BNT162b2 Vaccine Candidate Against COVID-19

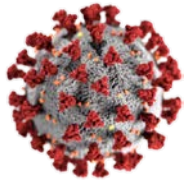
William Gruber, MD, FAAP, FIDSA
Senior Vice President Vaccine Clinical R&D
Pfizer

December 11, 2020

BNT162b2 Vaccine

Proposed Indication:

Prevention of Coronavirus Disease 2019 (COVID-19) caused by SARS-CoV-2



Individuals 16 years of age and older

DOSE LEVEL and REGIMEN	• **30 µg** • **2 doses given greater than or equal to 21 days apart**
PRESENTATION	• **5 dose multidose vial**
STORAGE ***	• **-80ºC to -60ºC** • **5 days at 2º-8ºC**

Non-Clinical Data

Key Nonclinical Studies with BNT162b2

Study No.	Study Description	Key Message
Toxicology Studies		
38166	17-Day, 2 or 3 Dose (1 Dose/Week) IM Toxicity in Rats With a 3 Week Recovery Period	**Completed with no safety concerns**
20GR142	17-Day IM Toxicity Study of BNT162b2(V9) and BNT162b3c in Wistar Han Rats with a 3-Week Recovery	**Completed with no safety concerns**
20256434	A Combined Fertility and Developmental Study (Including Teratogenicity and Postnatal Investigations) of BNT162b1, BNT162b2 and BNT162b3 by the Intramuscular Route in the Wistar Rat	**Ongoing with preliminary results mid-December 2020**
Pharmacology Studies		
VR-VTR-10671	BNT162b2 (V9) Immunogenicity and Evaluation of Protection against SARS-CoV-2 Challenge in Rhesus Macaques	**Completed and showed that BNT162b2 protects against SARS-CoV 2**

Vogel A, Kanevsky I, Che Y, et al. bioRxiv 2020.09.08.280818; doi: https://doi.org/10.1101/2020.09.08.280818 [preprint]4b

Clinical Safety, Immunogenicity, and Efficacy of BNT162b2

Efficacy & Safety Topics

- **Phase 1 German and US studies**
  - Safety
  - Immunogenicity
- **Phase 2/3 global study**
  - Study design
  - Primary/secondary objectives
  - COVID-19 definitions
  - Safety
  - Efficacy

BNT162b2 Phase 1 Studies

German Study
BNT162-01

- 18-55 years of age
- 12 active vaccine/cohort
- Safety, immunogenicity
- Cell Mediated Responses

US Study
C4591001

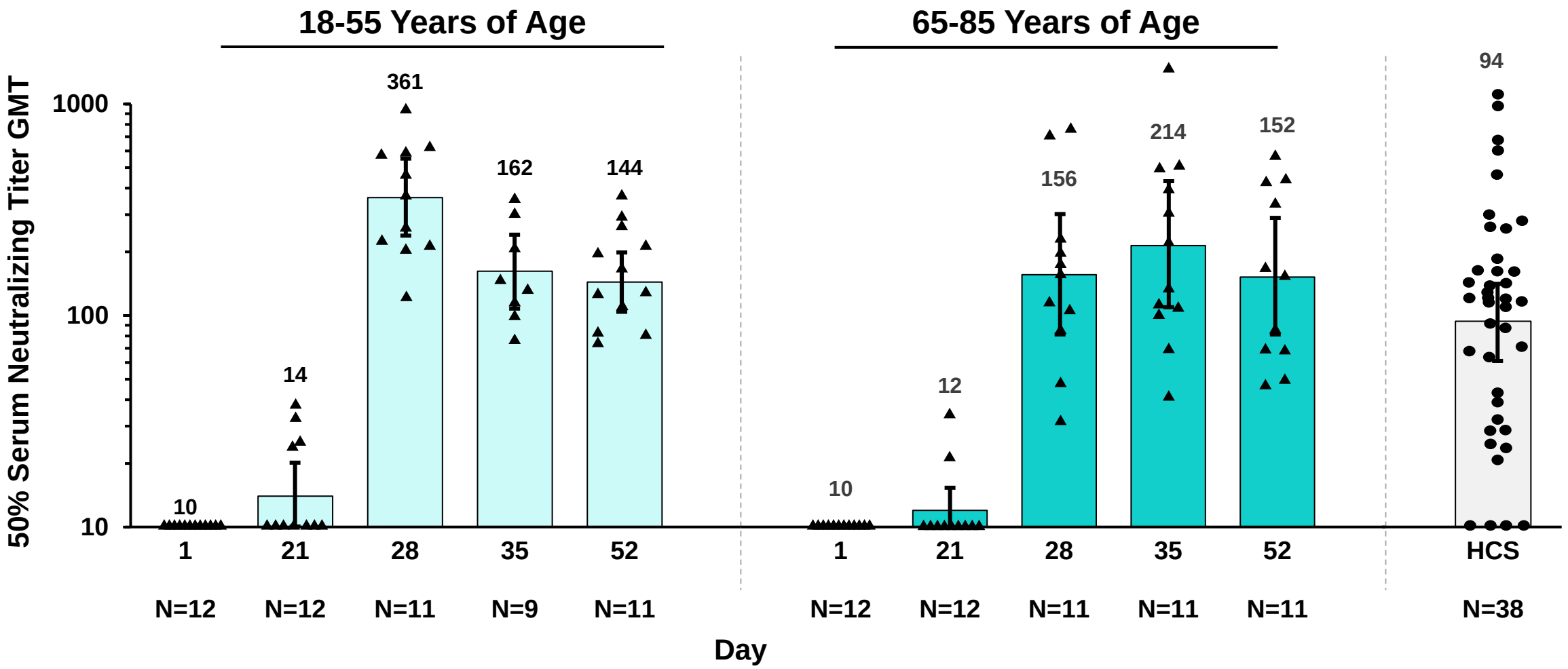
- 18-55 and 65-85 years of age
- 12 active vaccine, 3 placebo/cohort
- Safety, immunogenicity
- Reactogenicity by e-diary

Reactogenicity in Phase 1

- **Mild-moderate injection site pain observed frequently**
- **Fever and chills observed, generally mild-moderate**
- **Reactogenicity was generally higher after Dose 2 than Dose 1**
- **Reactogenicity events after each dose of BNT162b2 in older adults were milder and less frequent than those observed in younger adults**

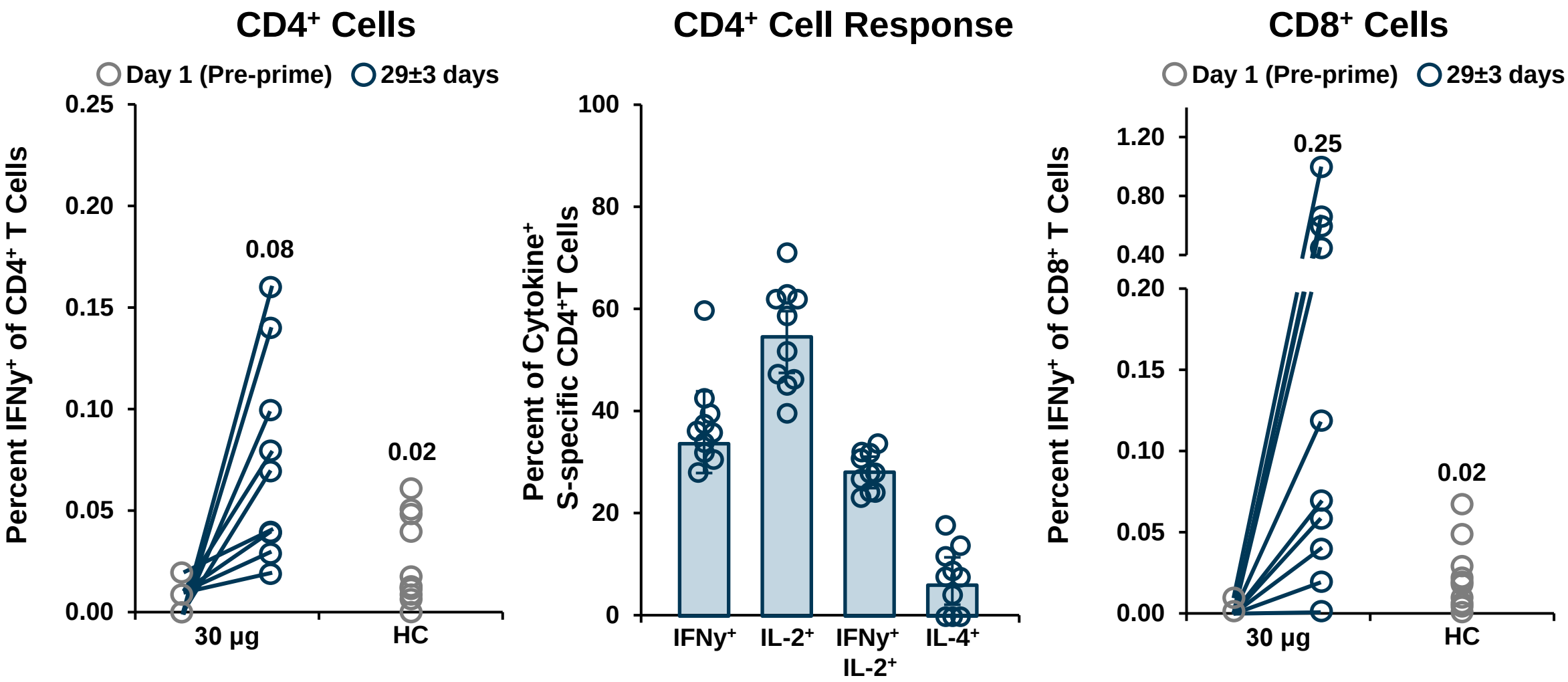
Sahin U, et al. *Nature*. 2020.
Walsh EE, et al. *N Engl J Med*. 2020

Two 30 µg Doses of BNT162b2 Induce Neutralizing Antibody Titers Comparable or Higher than Natural Infection



Walsh EE, et al. *N Engl J Med*. 2020

BNT162b2 Elicits Strong Th1-biased CD4+ and CD8+ T Cell Responses (German Trial)



Sahin et al., manuscript in preparation

Planned Subjects in Pivotal Study

- **44,000 healthy subjects enrollment target**
  - Stable chronic disease allowed
  - Stable HIV, HBV, HCV
- **At least 40% ages 56 years or older**
- **Balanced racial and ethnicity profile**
  - Black/African American
  - Asian
  - Hispanic/Latinx
- **Immunocompromised excluded**

Limited number of 12-15 yo not part of EUA application

Demographic Characteristics
Phase 2/3 (N=43,448)

		BNT162b2 (30 µg) N=21,720 n (%)	Placebo N=21,728 N (%)	Total N=43,448 n (%)
Sex	Male	11,183 (51.5)	10,942 (50.4)	22,125 (50.9)
	Female	10,537 (48.5)	10,786 (49.6)	21,323 (49.1)
Race	White	17,839 (82.1)	17,857 (82.2)	35,696 (82.2)
	Black or African American	2,091 (9.6)	2,107 (9.7)	4,198 (9.7)
	All others	1,790 (8.2)	1,764 (8.1)	3,554 (8.2)
Ethnicity	Hispanic/Latino	5,672 (26.1)	5,668 (26.1)	11,340 (26.1)
	Non-Hispanic/non-Latino	15,928 (73.3)	15,940 (73.4)	31,868 (73.3)
	Not reported	120 (0.6)	120 (0.6)	240 (0.6)
Age	16-55 Years	12,780 (58.8)	12,822 (59.0)	25,602 (58.9)
	>55 Years	8,940 (41.2)	8,906 (41.0)	17,846 (41.1)
	16-64 Years	17,176 (79.1)	17,190 (79.1)	34,366 (79.1)
	65-74 Years	3,620 (16.7)	3,646 (16.8)	7,266 (16.7)
	≥75 Years	924 (4.3)	892 (4.1)	1,816 (4.2)

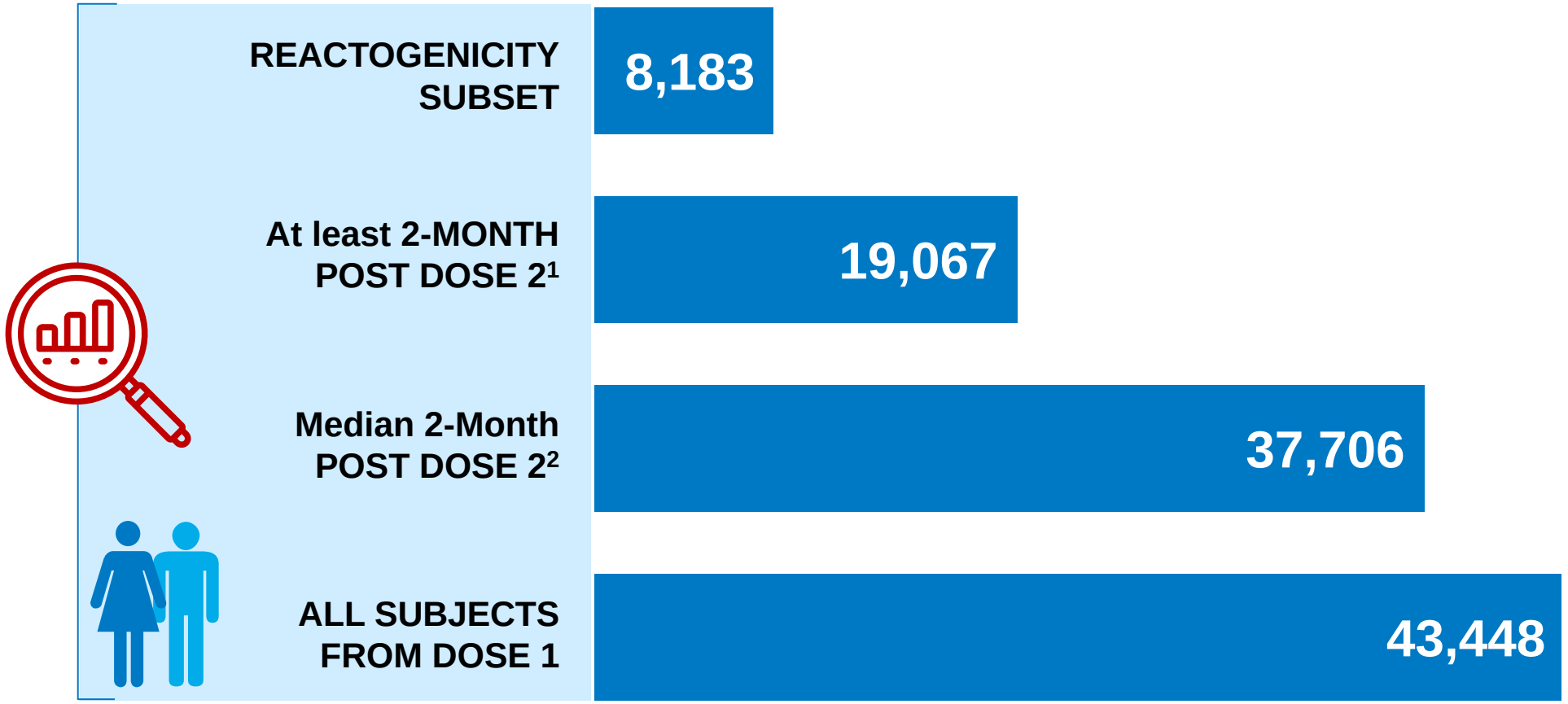
>9000 (20.9%)

