BNT162b2 [COMIRNATY® (COVID-19 Vaccine, mRNA)] Booster (Third) Dose

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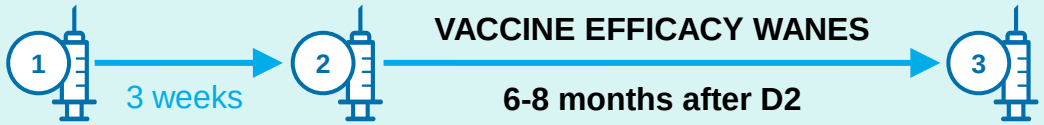
Data to Support Public Health Need for Booster

Data from Israel and the United States suggest vaccine protection against COVID-19 infection wanes approximately 6 to 8 months following the second dose

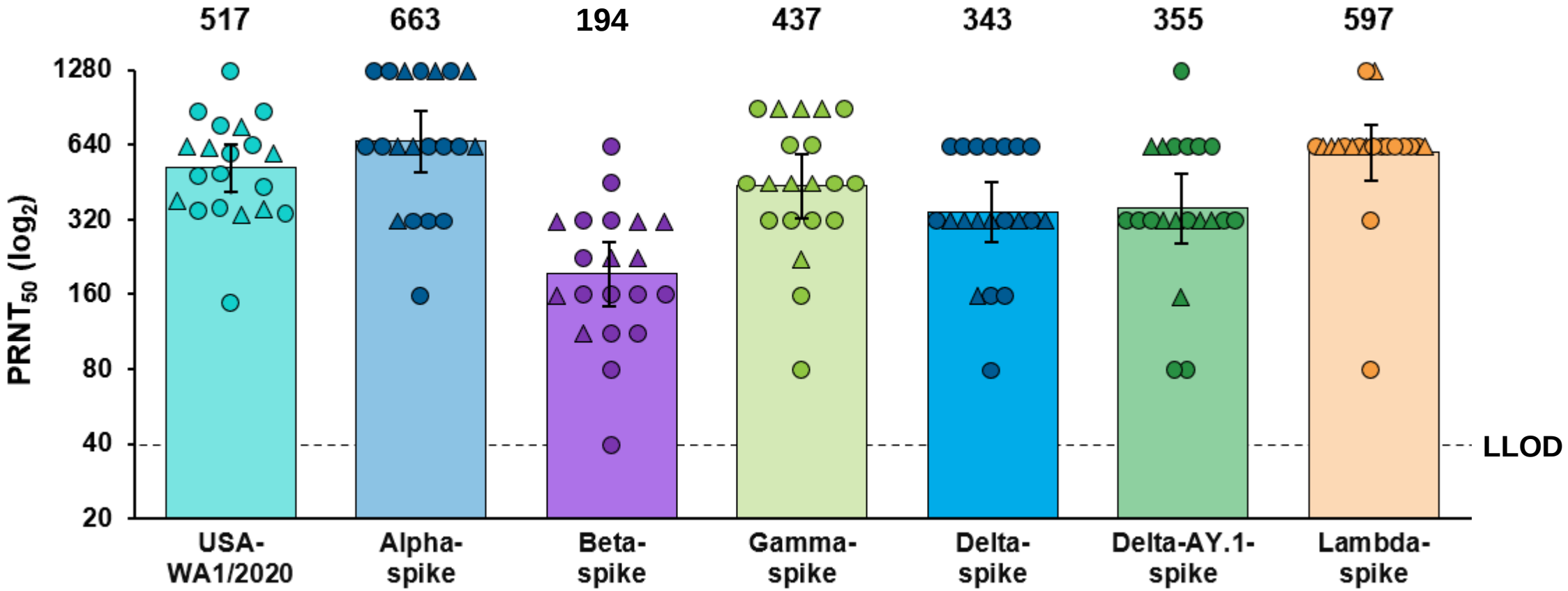


Data Source	Type	Result
Kaiser Permanente Southern California (KPSC)	Retrospective Cohort Study	• Reduction in VE is likely due to waning effectiveness rather than to Delta escaping vaccine protection
FDA requested analysis	Post-hoc	• Waning effectiveness over time
C4591001 substudy	RCT	• A booster dose of BNT162b2 has an acceptable safety profile and elicits robust immune responses
Israeli booster vaccination program	RWE	• Reactogenicity profile similar or better to that seen after the second primary series dose • Restores high levels of protection against COVID-19 outcomes

