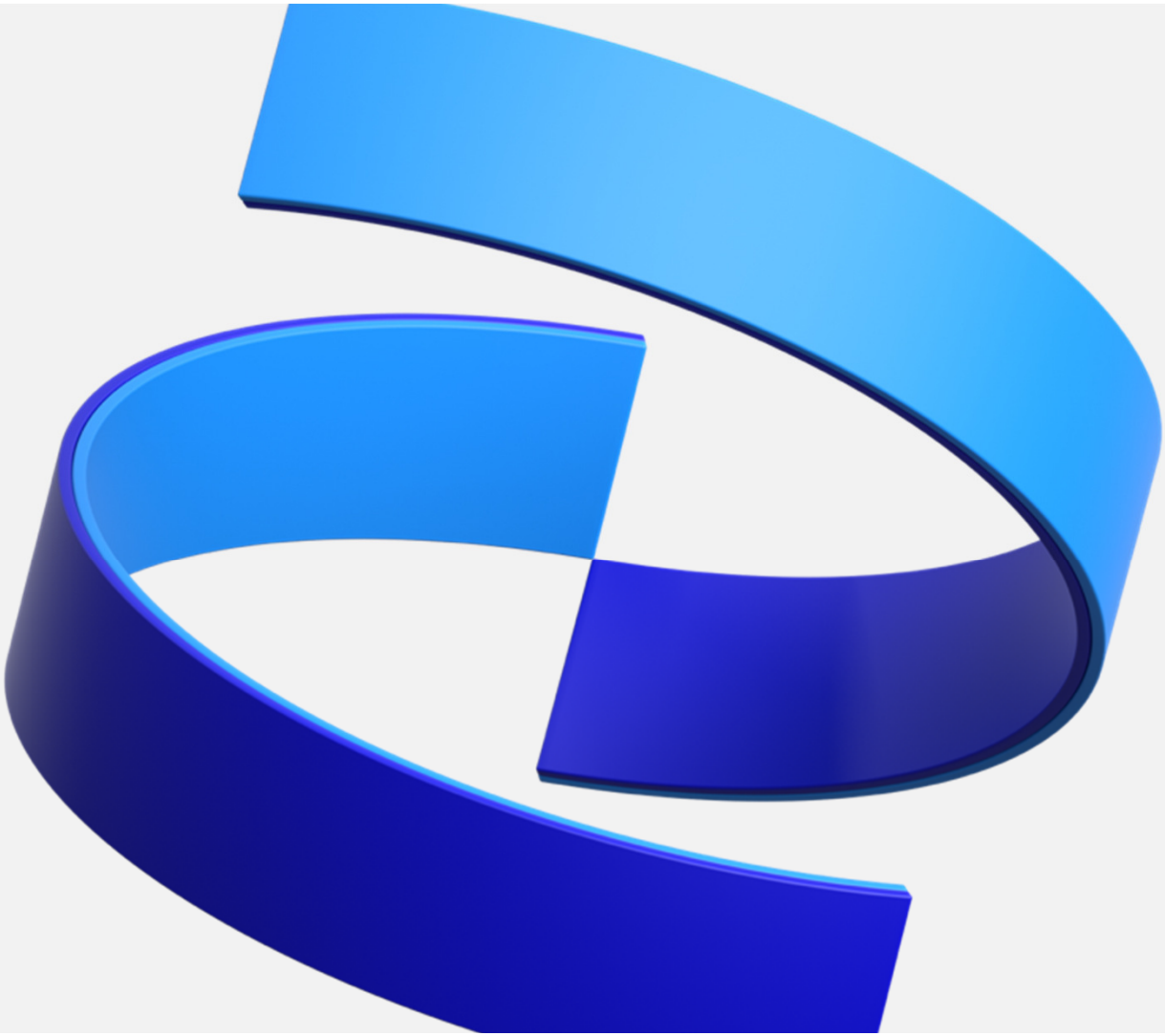
COVID-19 Vaccine BNT162b2 update

Presentation to the WHO Scientific Advisory Group of Experts (SAGE)
27 May 2021

Dr. Luis Jodar
SVP and CMO, Pfizer Vaccines on behalf of BionTech and Pfizer



Pfizer and BioNTech Attendees

Dr. Luis Jodar	Chief medical Officer, Pfizer Vaccines
Dr. Phil Dormitzer	Chief Scientific Officer– Pfizer Viral Vaccines
Dr. John Perez	Pfizer Vaccines Clinical Research & Development
Dr. Steve Lockhart	Pfizer COVID Vaccine Clinical Lead
Dr. Susan Mather	Pfizer Safety Surveillance & Risk Management
Dr. Dina Tresnan	Pfizer Safety Surveillance & Risk Management
Dr. Christian Lenz	Pfizer COVID Medical Lead, IDM
Dr. Donna Boyce	Pfizer Head of Regulatory Affairs, Vaccines

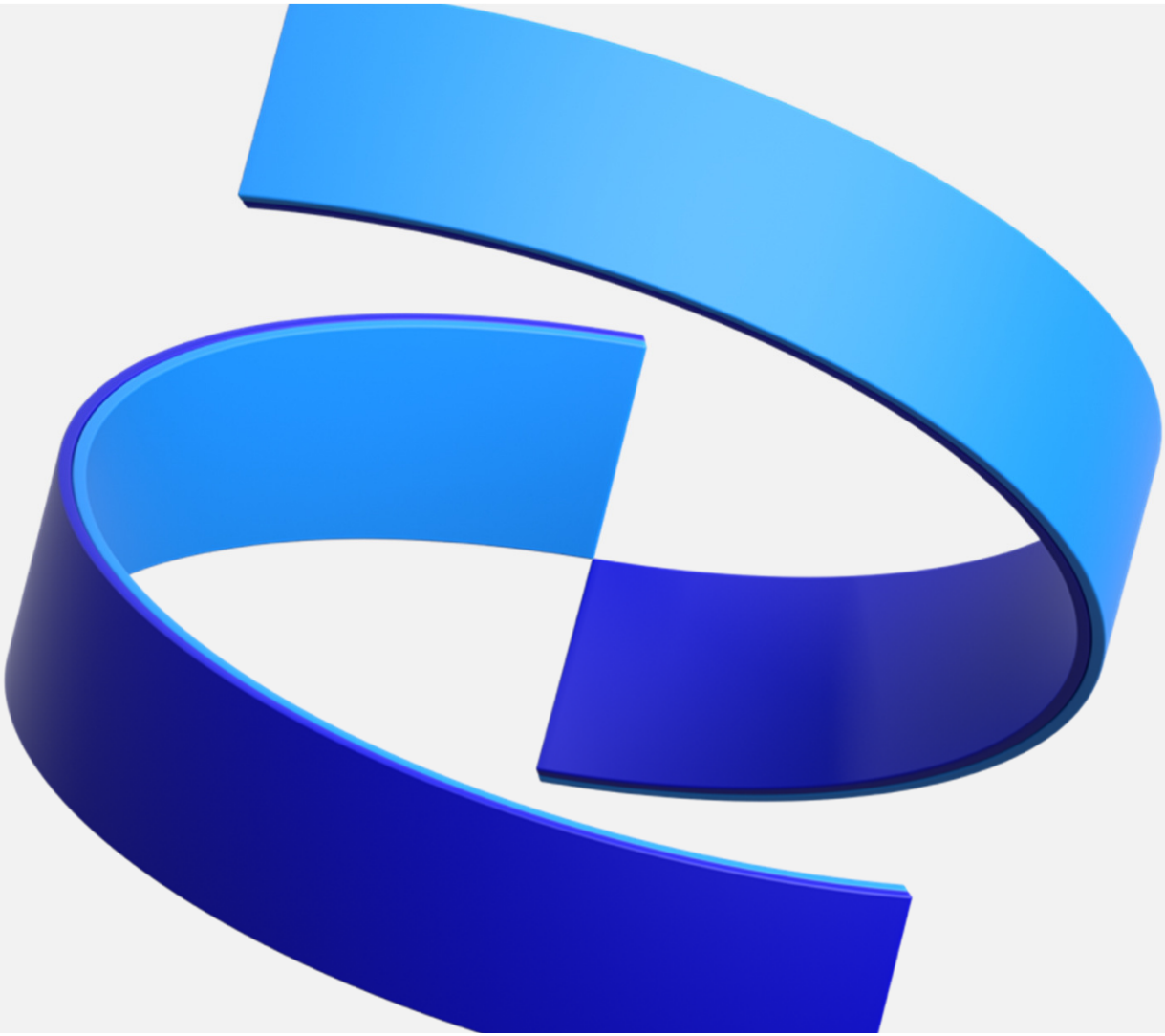
Dr. Özlem Türeci	Chief Medical Officer BioNTech
Dr. Eleni Lagkadinou	Clinical Development BioNTech
Dr. Shanti Pather	Global Medical Affairs BioNTech
Dr. Anoop Sagar	Global Medical Affairs BioNTech
Dr. Alexander Crocker-Buque	Global Medical Affairs BioNTech
Dr. Valeska Scharen-Guivel	Global Medical Affairs BioNTech
Dr. Ruben Rizzi	Global Regulatory Affairs BioNTech

