BNT162b2 (COVID-19 Vaccine, mRNA)
6 Months Through 4 Years of Age

Advisory Committee on Immunization Practices

June 17, 2022

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Presentation Agenda

1	**Introduction**	
2	**Phase 2/3 Clinical Data**	• Safety • Immunogenicity • Efficacy
3	**Benefit Risk**	

Clinical Data

Pfizer-BioNTech COVID-19 Vaccine BNT162b2 for Pediatric Populations: 6 Months to <5 Years - Study Overview

Phase 1

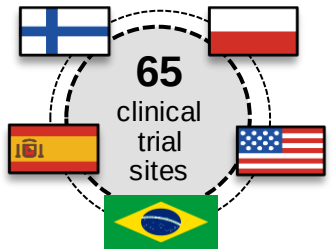
64
PARTICIPANTS

6 months through 4 years

Identification of preferred dose level

- **3 µg**
- **10 µg**

Phase 2/3



2:1
randomization

- **N=3,013** BNT162b2
- **N=1,513** Placebo (Saline)

Non-inferior immune responses have been established to infer vaccine efficacy

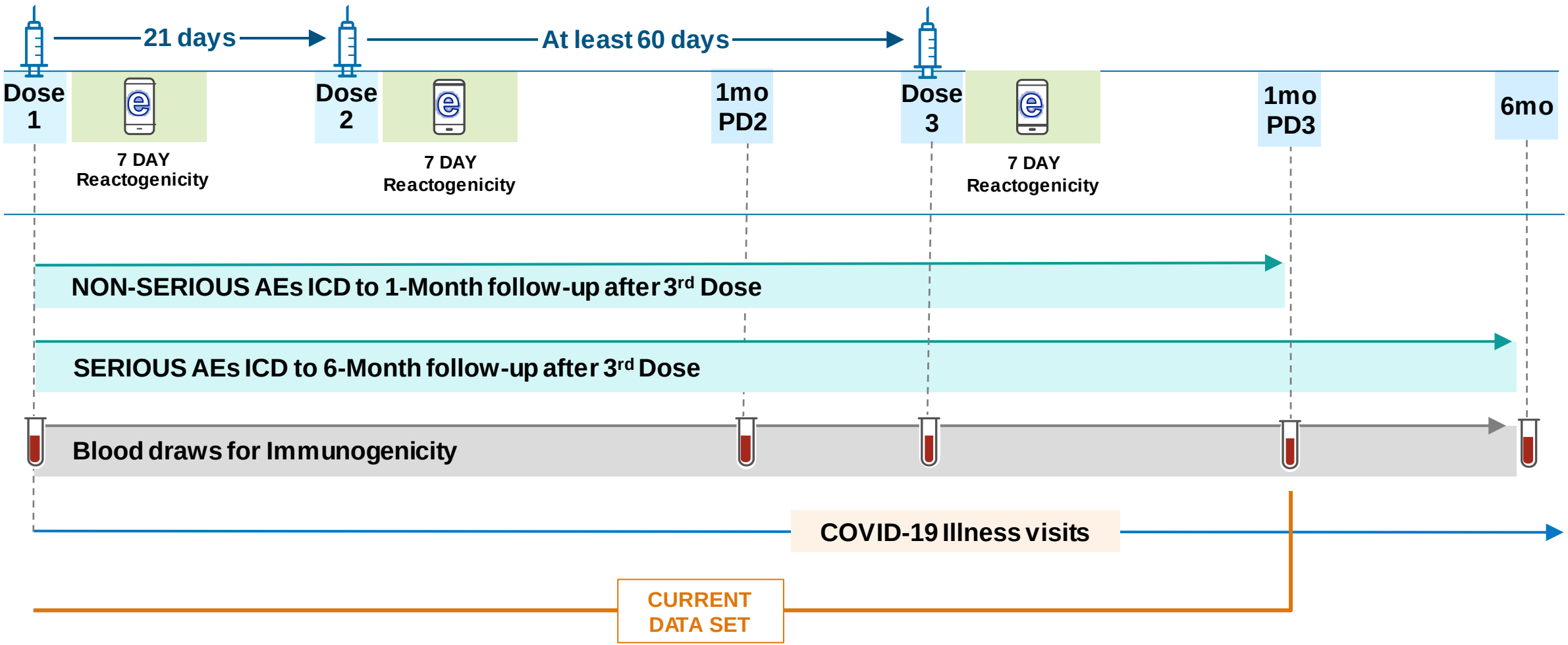
Children
6 months to <5-year-olds

COMPARED TO

16–25-year-olds
from the pivotal Phase 3 study

Although not required for EUA approval, COVID-19 surveillance was conducted permitting evaluation of vaccine efficacy

Phase 2/3 Timelines of Participants



Safety

Data Cut-off date: 29 April 2022

AGE
2 to <5

Demographics Were Balanced between Vaccine and Placebo Recipients

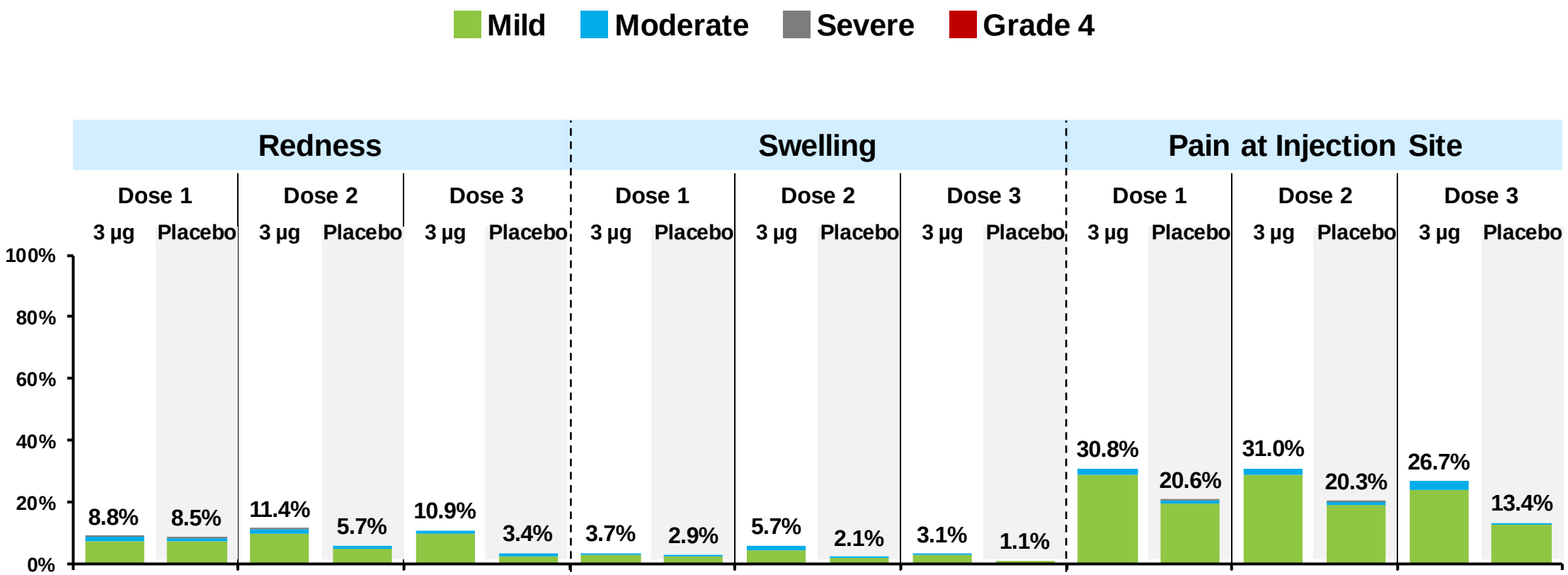
Phase 2/3 Safety Population (N=2750)