Safety

Safety Review by Independent Data Monitoring Committee

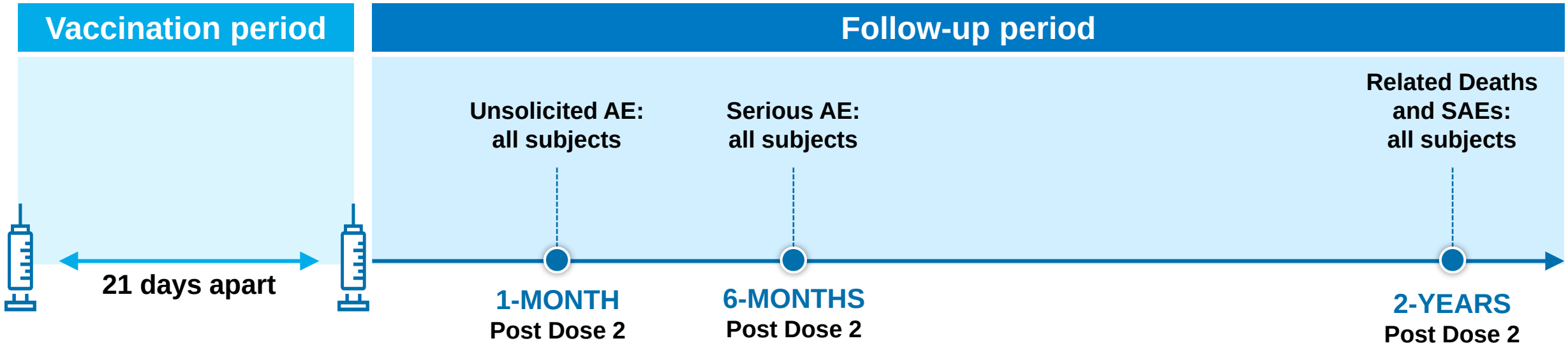
- **DMC consists of 4 adult/ pediatric infectious diseases experts, and one statistician all with expertise in assessing vaccine safety, immune response, and efficacy**
- **DMC meets weekly to review unblinded safety data**
- **DMC has identified no safety concerns during the duration of the clinical trial and recommended that study continues as planned at all safety reviews**

Summary of Safety Data



1. All subjects who have at least 2 months of safety follow-up post dose 2
2. 91.6% (34,532) had at least 1 month of safety follow-up post dose 2

Phase 2/3 Safety – Study Start 27 July, 2020



Active surveillance begins after 1st dose

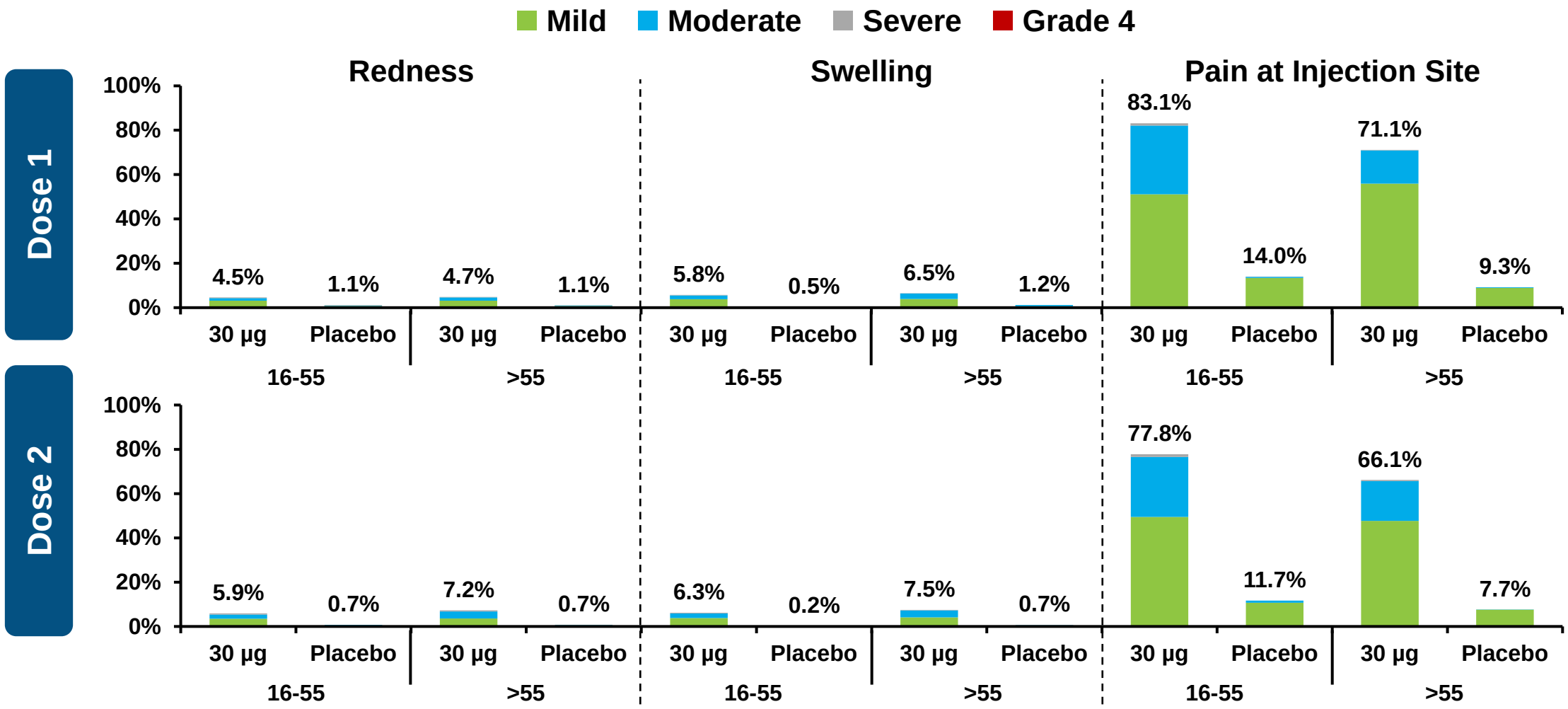
Potential COVID-19 symptoms **TRIGGER** telehealth or in-person visit and nasal swab

7 DAYS

7 DAYS

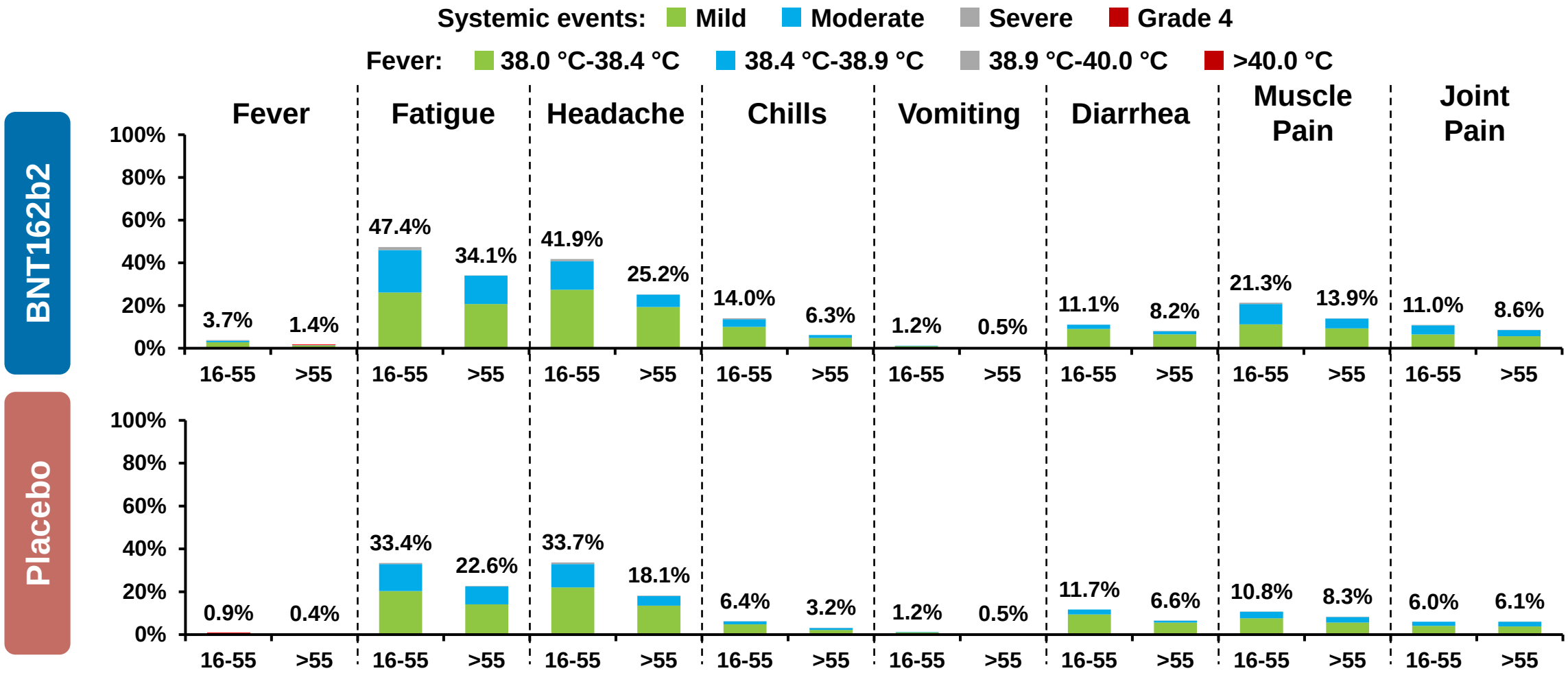
Reactogenicity:
at least 6000 subjects, at least 500 in each country

eDiary: Local Events Within 7 Days From Dose 1 and 2 in 16-55 and >55 Year Olds (N=8,183)



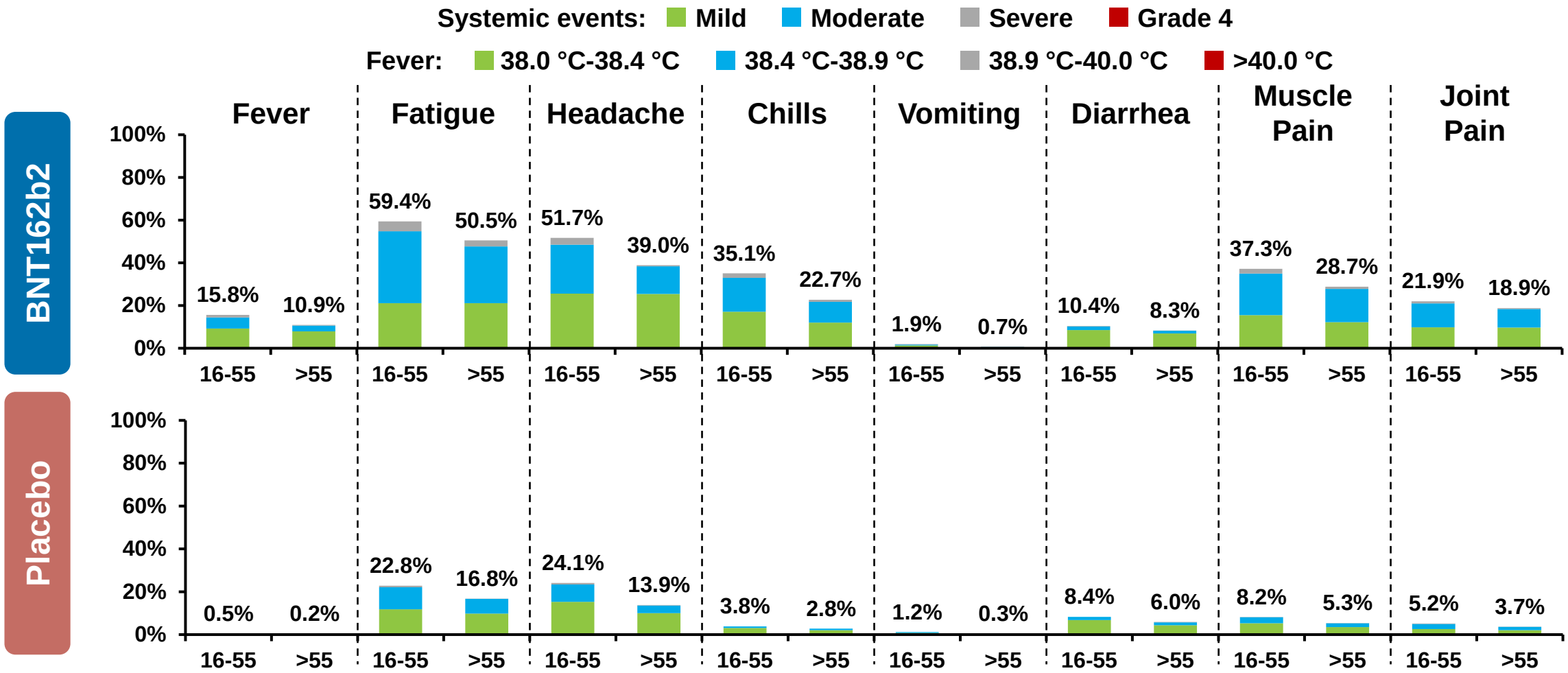
Redness and sweeling severity definition: Mild= >2-5cm, Moderate= >5-10 cm; Severe= >10 cm; Grade 4= necrosis
Pain at injection site severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization
Dose 1: 16-55 yrs N=4589; >55 yrs N=3594 Dose 2: 16-55 yrs N=4201 >55 yrs N=3306

eDiary: Systemic Events Within 7 Days From Dose 1 in 16-55 and >55 Year Olds (N=8,183)