Overview of Clinical Program

BNT162b2-elicited Sera Effectively Neutralize a Broad Range of SARS-CoV-2 Spike Variants After 2 Doses

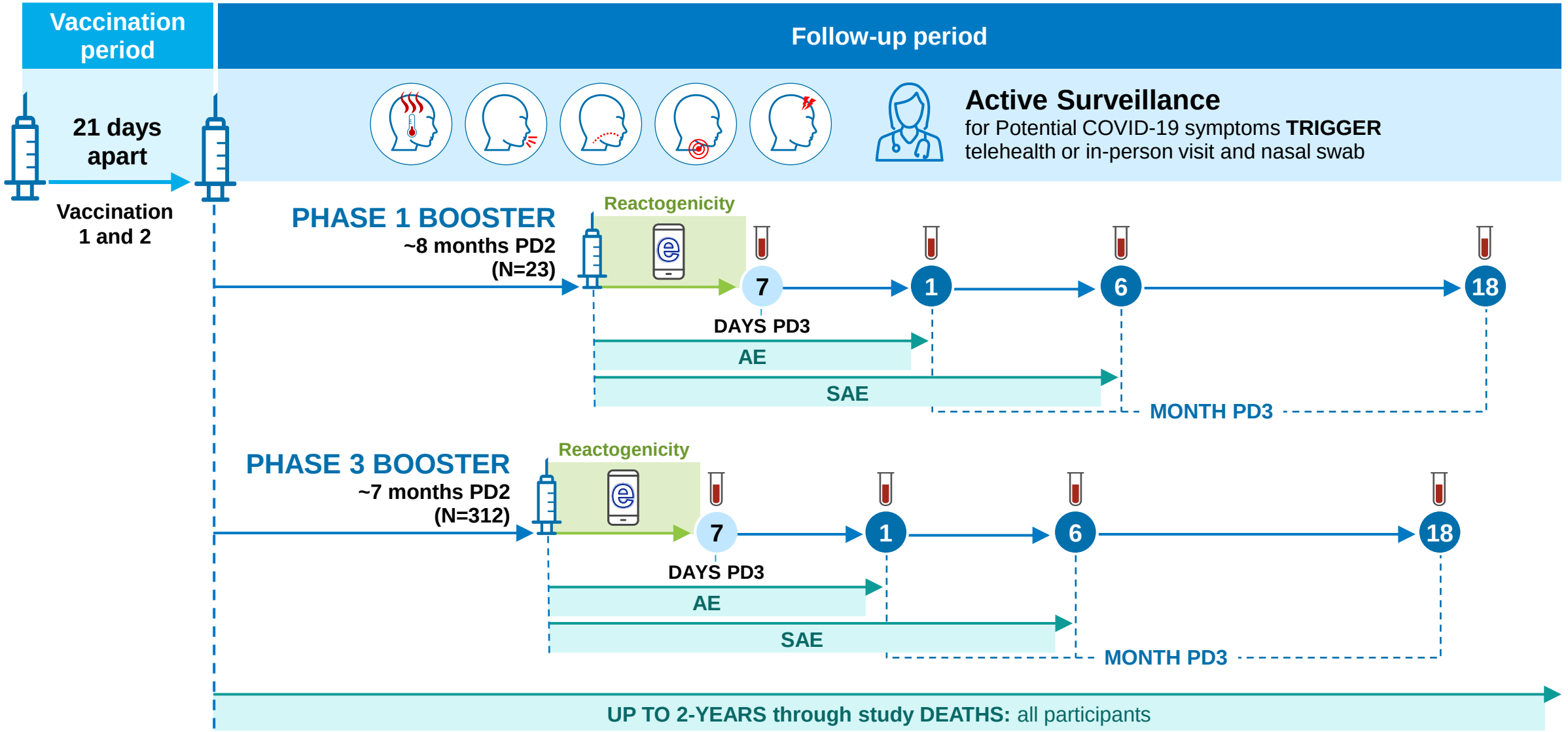
Viruses are isogenic, recombinant SARS-CoV-2 strains, with variant spike coding sequences on a common, USA-WA1/2020 genetic background