		BNT162b2 (3 µg) N=1835	Placebo N=915
Sex, n (%)	Male	901 (49.1)	471 (51.5)
	Female	934 (50.9)	444 (48.5)
Race, n (%)	White	1469 (80.1)	720 (78.7)
	Black or African American	94 (5.1)	41 (4.5)
	American Indian or Alaska native	<1%	<1%
	Asian	127 (6.9)	76 (8.3)
	Native Hawaiian or other Pacific Islander	<1%	<1%
	Multiracial	131 (7.1)	69 (7.5)
	Not reported	<1%	<1%
Ethnicity, n (%)	Hispanic/Latino	264 (14.4)	120 (13.1)
	Non-Hispanic/non-Latino	1568 (85.4)	795 (86.9)
	Not reported	<1%	0
Obese[a], n (%)	Yes	120 (6.5)	45 (4.9)
Baseline SARS-CoV-2 positive[b]	Yes	233 (12.7)	125 (13.7)
Comorbidities[c], n (%)	Yes	222 (12.1)	130 (14.2)

a. 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.
b. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
c. Participants who had at least one of the prespecified comorbidities based on MMWR 69(32);1081-1088 and/or obesity (BMI ≥ 95th percentile)

AGE
2 to <5

No Increase in Local Reactions from Dose 2 to 3 Mostly Mild to Moderate with No Grade 4 Events

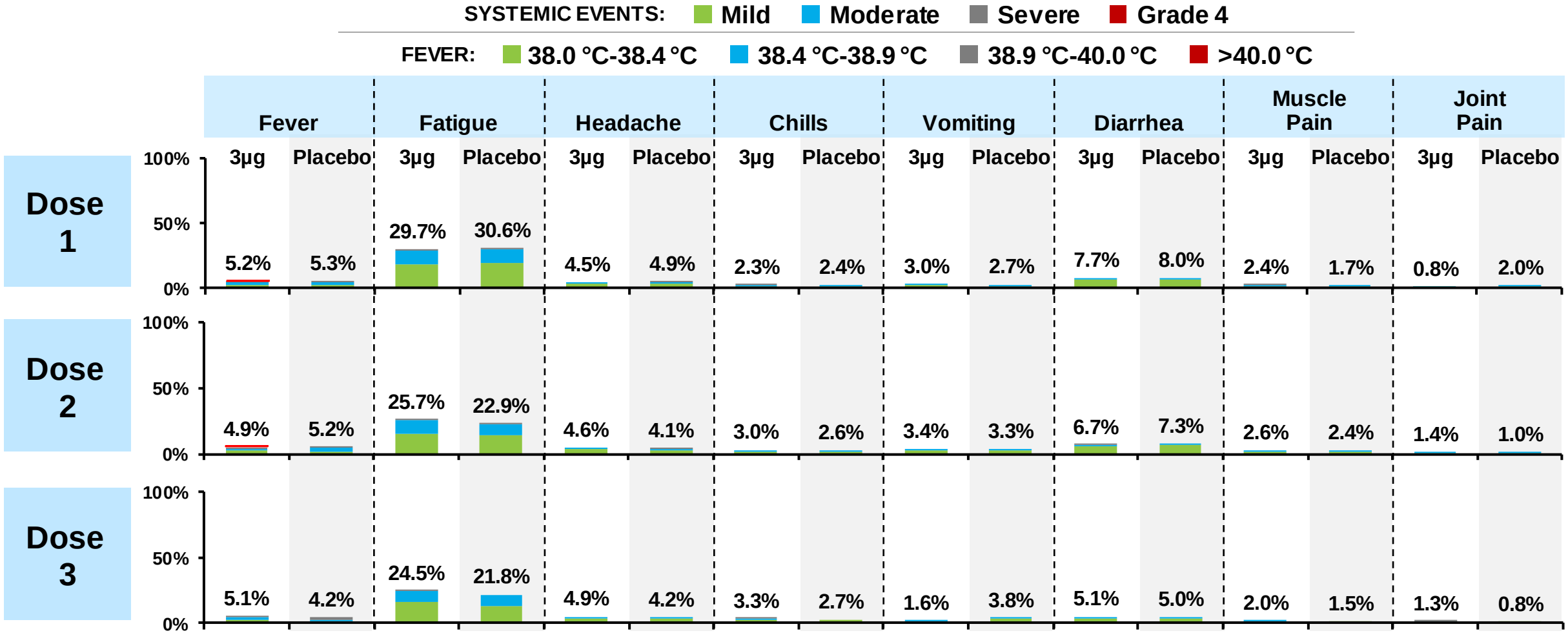


Redness and swelling severity definition: Mild= ≥0.5-2cm, Moderate= >2-7 cm; Severe= >7cm; Grade 4= necrosis (or exfoliative dermatitis for redness only)
Pain at injection site severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization
Dose 1: N=2734 Dose 2: N=2657 Dose 3: N=814

AGE
2 to <5

Systemic Events Within 7 Days After Each Dose Mostly Mild to Moderate

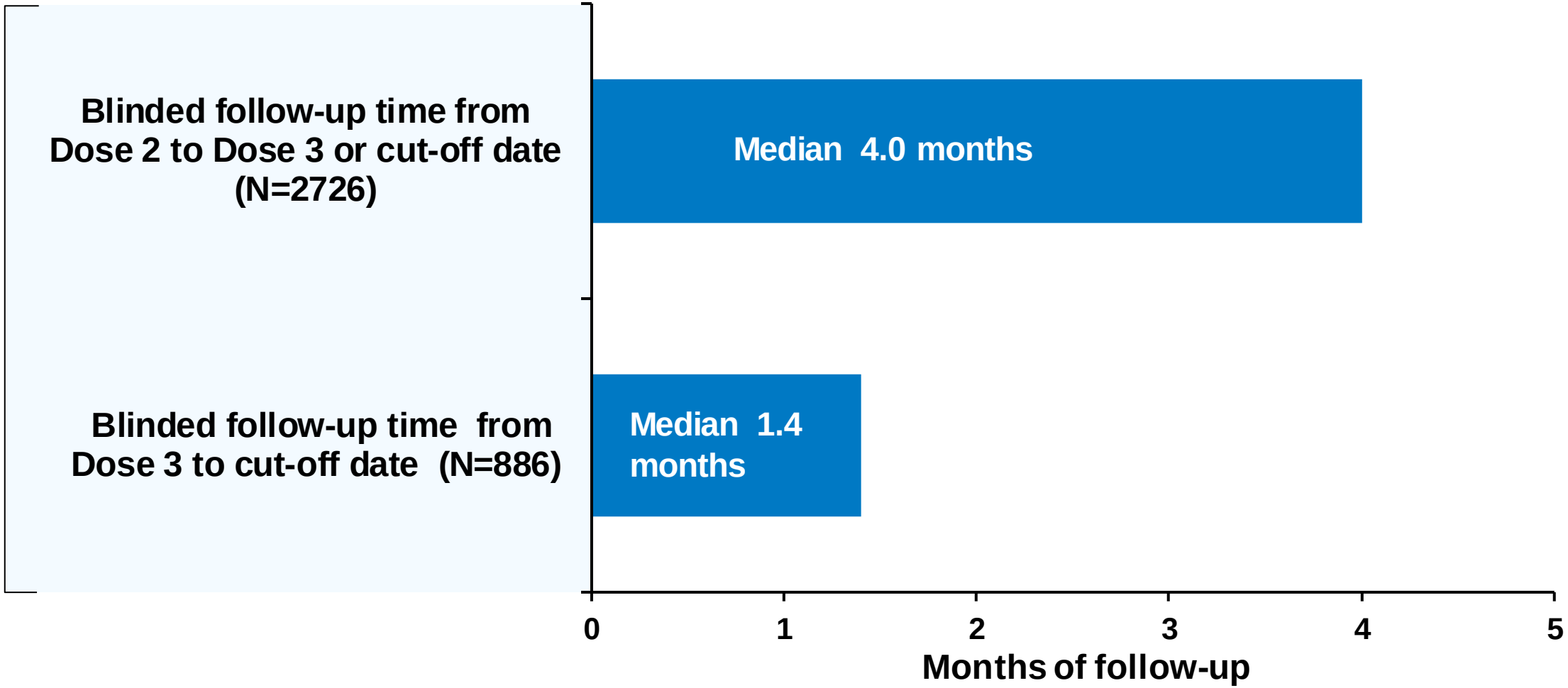
Similar incidence seen between BNT162b2 and placebo