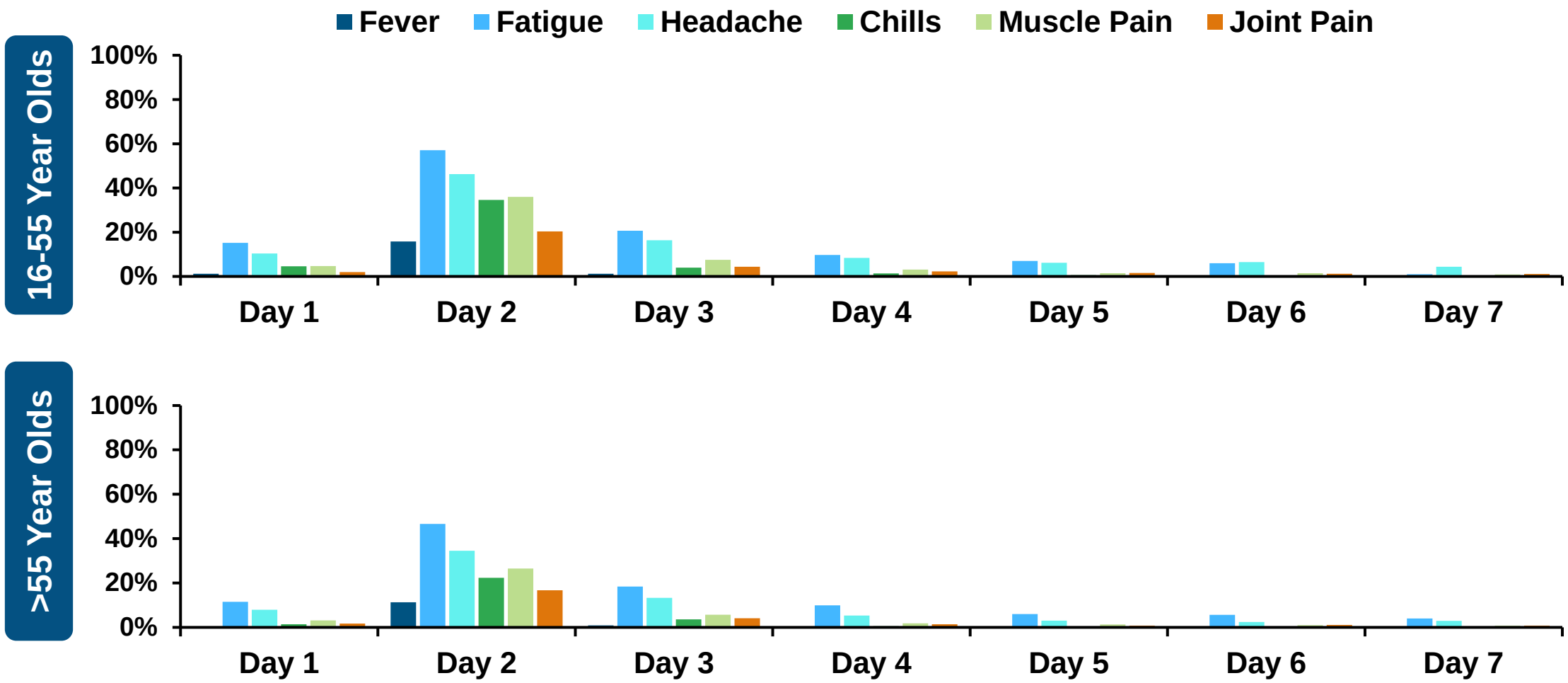
Fatigue, headache, chills, muscle pain, joint pain severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization
Vomiting severity definition: Mild=1-2 time in 24h; Moderate=>2times in 24h; Severe=Requires IV hydration; Grade 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: 18-55 yrs N=3529; 56-85 yrs N=3027 Dose 2: 18-55 yrs N=3345; 56-85 yrs N=2899

eDiary: Systemic Events Within 7 Days From Dose 2 in 16-55 and >55 Year Olds (N=8,183)



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: 18-55 yrs N=3529; 56-85 yrs N=3027 Dose 2: 18-55 yrs N=3345; 56-85 yrs N=2899

eDiary: Systemic Events Each Day From Dose 2 in 16-55 and >55 Year Olds (N=8,183) BNT162b2



Severe/Grade 3 Local Reactions Within 7 Days after each dose (N=8,183)

		BNT162b2 (30 µg) n (%)	Placebo N (%)
Dose 1	Pain at the injection site	28/4093 (0.7)	2/4090 (0.0)
	Redness	9/4093 (0.2)	6/4090 (0.1)
	Swelling	7/4093 (0.2)	3/4090 (0.1)
Dose 2	Pain at the injection site	33/3758 (0.9)	0/3749 (0.0)
	Redness	18/3758 (0.5)	1/3749 (0.0)
	Swelling	10/3758 (0.3)	1/3749 (0.0)

Fever >40°C or Severe/Grade 3 Systemic Events Within 7 Days of Dose 1 (N=8,183)

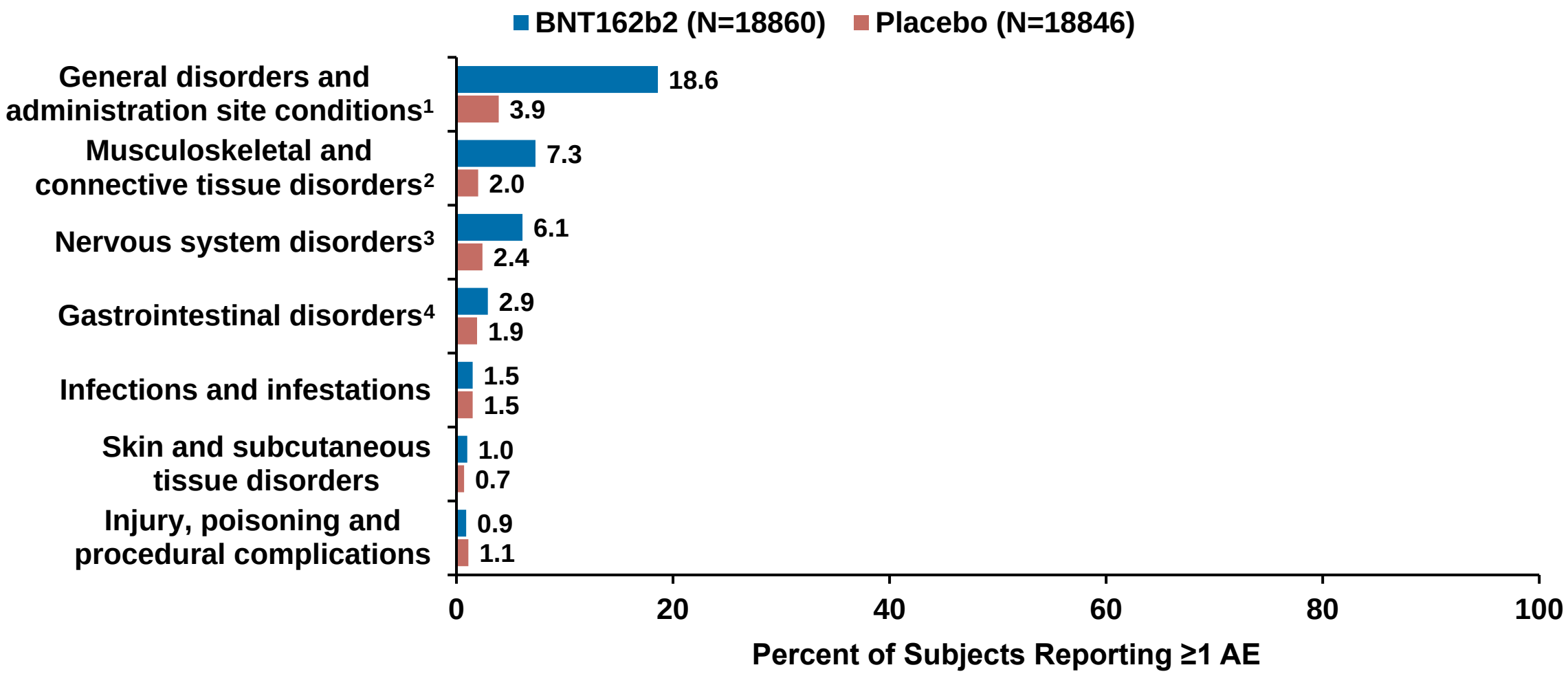
Dose 1	BNT162b2 (30 µg) n (%)	Placebo N (%)
Fever >40.0°C	1/4093 (0.0)	2/4090 (0.0)
Fatigue	35/4093 (0.9)	14/4090 (0.3)
Headache	25/4093 (0.6)	22/4090 (0.5)
Chills	9/4093 (0.2)	3/4090 (0.1)
Vomiting	0/4093 (0.0)	1/4090 (0.0)
Diarrhea	6/4093 (0.1)	2/4090 (0.0)
New or worsened muscle pain	14/4093 (0.3)	5/4090 (0.1)
New or worsened joint pain	7/4093 (0.2)	1/4090 (0.0)

Fever >40°C or Severe/Grade 3 Systemic Events Within 7 Days of Dose 2

Dose 2	BNT162b2 (30 µg) n (%)	Placebo N (%)
Fever >40.0°C	1/3758 (0.0)	0/3749 (0.0)
Fatigue	143/3758 (3.8)	16/3749 (0.4)
Headache	76/3758 (2.0)	19/3749 (0.5)
Chills	62/3758 (1.6)	0/3749 (0.0)
Vomiting	5/3758 (0.1)	0/3749 (0.0)
Diarrhea	6/3758 (0.2)	5/3749 (0.1)
New or worsened muscle pain	63/3758 (1.7)	4/3749 (0.1)
New or worsened joint pain	27/3758 (0.7)	5/3749 (0.1)

Adverse Events ≥1.0% by System Organ Class

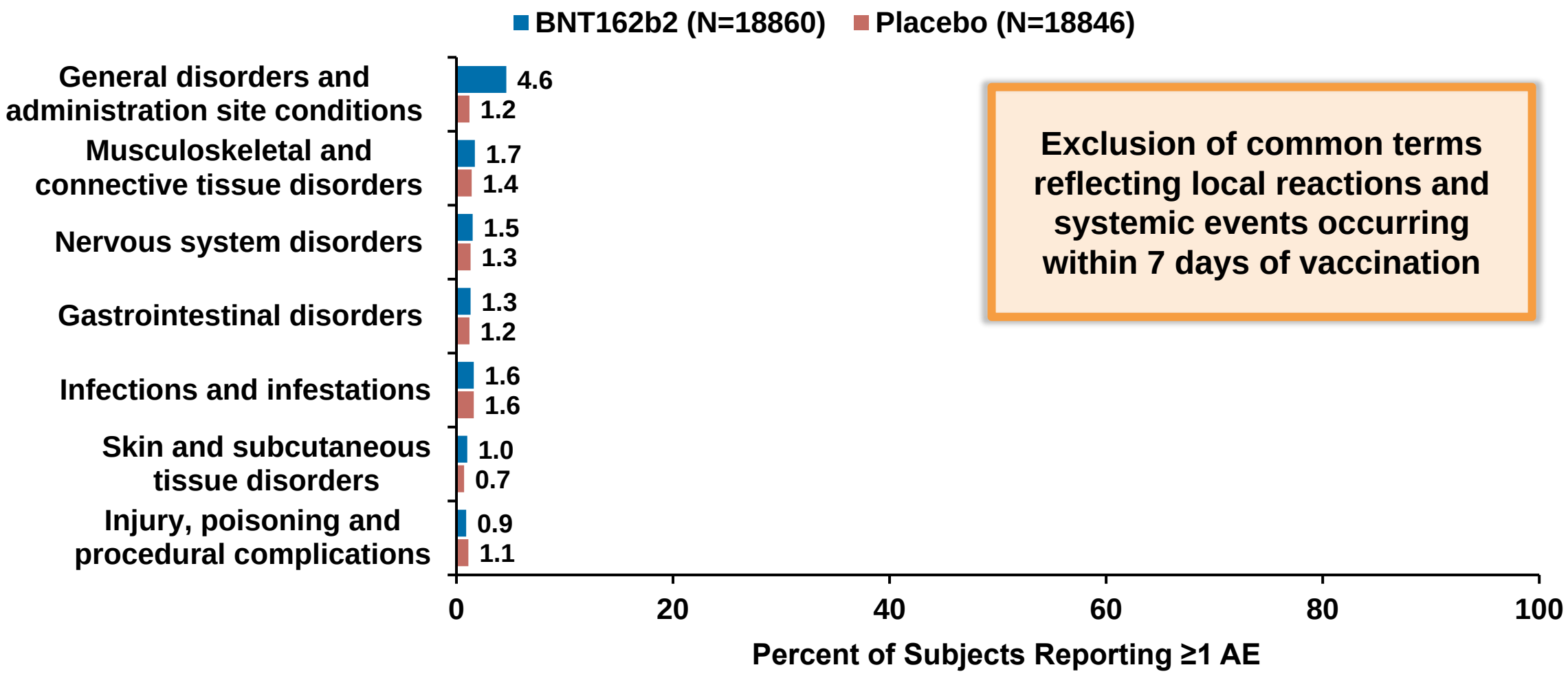
~50% of Subjects with ≥2 Months Post Dose 2 (N=37,706)



1. Predominantly reflect local reactions at the injection site and systemic reactions of fatigue and chills
2. Predominantly reflect myalgias and arthralgia's as part of systemic events
3. Predominantly reflects Headache
4. Predominantly reflects diarrhea and vomiting

