SAGE

Dr. Filip Dubovsky

December 16, 2021

Novavax and SII EUL Submissions

Novavax and the Serum Institute of India have filed 2 separate submissions to WHO for the Emergency Use Listing of NVX-CoV2373, to be marketed as Nuvaxovid™ and COVOVAX™, respectively.

- Both submissions leverage the same clinical and CMC modules.

WHO is conducting a harmonized and parallel review for EUL, the timing of which will be influenced by authorization from each related NRA of record.

- EMA - Novavax NRA of record
- DCGI – SII NRA of record

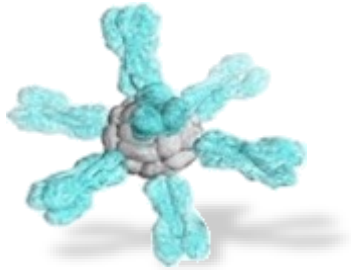
Novavax and SII are working in close coordination throughout the regulatory authorization process.

Agenda

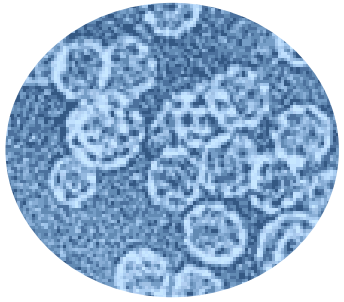
- Vaccine construct
- Pre-clinical Protection data
- Clinical Development Data
  - UK Phase 3 study
  - US/Mexico Phase 3 study
  - US/AU Phase 2 boosting study
- Integrated Data from Clinical Development Program
  - Immunogenicity
  - Reactogenicity
  - Adverse Drug Reactions
- Risk Management and Post-marketing plans

NOVAVAX VACCINE PLATFORM

RECOMBINANT PROTEIN NANOPARTICLES FORMULATED WITH MATRIX-M™



Recombinant protein nanoparticle



Matrix-M

Novavax Vaccine Platform

- Safety database includes >12,500 with exposure to nanoparticle vaccine
- Long-term safety in >2,500 with nanoparticle vaccine formulated with Matrix-M
  - Ebola
  - Respiratory Syncytial Virus (RSV)
  - Trivalent influenza
  - Quadrivalent influenza
- Additionally >30,000 participants in ongoing COVID-19 studies

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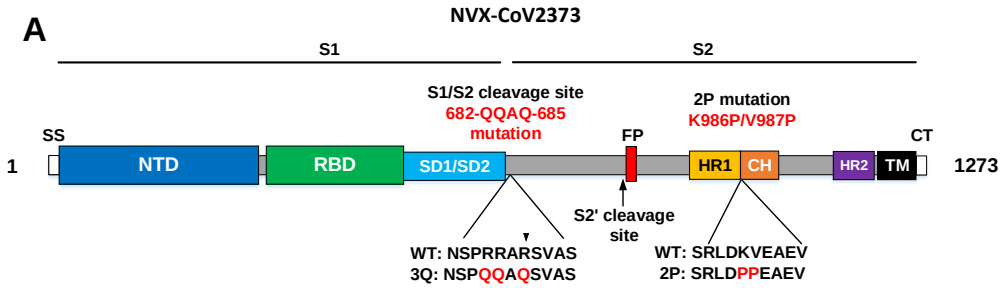
NVX-COV2373 VACCINE DESIGN

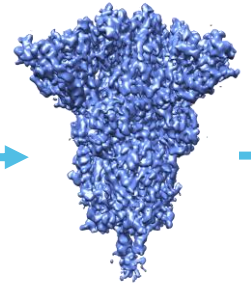
VACCINE PLATFORM TECHNOLOGY: NANOPARTICLE VACCINE FORMULATED WITH MATRIX-M1

Antigen expressed in baculovirus-*S. frugiperda* system
- Codon-optimized
- Full-length protein, including transmembrane domain
- Furin cleavage site mutated and protein stabilized