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=>2times 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
Dose 1: N=2734 Dose 2: N=2657; Dose 3: N=814

AGE
2 to <5

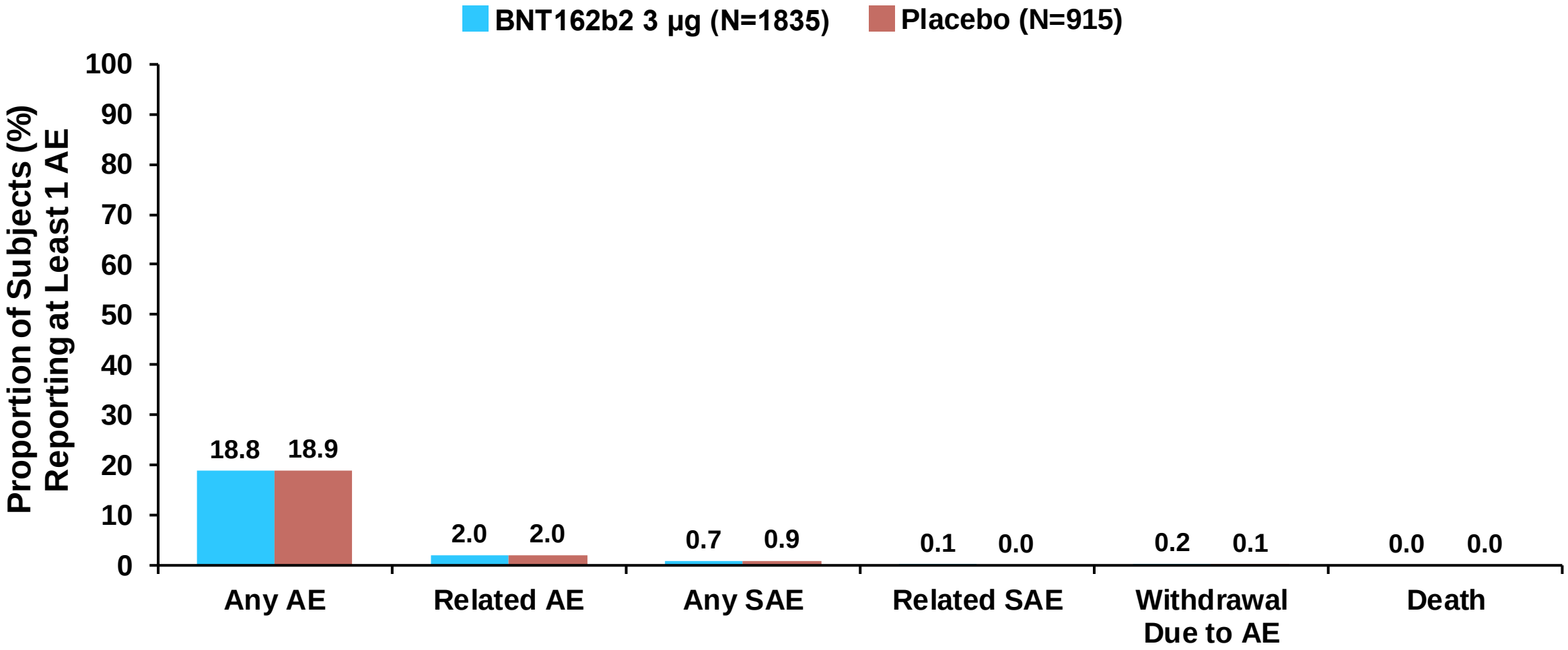
Safety Follow-up



AGE
2 to <5

Adverse Events: Similar Incidence Seen Between BNT162b2 and Placebo

Dose 1 to Data Cut-off (29 April 22)



AGE
6 mo. to <2

Demographics Were Balanced between Vaccine and Placebo Recipients

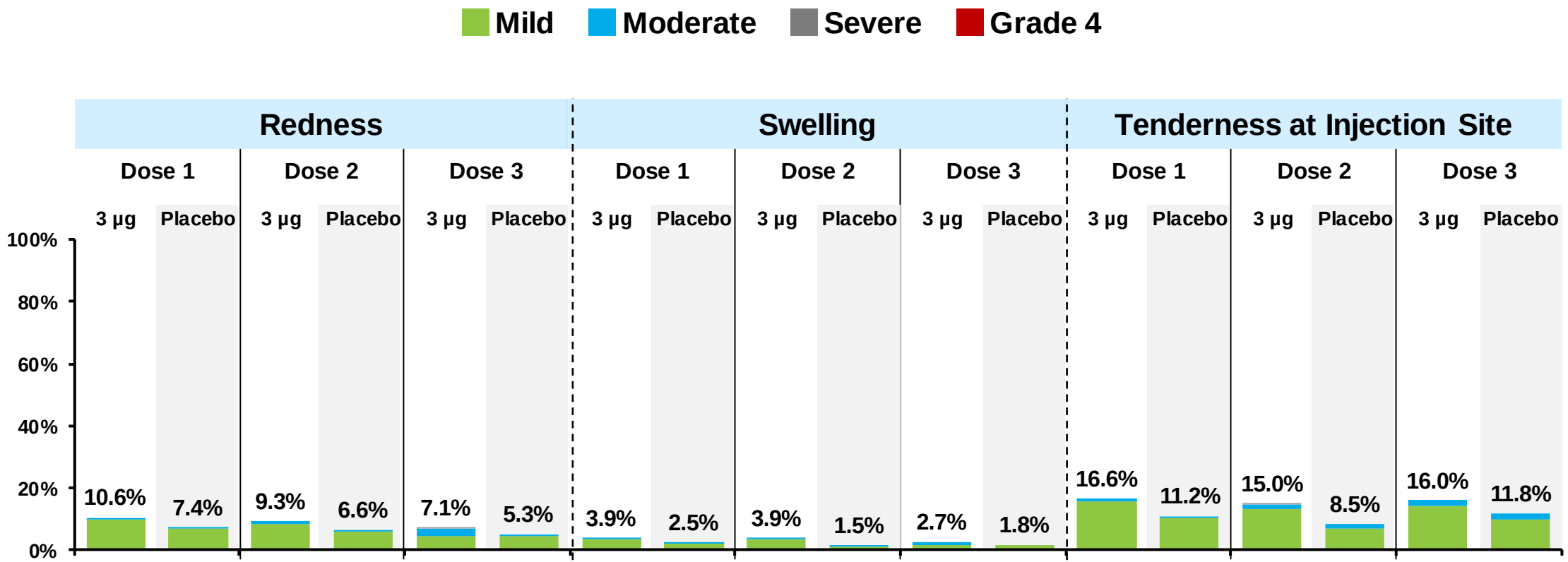
Phase 2/3 Safety Population (N=1776)

		BNT162b2 (3 µg) N=1178	Placebo N=598
Sex, n (%)	Male	589 (50.0)	291 (48.7)
	Female	589 (50.0)	307 (51.3)
Race, n (%)	White	922 (78.3)	480 (80.3)
	Black or African American	42 (3.6)	24 (4.0)
	American Indian or Alaska native	<1%	<1%
	Asian	91 (7.7)	40 (6.7)
	Multiracial	117 (9.9)	49 (8.2)
	Not reported	<1%	<1%
Ethnicity, n (%)	Hispanic/Latino	161 (13.7)	64 (10.7)
	Non-Hispanic/non-Latino	1014 (86.1)	530 (88.6)
	Not reported	<1%	<1%
Baseline SARS-CoV-2 positive[a]	Yes	89 (7.6)	44 (7.4)
Comorbidities[b], n (%)	Yes	50 (4.2)	34 (5.7)

a. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
b. Participants who had at least one of the prespecified comorbidities based on MMWR 69(32);1081-1088