Adverse Events ≥1.0% by System Organ Class

~50% of Subjects with ≥2 Months Post Dose 2 (N=37,706)



Exclusion of common terms reflecting local reactions and systemic events occurring within 7 days of vaccination

1. Predominantly reflect local reactions at the injection site and systemic reactions of fatigue and chills
2. Predominantly reflect myalgias and arthralgia's as part of systemic events
3. Predominantly reflects Headache
4. Predominantly reflects diarrhea and vomiting

Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2 – by Race

~38,000 Subjects for Phase 2/3 Analysis – Safety Population

	White		Black or African American		Hispanic/ Latino		Non-Hispanic/ Non-Latino		All Others	
Adverse Event	BNT162b2 (30 µg) N=15615 n (%)	Placebo N=15615 n (%)	BNT162b2 (30 µg) N=1694 n (%)	Placebo N=1722 n (%)	BNT162b2 (30 µg) N=5253 n (%)	Placebo N=5269 n (%)	BNT162b2 (30 µg) N=13436 n (%)	Placebo N=13407 n (%)	BNT162b2 (30 µg) N=1492 n (%)	Placebo N=1448 n (%)
Any event	4252 (27.2)	1991 (12.8)	269 (15.9)	176 (10.2)	1429 (27.2)	834 (15.8)	3621 (26.9)	1511 (11.3)	550 (36.9)	189 (13.1)
Related[a]	3234 (20.7)	748 (4.8)	194 (11.5)	87 (5.1)	940 (17.9)	278 (5.3)	2959 (22.0)	669 (5.0)	487 (32.6)	118 (8.1)
Severe	185 (1.2)	94 (0.6)	14 (0.8)	11 (0.6)	71 (1.4)	38 (0.7)	149 (1.1)	71 (0.5)	21 (1.4)	4 (0.3)
Life-threatening	16 (0.1)	17 (0.1)	0	3 (0.2)	4 (0.1)	4 (0.1)	14 (0.1)	16 (0.1)	2 (0.1)	0
Any SAE	81 (0.5)	71 (0.5)	11 (0.6)	9 (0.5)	27 (0.5)	21 (0.4)	76 (0.6)	60 (0.4)	11 (0.7)	1 (0.1)
Related[a]	2 (0.0)	0	0	0	0	0	3 (0.0)	0	1 (0.1)	0
Severe	44 (0.3)	41 (0.3)	7 (0.4)	6 (0.3)	13 (0.2)	16 (0.3)	44 (0.3)	32 (0.2)	6 (0.4)	1 (0.1)
Life-threatening	16 (0.1)	16 (0.1)	0	3 (0.2)	4 (0.1)	4 (0.1)	14 (0.1)	15 (0.1)	2 (0.1)	0
Any AE leading to withdrawal	29 (0.2)	18 (0.1)	3 (0.2)	6 (0.3)	9 (0.2)	2 (0.0)	25 (0.2)	23 (0.2)	2 (0.1)	1 (0.1)
Related[a]	13 (0.1)	4 (0.0)	1 (0.1)	3 (0.2)	3 (0.1)	0	11 (0.1)	7 (0.1)	0	0
Severe	13 (0.1)	6 (0.0)	0	1 (0.1)	4 (0.1)	0	9 (0.1)	7 (0.1)	0	0
Life-threatening	1 (0.0)	4 (0.0)	0	0	0	2 (0.0)	2 (0.0)	2 (0.0)	1 (0.1)	0
Death	1 (0.0)	2 (0.0)	0	0	0	1 (0.0)	1 (0.0)	1 (0.0)	0	0

a. Assessed by the investigator as related to investigational product.

Serious Adverse Events by System Organ Class ≥0.1%
All Enrolled Subjects (N=43,448)

	BNT162b2 (30 µg) N=21621 n (%)	Placebo N=21631 n (%)
Any event	126 (0.6)	111 (0.5)
Infections and infestations	27 (0.1)	17 (0.1)
Cardiac disorders	18 (0.1)	18 (0.1)
Nervous system disorders	18 (0.1)	16 (0.1)
Neoplasms benign, malignant and unspecified (incl. cysts and polyps)	11 (0.1)	8 (0.0)
Injury, poisoning and procedural complications	8 (0.0)	12 (0.1)

Deaths

All Enrolled Subjects (N=43,448)

	BNT162b2 (30 µg) N=21720 n (%)	Placebo N=21728 n (%)
Deaths	**2 (0.0)**	**4 (0.0)**

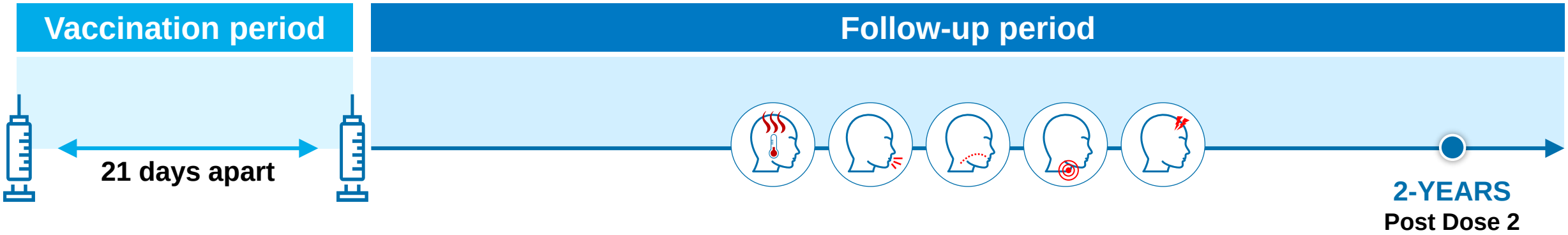
Safety Conclusions

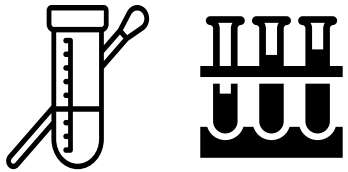
- **Tolerability and safety profile of BNT162b2 at 30 µg administered as a 2-dose regimen 21 days apart is favorable**

- **No clinically significant safety findings other than mild or moderate reactogenicity were identified**

Efficacy

Phase 2/3 Efficacy Analysis





Prior infection status

Before each dose

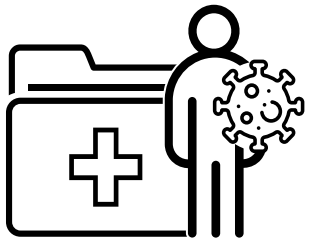
- Swab for SARS-CoV-2 PCR
- Blood for N-antigen antibodies

Active surveillance begins after 1st dose

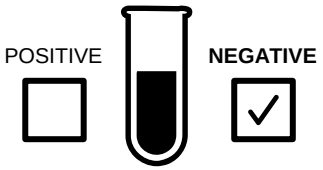
Potential COVID-19 symptoms **TRIGGER** telehealth or in-person visit and nasal swab

*Only primary and secondary endpoints after dose 2

COVID-19 First Primary Endpoint Case Definition



COVID-19 Case



Baseline **NEGATIVE** by serology & PCR

=

1 or more
of these symptoms

Fever	**New or increased cough**	**New or increased shortness of breath**
Chills	**New or increased muscle pain**	**New loss of taste/smell**
Sore throat	**Diarrhea**	**Vomiting**

+

Positive validated PCR in central laboratory

CDC definition also includes fatigue, headache, nasal congestion or runny nose, and nausea

First COVID-19 Occurrence From 7 Days After Dose 2

Phase 2/3 Efficacy – Final Analysis

Subjects WITHOUT Evidence of Infection Prior to 7 days after Dose 2

	BNT162b2 (30 µg) N=18,198		Placebo N=18,325				
Efficacy Endpoint	n	Surveillance Time (n)	n	Surveillance Time (n)	VE (%)	(95% CI)	Pr (VE >30%)
First COVID-19 occurrence ≥7 days after Dose 2	8	2.214 (17,411)	162	2.222 (17,511)	95.0	(90.3, 97.6)	>0.9999

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint..
Pr=Posterior probability

First COVID-19 Occurrence From 7 Days After Dose 2

Phase 2/3 Efficacy – Final Analysis: Subgroups

Subjects WITHOUT Evidence of Infection Prior to 7 days after Dose 2

		BNT162b2 N=18,198 n	Placebo N=18,325 n	VE (%)	(95% CI)
Overall		8	162	95.0	(90.0, 97.9)
Age	18-64 years	7	143	95.1	(89.6, 98.1)
	65-74 years	1	14	92.9	(53.1, 99.8)
	≥75 years	0	5	100.0	(-13.1, 100.0)
Sex	Male	3	81	96.4	(88.9, 99.3)
	Female	5	81	93.7	(84.7, 98.0)
Race	White	7	146	95.2	(89.8, 98.1)
	Black or African American	0	7	100.0	(31.2, 100.0)
	All Others	1	9	89.3	(22.6, 99.8)
Ethnicity	Hispanic/Latino	3	53	94.4	(82.7, 98.9)
	Non-Hispanic/Non-Latino	5	109	95.4	(88.9, 98.5)
Country	Argentina	1	35	97.2	(83.3, 99.9)
	Brazil	1	8	87.7	(8.1, 99.7)
	USA	6	119	94.9	(88.6, 98.2)

First COVID-19 Occurrence From 7 Days After Dose 2

Phase 2/3 Efficacy – Final Analysis: Risk Factor Subgroups

Subjects WITHOUT Evidence of Infection Prior to 7 days after Dose 2

		BNT162b2 N=18,198 n	Placebo N=18,325 n	VE (%)	(95% CI)
Overall		8	162	95.0	(90.0, 97.9)
At risk[1]	Yes	4	86	95.3	(87.7, 98.8)
	No	4	76	94.7	(85.9, 98.6)
Age group at risk	16-64 and not at risk	4	69	94.2	(84.4, 98.5)
	16-64 and at risk	3	74	95.9	(87.6, 99.2)
	≥65 and not at risk	0	7	100.0	(29.0, 100.0)
	≥65 and at risk	1	12	91.7	(44.2, 99.8)
Obese[2]	Yes	3	67	95.4	(86.0, 99.1)
	No	5	95	94.8	(87.4, 98.3)
Age group and obese	16-64 and not obese	4	83	95.2	(87.3, 98.7)
	16-64 and obese	3	60	94.9	(84.4, 99.0)
	≥65 and not at obese	1	12	91.8	(44.5, 99.8)
	≥65 and obese	0	7	100.0	(27.1, 100.0)

[1] At least one of Charlson Comorbidity index or obesity
[2] Obesity: BMI ≥ 30 kg/m^2

First COVID-19 Occurrence From 7 Days After Dose 2 by Comorbidity Status – Evaluable Efficacy (7 Days) Population

Subjects WITHOUT Evidence of Infection Prior to 7 days after Dose 2

	BNT162b2 (30 µg) N=18,198		Placebo N=18,325			
	n	Surveillance Time (n)	n	Surveillance Time (n)	VE (%)	(95% CI)
Overall	8	2.214 (17,411)	162	2.222 (17,511)	95.0	(90.0, 97.9)
Comorbidity						
No comorbidity	4		76		94.7	(85.9, 98.6)
Any comorbidity	4		86		95.3	(87.7, 98.8)
Any malignancy	1		4		75.7	(-145.8, 99.5)
Cardiovascular	0		5		100.0	(-0.8, 100.0)
Chronic pulmonary disease	1		14		93.0	(54.1, 99.8)
Diabetes	1		19		94.7	(66.8, 99.9)
Obese (≥30.0 kg/m^2)	3		67		95.4	(86.0, 99.1)
Hypertension	2		44		95.4	(82.6, 99.5)
Diabetes (including gestational diabetes)	1		20		95.0	(68.7, 99.9)

First COVID-19 Occurrence From 7 Days After Dose 2

Phase 2/3 Efficacy – Final Analysis

Subjects WITH or WITHOUT Evidence of Infection Prior to 7 days after Dose 2

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) N=19,965		Placebo N=20,172				
Efficacy Endpoint	n	Surveillance Time (n)	n	Surveillance Time (n)	VE (%)	(95% CI)	Pr (VE >30%)
First COVID-19 occurrence ≥7 days after Dose 2	9	2.332 (18,559)	169	2.345 (18,708)	94.6	(89.9, 97.3)	>0.9999

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint..
Pr=Posterior probability

Definition of Severe COVID-19 Case Per FDA Guidance

- **Any of the following:**
  - Admission to ICU
  - Clinical signs at rest indicative of severe systemic illness (RR ≥30 breaths per minute, HR ≥125 beats per minute, SpO2 ≤93% on room air at sea level, or PaO2/FiO2 <300 mm Hg)
  - Evidence of shock (SBP <90 mm Hg, DBP <60 mm Hg, or requiring vasopressors)
  - Significant acute renal, hepatic, or neurologic dysfunction
  - Respiratory failure (defined as needing high-flow oxygen, non-invasive ventilation, mechanical ventilation, or ECMO)
  - Death

BNT162b2 Protects Against Severe Disease

Phase 2/3 Efficacy – Final Analysis (FDA definition)

	BNT162b2 (30 µg) N=18,198		Placebo N=18,325				
Efficacy Endpoint	n	Surveillance Time (n)	n	Surveillance Time (n)	VE (%)	(95% CI)	Pr (VE >30%)
First Severe COVID-19 occurrence >7 days after Dose 2	1	2.215 (17,411)	3	2.232 (17,511)	66.4	(-124.8, 96.3)	0.7429

	BNT162b2 (30 µg) N=21,669		Placebo N=21,686			
Efficacy Endpoint	n	Surveillance Time (n)	n	Surveillance Time (n)	VE (%)	(95% CI)
First Severe COVID-19 occurrence after Dose 1	1	4.021 (21,314)	9	4.006 (21,259)	88.9	(20.1, 99.7)

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint..
Pr=Posterior probability

BNT162b2 Protects Against Severe Disease

Phase 2/3 Efficacy – Final Analysis (CDC definition)

Severe Disease Severe illness - CDC definition: hospitalization, admission to the ICU, intubation or mechanical ventilation, or death