Agenda

- **BNT162b2 vaccine update on VOC and booster plans**

- **Safety, Immunogenicity and Efficacy of BNT162b2 vaccine in 12-15 years old**

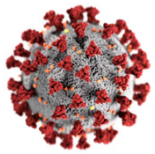
BNT162b2 vaccine update on VOC and booster plans



BNT162b2 Vaccine

Proposed Indication:

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



Individuals 12 years of age and older (FDA EUA)

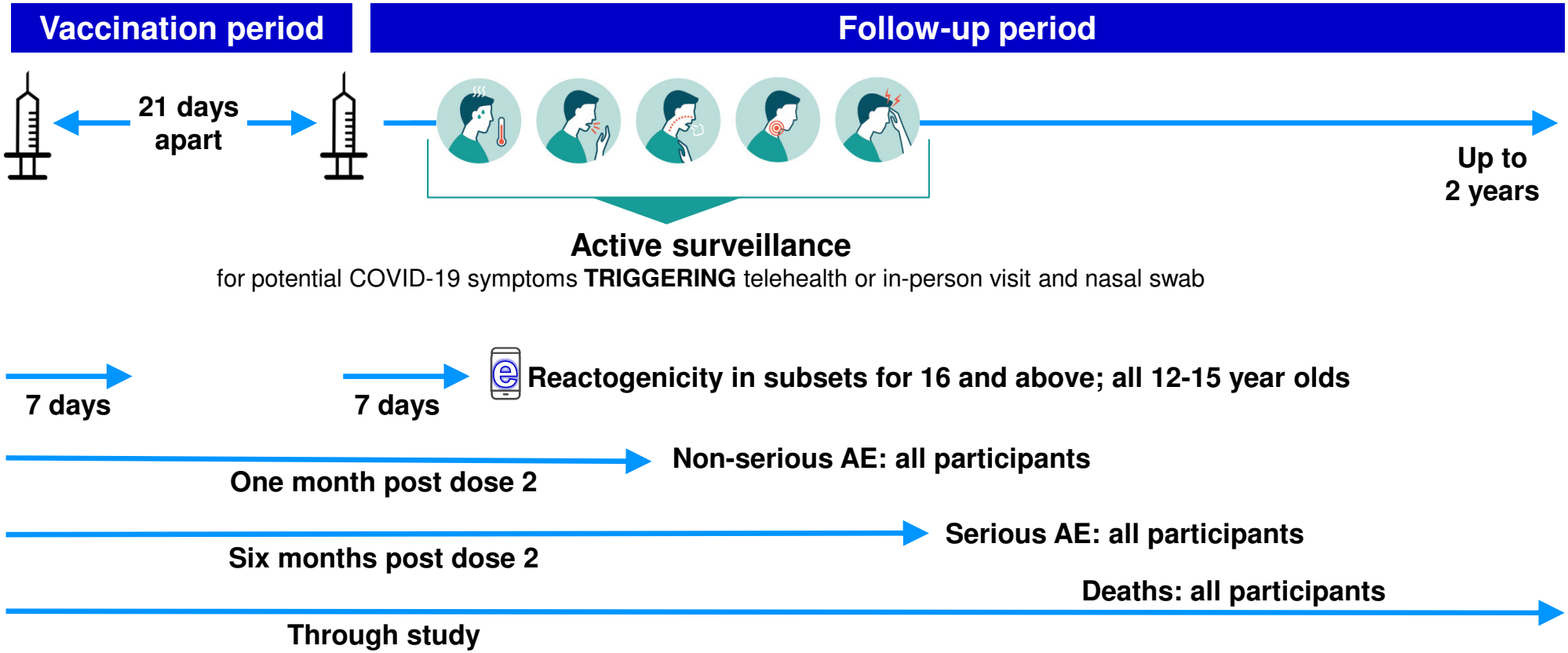
DOSE LEVEL and REGIMEN	• 30 µg • 2 doses given greater than or equal to 21 days apart
PRESENTATION	• 6 dose multidose vial
STORAGE	• -80ºC to -60ºC up to 6 months • -15ºC to -25ºC up to 2 weeks • 2º-8ºC up to 31 days

Subjects in Pivotal Phase 2/3 Study

- **~46,000 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

Phase 2/3 Safety/Efficacy Schema – Started 27 July, 2020



The first primary efficacy endpoint evaluation, individuals with NO evidence of prior/ current infection before each dose. Determined by a swab at the time of each dose and evidence of COVID by PCR or
by obtaining blood specimen for N-antigen antibodies at the time of the first dose to indicate evidence of prior infection

BioNTech/Pfizer vaccine efficacy remains high up to 6 Months following 2nd dose

Subjects Without Evidence of Infection Prior to 7 days after Dose 2 (C4591001)