Circles: 2 weeks PD2
Triangles: 4 weeks PD2

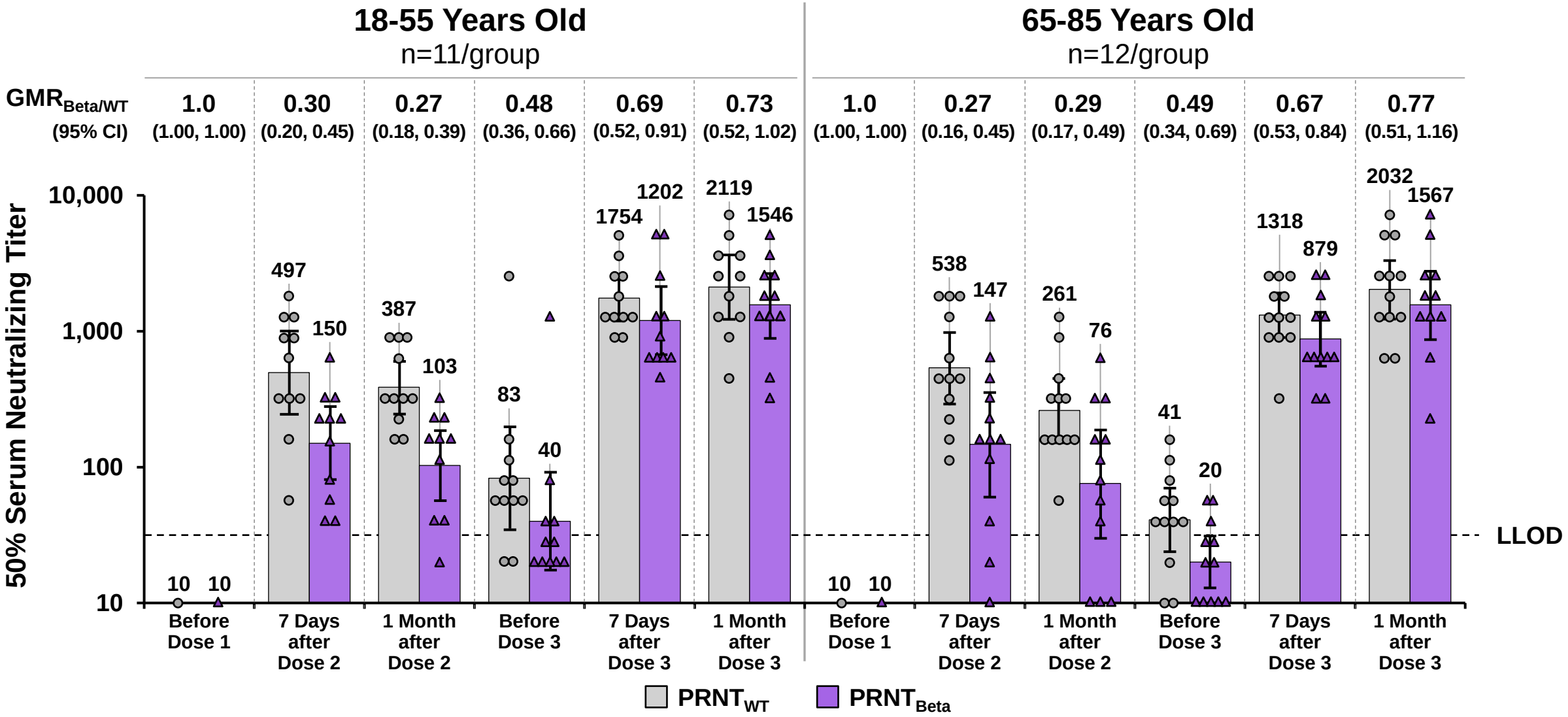
Data from Liu et al., 2021, Nature DOI: ; L10.1038/s41586-021-03693-y; Liu et al., 2021 NEJM, DOI: 10.1056/NEJMc2102017; Delta-AY.1, Lambda data submitted for publication

3rd Dose Evaluated in Both Phase 1 and Phase 3 Participants from Original Pivotal Trial