Drug Substance
- Native conformation trimers
- Stable PS80 nanoparticle

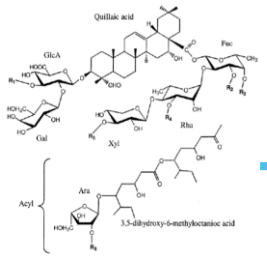
Drug Product
- Co-formulated with adjuvant
- Dispensed in vial
- Stored 2-8^{O} C

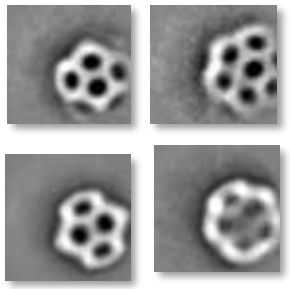


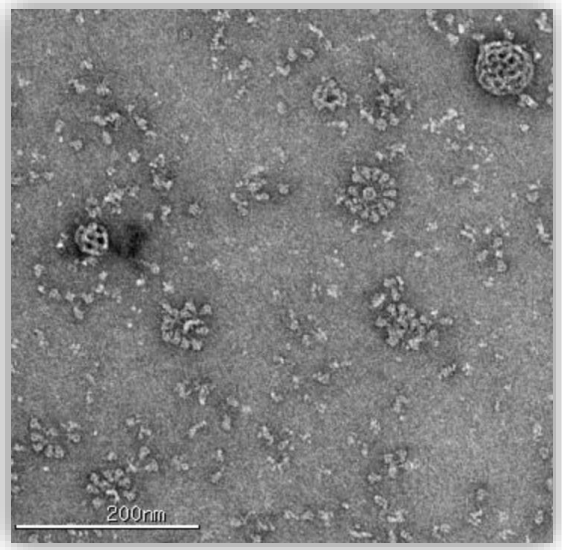


Matrix-M adjuvant
- Purified from *Quillaja saponaria molina*

Matrix-M Adjuvant







Bangaru et al. bioRxiv 06 August 2020 and Tian et al. bioRxiv 30 June 2020

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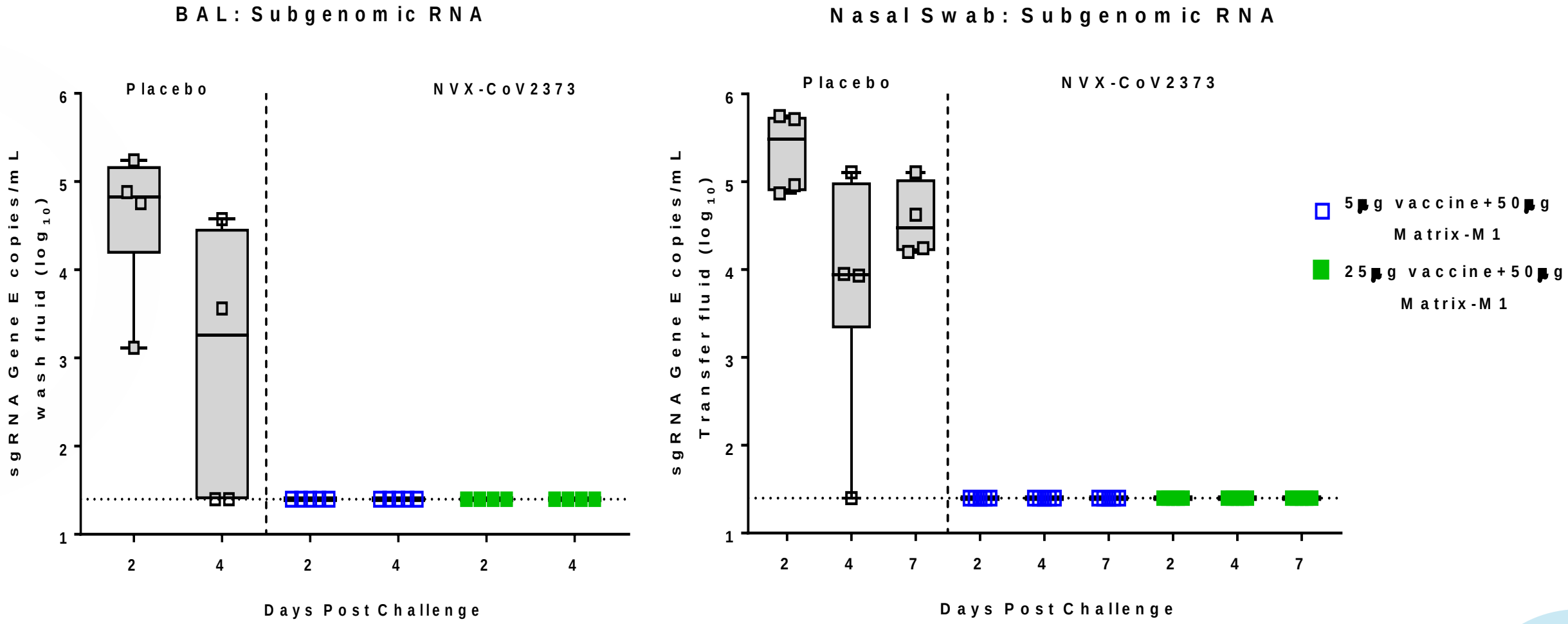
Rhesus Macaques: Upper and Lower airway protection