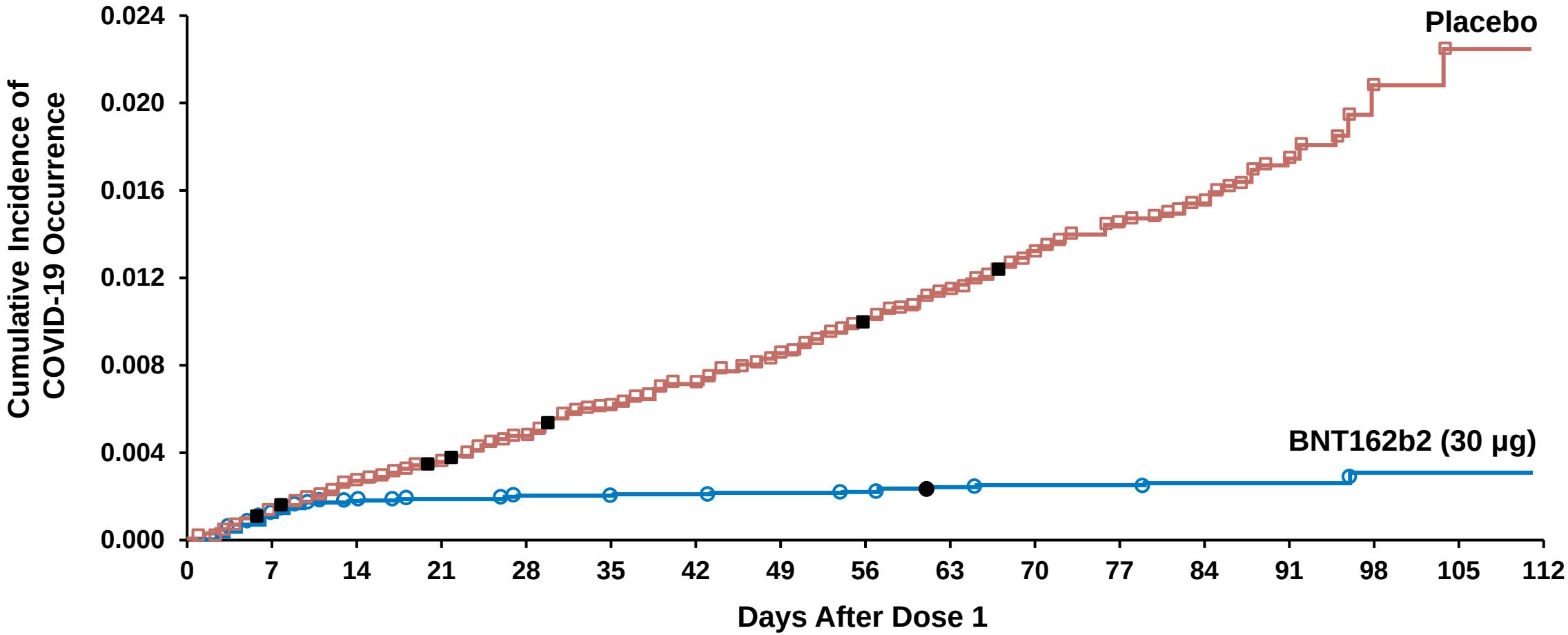
	BNT162b2 (30 µg) N=18,198		Placebo N=18,325			
Efficacy Endpoint	**n**	**Surveillance Time (n)**	**n**	**Surveillance Time (n)**	**VE (%)**	**(95% CI)**
First Severe COVID-19 occurrence >7 days after Dose 2	**0**	**2.215 (17,399)**	**5**	**2.229 (17,495)**	**100**	**(-9.9, 100)**

	BNT162b2 (30 µg) N=21,669		Placebo N=21,686			
Efficacy Endpoint	**n**	**Surveillance Time (n)**	**n**	**Surveillance Time (n)**	**VE (%)**	**(95% CI)**
First Severe COVID-19 occurrence after Dose 1	**1**	**4.018 (21,299)**	**14**	**4.001 (21,238)**	**92.9**	**(53.2, 99.8)**

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint..

Cumulative Incidence of COVID-19 After Dose 1



Solid fill marker indicates subjects with severe COVID-19

First COVID-19 Occurrence After Dose 1

	BNT162b2 (30 µg) N=21,669 n	Placebo N=21,686 n	VE (%)	(95% CI)
COVID-19 occurrence after Dose 1	50	275	82.0	(75.6, 86.9)
After Dose 1 and before Dose 2	39	82	52.4	(29.5, 68.4)
Dose 2 to 7 days after Dose 2	2	21	90.5	(61.0, 98.9)
≥7 days after Dose 2	9	172	94.8	(89.8, 97.6)

Efficacy Conclusions

- **Both primary objectives met success criteria**
- **In individuals without prior SARS-CoV-2 infection, observed Vaccine efficacy against COVID-19 occurring at least 7 days after Dose 2 was 95%, with high probability (97.5%) that the true vaccine efficacy is at least 90%**
- **Observed Vaccine Efficacy was >93% for the first primary endpoint across age, race, ethnicity, and at-risk subgroups**

Efficacy Conclusions (Continued)

- **Per FDA definition, 9 severe COVID-19 cases were observed in the placebo group and 1 in the BNT162b2 group after Dose 1.**
- **Early onset of protection is apparent from the cumulative incidence curve, with divergence by 14 days after Dose 1**
- **Overall, the efficacy results show that BNT162b2 at 30 µg provides protection against COVID-19 in participants who had or did not have prior SARS-CoV-2 infection**

Pharmacovigilance & Pharmacoepidemiology Plan

Pharmacovigilance

- Expanded intake capability with AE portal
- Active follow-up of safety reports
- Frequent signal detection and evaluation
- Post-approval safety monitoring
- Clinical studies in vulnerable populations

Pharmacoepidemiology Studies

- Safety event background rates (contextualization)
- Extended follow up (30 months) for high-severity low-incidence events in large populations
- Vaccine effectiveness

Proactive Risk minimization

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

Collaborate with Vaccine Safety Stakeholders

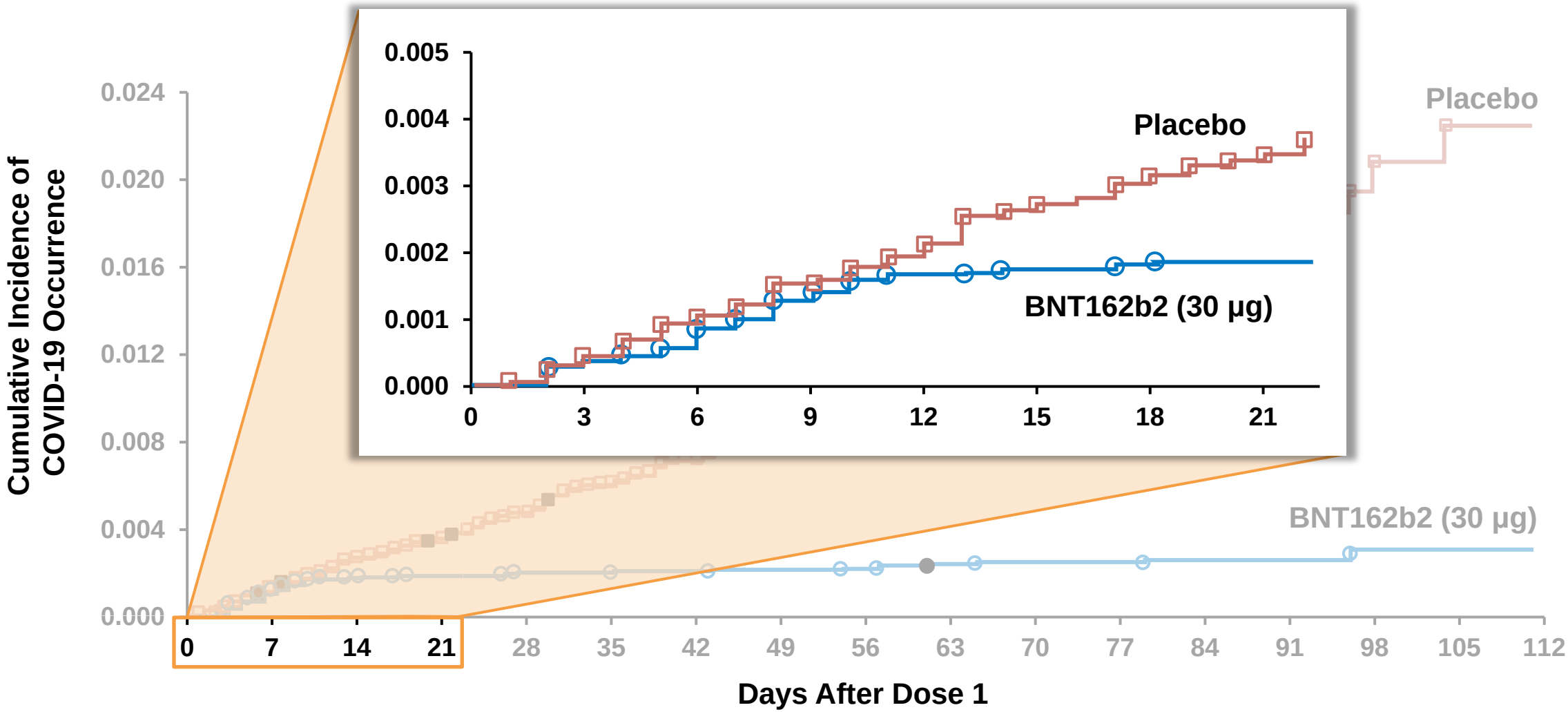
- Interface with CDC (VAERS, V-SAFE, VSD, CISA) to optimize pharmacovigilance activities
- Collaborate with international groups to ensure consistent approach to PV

Plans for BNT162b2 Clinical Studies Beyond Adult Efficacy and Safety

- **Persistence of immunogenicity, efficacy and longer term safety in pivotal study C4591001 continue**
- **Boostability**
- **Dose ranging and studies in pediatrics**
- **Use in pregnancy**
- **Use in Immunocompromised**
- **Refrigerator stable second-generation formulation**
- **Co-administration of influenza vaccine being considered**

Back up slides: Efficacy

Cumulative Incidence of COVID-19 After Dose 1



Solid fill marker indicates subjects with severe COVID-19

BNT162b2 Protects Against Severe Disease Severe illness - CDC definition: hospitalization, admission to the ICU, intubation or mechanical ventilation, or death" Phase 2/3 Efficacy – Final Analysis

Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC-Definition From 7 Days After Dose 1 – Dose 1 All-Available Efficacy Population

	BNT162b2 (30 µg) N=21,669		Placebo N=21,686			
Efficacy Endpoint	n	Surveillance Time (n)	n	Surveillance Time (n)	VE (%)	(95% CI)
First Severe COVID-19 occurrence	1	4.018 (21,299)	14	4.001 (21,238)	92.9	(53.2, 99.8)
First Severe COVID-19 occurrence after Dose 1 to before Dose 2	1		8		87.5	(6.8, 99.7)
First Severe COVID-19 occurrence Dose 2 to 7 days after Dose 2	0		1		100.0	(-3800.0, 100.0)
First Severe COVID-19 occurrence >7 days after Dose 2	0	2.215 (17,399)	14	2.229 (17,495)	100	(-9.9, 100)

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint..

Characterization of Severe COVID-19 CDC Definition Occurrence After Dose 1

	Placebo cases														BNT Cases
	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13	#14	#15
Hospitalized due to COVID-19 illness	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Admission to an ICU		Y									Y		Y		
Needs mechanical ventilation											Y				
Ethnicity															
Hispanic/Latino		Y		Y	Y	Y	Y	Y	Y	Y	Y	Y			
Non-Hispanic/non-Latino	Y		Y										Y	Y	Y

Characterization of Severe COVID-19 CDC Definition Occurrence After Dose 1 By Comorbidity Status

	Placebo cases														BNT Cases
	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13	#14	#15
Any Malignancy															
Cardiovascular			Y												
Chronic pulmonary disease		Y					Y						Y		
Diabetes	Y	Y	Y												Y
Obese (≥30.0 kg/m^2)	Y	Y	Y					Y					Y	Y	
Hypertension		Y	Y			Y	Y						Y		
Gestational diabetes															

Real-world, Test-negative Design (TND) Vaccine Effectiveness Studies

Against severe, important endpoints like:

- Hospitalization
- Emergency Dept. (ED) visits

In specific populations:

- Race/ethnicity
- Elderly
- Nursing home residents
- Healthcare workers

Understand VE:

- When vaccine is used in “real-world” conditions outside controlled trial
- In broader populations