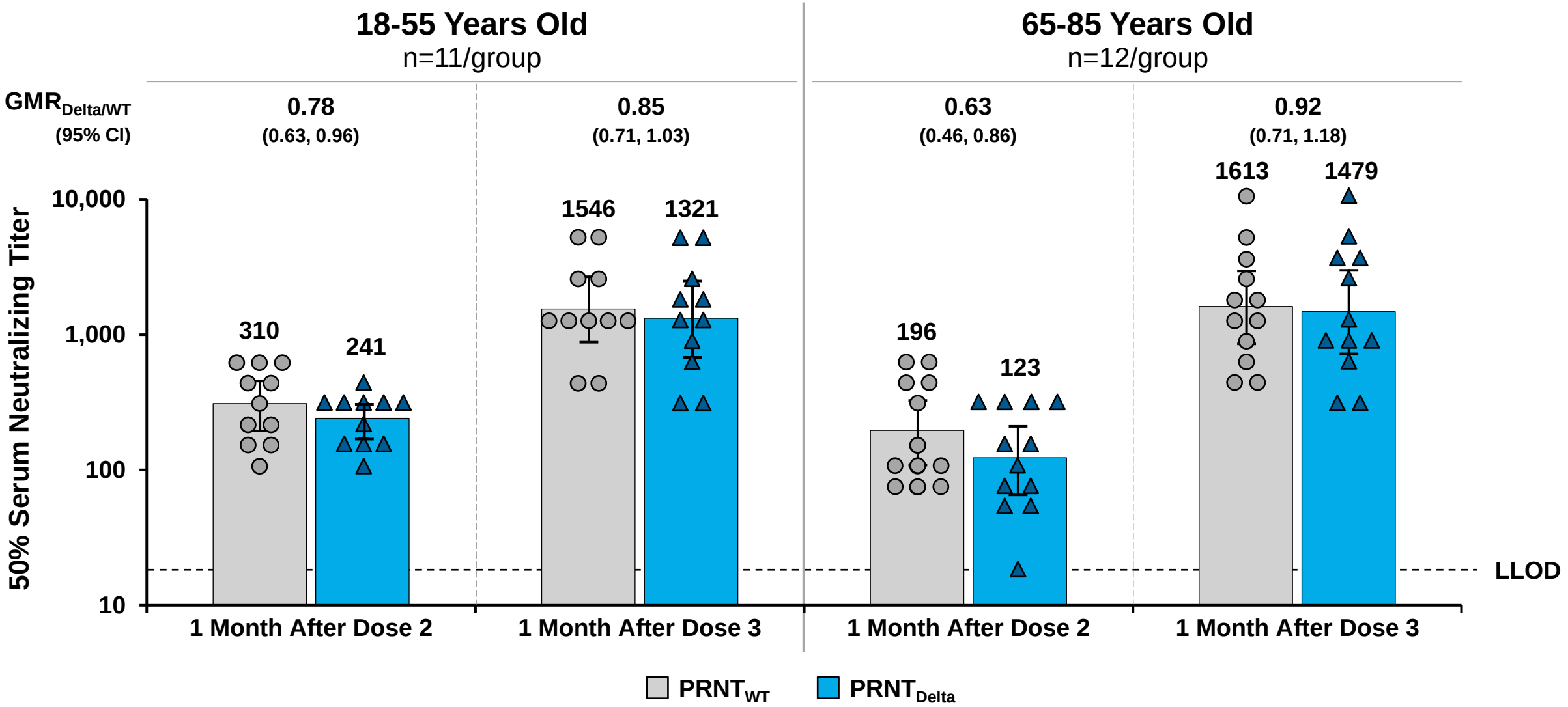
Summary of Data for BNT162b2 Booster (3rd Dose) Administered in C4591001: Phase 1

Post-dose 3 BNT162b2 GMTs Indicate a Substantial Boost and Reduced Gap Between WT and Beta Neutralization



SARS-CoV-2 Neutralization with BNT162b2 Vaccine Dose 3 | NEJM (openathens.net), DOI: 10.1056/NEJMc2113468

Post-dose 3 BNT162b2 GMTs Indicate a Substantial Boost to the Delta Variant Similar to Wild Type



SARS-CoV-2 Neutralization with BNT162b2 Vaccine Dose 3 | NEJM (openathens.net), DOI: 10.1056/NEJMc2113468.