Vaccinated Day 0 and Day 21; Challenged with SARS-CoV-2 wild-type 1.05 x 10^6 PFU IN/IT on Day 38
No viral replication detected in upper or lower airway following experimental wild-type challenge

Partner: OWS
Sponsor: Novavax



Gorman et al. Cell Reports Medicine Sep 2021

NVX-COV2373 CLINICAL DEVELOPMENT PROGRAM

Phase 3 US & Mexico	*N=29,960*	▪ Licensure-enabling safety in US population ▪ Licensure-enabling efficacy in US populations
Phase 3 United Kingdom Heath et al. NEJM 30 June 2021 Toback et al. Lancet ID in Press	*N=15,203*	▪ Licensure-enabling safety data ▪ Licensure-enabling efficacy data ▪ Safety of co-administration with influenza vaccine
Phase 2b South Africa Shinde et al. NEJM 20 May 2021	*N=4,422*	▪ Evaluated preliminary efficacy ▪ Defined safety profile ▪ HIV+ subgroup
Phase 1/2 US & Australia Keech et al. NEJM 02 September 2020 Formica et al. PLoS Medicine Oct 2021	*N=131 Phase 1* *N=1,288 Phase 2*	▪ Established dose level in younger and older adults ▪ Confirmed need for adjuvant and 2 dose schedule ▪ Defined immunologic phenotype ▪ Described preliminary safety profile

