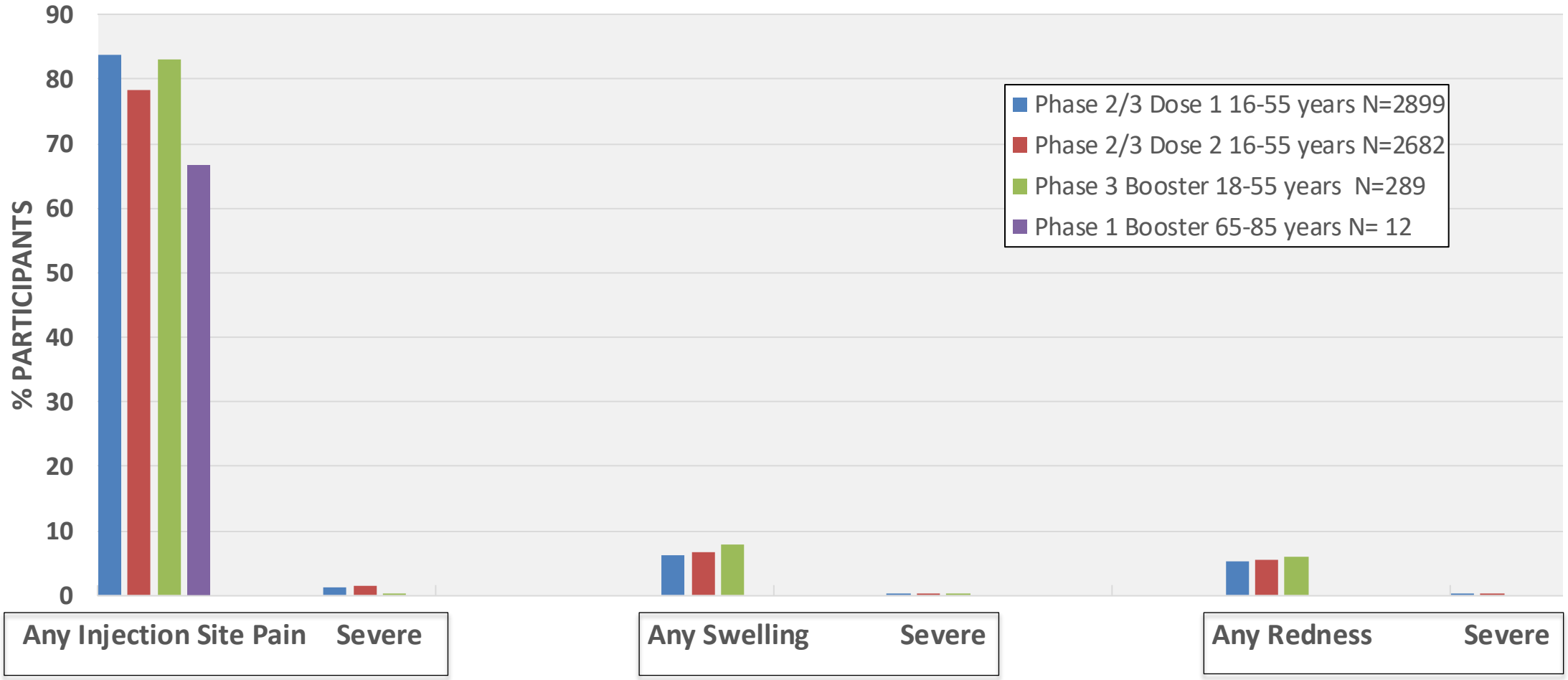
Safety Populations and Length of Follow-up