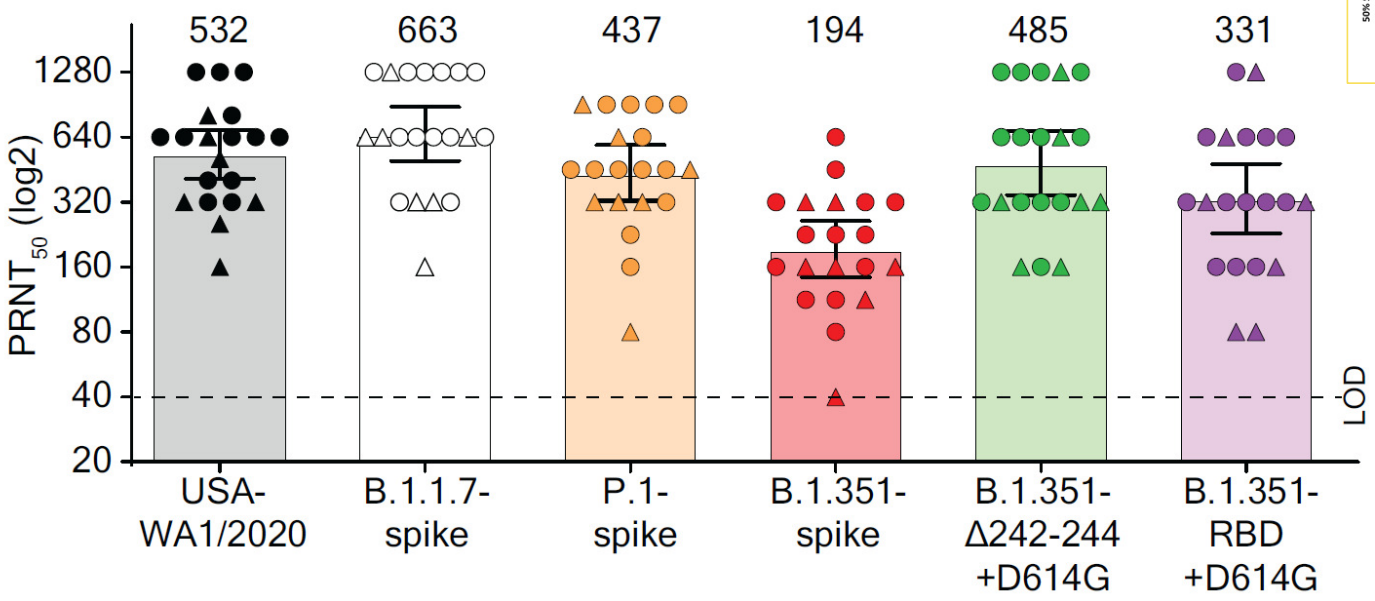
Subjects 16 – 85 Years of Age	BNT162b2 (30 µg) N=20,998		Placebo N=21,096		
Efficacy Endpoint	n	Surveillance Time (n)	n	Surveillance Time (n)	Vaccine efficacy (%)
First COVID-19 occurrence >7 days after Dose 2	77	6.247 (20712)	850	6.003 (20713)	**91.3**
First Severe COVID-19 occurrence >7 days after Dose 2	0*	6.250 (20688)	32	6.108 (20680)	**100.0**

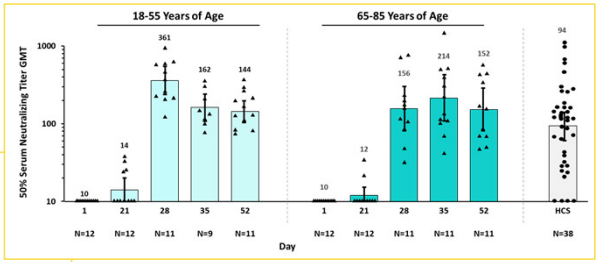
*Based on CDC definitions; 1 severe case observed in vaccine group based on FDA definition

The landmark trial enrolled 46,331 participants at 153 clinical sites around the world

Neutralization of SARS-CoV2 emerging variants by BNT162b2-elicited sera

BNT162b2 mRNA vaccine immune sera (n=15 participants) tested against 5 recombinant viruses covering key variants B.1.1.7, B.1.351, P.1. vs. the wildtype Wa-1 genetic background[1]





- B.1.1.7-spike and P.1-spike virus neutralization was roughly equivalent
- B.1.351-spike virus neutralization still robust but ~2.7-fold lower
- Mutations in receptor binding site (K417N, E484K, N501Y) affect neutralization more than 242-244 deletion in spike N-terminal domain

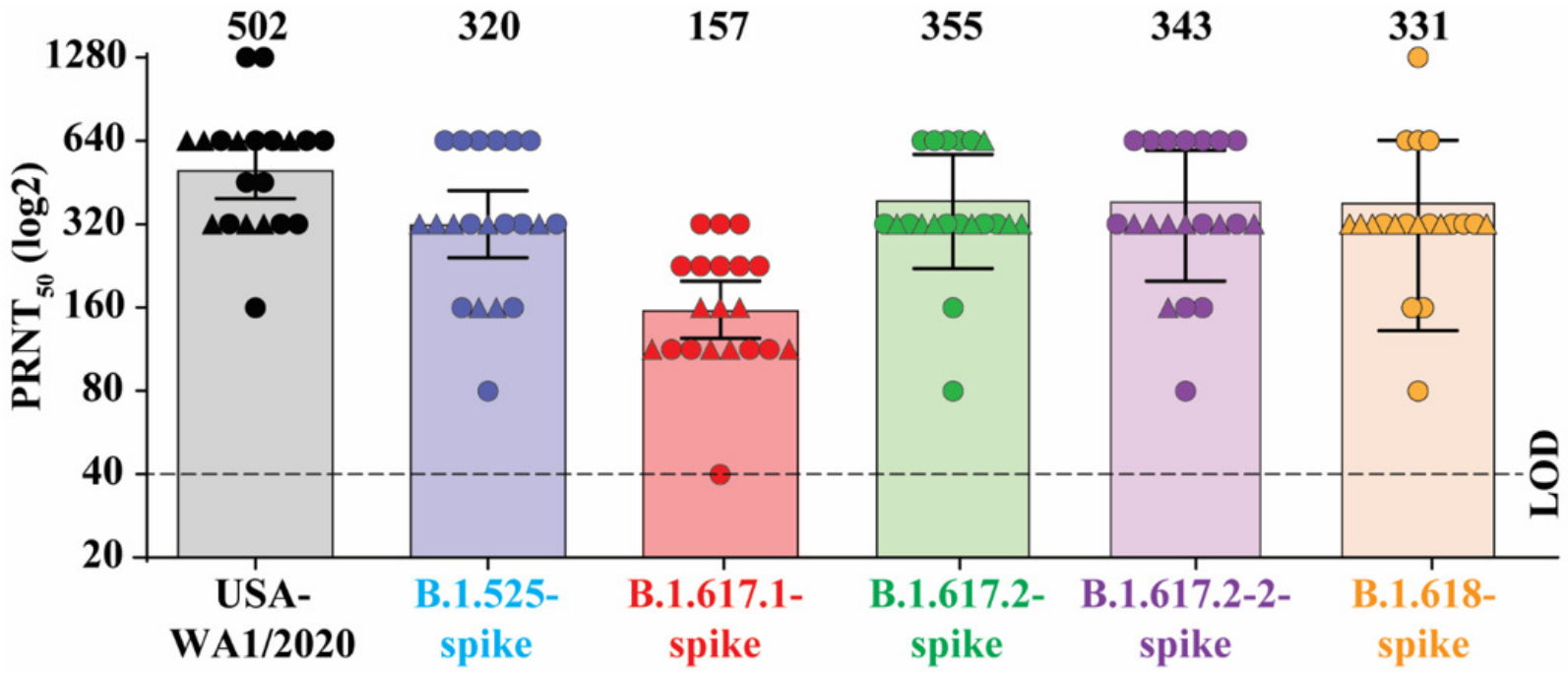
- **Reduced variant neutralization titers are much higher than the barely detectable titers observed after 1 dose of BNT162b2, when strong efficacy was already observed in pivotal Ph 3 trial[2]**