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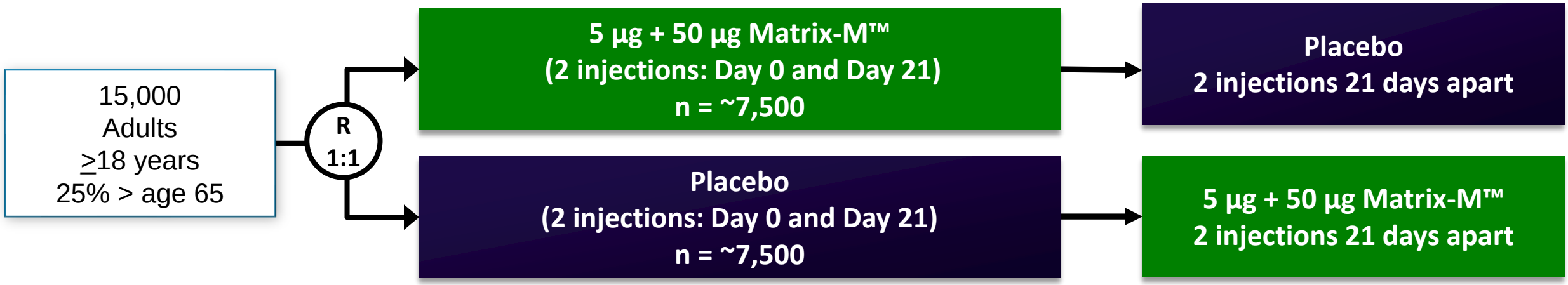
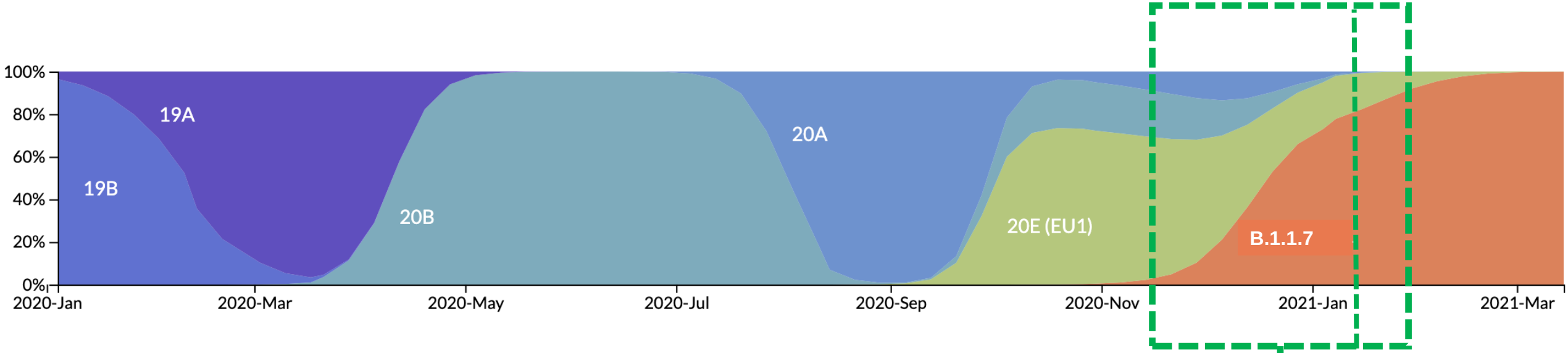
UK PHASE 3 STUDY DESIGN

Randomized, observer-blinded, placebo-controlled trial evaluating efficacy, immunogenicity and safety



- Primary endpoint: PCR-positive symptomatic mild, moderate or severe COVID-19 illness diagnosed ≥ 7 days after second dose
- Cross-over planned following Final Analysis

UK B.1.1.7 MUTANT STRAIN INCREASED IN PREVALENCE DURING EFFICACY COLLECTION WINDOW



Dose 1: September 28 – November 28

Dose 2: October 19 – January 13

Efficacy Endpoint Accrual:
Interim Analysis: November 10 – January 10
Final Analysis: January 10 – January 24

Figure Source: Nextstrain.org

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FINAL ANALYSIS SUBJECT DISPOSITION, DEMOGRAPHICS, AND BLINDED BASELINE CHARACTERISTICS

Number of randomized participants: N=15,187 (Vaccine = 7,593; placebo 7,594)

- Discontinuation: Vaccine = 2.3%; Placebo 2.7%

	Placebo	Vaccine
Median age	55	55
>65 years	27.2%	27.3%
Medical Comorbidity	44.9%	44.5%
Gender: male	51.8%	51.4%
Race: White	94.5%	94.2%
Median weight (kg)	79.0	78.8
Baseline PCR +	0.6%	0.6%
Baseline seropositive	4.1%	4.4%

HIGH-LEVEL SAFETY SUMMARY THROUGH CROSS-OVER

SERIOUS AND SEVERE ADVERSE EVENTS WERE INFREQUENT AND BALANCED

2019nCoV-302	NVX-CoV2373 N=7,569	Placebo N=7,570
Any adverse event through Day 49	12.3%	11.1%
Any severe adverse event	0.4%	0.4%
Adverse Event of special Interest		
Potentially immune mediated	≤ 0.1%	≤ 0.1%
COVID-19 related	≤ 0.1%	≤ 0.1%
Serious Adverse Events	0.1%	0.2%
Deaths	0.03%	0.01%