AGE
6 mo. to <2

Local Reactions were Mostly Mild to Moderate with No Grade 4 Events

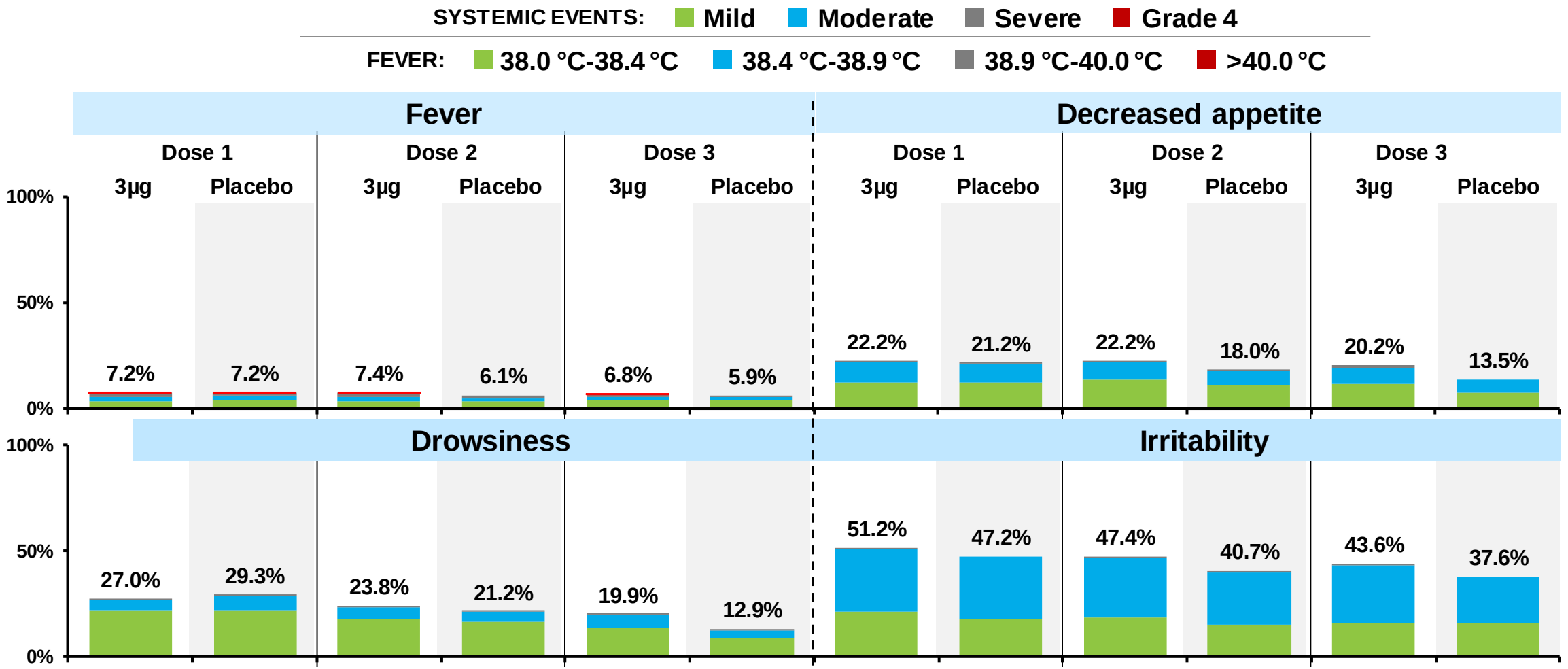


Redness and swelling severity definition: Mild= ≥0.5-2cm, Moderate= >2-7 cm; Severe= >7cm; Grade 4= necrosis (or exfoliative dermatitis for redness only)
Tenderness at injection site severity definition: Mild=hurts with gentle touch; Moderate=crying with gentle touch; Severe=limitation of limb movement; Grade 4=ER visit or hospitalization
Dose 1: N=1768; Dose 2: N=1738; Dose 3: N=535

AGE
6 mo. to <2

Systemic Events Within 7 Days After Each Dose Mostly Mild to Moderate

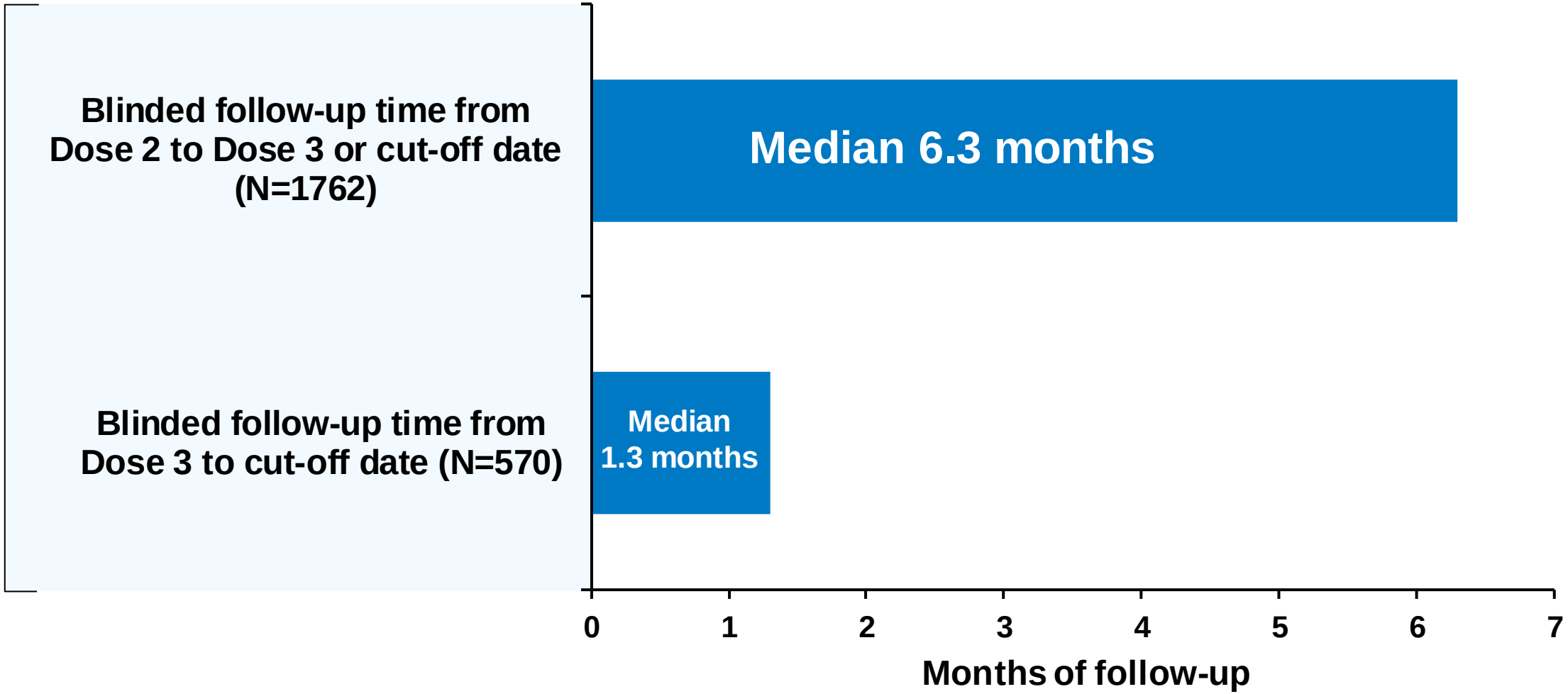
Similar incidence seen between BNT162b2 and placebo



Decreased appetite severity definition: Mild=decreased interest in eating; Moderate=decreased oral intake; Severe=refusal to feed; Grade 4=ER visit or hospitalization
Drowsiness severity definition: Mild=increased/prolonged sleeping; Moderate: slightly subdued; Severe=Disabling/not interested in daily activity; Grade 4=ER visit or hospitalization
Irritability severity definition: Mild=easily consolable; Moderate=requires increased attention; Severe=inconsolable; Grade 4=ER visit or hospitalization
Dose 1: N= 1768; Dose 2: N= 1738; Dose 3: N=535