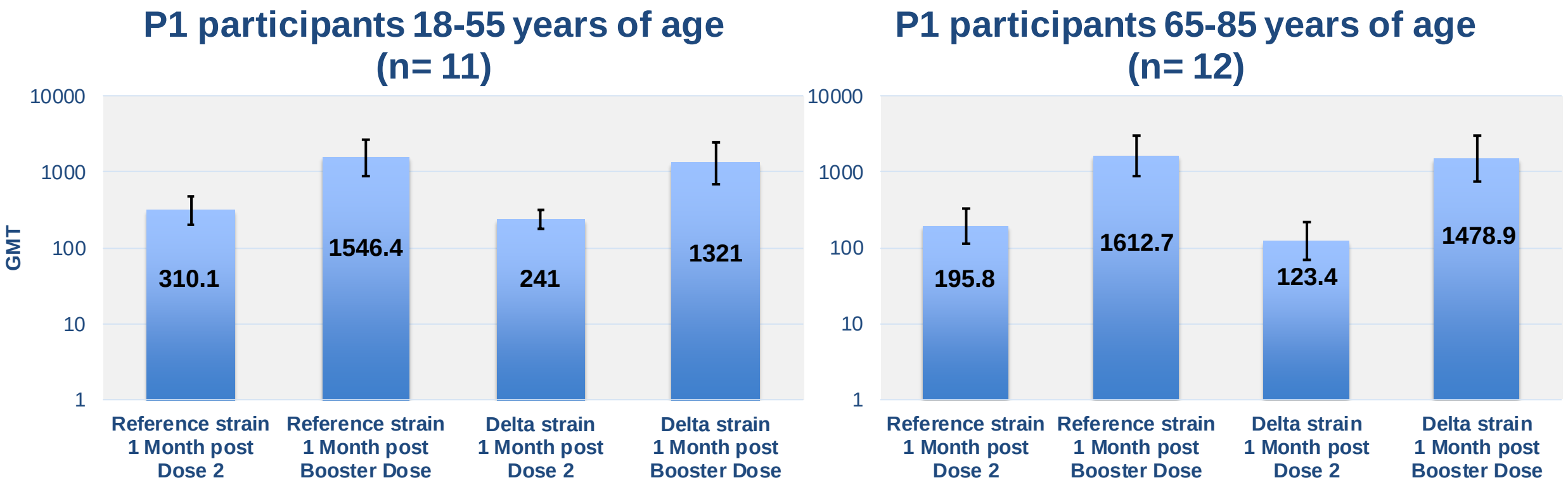
Length of Follow-up	Phase 3 18-55 Years Nb=306 nc (%)	Phase 1 18-55 & 65-85 Years N=23 n (%)
Dose 3 to cutoff date[a]		
<2 Months	1 (0.3)	
≥2 - <4 Months	305 (99.7)	
Mean	2.7	
Median	2.6	
Min, max	1.1, 2.8	