Table 14.3.1.1.3/ Listing 16.2.7.8

FINAL PRIMARY EFFICACY ANALYSIS

	Final Analysis	
	NVX-CoV2373 (n=7,020)	Placebo (n=7,020)
Total	**10**	**96**
Mild	*1*	*28*
Moderate	*9*	*63*
Severe	*0*	*5*
Vaccine Efficacy	**89.7%** (95% CI: 80.2, 94.6)	

- Statistical success criteria included lower bound of 95% CI >30%
- All Severe cases in placebo group
- Adults >65 years of age; 9/10 in placebo group VE = 88.9% (95% CI: 12.8; 98.6)

Primary Endpoint: PCR-confirmed mild, moderate, or severe COVID-19 illness occurring ≥7 days after second dose in baseline seronegative participants

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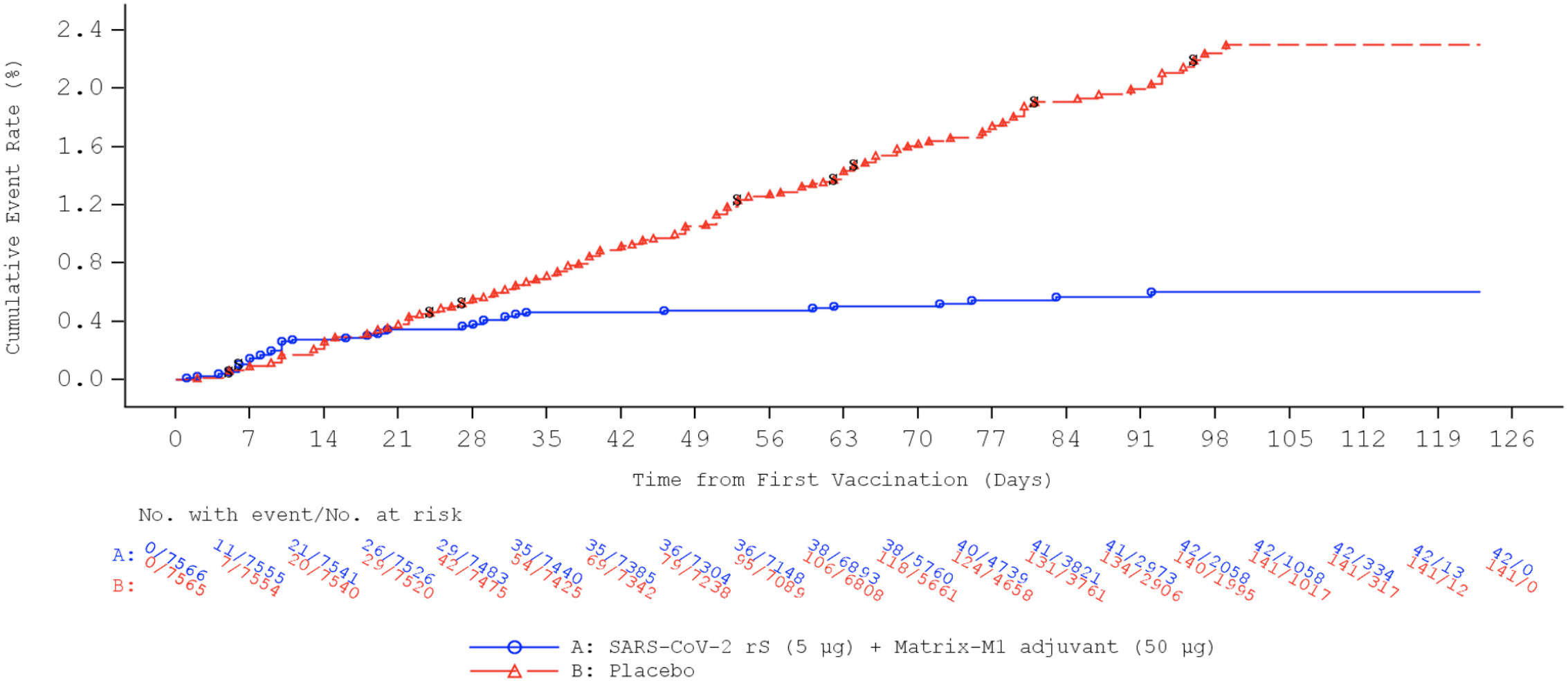
PCR-CONFIRMED MILD, MODERATE OR SEVERE COVID-19 DISEASE ONSET FROM FIRST VACCINATION INTENTION-TO-TREAT ANALYSIS SET