Studies will complement CDC planned effectiveness studies

Back up slides: Safety

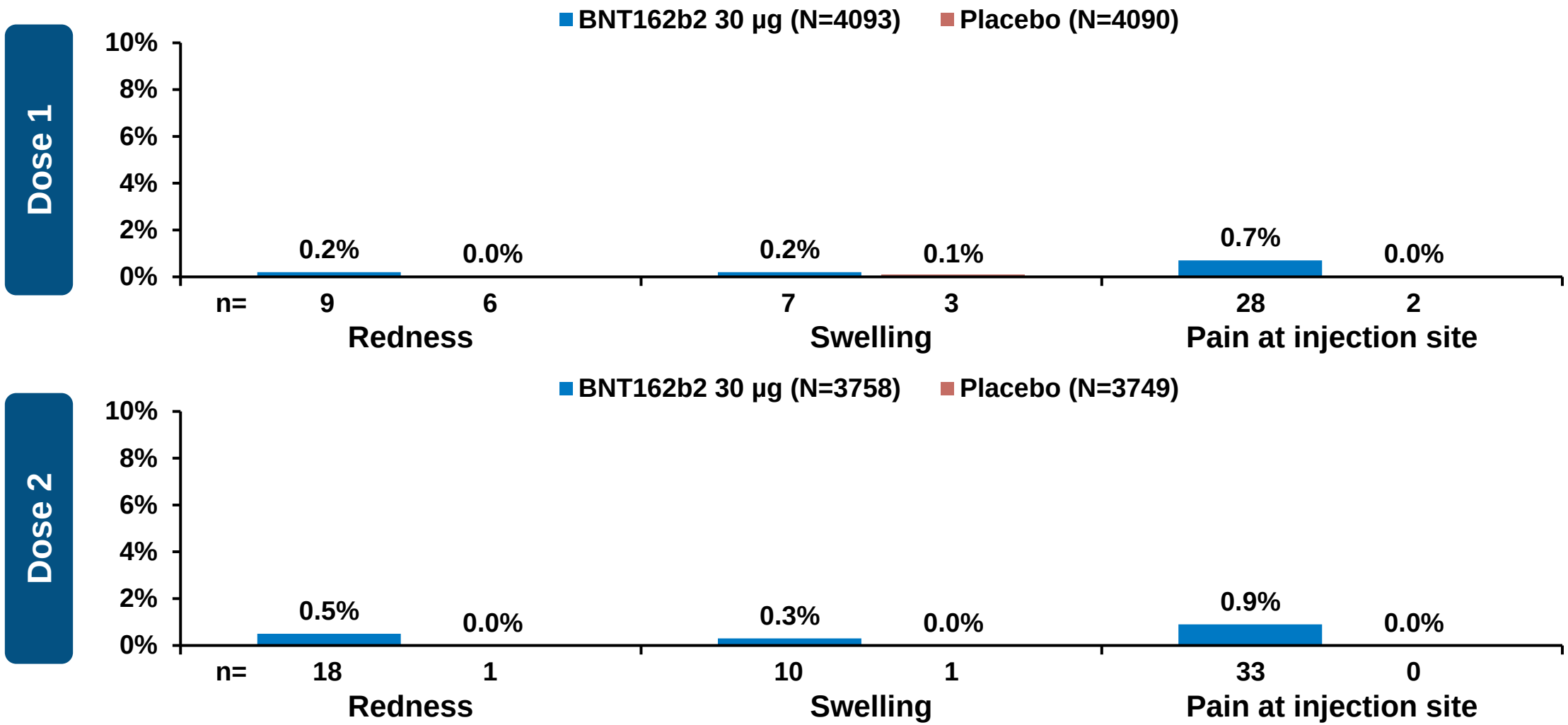
Reactogenicity Overview – Subjects Reporting ≥1 Solicited Injection Site Reaction

Safety Population (Participants who Received at Least 1 Dose of Study Intervention)

	BNT162b2 (30 µg) N=4108 n (%)	Placebo N=4106 n (%)
Solicited injection site reaction within 7 days after each dose	3481 (84.7)	748 (18.2)
Grade 3 solicited injection site reaction		
After Dose 1	N=4093	N=4090
Pain at the injection site	28 (0.7)	2 (0.0)
Redness	9 (0.2)	6 (0.1)
Swelling	7 (0.2)	3 (0.1)
After Dose 2	N=3758	N=3749
Pain at the injection site	33 (0.9)	0 (0.0)
Redness	18 (0.5)	1 (0.0)
Swelling	10 (0.3)	1 (0.0)

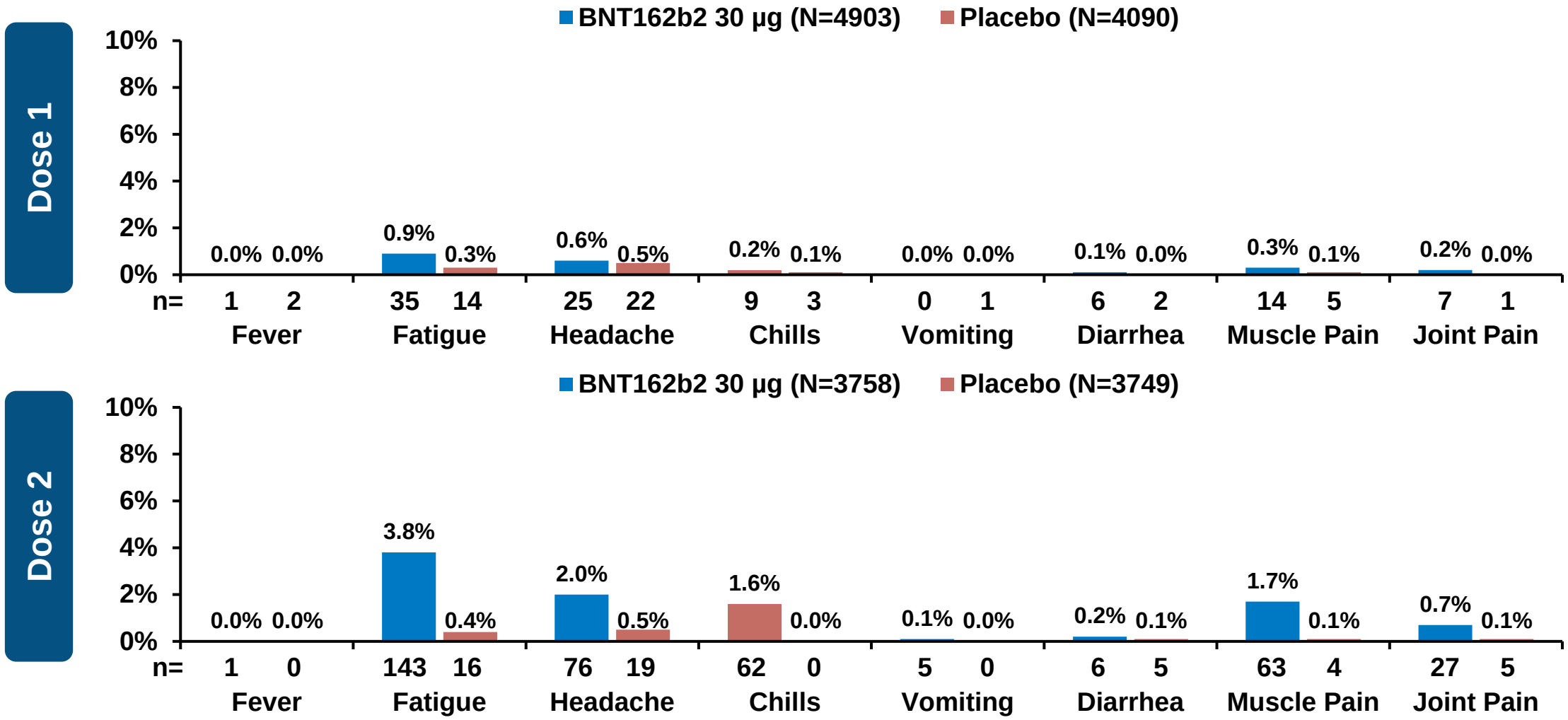
Reactogenicity Overview – Subjects Reporting ≥1 Solicited Injection Site Reaction

Safety Population (Participants who Received at Least 1 Dose of Study Intervention)



Reactogenicity Overview – Subjects Reporting ≥1 Solicited Systemic Adverse Event

Safety Population (Participants who Received at Least 1 Dose of Study Intervention)



Back up slides: Individual AEs by Race and Ethnicity tables

Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2 – by Race: Black or African American

~38,000 Subjects for Phase 2/3 Analysis – Safety Population

Adverse Event	BNT162b2 (30 µg) N=1694 n (%)	Placebo N=1722 n (%)
Any event	269 (15.9)	176 (10.2)
Related[a]	194 (11.5)	87 (5.1)
Severe	14 (0.8)	11 (0.6)
Life-threatening	0	3 (0.2)
Any serious adverse event	11 (0.6)	9 (0.5)
Related[a]	0	0
Severe	7 (0.4)	6 (0.3)
Life-threatening	0	3 (0.2)
Any adverse event leading to withdrawal	3 (0.2)	6 (0.3)
Related[a]	1 (0.1)	3 (0.2)
Severe	0	1 (0.1)
Life-threatening	0	0
Death	0	0

a. Assessed by the investigator as related to investigational product.

Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2 – by Race: White

~38,000 Subjects for Phase 2/3 Analysis – Safety Population

Adverse Event	BNT162b2 (30 µg) N=15615 n (%)	Placebo N=15615 n (%)
Any event	4252 (27.2)	1991 (12.8)
Related[a]	3234 (20.7)	748 (4.8)
Severe	185 (1.2)	94 (0.6)
Life-threatening	16 (0.1)	17 (0.1)
Any serious adverse event	81 (0.5)	71 (0.5)
Related[a]	2 (0.0)	0
Severe	44 (0.3)	41 (0.3)
Life-threatening	16 (0.1)	16 (0.1)
Any adverse event leading to withdrawal	29 (0.2)	18 (0.1)
Related[a]	13 (0.1)	4 (0.0)
Severe	13 (0.1)	6 (0.0)
Life-threatening	1 (0.0)	4 (0.0)
Death	1 (0.0)	2 (0.0)

a. Assessed by the investigator as related to investigational product.

Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2 – by Race: All Others

~38,000 Subjects for Phase 2/3 Analysis – Safety Population

Adverse Event	BNT162b2 (30 µg) N=1492 n (%)	Placebo N=1448 n (%)
Any event	550 (36.9)	189 (13.1)
Related[a]	487 (32.6)	118 (8.1)
Severe	21 (1.4)	4 (0.3)
Life-threatening	2 (0.1)	0
Any serious adverse event	11 (0.7)	1 (0.1)
Related[a]	1 (0.1)	0
Severe	6 (0.4)	1 (0.1)
Life-threatening	2 (0.1)	0
Any adverse event leading to withdrawal	2 (0.1)	1 (0.1)
Related[a]	0	0
Severe	0	0
Life-threatening	1 (0.1)	0
Death	0	0

a. Assessed by the investigator as related to investigational product.
All others=American Indian or Alaska native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories

Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2 – by Ethnicity: Hispanic/Latino

~38,000 Subjects for Phase 2/3 Analysis – Safety Population

Adverse Event	BNT162b2 (30 µg) N=5253 n (%)	Placebo N=5269 n (%)
Any event	1429 (27.2)	834 (15.8)
Related[a]	940 (17.9)	278 (5.3)
Severe	71 (1.4)	38 (0.7)
Life-threatening	4 (0.1)	4 (0.1)
Any serious adverse event	27 (0.5)	21 (0.4)
Related[a]	0	0
Severe	13 (0.2)	16 (0.3)
Life-threatening	4 (0.1)	4 (0.1)
Any adverse event leading to withdrawal	9 (0.2)	2 (0.0)
Related[a]	3 (0.1)	0
Severe	4 (0.1)	0
Life-threatening	0	2 (0.0)
Death	0	1 (0.0)

a. Assessed by the investigator as related to investigational product.

Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2 – by Ethnicity: Non-Hispanic/Non-Latino

~38,000 Subjects for Phase 2/3 Analysis – Safety Population

Adverse Event	BNT162b2 (30 µg) N=13436 n (%)	Placebo N=13407 n (%)
Any event	3621 (26.9)	1511 (11.3)
Related[a]	2959 (22.0)	669 (5.0)
Severe	149 (1.1)	71 (0.5)
Life-threatening	14 (0.1)	16 (0.1)
Any serious adverse event	76 (0.6)	60 (0.4)
Related[a]	3 (0.0)	0
Severe	44 (0.3)	32 (0.2)
Life-threatening	14 (0.1)	15 (0.1)
Any adverse event leading to withdrawal	25 (0.2)	23 (0.2)
Related[a]	11 (0.1)	7 (0.1)
Severe	9 (0.1)	7 (0.1)
Life-threatening	2 (0.0)	2 (0.0)
Death	1 (0.0)	1 (0.0)

a. Assessed by the investigator as related to investigational product.

Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2 – by Ethnicity: Not Reported

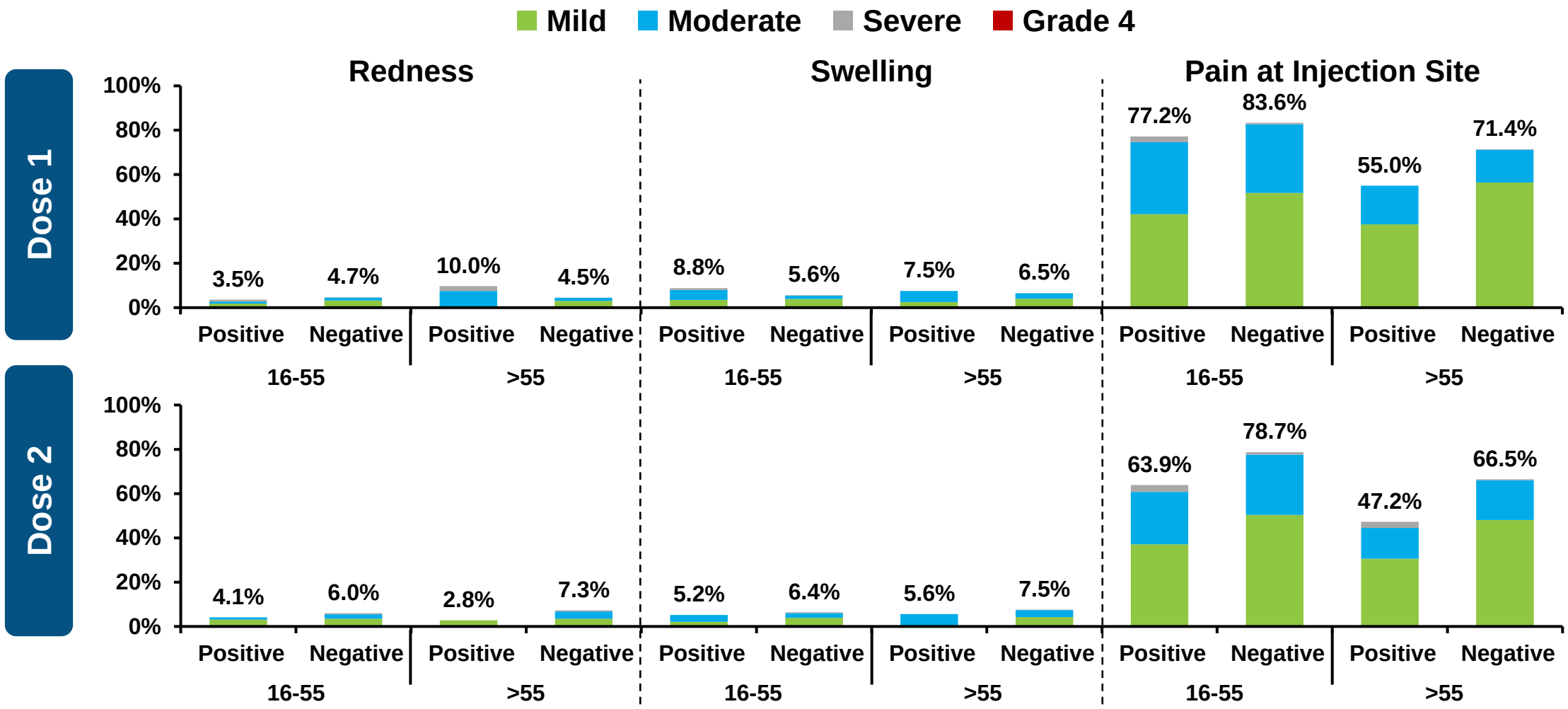
~38,000 Subjects for Phase 2/3 Analysis – Safety Population

Adverse Event	BNT162b2 (30 µg) N=112 n (%)	Placebo N=109 n (%)
Any event	21 (18.8)	11 (10.1)
Related[a]	16 (14.3)	6 (5.5)
Severe	0	0
Life-threatening	0	0
Any serious adverse event	0	0
Related[a]	0	0
Severe	0	0
Life-threatening	0	0
Any adverse event leading to withdrawal	0	0
Related[a]	0	0
Severe	0	0
Life-threatening	0	0
Death	0	0

a. Assessed by the investigator as related to investigational product.