1. Liu, Y., et al. (2021). "Neutralizing Activity of BNT162b2-Elicited Serum." New England Journal of Medicine March 8, 2021; 2. Pfizer (2020). BNT162b2 EUA Presentation to FDA VRBPAC. VRBPAC. FDA, US FDA: 12 Dec 2020;

100% Observed Efficacy of BNT162b2 Against B.1.351 in a Sub-Analysis of Data from South Africa

- The vaccine efficacy estimate for B.1.351 was part of the pivotal phase 2/3 clinical study with a cut-off date of 13 March and was calculated in a sub-analysis at the South African site of the pivotal phase 2/3 trial.
- There were 291 vaccinated with BNT162b2 and 276 received placebo.
- 9 cases of COVID-19 observed without evidence of prior SAR-CoV-2 infection
- Case split: BNT162b2 – 0, placebo – 9
- Nasal swabs from 8 of the cases yielded viral sequence of B.1.351
- Observed vaccine efficacy against B.1.351 in the South Africa sub-analysis = 100% (95% CI [53.5, 100.0])

Neutralization of SARS-CoV2 emerging variants by BNT162b2-elicited sera



USA-WA1/2020 – wild type virus; B.1.525-spike – Nigerian variant virus;
B.1.617-1, B.1.617-2, B.1.617.2-vs, B.1.618 – Indian variant viruses

Real world effectiveness against B.1.1.7 and B.1.617.2 in the UK

Table 2: Vaccine effectiveness against S-gene target negative (B.1.1.7) and S-gene target positive (B.1.617.2)

Vaccination status	Test negative controls	B.1.1.7 or S-gene target negative			B.1.617.2 or S-gene target positive		
		cases	cases:controls	aVE(%)	cases	cases:controls	aVE(%)
Unvaccinated	58253	4891	0.084	base	695	0.012	base
Any vaccine							
Dose 1	32703	1481	0.045	51.1 (47.3 to 54.7)	279	0.009	33.5 (20.6 to 44.3)
Dose 2	8483	74	0.009	86.8 (83.1 to 89.6)	27	0.003	80.9 (70.7 to 87.6)
BNT162b2							
Dose 1	7036	344	0.049	49.2 (42.6 to 55.0)	49	0.007	33.2 (8.3 to 51.4)
Dose 2	6412	28	0.004	93.4 (90.4 to 95.5)	13	0.002	87.9 (78.2 to 93.2)

From Bernal et al., medRxiv 2021. DOI:10.1101/2021.05.22.21257658v1

Prototype clinical study evaluating updated variant of concern vaccine and booster with current vaccine

BNT162b2-experienced	Day 1	Day 7	Month 1	Month 6	Month 18
1 Current vaccine					
2 Updated vaccine			 *		

* After unblinding, a subset of participants will receive a 2nd dose of BNT162b2$_{VOC}$ at 1 month, with blood draws 7 days and 1 month later

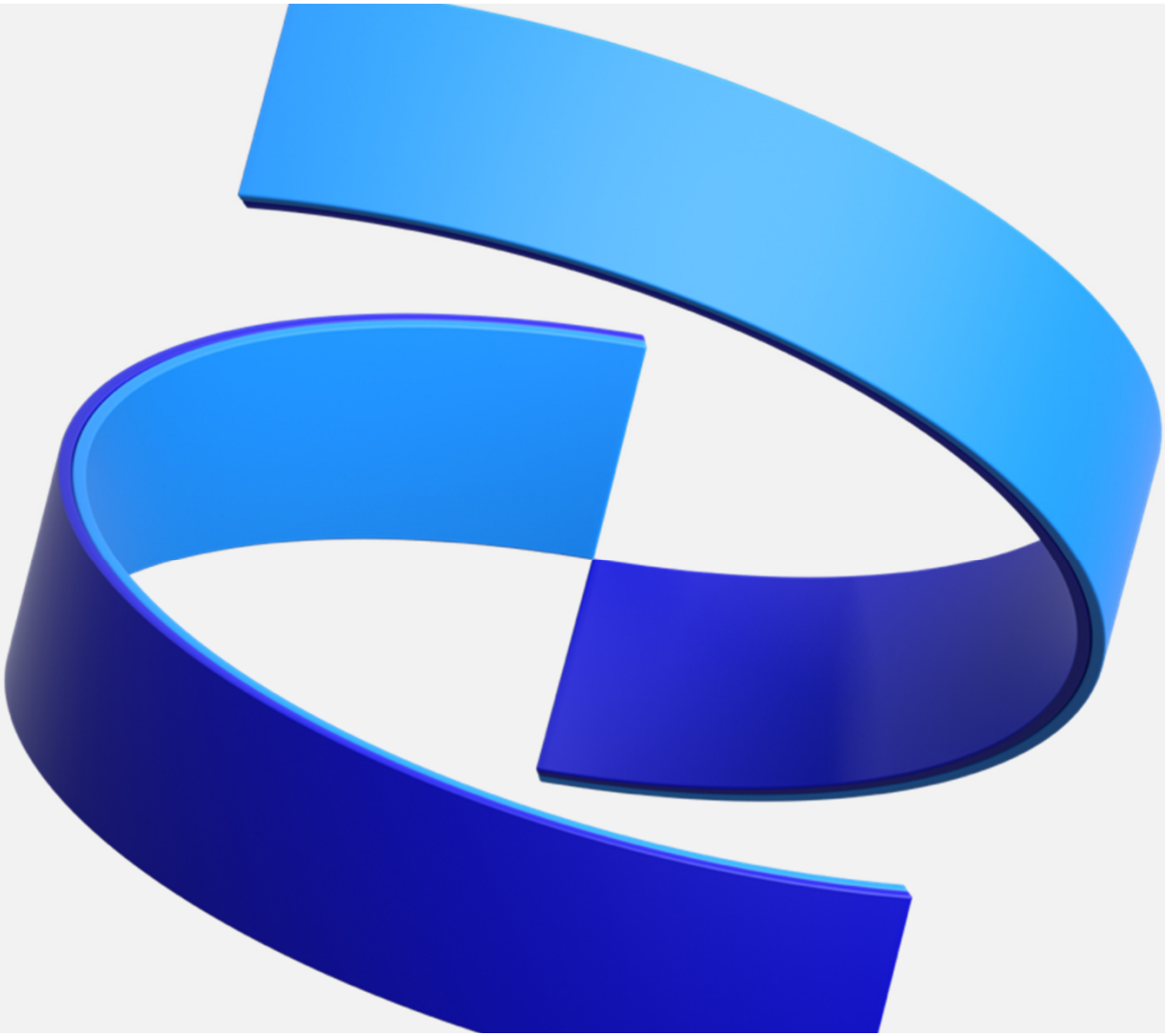
BNT162b2-naïve**	Day 1	Day 21	7 Days PD2	1 Month PD2	6 Months PD2	18 Months PD2
3 Updated vaccine						