PCR-CONFIRMED MILD, MODERATE OR SEVERE COVID-19

ONSET 7+ DAYS AFTER 2ND VACCINATION IN BASELINE SERONEGATIVE, PER-PROTOCOL POPULATION

	Final Analysis					
	NVX-CoV2373 (n=7020)			Placebo (n=7020)		
	B.1.1.7	Prototype	No Data	B.1.1.7	Prototype	No Data
PCR-Confirmed COVID-19 (Mild, Moderate, Severe)	8	1	1	58	28	10
Mild	1	0	0	15	9	4
Moderate	7	1	1	39	18	6
Severe	0	0	0	4	1	0

PCR-fingerprinting from Final Analysis identified 62% (66/106 strains) as B.1.1.7 variants

- Post-hoc Final Analysis: **96.4%** (95% CI 73.8, 99.5) vs prototype strain & **86.3%** (95% CI 71.3, 93.5) vs B.1.1.7
- All Severe cases in placebo group, 4/5 severe cases attributed to B.1.1.7

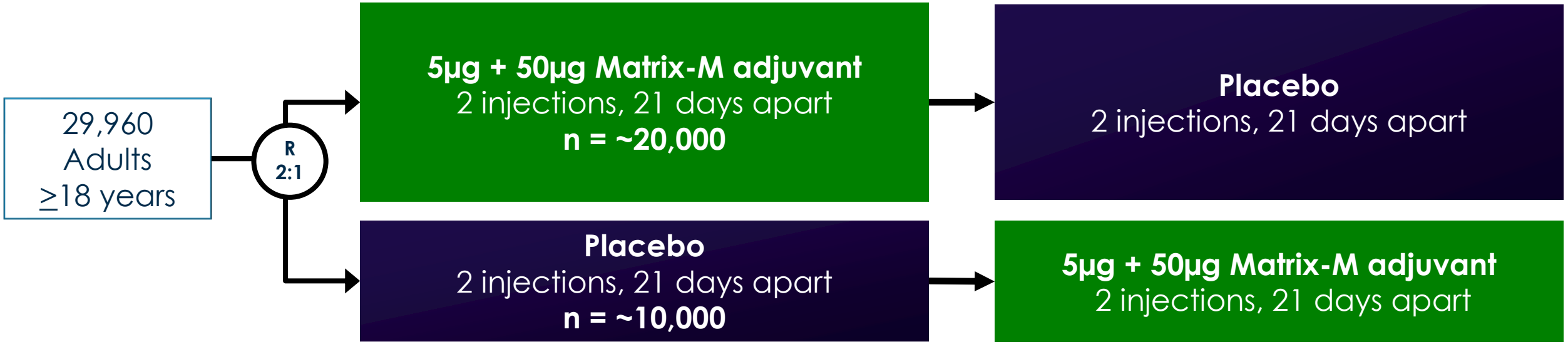
FORREST PLOT FINAL ANALYSIS

Subgroup	Placebo (N=7019)	NVX-CoV2373 (N=7020)	Vaccine Efficacy, % (95% CI)
	No. of events/total no. at risk		
Per-protocol population	96/7019	10/7020	89.7 (80.2, 94.6)
Age, years			
≥18 to <65	87/5062	9/5067	89.8 (79.7, 95.5)
≥65 to <85	9/1957	1/1953	88.9 (20.2, 99.7)
Race			
White			90.7 (80.8, 96.1)
Minority races (all)			75.7 (-21.6, 97.5)
Strain			
Prototype strain			96.4 (73.8, 99.5)
B.1.1.7 variant			86.3 (71.3, 93.5)
Comorbidity			
Yes	33/3143	3/3117	90.9 (70.4, 97.2)
No	63/3876	7/3903	89.1 (76.2, 95.0)