AGE
6 mo. to <2

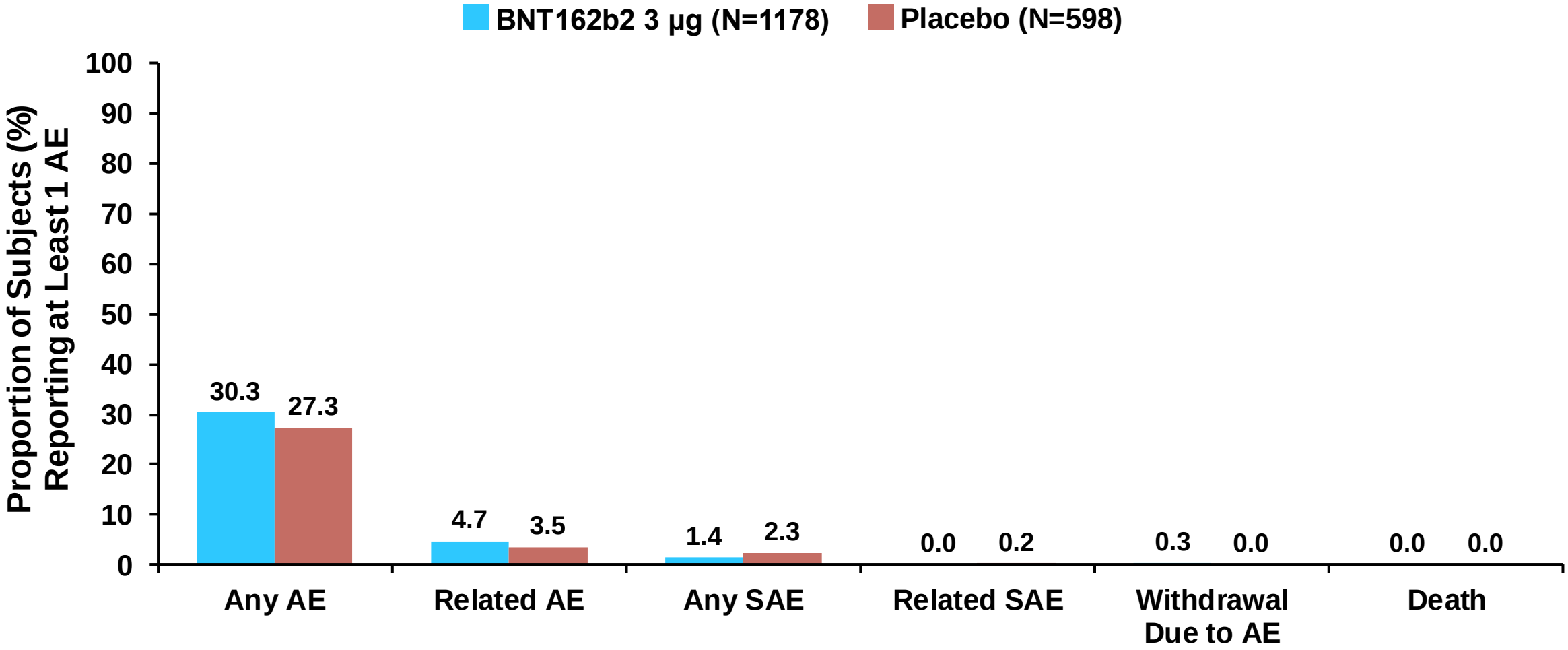
Safety Follow-up



AGE
6 mo. to <2

Adverse Events: Similar Incidence Between BNT162b2 and Placebo with No Meaningful Difference Noted

Dose 1 to Data Cut-off (29 April 22)



AGE
6 mo. to <5

Few Adverse Events of Special Interest (AESIs) Were Reported

- **FDA AESIs (both age groups):**
  - Predominant categories were potential angioedema and hypersensitivity comprising mainly urticarias and rashes
  - Similar incidence between BNT162b2 and placebo for these categories
- **CDC Defined AESIs:**
  - No vaccine related anaphylaxis
  - No myocarditis/pericarditis
  - No Bell's palsy (or facial paralysis/paresis)
  - No MIS-C

AGE
6 mo. to <5

Favorable Safety Profile and Well-tolerated

Phase 2/3 Safety Population (N=4,526)

- Vaccine reactions were mostly mild to moderate and short lived, with systemic reactions comparable to placebo
- Reactions were comparable after dose 1, 2, and 3
- The unsolicited AE profile mostly reflected reactogenicity or common childhood illnesses
- The favorable safety profile should encourage vaccine adherence for each of the three doses

Immunogenicity

AGE
2 to <5

Immunobridging Criteria Were Not Met for GMR, But Were Met for Seroresponse After Dose 2

Post-dose 2 Compared to 16 to 25 Years of Age Post-dose 2

GMR	Dosing/Sampling Time Point	BNT162b2 (3 µg) 2 to <5 years n	BNT162b2 (3 µg) 2 to <5 years GMT (95% CI)	BNT162b2 (30 µg) 16-25 years n	BNT162b2 (30 µg) 16-25 years GMT (95% CI)	2 to <5 years / 16-25 years GMR (95% CI)	2 to <5 years / 16-25 years Met Immuno-bridging (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)	2 / 1 Month	243	763.9 (688.5, 847.5)	252	1255.4 (1131.2, 1393.3)	0.61 (0.53, 0.70)	N

Immunobridging is declared if the lower bound of the 95% confidence interval of the GMR is > 0.67 and the GMR is ≥0.8

Seroresponse	Dosing/Sampling Time Point	BNT162b2 (3 µg) 2 to <5 years N	BNT162b2 (3 µg) 2 to <5 years n (%) (95% CI)	BNT162b2 (30 µg) 16-25 years N	BNT162b2 (30 µg) 16-25 years n (%) (95% CI)	Difference in % 2 to <5 years - 16-25 years % (95% CI)	Difference in % 2 to <5 years - 16-25 years Met Immuno-bridging (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)	2 / 1 Month	243	235 (96.7) (93.6, 98.6)	251	245 (97.6) (94.9, 99.1)	-0.9 (-4.3, 2.3)	Y (but success not declared)

Seroresponse defined as achieving a ≥4 fold rise from baseline (before Dose 1)
Immunobridging is declared if the lower bound of the 95% confidence interval for the percentage difference is greater than -10

AGE
2 to <5

Immunobridging of Geometric Mean Ratio's was Highly Favorable With ≥65 Year-old Participants After Dose 2

Post-dose 2 Compared to ≥65 Years of Age Post-dose 2

GMR	Dosing/Sampling Time Point	BNT162b2 (3 µg) 2 to <5 years n	BNT162b2 (3 µg) 2 to <5 years GMT (95% CI)	BNT162b2 (30 µg) ≥65 years N	BNT162b2 (30 µg) ≥65 years GMT (95% CI)	2 to <5 years / ≥65 years GMR (95% CI)
SARS-CoV-2 neutralization assay - NT50 (titer)	2 / 1 Month	149	830.0 (727.0, 947.6)	149	431.8 (368.1, 506.6)	1.92 (1.56, 2.36)

Vaccine Efficacy in the ≥65 year olds was 94.5% (95% Confidence Intervals: 88.3, 97.8)*, so a non-inferior immune response seen in the 2 to <5 year olds is likely to predict efficacy

*Table 19: BLA C4591001 Vaccines Study Report: Interim Report – 6 Month Update: A Phase 1/2/3, Placebo Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals

AGE
6 mo. to <2

Immunobridging Criteria Met for Both GMR and Seroresponse After Dose 2

Post-dose 2 Compared to 16 to 25 Years of Age Post-dose 2

GMR	Dosing/Sampling Time Point	BNT162b2 (3 µg) 6 months to <2 years n	BNT162b2 (3 µg) 6 months to <2 years GMT (95% CI)	BNT162b2 (30 µg) 16-25 years n	BNT162b2 (30 µg) 16-25 years GMT (95% CI)	6mo to <2y / 16-25 years GMR (95% CI)	6mo to <2y / 16-25 years Met Immuno-bridging (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)	2 / 1 Month	245	979.7 (893.2, 1074.6)	238	946.8 (850.8, 1053.7)	1.03 (0.90, 1.19)	Y

Immunobridging is declared if the lower bound of the 95% confidence interval of the GMR is > 0.67 and the GMR is ≥0.8