** COVID-19 vaccine-naïve and have not experienced COVID-19
PD2 = Post dose 2

This study is a pivotal non-inferiority study and is ongoing; data are not yet available

We have a process to be ready in less than 100 days to have a new variant vaccine, if needed, to start mass vaccination

Safety, Immunogenicity, and Efficacy of BNT162b2 in Subjects 12–15-years-old



Phase 2/3 Safety Schema – Started 27 July, 2020

Vaccination period | **Follow-up period**

Active surveillance
for potential COVID-19 symptoms **TRIGGERING**
telehealth or in-person visit and nasal swab

7 days — **7 days** — **Reactogenicity in subsets for 16 and above; all 12-15 year olds**

One month post dose 2 — **Non-serious AE: all participants**

Six months post dose 2 — **Serious AE: all participants**

Through study — **Deaths: all participants**

- All 12-15 year olds had e-diaries to capture solicited events (N=2260)
- A random subset of 16-25 year olds had e-diaries (N=1097)
- Prior history of symptomatic COVID-19/MIS-C were excluded

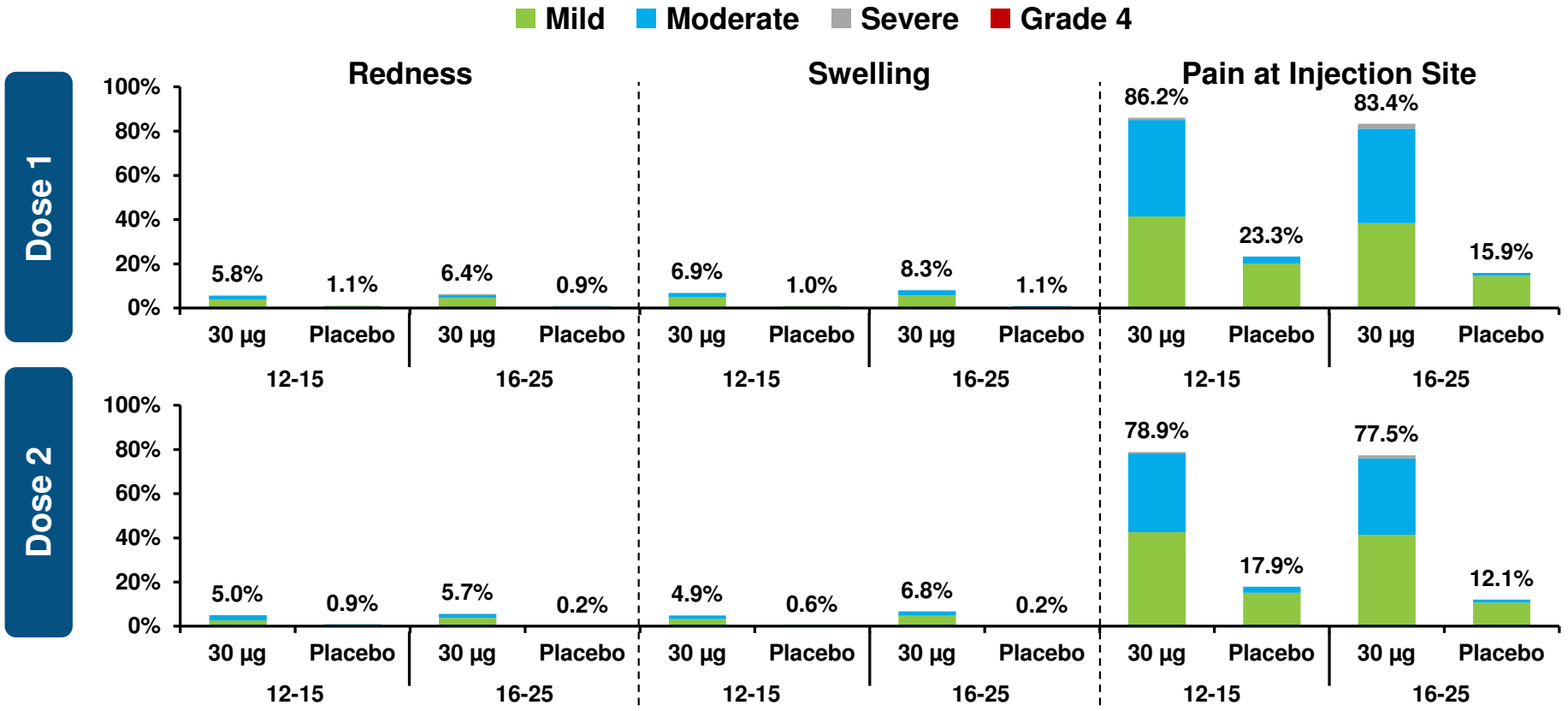
Demography for 12-15 and 16-25 year olds (Safety population)

		BNT162b2		Placebo	
		12-15 Years (N=1131) n (%)	16-25 Years (N=1867) n (%)	12-15 Years (N=1129) n (%)	16-25 Years (N=1903) n (%)
Sex	Male	567 (50.1)	921 (49.3)	585 (51.8)	882 (46.3)
	Female	564 (49.9)	946 (50.7)	544 (48.2)	1021 (53.7)
Race	White	971 (85.9)	1443 (77.3)	962 (85.2)	1510 (79.3)
	Black or African American	52 (4.6)	189 (10.1)	57 (5.0)	179 (9.4)
	American Indian or Alaska native	4 (0.4)	32 (1.7)	3 (0.3)	18 (0.9)
	Asian	72 (6.4)	108 (5.8)	71 (6.3)	108 (5.7)
	Native Hawaiian or other Pacific Islander	3 (0.3)	10 (0.5)	0	3 (0.2)
	Multiracial	23 (2.0)	76 (4.1)	29 (2.6)	74 (3.9)
	Not reported	6 (0.5)	9 (0.5)	7 (0.6)	11 (0.6)
Racial desig.	Japanese	5 (0.4)	3 (0.2)	2 (0.2	6 (0.3)
Ethnicity	Hispanic/Latino	132 (11.7)	604 (32.4)	130 (11.5)	575 (30.2)
	Non-Hispanic/non-Latino	997 (88.2)	1259 (67.4)	996 (88.2)	1322 (69.5)
	Not reported	2 (0.2)	4 (0.2)	3 (0.3)	6 (0.3)
Country	USA	1131 (100.0)	1333 (71.4)	1129 (100.0)	1364 (71.7)
	Others*	0	534 (28.6)	0	539 (28.3)