Summary of Data for BNT162b2 Booster (3rd Dose) Administered in C4591001: Phase 3

Subjects Receiving 3rd Dose were Representative of US 18-55 Year Olds in Parent Study

		SAFETY POPULATION
		BNT162b2 N=306
Sex, n (%)	Male	140 (45.8)
	Female	166 (54.2)
Race, n (%)	White	249 (81.4)
	Black or African American	28 (9.2)
	American Indian or Alaska Native	2 (0.7)
	Asian	16 (5.2)
	Native Hawaiian or other Pacific Islander	1 (0.3)
	Multiracial	4 (1.3)
	Not reported	6 (2.0)
Ethnicity, n (%)	Hispanic/Latino	85 (27.8)
	Non-Hispanic/non-Latino	219 (71.6)
	Not reported	2 (0.7)
Comorbidity[a]	Present	174 (56.9)
Age at booster vaccination (years)	Mean (SD)	41.3 (9.44)
	Min, Max	(19,55)
Time from Dose 2 to booster dose (months)	Mean (SD)	6.8 (0.56)
	Min, Max	(4.8. 8.0)

a. One or more Charlson comorbidity index, hypertension or obese

Immunogenicity

Geometric Mean Ratio of Neutralization Titers Non-inferiority Criterion (Post-dose 3 vs. Post-dose 2) was Met, with Titers ~3-fold Higher

		Booster Evaluable Immunogenicity Population			
		1 Month Post Booster (Dose 3)	1 Month After Dose 2	1M Post Booster/1M PD2[a]	
Assay	N	GMT (95% CI)	GMT (95% CI)	GMR (97.5% CI)	Met NI (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)	210	2476.4 (2210.1, 2774.9)	753.7 (658.2, 863.1)	3.29 (2.76, 3.91)	Yes

a. Noninferiority is declared if the lower bound of the 97.5% confidence interval is > 0.67 and the point estimate of the GMR is ≥0.8
NT50 = 50% neutralizing titers (Booster Evaluable Immunogenicity Population)

Noninferiority of Booster Dose Demonstrated Based on Proportion of Subjects with a Seroresponse

Seroresponse is defined as achieving a ≥4-fold rise from baseline (before Dose 1)

		Booster Evaluable Immunogenicity Population		
		1 Month Post Booster (Dose 3)	1 Month After Dose 2	1M Post Booster - 1M PD2[a]
Assay	N	n (%) (95% CI)	n (%) (95% CI)	% (97.5% CI)
SARS-CoV-2 neutralization assay - NT50 (titer)	198	197 (99.5) (97.2, 100.0)	194 (98.0) (94.9, 99.4)	1.5 (-0.7, 3.7)

a. Noninferiority is declared if the lower bound of the 2-sided 97.5% confidence interval for the percentage difference is greater than -10
If the baseline measurement is below the LLOQ, a postvaccination assay result ≥4 × LLOQ is considered a seroresponse