Seroresponse	Dosing/Sampling Time Point	BNT162b2 (3 µg) 6 months to <2 years N	BNT162b2 (3 µg) 6 months to <2 years n (%) (95% CI)	BNT162b2 (30 µg) 16-25 years N	BNT162b2 (30 µg) 16-25 years n (%) (95% CI)	Difference in % 6mo to <2y - 16-25 years % (95% CI)	Difference in % 6mo to <2y - 16-25 years Met Immuno-bridging (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)	2 / 1 Month	245	240 (98.0) (95.3, 99.3)	238	229 (96.2) (92.9, 98.3)	1.7 (-1.4, 5.2)	Y

Seroresponse defined as achieving a ≥4 fold rise from baseline (before Dose 1)
Immunobridging is declared if the lower bound of the 95% confidence interval for the percentage difference is greater than -10

AGE
2 to <5

Immunobridging Criteria Met for Both GMR and Seroresponse in Participants Without Prior Infection

Post-dose 3 Compared to 16 to 25 Years of Age Post-dose 2

	BNT162b2 (3 µg) 2 to <5 Years 1M Post-Dose 3		BNT162b2 (30 µg) 16-25 years 1M Post-Dose 2		2 to <5 / 16-25 years	
GMR	**n**	**GMT (95% CI)**	**n**	**GMT (95% CI)**	**GMR (95% CI)**	**Met Criteria (Y/N)**
SARS-CoV-2 neutralization assay - NT50 (titer)	143	1535.2 (1388.2, 1697.8)	170	1180.0 (1066.6, 1305.4)	1.30 (1.13, 1.50)	Y

Immunobridging is declared if the lower bound of the 95% confidence interval of the GMR is > 0.67 and the GMR is ≥0.8 and ≥1 per FDA criteria

	BNT162b2 (3 µg) 2 to <5 Years 1M Post-Dose 3		BNT162b2 (30 µg) 16-25 years 1M Post-Dose 2		Difference in % 2 to <5 - 16-25 years	
Seroresponse	**N**	**n (%) (95% CI)**	**N**	**n (%) (95% CI)**	**% (95% CI)**	**Met Criteria (Y/N)**
SARS-CoV-2 neutralization assay - NT50 (titer)	141	141 (100.0) (97.4, 100.0)	170	168 (98.8) (95.8, 99.9)	1.2 (-1.5, 4.2)	Y

Seroresponse defined as achieving a ≥4 fold rise from baseline (before Dose 1).
Immunobridging is declared if the lower bound of the 95% confidence interval for the percentage difference is greater than -10

AGE
6 mo. to <2

Immunobridging Criteria Met for Both GMR and Seroresponse in Participants Without Prior Infection

Post-dose 3 Compared to 16 to 25 Years of Age Post-dose 2

	BNT162b2 (3 µg) 6M to <2 Years 1M Post-Dose 3		BNT162b2 (30 µg) 16-25 years 1M Post-Dose 2		6M to <2 / 16-25 years	
GMR	**n**	**GMT (95% CI)**	**n**	**GMT (95% CI)**	**GMR (95% CI)**	**Met Criteria (Y/N)**
SARS-CoV-2 neutralization assay - NT50 (titer)	82	1406.5 (1211.3, 1633.1)	170	1180.0 (1066.6, 1305.4)	1.19 (1.00, 1.42)	Y

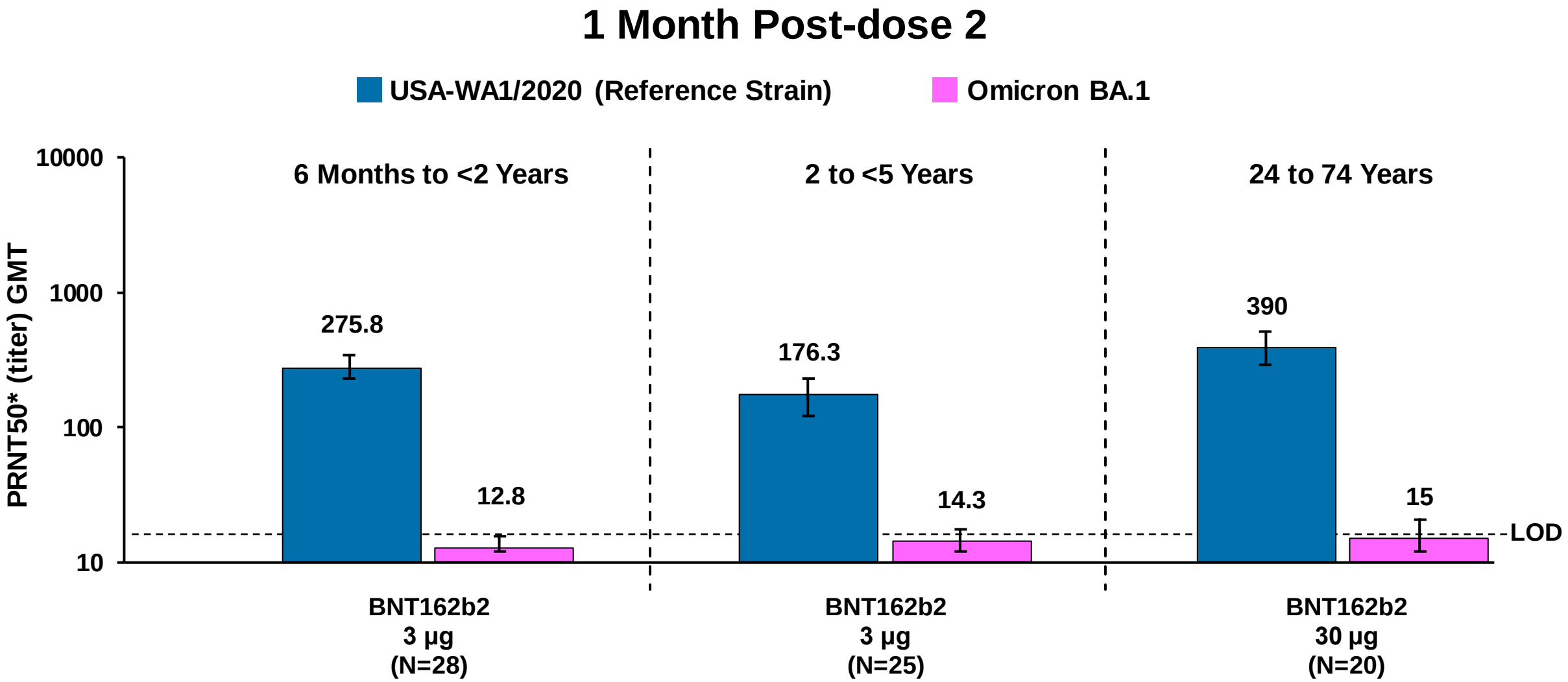
Immunobridging is declared if the lower bound of the 95% confidence interval of the GMR is > 0.67 and the GMR is ≥0.8 and ≥1 per FDA criteria

	BNT162b2 (3 µg) 6M to <2 Years 1M Post-Dose 3		BNT162b2 (30 µg) 16-25 years 1M Post-Dose 2		Difference in % 6M to <2 - 16-25 years	
Seroresponse	**N**	**n (%) (95% CI)**	**N**	**n (%) (95% CI)**	**% (95% CI)**	**Met Criteria (Y/N)**
SARS-CoV-2 neutralization assay - NT50 (titer)	80	80 (100.0) (95.5, 100.0)	170	168 (98.8) (95.8, 99.9)	1.2 (-3.4, 4.2)	Y

Seroresponse defined as achieving a ≥4 fold rise from baseline (before Dose 1).
Immunobridging is declared if the lower bound of the 95% confidence interval for the percentage difference is greater than -10

AGE
6 mo. to <5

Robust Immune Response After 2 Doses to Reference Strain with Low Immune Responses to Omicron