Safety: Local Reactogenicity for 7 Days After Each Dose



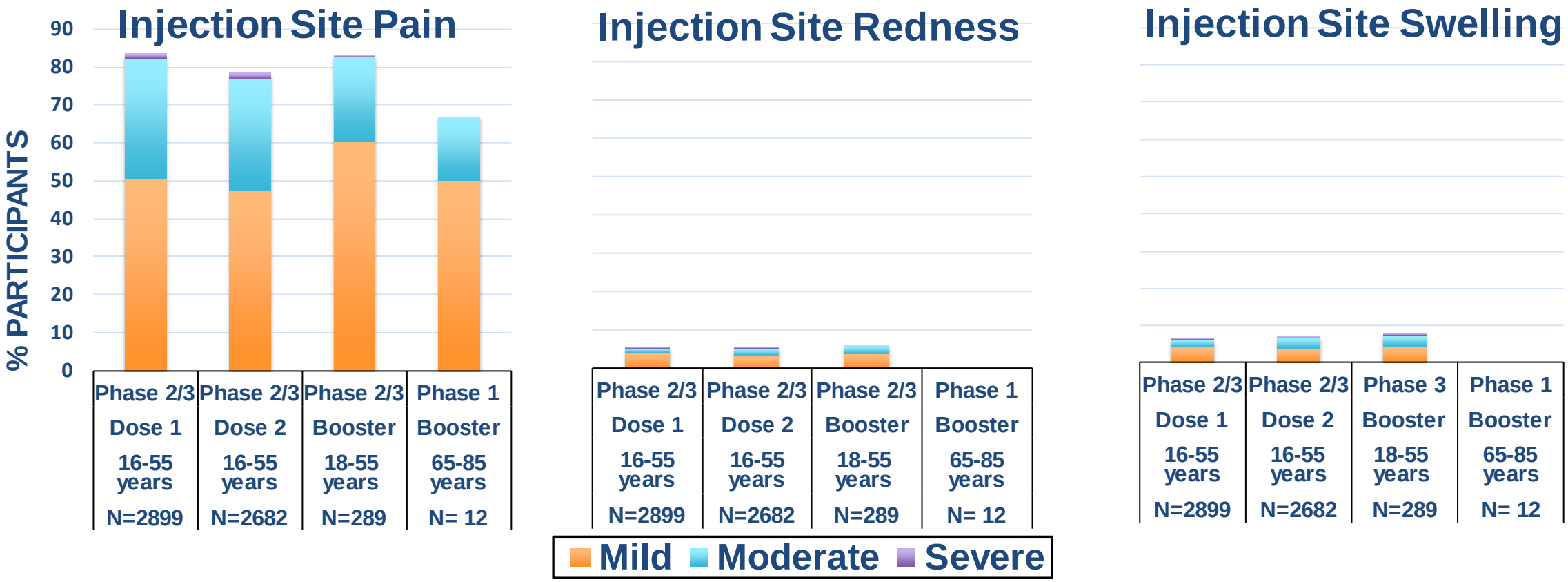
Exploratory Immunogenicity Analysis of Neutralization Activity Against USA_WA1/2020 Strain and Delta Variant

Booster all-available immunogenicity population



Limitations in the interpretation of the data include: small sample size and use of a non-validated SARS-CoV-2 plaque reduction neutralization assay with the USA_WA1/2020 and Delta variant input virus

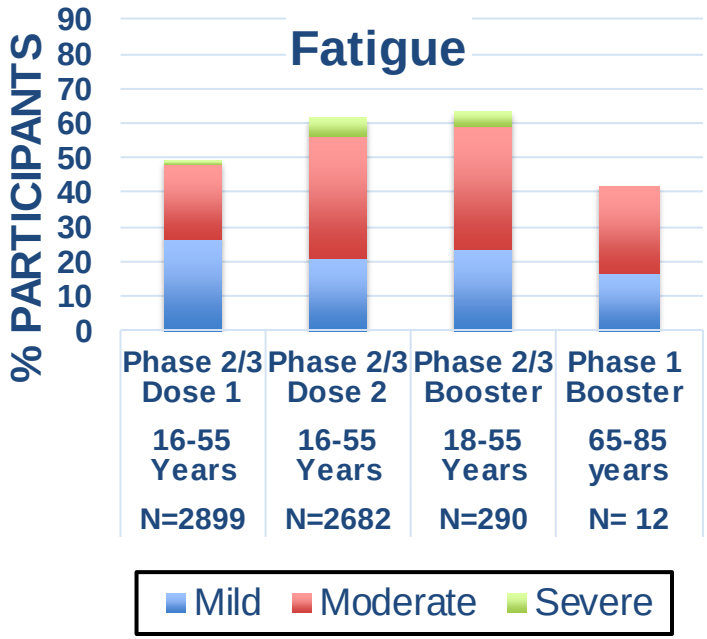
Safety: Local Reactogenicity (7 Days After Each Dose)