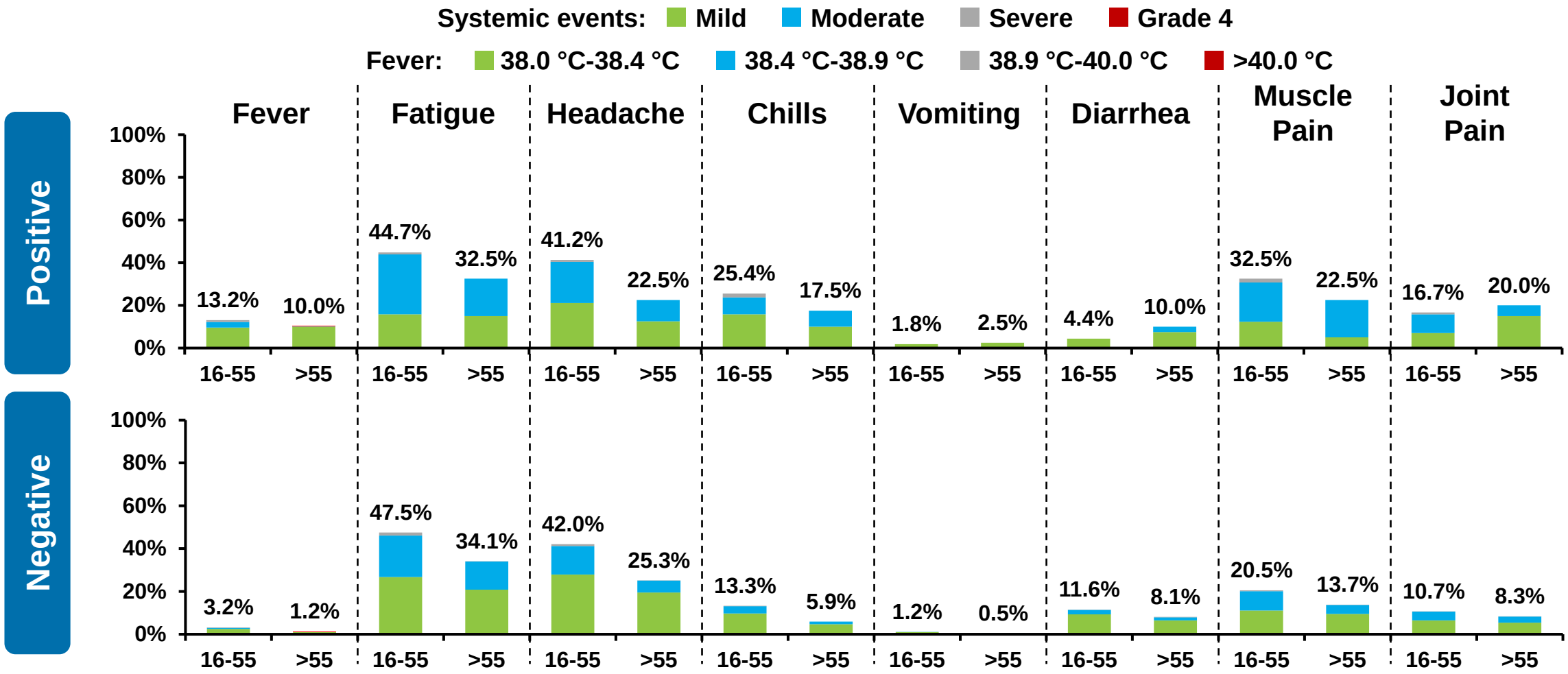
Back up slides: AEs Tables by Serostatus

eDiary: Local Events Within 7 Days From Dose 1 and 2 in 16-55 and >55 Year Olds BNT162b2 By Baseline SARS-CoV-2 Status



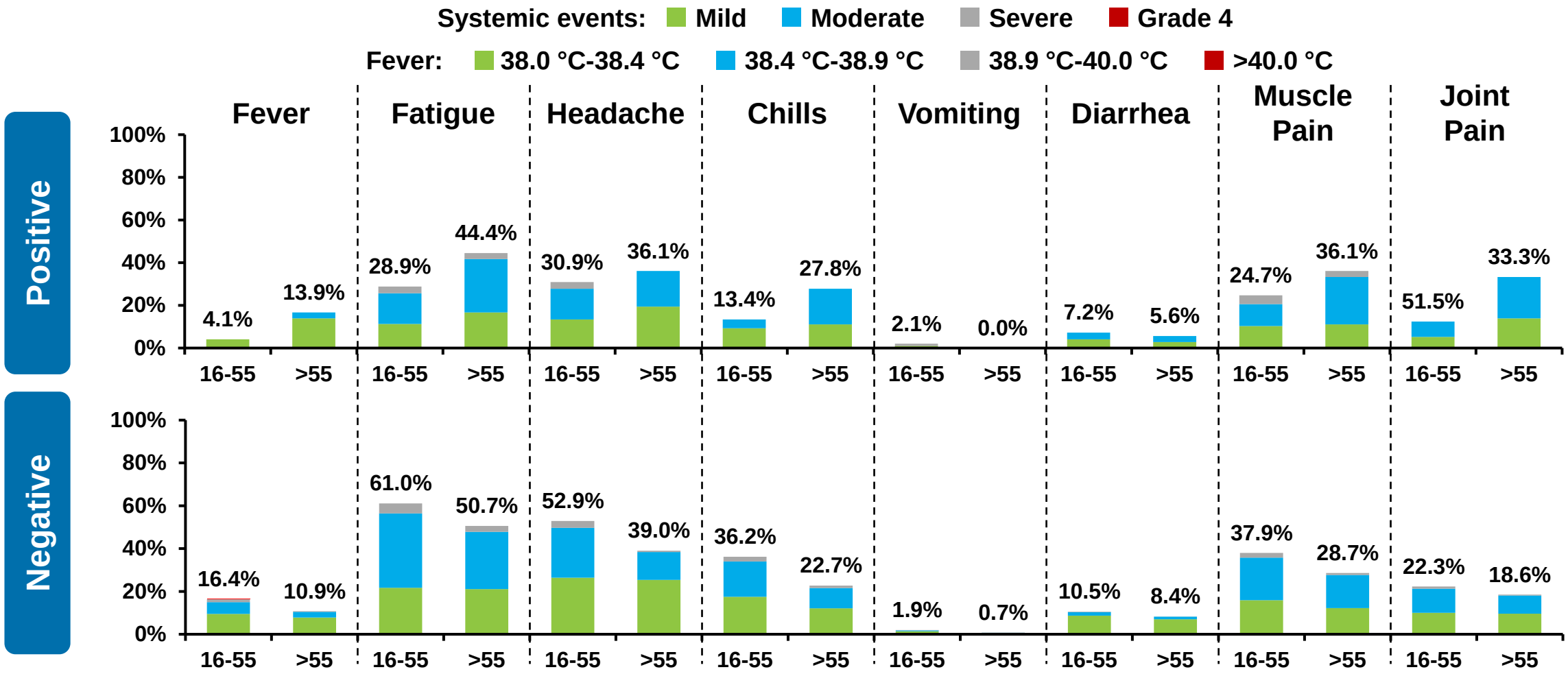
Redness and sweeling severity definition: Mild= >2-5cm, Moderate= >5-10 cm; Severe= >10 cm; Grade 4= necrosis
Pain at injection site severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization

eDiary: Systemic Events Within 7 Days From Dose 1 in 16-55 and >55 Year Olds BNT162b2 By SARS-CoV-2 Baseline Status



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

eDiary: Systemic Events Within 7 Days From Dose 2 in 16-55 and >55 Year Olds BNT162b2 SARS-CoV-2 By Baseline Status



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

Severe/Grade 3 Local Reactions Within 7 Days after each dose BNT162b2 By Baseline SARS-CoV-2 Status

		Positive	Placebo	Negative	Placebo
Dose 1	Pain at the injection site	3/154 (1.9)	1/164 (0.6)	23/3893 (0.6)	1/3886 (0.0)
	Redness	2/154 (1.3)	2/164 (1.2)	7/3893 (0.2)	3/3886 (0.1)
	Swelling	1/154 (0.6)	1/164 (0.6)	6/3893 (0.2)	1/3886 (0.0)
Dose 2	Pain at the injection site	4/133 (3.0)	0/145 (0.0)	29/3590 (0.8)	0/3568 (0.0)
	Redness	0/133 (0.0)	1/145 (0.7)	18/3590 (0.5)	0/3568 (0.0)
	Swelling	0/133 (0.0)	0/145 (0.0)	10/3590 (0.3)	1/3568 (0.0)

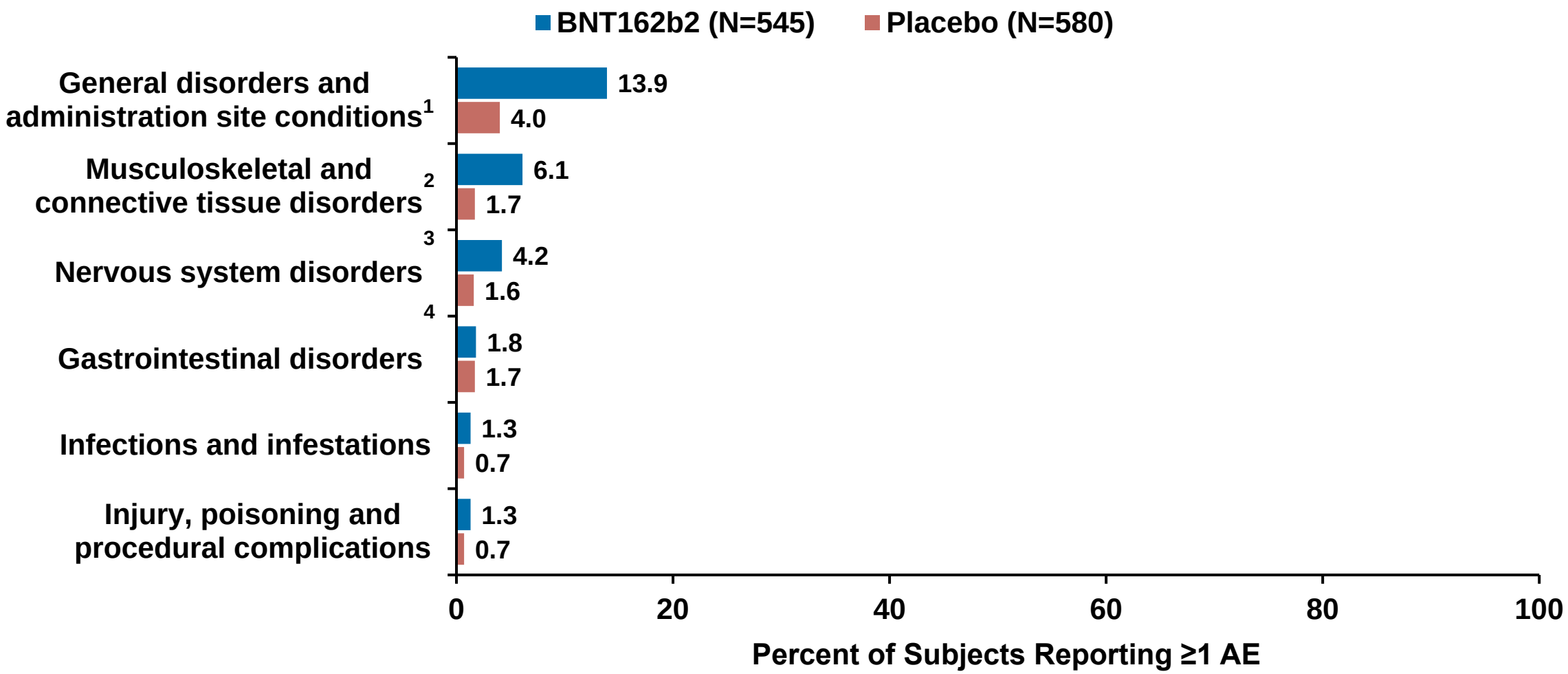
Severe/Grade 3 Systemic Events Within 7 Days of Dose 1 BNT162b2 By Baseline SARS-CoV-2 Status

Dose 1	Positive	Placebo	Negative	Placebo
Fever >40.0°C	0/154 (0.0)	1/164 (0.6)	1/3893 (0.0)	1/3886 (0.0)
Fatigue	1/154 (0.6)	0/164 (0.0)	31/3893 (0.8)	14/3886 (0.4)
Headache	1/154 (0.6)	3/164 (1.8)	21/3893 (0.5)	18/3886 (0.5)
Chills	2/154 (1.3)	0/164 (0.0)	5/3893 (0.1)	3/3886 (0.1)
Vomiting	0/154 (0.0)	0/164 (0.0)	0/3893 (0.0)	0/3886 (0.0)
Diarrhea	0/154 (0.0)	0/164 (0.0)	6/3893 (0.2)	1/3886 (0.0)
New or worsened muscle pain	2/154 (1.3)	0/164 (0.0)	10/3893 (0.3)	5/3886 (0.1)
New or worsened joint pain	1/154 (0.6)	0/164 (0.0)	4/3893 (0.1)	1/3886 (0.0)