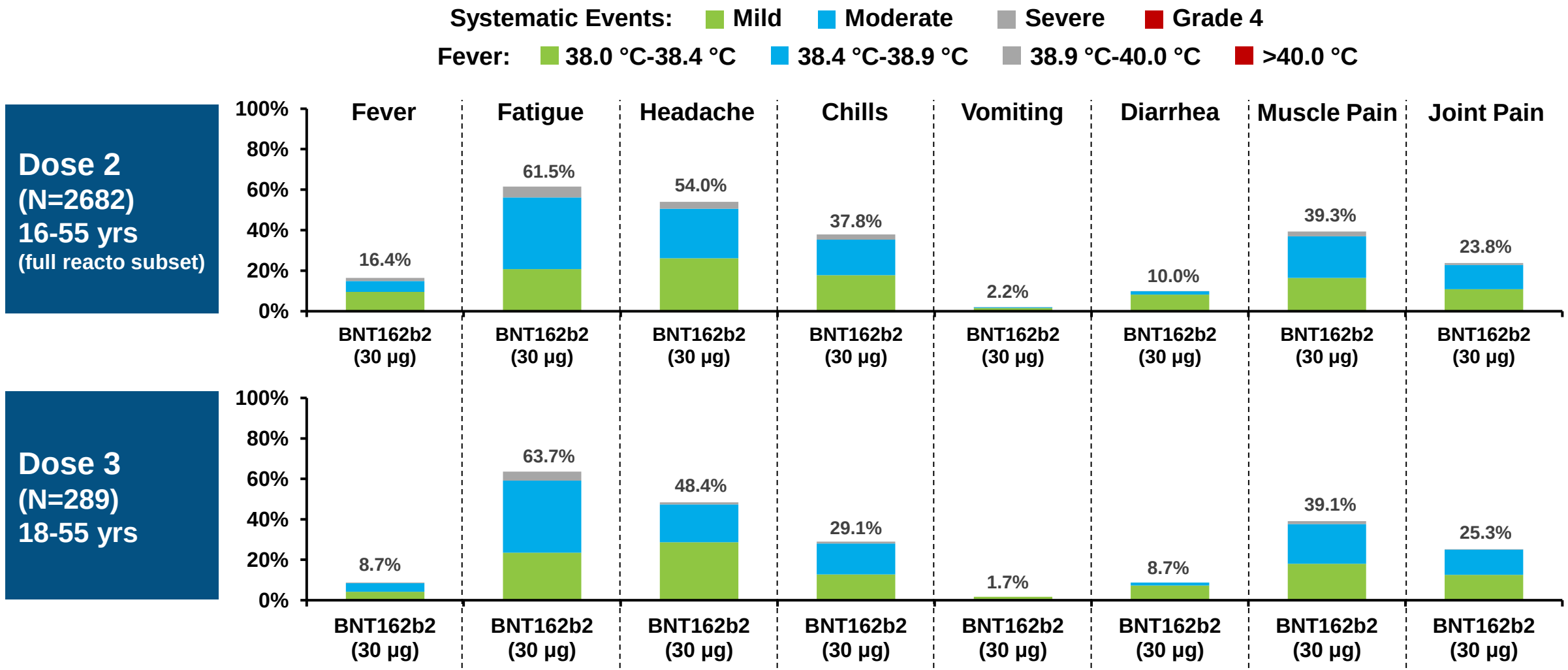
Safety

Follow-up Time for Booster Dose

		BNT162b2 (30µg) Booster (3rd) Dose N=306
Total exposure from booster vaccination to cutoff date (months)	Mean (SD)	2.7 (0.15)
	Median	2.6
	Min, Max	(1.1, 2.8)
Total exposure from Dose 2 to cutoff date (months)	Mean (SD)	9.4 (0.57)
	Median	9.5
	Min, Max	(7.5, 10.8)

Data cutoff date 17Jun2021

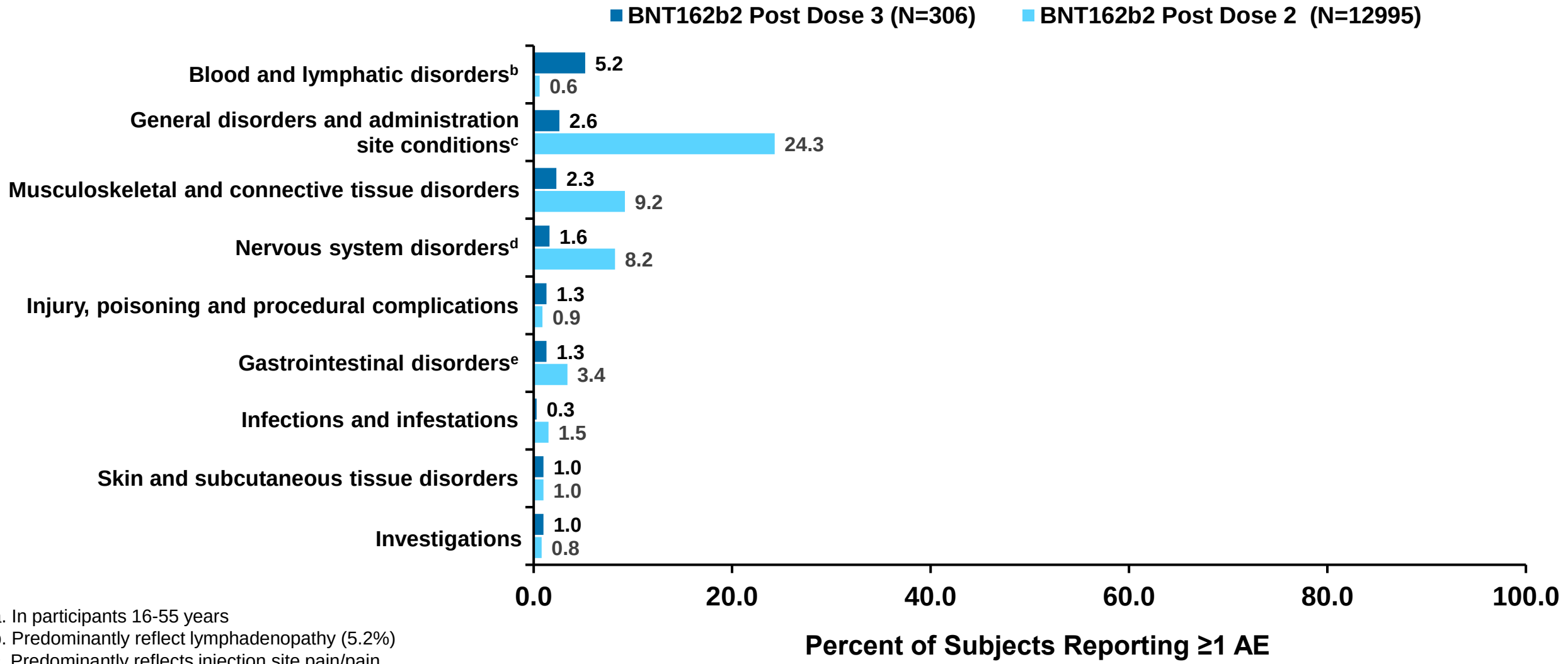
Systemic Events by Maximum Severity within 7 Days of 3rd Dose Similar to Post-dose 2 in Parent Study