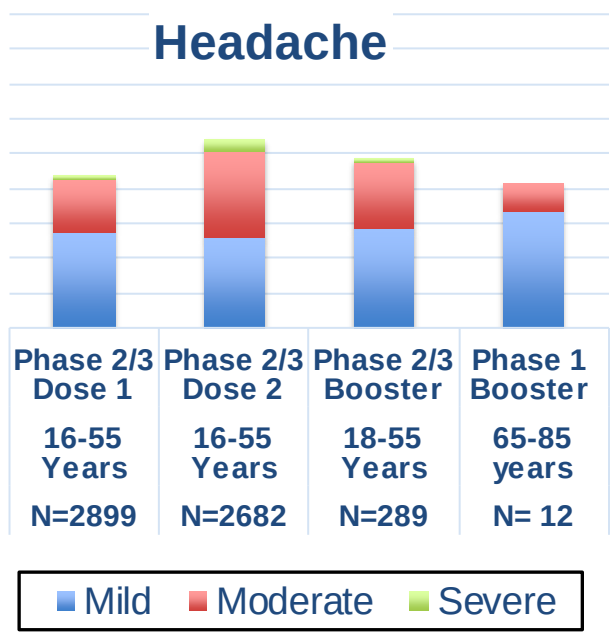


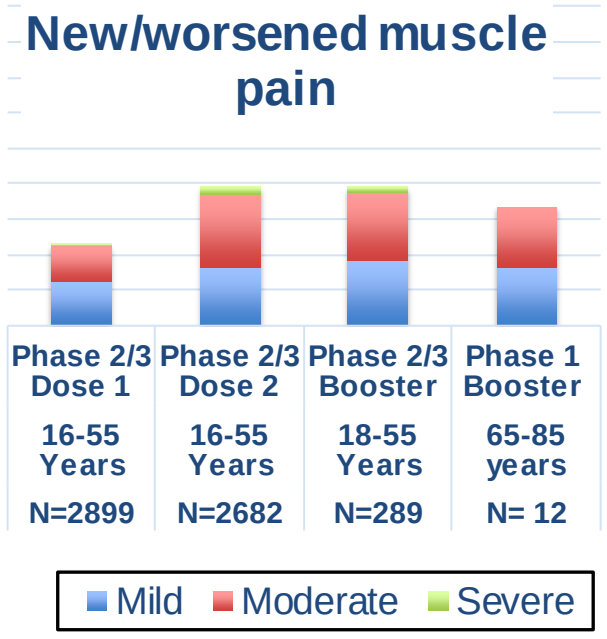
Phase 2/3 Dose 1 and 2 participants from reactogenicity subset; N= number of paticipants reporting at least 1 yes or no response for the specified reaction after the specified dose.

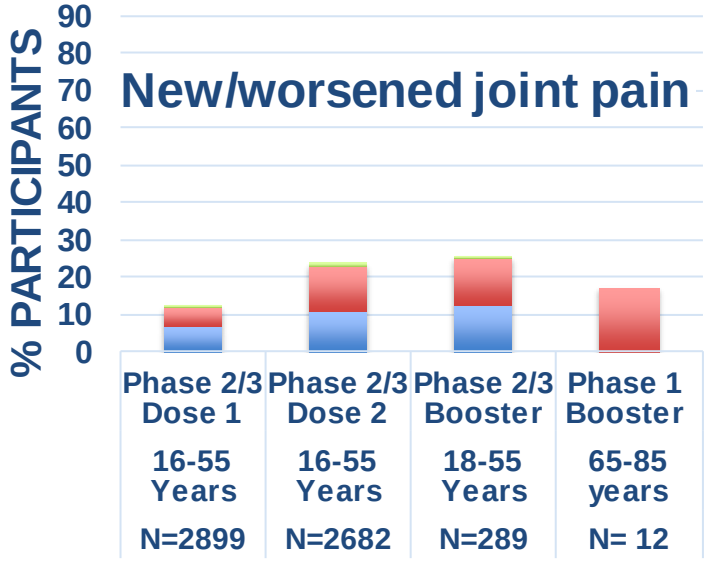
Redness and swelling: mild= >2.0 to 5.0 cm; moderate:= >5.0 to 10.0 cm; severe= >10.0 cm
Pain: mild= does not interfere with activity; moderate= interferes with activity; severe= prevents daily activity