Severe/Grade 3 Systemic Events Within 7 Days of Dose 2 (N=8,183) BNT162b2 By Baseline SARS-CoV-2 Status

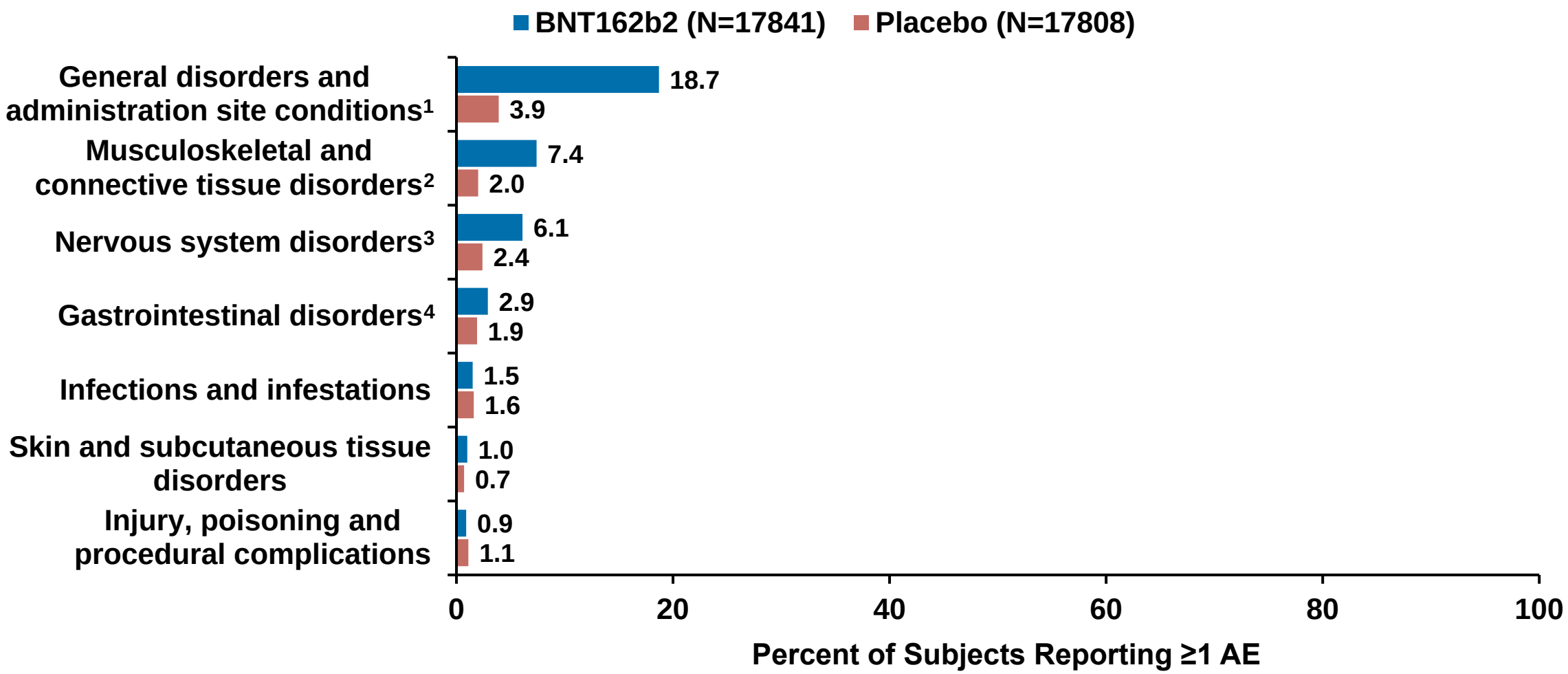
Dose 2	Positive	Placebo	Negative	Placebo
Fever >40.0°C	0/133 (0.0)	0/145 (0.0)	1/3590 (0.0)	0/3568 (0.0)
Fatigue	4/133 (3.0)	1/145 (0.7)	138/3590 (3.8)	15/3568 (0.4)
Headache	3/133 (2.3)	3/145 (2.1)	73/3590 (2.0)	16/3568 (0.4)
Chills	0/133 (0.0)	0/145 (0.0)	61/3590 (1.7)	0/3568 (0.0)
Vomiting	1/133 (0.8)	0/145 (0.0)	4/3590 (0.1)	0/3568 (0.0)
Diarrhea	0/133 (0.0)	2/145 (1.4)	6/3590 (0.2)	3/3568 (0.1)
New or worsened muscle pain	5/133 (3.8)	0/145 (0.0)	58/3590 (1.6)	4/3568 (0.1)
New or worsened joint pain	0/133 (0.0)	0/145 (0.0)	26/3590 (0.7)	5/3568 (0.1)

Adverse Events ≥1.0% by System Organ Class
≥50% of Subjects with at least 2 Months Post Dose 2 ~38,000 subjects SARS-CoV-2 Positive at Baseline



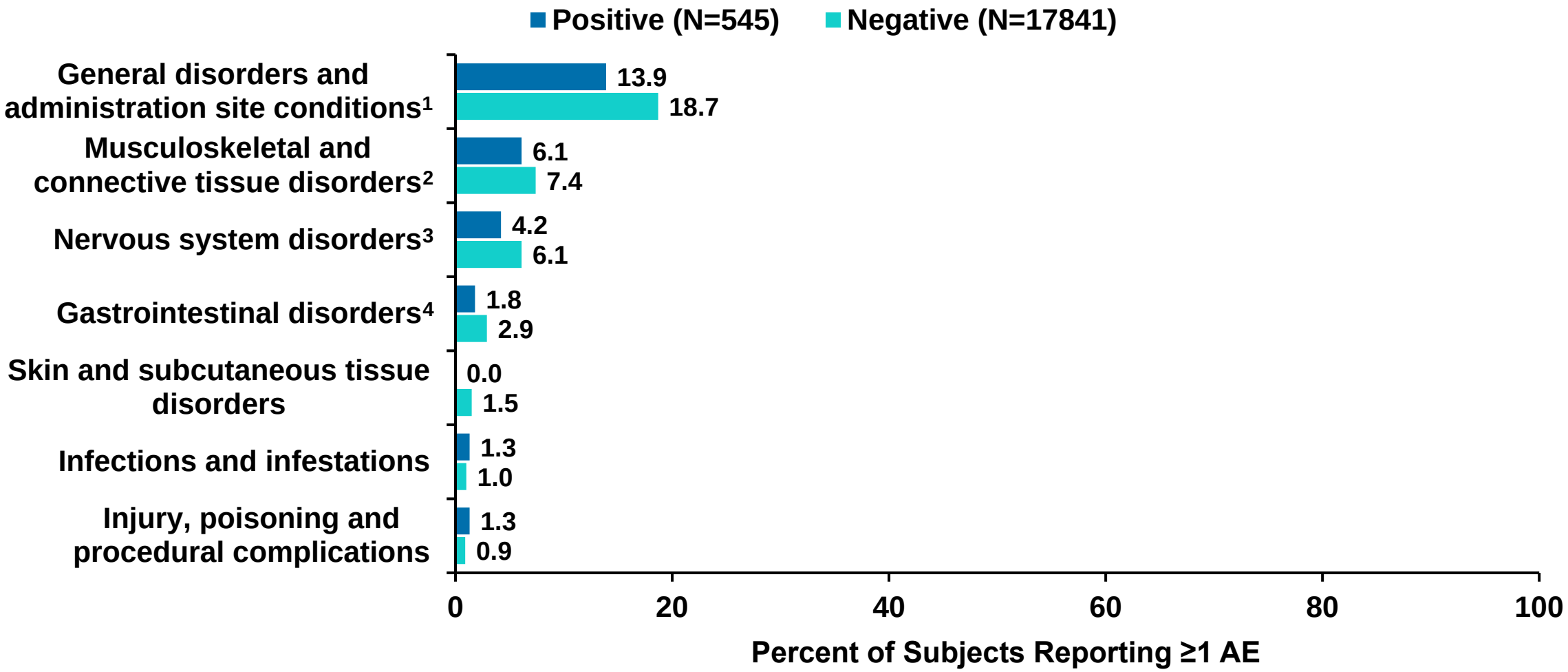
1. Predominantly reflect local reactions at the injection site and systemic reactions of fatigue and chills
2. Predominantly reflect myalgias and arthralgia's as part of systemic events
3. Predominantly reflects Headache
4. Predominantly reflects diarrhea and vomiting

Adverse Events ≥1.0% by System Organ Class
≥ 50% of Subjects with at least 2 Months Post Dose 2 ~38,000 subjects SARS-CoV-2 Negative at Baseline



1. Predominantly reflect local reactions at the injection site and systemic reactions of fatigue and chills
2. Predominantly reflect myalgias and arthralgia's as part of systemic events
3. Predominantly reflects Headache
4. Predominantly reflects diarrhea and vomiting

Adverse Events ≥1.0% by System Organ Class
≥ 50% of Subjects with at least 2 Months Post Dose 2 ~38,000 subjects SARS-CoV-2 status at Baseline



1. Predominantly reflect local reactions at the injection site and systemic reactions of fatigue and chills
2. Predominantly reflect myalgias and arthralgia's as part of systemic events
3. Predominantly reflects Headache
4. Predominantly reflects diarrhea and vomiting

Serious Adverse Events by System Organ Class ≥0.1%

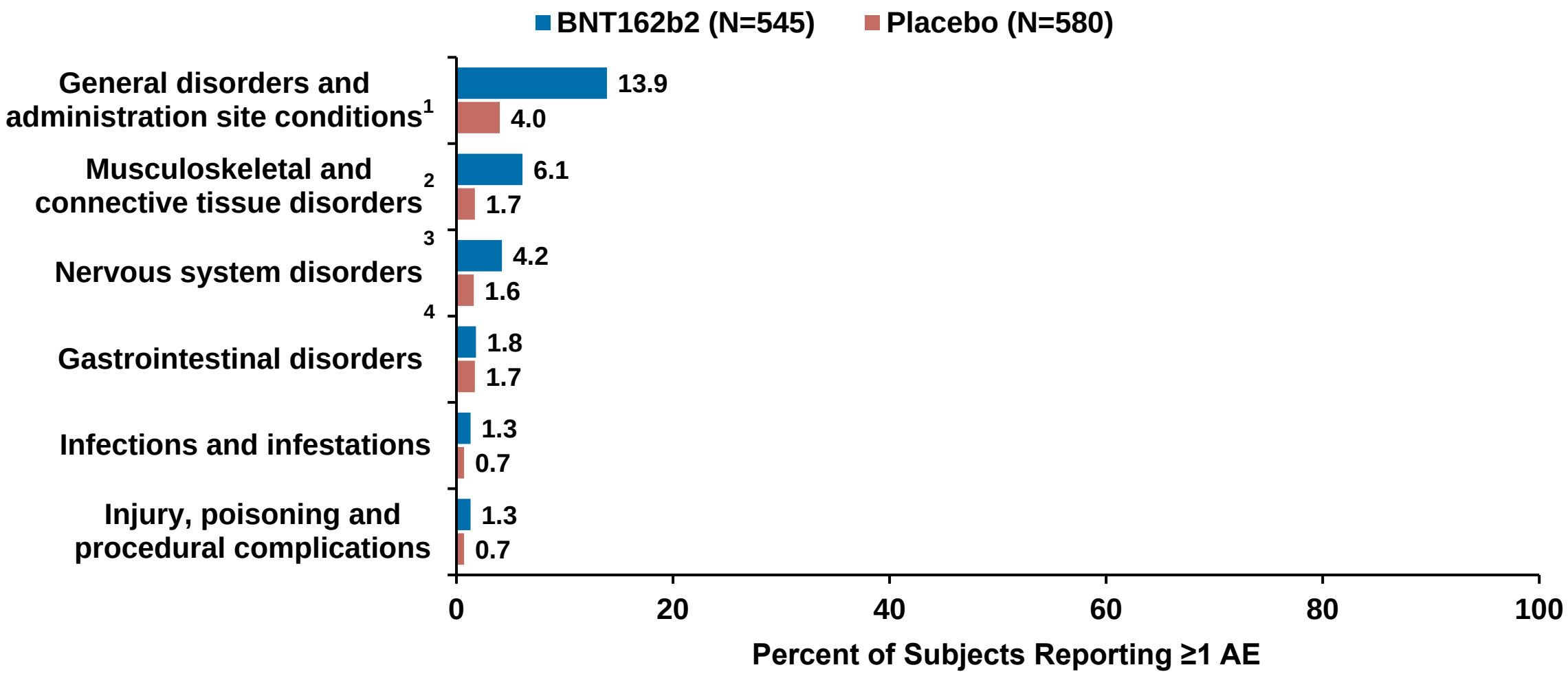
~38,000 subjects by SARS-CoV-2 baseline status

Baseline Positive	BNT162b2 (30 µg) N=545 n (%)	Placebo N=580 n (%)
Infections and infestations	1 (0.2)	0 (0.0)
Injury, poisoning and procedural complications	1 (0.2)	0 (0.0)
Pregnancy, puerperium and perinatal conditions	0 (0.0)	1 (0.1)
Vascular disorders	2 (0.4)	0 (0.0)

Baseline Negative	BNT162b2 (30 µg) N=17841 n (%)	Placebo N=17808 n (%)
Infections and infestations	24 (0.1)	14 (0.1)
Nervous system disorders	15 (0.1)	13 (0.1)
Cardiac disorders	14 (0.1)	12 (0.1)
Injury, poisoning and procedural complications	5 (0.0)	11 (0.1)

3 related SAEs in the BNT group in baseline SARS-CoV-2 negative

Adverse Events ≥1.0% by System Organ Class
≥50% of Subjects with at least 2 Months Post Dose 2 ~38,000 subjects SARS-CoV-2 Positive at Baseline



1. Predominantly reflect local reactions at the injection site and systemic reactions of fatigue and chills
2. Predominantly reflect myalgias and arthralgia's as part of systemic events
3. Predominantly reflects Headache
4. Predominantly reflects diarrhea and vomiting