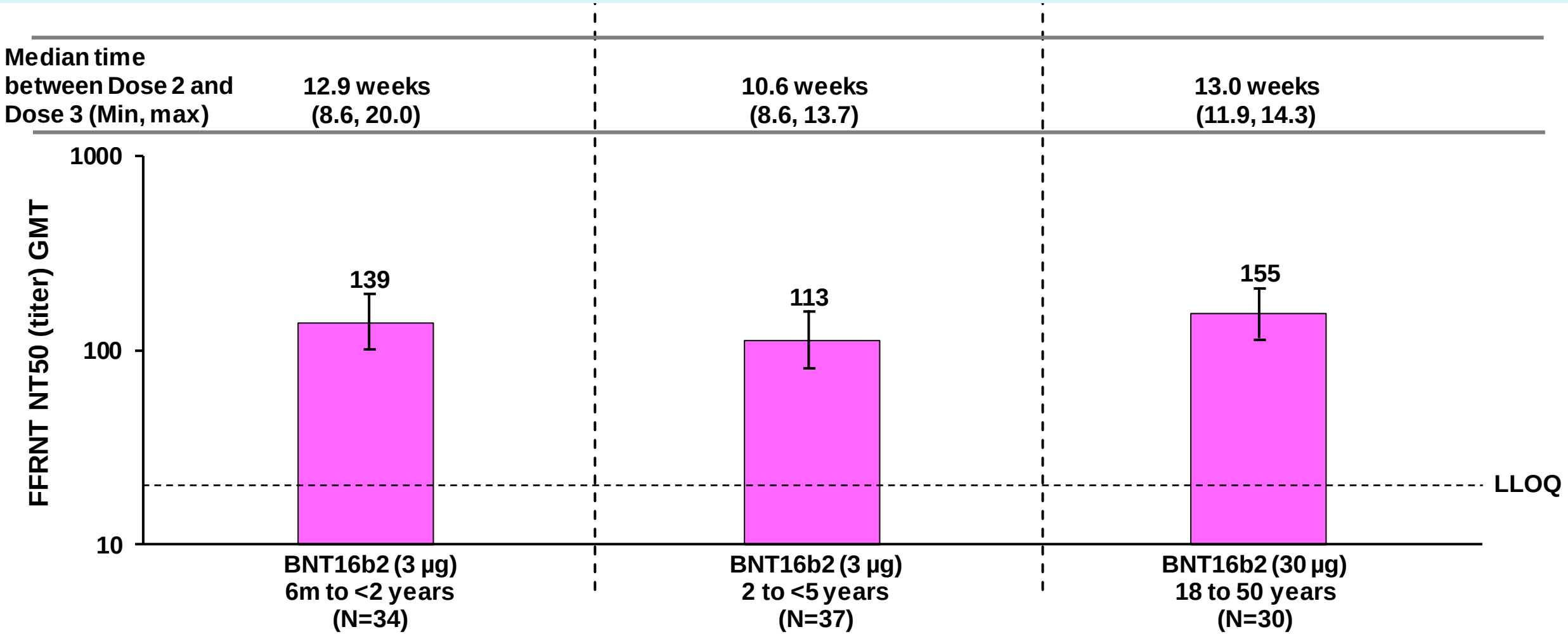


*PRNT50 = 50% Plaque Reducing neutralizing titers

AGE
6 mo. to <5

Similar Neutralizing Responses to Omicron Observed Across Age Groups One Month After The 3rd Dose

Subjects WITHOUT evidence of existing or preexisting SARS-CoV-2 infection



AGE
6 mo. to <5

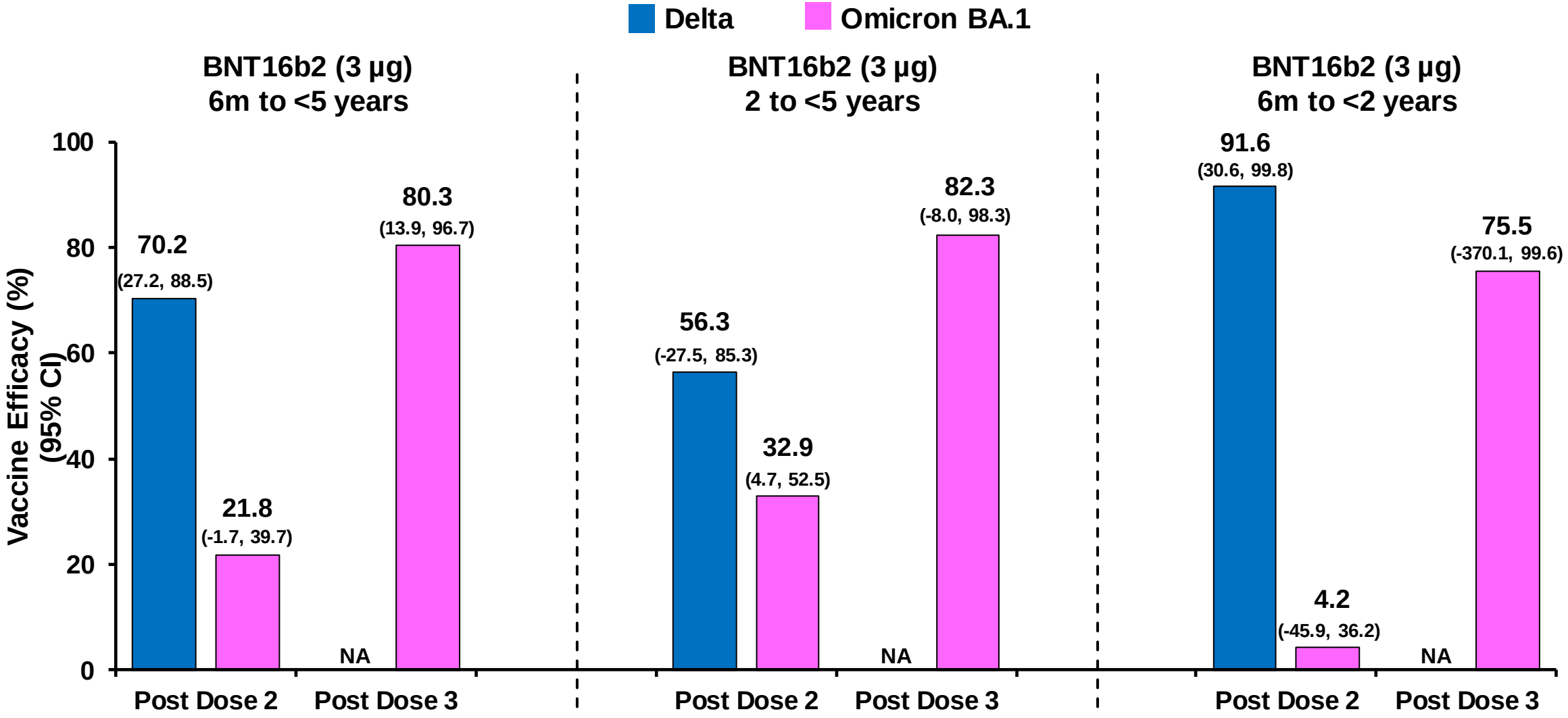
Immunogenicity Conclusions

- **Immunobridging criteria were partially met after dose 2**
- **Immunobridging criteria (post-dose 3 in young children to post-dose 2 in young adults) were met for both age groups inferring effectiveness**
- **Omicron neutralizing titers were much higher after the 3rd dose**
- **As has been observed in other populations, a 3rd dose in young children is likely to be associated with high protection against COVID-19 due to Omicron**

Efficacy

AGE
6 mo. to <5

High Observed Efficacy After 3rd Dose Against Omicron



NA - Not applicable as Delta cases post Dose 3 did not occur during this time period.