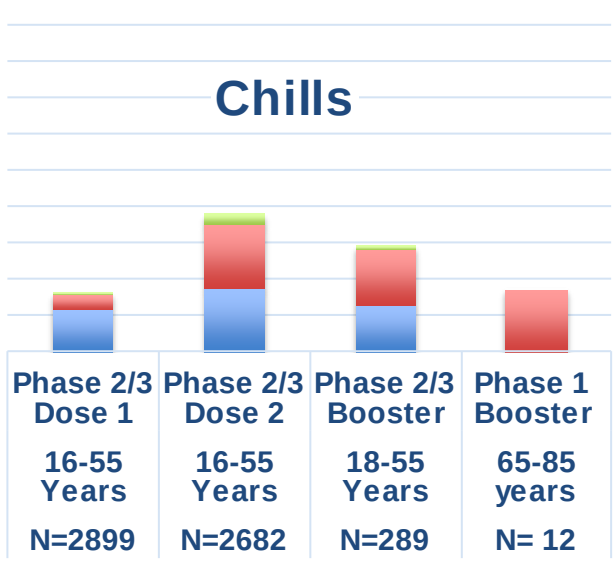
Safety: Systemic Reactogenicity (7 Days After Each Dose)









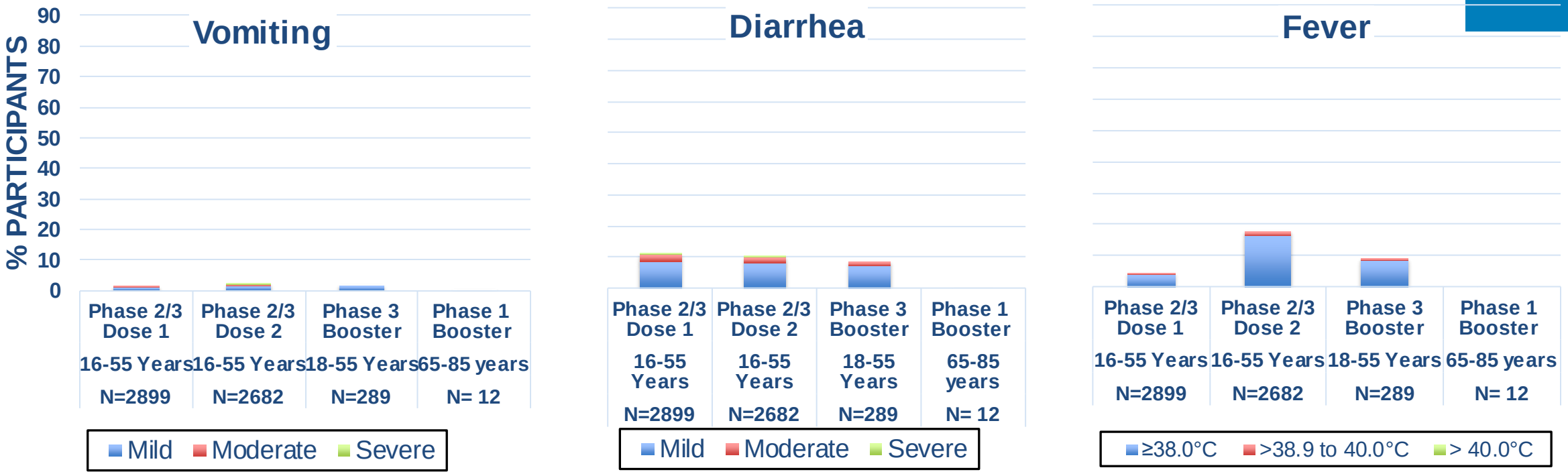


Phase 2/3 Dose 1 and 2 participants from reactogenicity subset

N= number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose

Mild= does not interfere with activity; Moderate= some interference with activity; Severe= prevents daily activity

Safety: Systemic Reactogenicity (7 Days After Each Dose)