*Argentina, Brazil, Germany, South Africa, Turkey

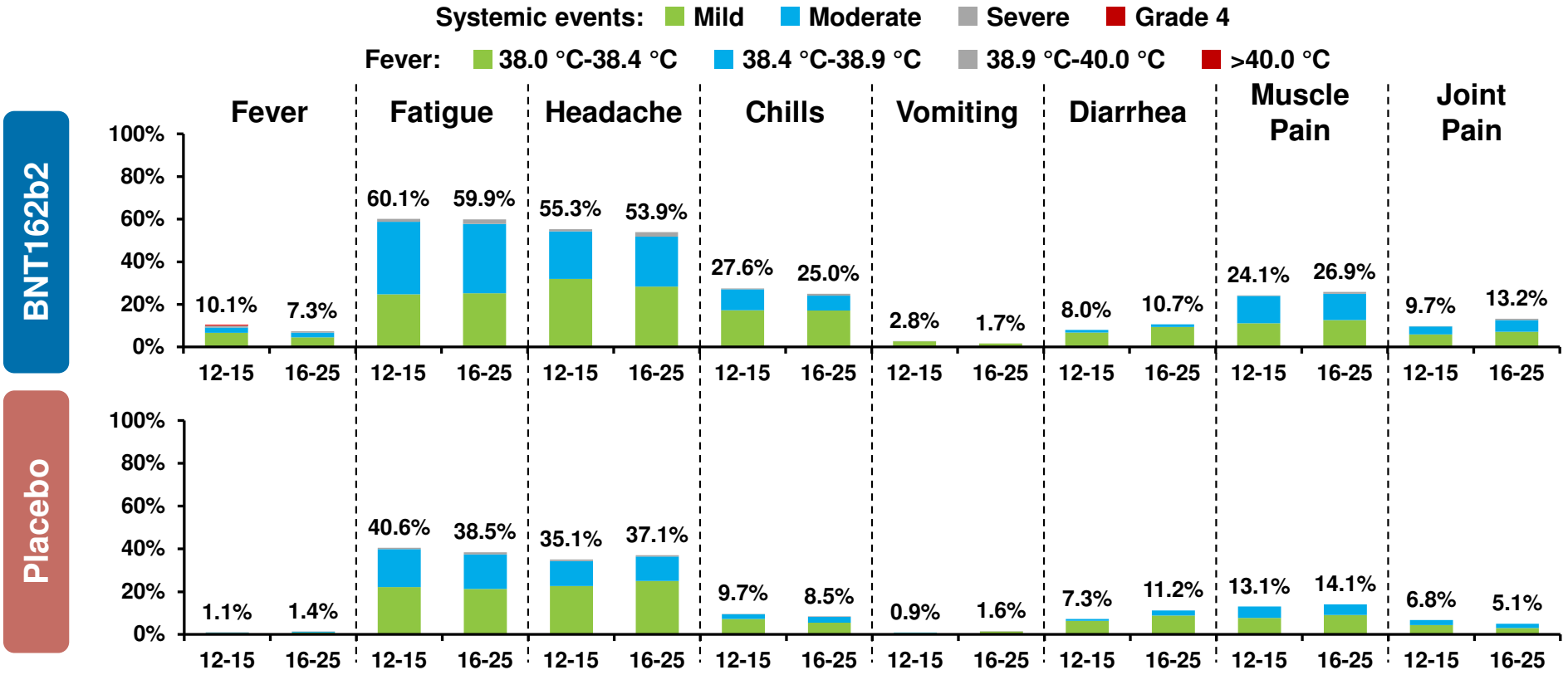
Note: All 12-15 year olds from the US; ~72% of 16-25 year olds from the US

Subjects Reporting Local Reactions, by Maximum Severity, Within 7 Days After Each Dose in 12-15 and 16-25 Year Olds



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: 12-15 yrs N=2254; 16-25 yrs N=1084 Dose 2: 12-15 yrs N=2175 16-25 yrs N=984

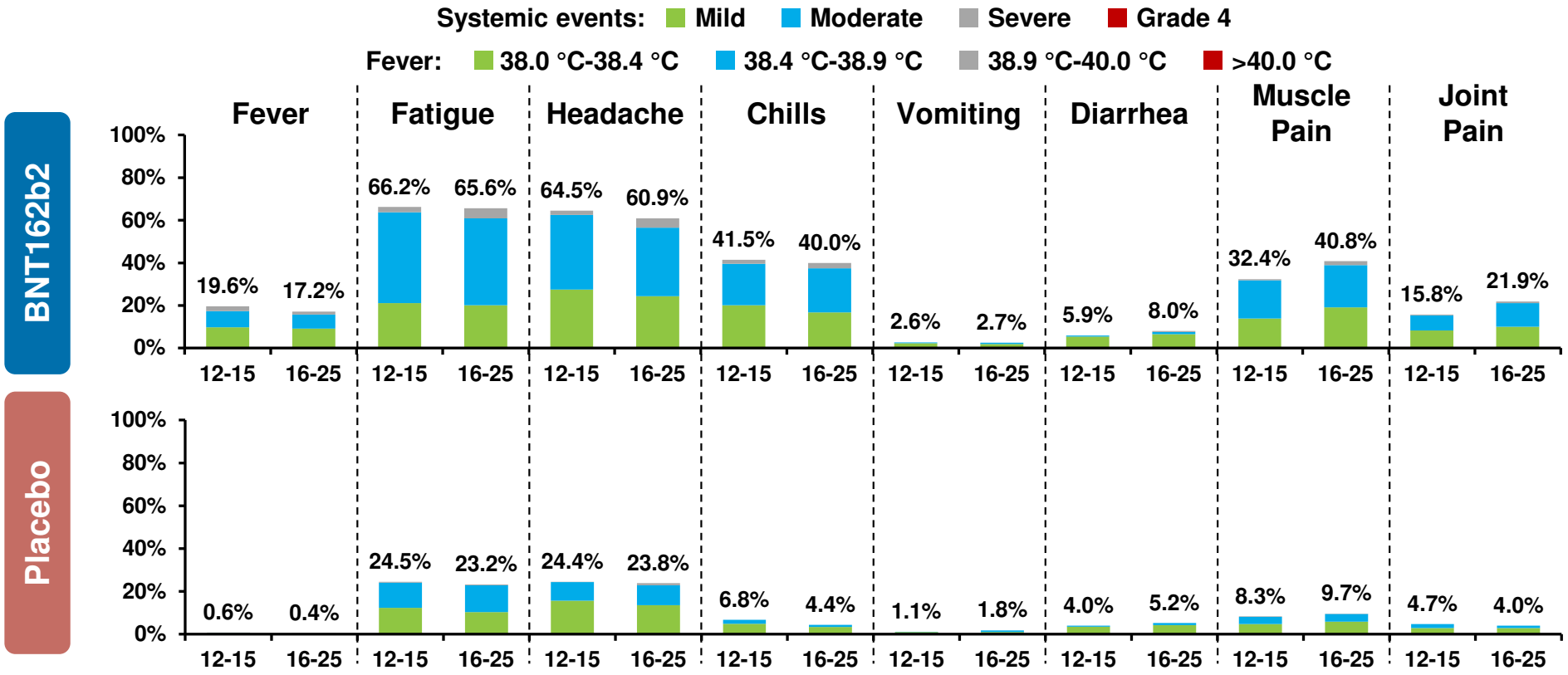
Subjects Reporting Systemic Events, by Maximum Severity, Within 7 Days After **Dose 1** in 12-15 and 16-25 Year Olds