Fatigue, headache, chills, muscle pain, joint pain severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization
Vomiting severity definition: Mild=1-2 time in 24h; Moderate=>2 times in 24h; Severe=Requires IV hydration; Grade 4=ER visit or hospitalization
Diarrhea severity definition: Mild=2-3 times in 24h; Moderate=4-5 times in 24h; Severe=6 or more times in 24h; Grade 4=ER visit or hospitalization

Adverse Events by System Organ Class ≥1% 1 Month Post 3rd Dose Overall Less than Those Post-dose 2 in Parent Study[a]

Safety Population



a. In participants 16-55 years
b. Predominantly reflect lymphadenopathy (5.2%)
c. Predominantly reflects injection site pain/pain
d. Predominantly reflects headache
e. Predominantly reflects nausea

One Serious Adverse Event Through Median 2.6 Months Follow-up, Assessed as Unrelated to Vaccination

	BNT162b2 (30 µg) N=306 n (%)
Any event	**1 (0.3)**
Acute myocardial infarction	**1 (0.3)**

Ongoing and Active Pharmacovigilance and Pharmacoepidemiology

Pharmacovigilance

- Expanded intake capability with web-based AE portal
- Active follow-up of safety reports
- Frequent signal detection and evaluation
- Post-approval safety monitoring
- Continued pharmacovigilance for adverse events of special interest including anaphylaxis and myocarditis

Proactive Risk minimization

- Labeling & Educational Materials
- Real-time product quality monitoring (cold-chain)

Pharmacoepidemiology Studies

- Extended follow up (for high-severity low-incidence events in large populations)
- Safety surveillance studies (including analysis of booster dose and myocarditis)
- Vaccine effectiveness
- Event background rate (contextualization)

Collaborate with Vaccine Safety Stakeholders

- Interface with CDC (VAERS, V-SAFE, VSD, CISA) to optimize pharmacovigilance activities
- Collaborate with international groups to ensure consistent approach to PV

Summary of Safety and Immunogenicity

Safety and Immunogenicity Data Meet FDA Criteria for Booster Dose ≥16 Years of Age

Phase 1

- Resulted in acceptable safety profile
- Elicited robust immune responses against the wild-type (reference strain), Beta and Delta variants of concern support effectiveness to be inferred against Delta variant

Phase 3

- Safety profile similar or better than dose 2
- Elicited immune responses against wild-type non-inferior to responses observed post dose 2
- Met protocol pre-specified immunobridging success criteria for GMTs and seroresponse rates

BNT162b2 demonstrated high efficacy (>90%) against COVID-19 and safety in the pivotal clinical trial after a 2-dose primary series

While VE against severe disease and hospitalization remains high in most populations in the US, data from Israel predicts this may not be sustained