Phase 2/3 Dose 1 and 2 participants from reactogenicity subset

N= number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose

Vomiting: mild= 1 to 2 times in 24 hours; moderate= >2 times in 24 hours; severe= requires intravenous hydration

Diarrhea: mild= 2 to 3 loose stools in 24 hours; moderate= 4 to 5 loose stools in 24 hours; severe= 6 or more loose stools in 24 hours

Safety: Local Reactogenicity for 7 Days After Each Dose

	Phase 2/3 Dose 1 16-55 years N=2899* n (%)	Phase 2/3 Dose 2 16-55 years N=2682* n (%)	Phase 3 Booster 18-55 years N=289 n (%)	Phase 1 Booster 65-85 years N= 12 n (%)
Any Injection Site Pain[a]	**2426 (83.7)**	**2101 (78.3)**	**240 (83.0)**	**8 (66.7)**
Mild	1464 (50.5)	1274 (47.5)	174 (60.2)	6 (50.0)
Moderate	923 (31.8)	788 (29.4)	65 (22.5)	2 (16.7)
Severe	39 (1.3)	39 (1.5)	1 (0.3)	0 (0)
Any Swelling[b]	**184 (6.3)**	**183 (6.8)**	**23 (8.0)**	**0 (0)**
Mild	124 (4.3)	110 (4.1)	13 (4.5)	0 (0)
Moderate	54 (1.9)	66 (2.5)	9 (3.1)	0 (0)
Severe	6 (0.2)	7 (0.3)	1 (0.3)	0 (0)
Any Redness[b]	**156 (5.4)**	**151 (5.6)**	**17 (5.9)**	**0 (0)**
Mild	113 (3.9)	90 (3.4)	10 (3.5)	0 (0)
Moderate	36 (1.2)	50 (1.9)	7 (2.4)	0 (0)
Severe	7 (0.2)	11 (0.4)	0 (0)	0 (0)

**= Reactogenicity subset; N= number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. n = Number of participants with the specified characteristic*

a. Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity

b. Mild: >2.0 to 5.0 cm; moderate: >5.0 to 10.0 cm; severe: >10.0 cm; Grade 4: necrosis (redness and swelling categories) or exfoliative dermatitis (redness category only)

Booster Dose Sub-Study

Global Phase 1/2/3 study in individuals ≥12 years of age (**C4591001**)

Booster Dose Sub-Study

Phase 1: participants 18-55 and 65-85 years of age randomized to receive 10, 20, or 30 µg of BNT162b2 were offered booster vaccination with BNT162b2 at 30 µg, approximately 6 to 12 months after their second dose of BNT162b2.

- A total of 11 participants 18-55 years of age and 12 participants 65-85 years of age received a booster dose of BNT162b2.

Phase 2/3: participants ≥ 12 years of age were randomized to receive 30 µg of BNT162b2 or placeboPhase 3 of the study included the primary efficacy endpoint.

- A total of 306 Phase 2/3 participants **18 55 years of age** received a booster dose of BNT162b2 at 30 µg, approximately 6 months after their second dose of BNT162b2 (starting March 2021).

Booster Dose Administration Timing

Months since Dose 2	Phase 1 18-55 Years N=11 n (%)	Phase 1 65-85 Years N=12 n (%)	Phase 2/3 18-55 Years N=312 n (%)
<5 Months	0 (0)	0 (0)	1 (0.3)
≥5 - <6 Months	0 (0)	0 (0)	28 (9.0)
≥6 - <7 Months	0 (0)	0 (0)	155 (49.7)
≥7 - ≤8 Months	-	-	128 (41.0)
≥7 - <8 Months	3 (27.3)	0 (0)	-
≥ 8- <9 Months	8 (72.7)	12 (100)	-
Mean (SD)	8.2 (0.27)	8.4 (0.12)	6.8 (0.56)
Median	8.2	8.4	6.8
Min, max	7.9, 8.8	8.2, 8.5	4.8, 8.0

N = number of participants in the specified group. This value is the denominator for the percentage calculations.
n = Number of participants with the specified characteristic.