A 14 year old in the BNT162b2 group had Grade 4 pyrexia (40.4 °C) on Day 2 after Dose 1, with temperature returning to normal within 2 days

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: 12-15 yrs N=2254; 16-25 yrs N=1084

Subjects Reporting Systemic Events, by Maximum Severity, Within 7 Days After **Dose 2** in 12-15 and 16-25 Year Olds



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
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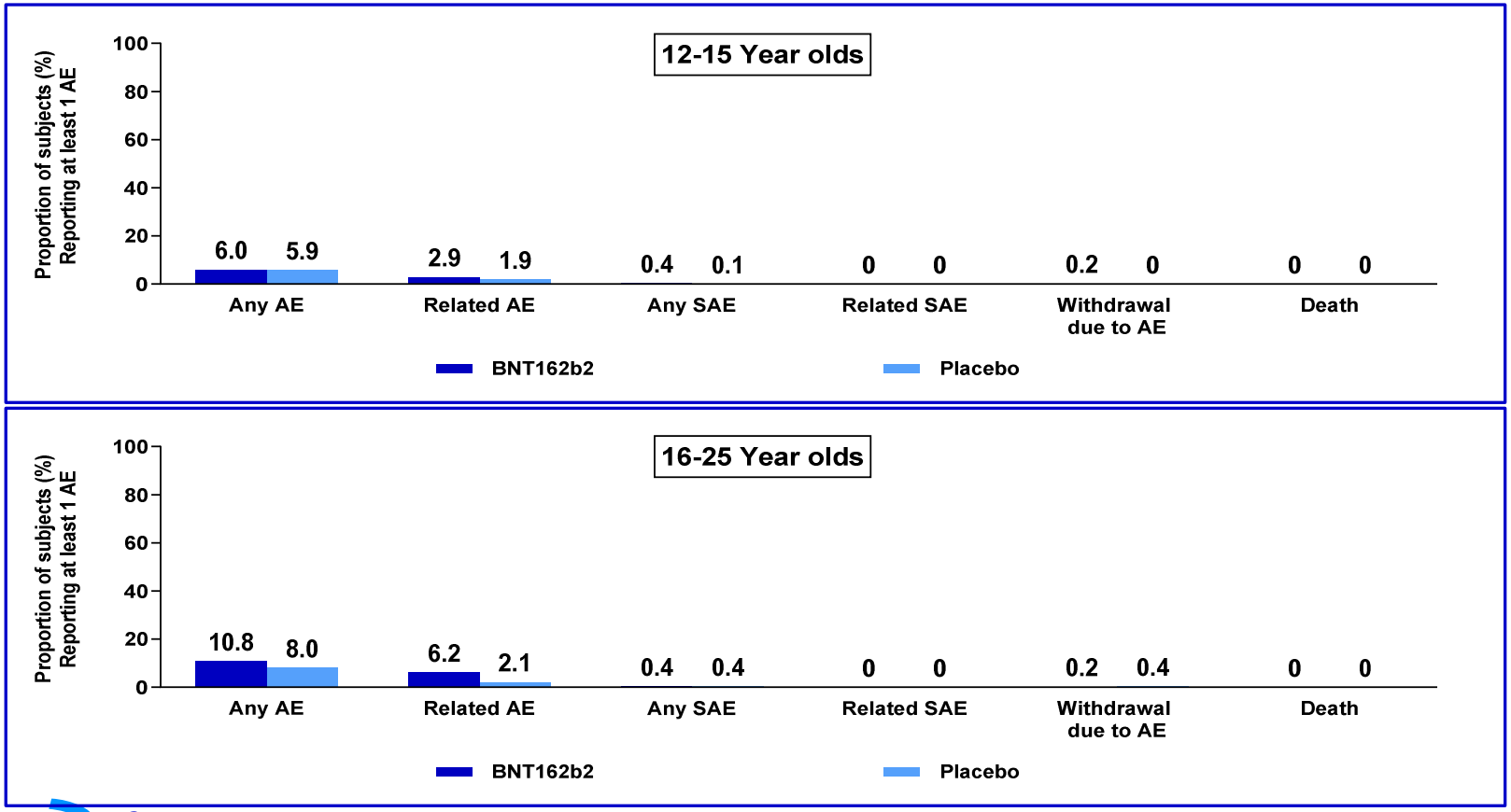
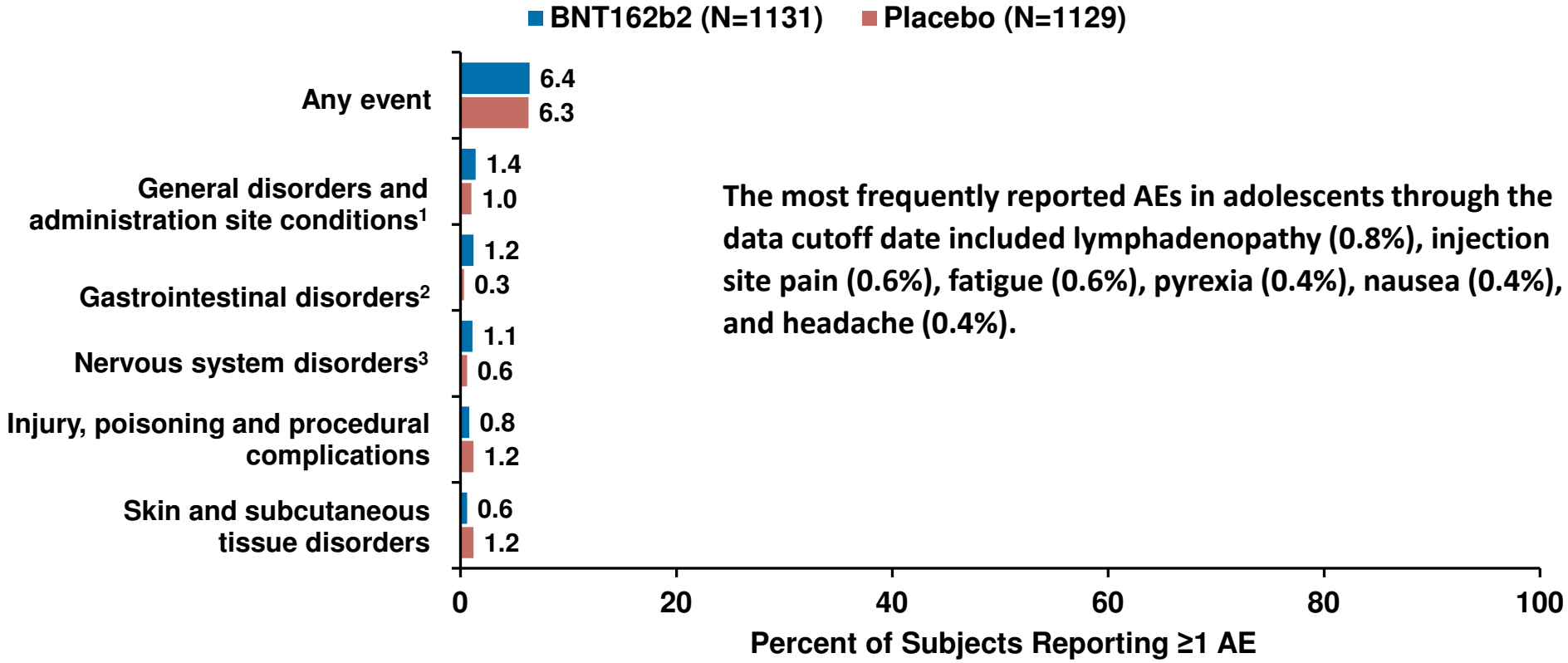
Diarrhea severity definition: Mild=2-3 times in 24h; Moderate=4-5 times in 24h; Severe=6 or more times in 24h; Grade 4=ER visit or hospitalization
Dose 2: 12-15 yrs N=2175 16-25 yrs N=984