AGE
6 mo. to <5

Vaccine Efficacy from 7 Days After Dose 2 to Before Dose 3

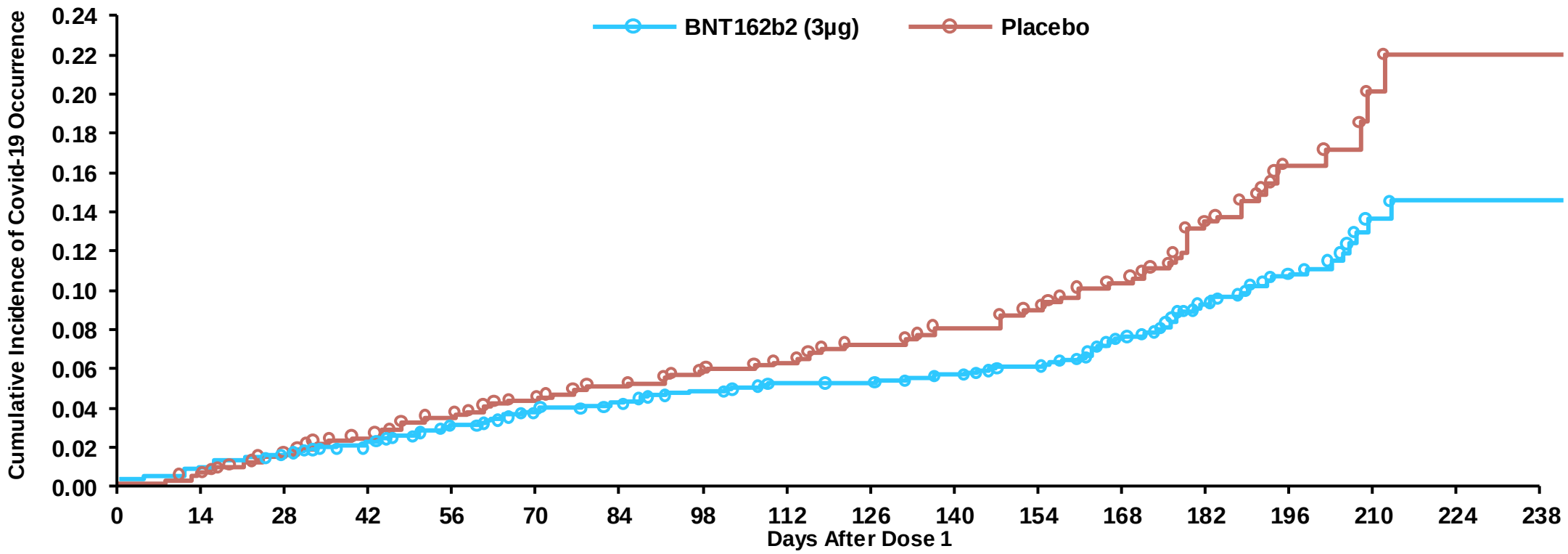
Evaluable Population

	6 months to <5 years		2 to <5 years		6 months to <2 years	
	Case Split (BNT162b2:Placebo)	VE (95% CI)	Case Split (BNT162b2:Placebo)	VE (95% CI)	Case Split (BNT162b2:Placebo)	VE (95% CI)
Without prior evidence of SARS-CoV-2 infection	163:113	28.3% (8.0%, 43.9%)	90:69	35.9% (11.0%, 53.7%)	73:44	16.1% (-24.9%, 43.1%)
With or without prior evidence of SARS-CoV-2 infection	173:120	27.0% (7.1%, 42.5%)	97:73	34.3% (9.7%, 52.0%)	76:47	15.6% (-24.2%, 42.1%)

AGE
2 to <5

Cumulative Incidence Curves Show Increasing Separation at Later Timepoints

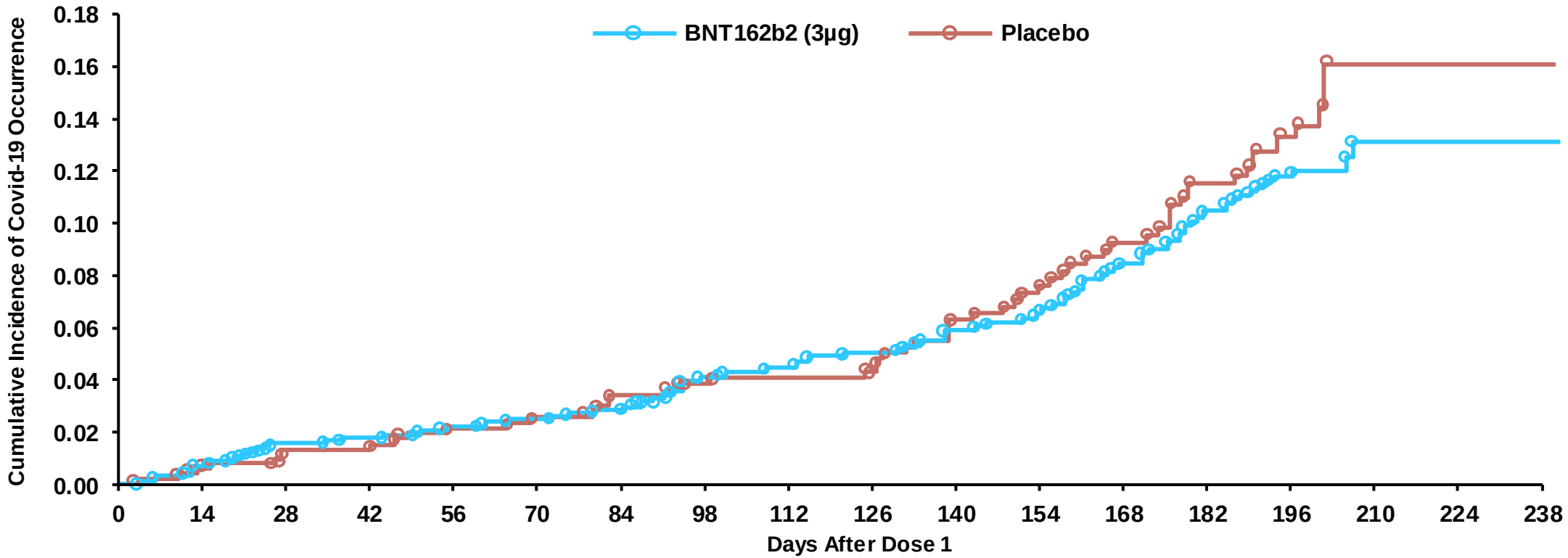
Dose 1 All Available Population



AGE
6 mo. to <2

Cumulative Incidence Curves Show Increasing Separation at Later Timepoints

Dose 1 All Available Population



AGE
6 mo. to <5

Vaccine Efficacy 80% Post-dose 3 During a Period When Omicron Was Predominant

Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 3

	BNT162b2 (3 µg)		Placebo			
	n / N	Surveillance Time (n)	n / N	Surveillance Time (n)	VE (%)	(95% CI)
6 months to <5 years	3 / 992	0.086 (758)	7 / 464	0.039 (348)	80.3	(13.9, 96.7)
2 to <5 years	2 / 606	0.056 (481)	5 / 280	0.025 (209)	82.3	(-8.0, 98.3)
6 months to <2 years	1 / 386	0.030 (277)	2 / 184	0.015 (139)	75.5	(-370.1, 99.6)

All the cases post-dose 3 occurred after February 7, 2022 and were confirmed to be omicron

Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint

AGE
6 mo. to <5

Descriptive Efficacy Conclusions

- As demonstrated in other pediatric and adult age groups, two doses of BNT162b2 are protective against variants of concern such as Delta, but do not provide adequate protection against Omicron

- As demonstrated in other pediatric and adult age groups, a third dose is necessary to provide high protection against Omicron

Ongoing and Active Pharmacovigilance and Pharmacoepidemiology (Pediatric)

Pharmacoepidemiology Studies for Ages 6 Months and Up

5 Studies that include pediatric patients:

- >100M persons in source populations
- All evaluate post-vaccination myocarditis
- 4 evaluate long-term sequelae outcomes

Proactive Risk Mitigation

- Labeling
- Educational materials
- Vial differentiation

Pharmacovigilance

- **Detect unexpected safety events rapidly**
- Spontaneous report collection
- Active follow-up
- Frequent signal detection and evaluation

Potential Benefits of Vaccinating Children 6m to <5y of Age Outweigh Known/Potential Risks

- **Children 6 months to <5 years of age are currently unprotected**
- **Protection against COVID-19 is critical – particularly given the unpredictability of future waves or emergence of new variants**
- **Available safety, immunogenicity, and efficacy data support a favorable benefit-risk profile for administration of 3 doses of BNT162b2 at 3µg to children 6 months to <5 years of age**

Acknowledgments

Pfizer and BioNTech wish to thank:

- **The clinical trial participants and their families**
- **Sites, investigators, CRO, our partners and their staff**
- **FDA guidance to assess this urgent medical need**

Questions?

Advisory Committee on Immunization Practices

June 17, 2022