Overall Adverse Events from Dose 1 to 1 Month Post Dose 2
12-15 (N=2260) and 16-25 (Reactogenicity subset N=1097) year olds



- Overall, small number of adverse events: more in the 16-25 year olds
- Related AE due to reactogenicity events captured as AEs
- No related SAE's
- No deaths

Adverse Events ≥1.0% by System Organ Class for 12-15 year olds from Dose 1 to Data Cut-off Date (13 Mar 2021)



The most frequently reported AEs in adolescents through the data cutoff date included lymphadenopathy (0.8%), injection site pain (0.6%), fatigue (0.6%), pyrexia (0.4%), nausea (0.4%), and headache (0.4%).

1. Predominantly reflect local reactions at the injection site and systemic reactions of fever and fatigue
2. Predominantly reflect nausea and diarrhea
3. Predominantly reflects Headache

Serious Adverse Events by SOC/PT from Dose 1 to Data Cut-off Date 12-15 year olds

System Organ Class/PT	BNT162b2 (30 µg) (N=1131)		Placebo (N=1129)	
	n	%	n	%
ANY EVENT	5	0.4	2	0.1
GASTROINTESTINAL DISORDERS	1	0.1	0	0
*Abdominal pain	1	0.1	0	0
*Constipation	1	0.1	0	0
INFECTIONS AND INFESTATIONS	0	0	2	0.2
#Appendicitis	0	0	2	0.2
#Focal peritonitis	0	0	1	0.1
NERVOUS SYSTEM DISORDERS	1	0.1	0	0
*Neuralgia	1	0.1	0	0
PSYCHIATRIC DISORDERS	4	0.4	0	0
Depression	3	0.3	0	0
Anxiety	1	0.1	0	0
Suicidal ideation	1	0.1	0	0

*Abdominal pain, constipation and neuralgia were in the same participant

#Appendicitis and focal peritonitis were in the same participant

Overall safety conclusions for 12-15 year olds

- **Reactogenicity: BNT162b2 was well tolerated in subjects 12-15 years old and showed a similar pattern to that seen in 16-25 year olds**
  - Pain at the injection site, fatigue, headaches, chills, joint pain and muscle pain were the most predominant as well as fever
  - Increased systemic events after dose 2 was similar to that seen with 16-25 year olds

- **Adverse events overall were few**
  - Highest incidence was in the General Disorders and Administration Site Conditions, reflecting local and systemic reactogenicity events
  - Lymphadenopathy was identified as related to vaccination
  - There were no related SAEs
  - No deaths were reported

Noninferiority Between 12-15 and 16-25 years Of Age Was Met Geometric Mean Ratio (GMR) in Neutralization Titers

(Without prior infection)

		BNT162b2 (30 µg)					
		12-15 year		16-25 years		12-15/16-25 years	
Assay	Dosing/ Sampling Time Point	n	GMT (95% CI)	n	GMT (95% CI)	GMR (95% CI)	Met NI (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)	2 / 1 Month	190	1239.5 (1095.5, 1402.5)	170	705.1 (621.4, 800.2)	1.76 (1.47, 2.10)	Y

- Noninferiority is declared if the lower bound of the 95% confidence interval is > 0.67
- LBCI for GMR >1 indicating a statistically greater response in 12-15 that 16-25 year olds

First COVID-19 Occurrence From 7 Days After Dose 2

Subjects 12-15 Years of Age – Evaluable Efficacy Population

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

	BNT162b2 (30 µg) N=1005		Placebo N=978			
Efficacy Endpoint	**n**	**Surveillance Time (n)**	**n**	**Surveillance Time (n)**	**VE (%)**	**(95% CI)**
First COVID-19 occurrence ≥7 days after Dose 2	**0**	**0.154 (1001)**	**16**	**0.147 (972)**	**100.0**	**(75.3, 100.0)**

- There were no severe COVID-19 cases

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint.
The analysis is descriptive; no hypothesis test

First COVID-19 Occurrence From 7 Days After Dose 2

Subjects 12-15 Years of Age – Evaluable Efficacy Population

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

	BNT162b2 (30 µg) N=1119		Placebo N=1110			
Efficacy Endpoint	**n**	**Surveillance Time (n)**	**n**	**Surveillance Time (n)**	**VE (%)**	**(95% CI)**
First COVID-19 occurrence ≥7 days after Dose 2	**0**	**0.170 (1109)**	**18**	**0.163 (1094)**	**100.0**	**(78.1, 100.0)**

- There were no severe COVID-19 cases

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint.
The analysis is descriptive; no hypothesis test

Immunogenicity & Efficacy Conclusions

- Immune response to Pfizer-BioNTech COVID-19 Vaccine in SARS-CoV-2 50% neutralizing titers in adolescents 12-15 years of age was noninferior to (and in fact exceeded) the immune response in young adults 16-25 years of age, which provides immunobridging for adolescents in pivotal Study C4591001.
- In the adolescent group, efficacy analyses based on cases reported from at least 7 days after Dose 2 through the data cutoff date, the observed VE was **100%** (95% CI: 75.3%, 100%) for individuals without evidence of prior SARS-CoV-2 infection before and during vaccination regimen, and **100%** (2-sided 95% CI: 78.1%, 100%) for those with or without evidence of prior SARS-CoV-2 infection before and during vaccination regimen.
- No severe cases were reported in the 12-15 years of age group as of the cutoff date.
- Overall, these immunogenicity and efficacy data strongly support BNT162b2 use in adolescents 12-15 years of age.

Thank you
Questions?