PREVENT-19 PHASE 3 TRIAL DESIGN

PREVENT-19
PRE-fusion Protein Subunit Vaccine Efficacy Novavax Trial | COVID-19

Randomized, observer-blinded, placebo-controlled trial evaluating efficacy, immunogenicity and safety



- **Primary endpoint**: PCR-positive symptomatic mild, moderate or severe COVID-19 illness diagnosed ≥ 7 days after second dose
- 2:1 randomization

Protocol version 8.0 posted on Novavax.com

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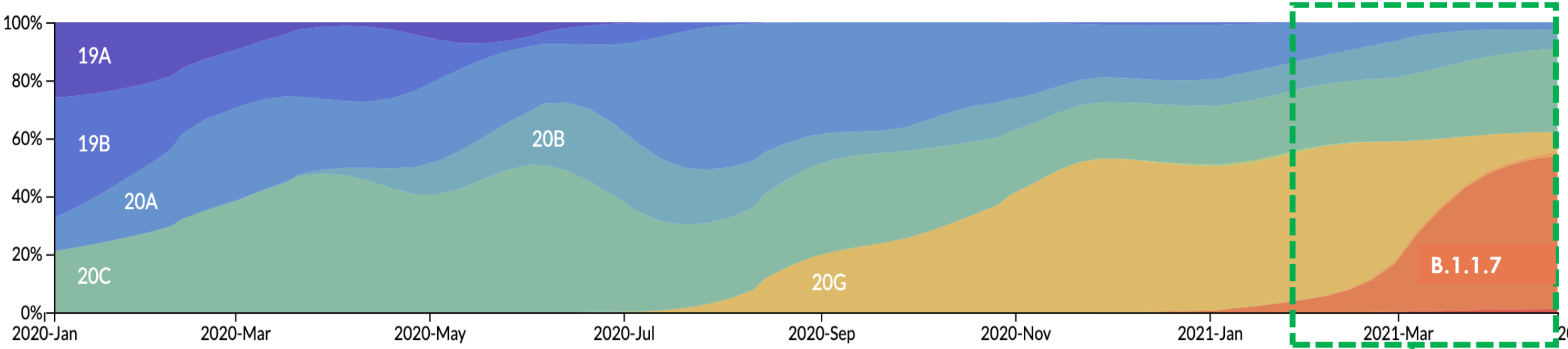
VARIANTS EMERGED DURING THE EFFICACY COLLECTION WINDOW

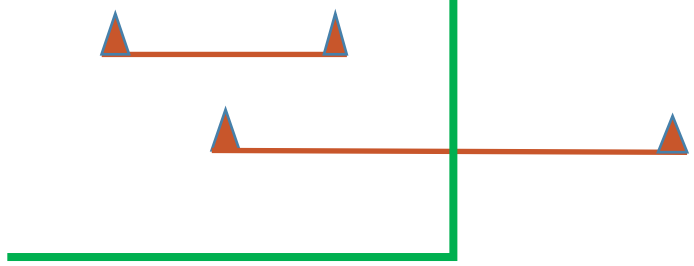
PREVENT-19
PRE-fusion Protein Subunit Vaccine Efficacy Novavax Trial | COVID-19



Dose 1: December 27 – February 18

Dose 2: January 18 – March 26

Efficacy Endpoint Accrual:
January 25 – April 30



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DEMOGRAPHICS OF TOTAL ENROLLED POPULATION
UNITED STATES: 113 SITES | MEXICO: 6 SITES

PREVENT-19
PRE-fusion Protein Subunit Vaccine Efficacy Novavax Trial | COVID-19

	NVX-CoV-2373	Placebo
Randomized	19,745	9,836
USA | Mexico	94.0% | 6.0%	94.0% | 6.0%
Female	47.2%	48.8%
Age >65	12.6%	12.6%
Race		
White	74.9%	75.0%
Black or African American	11.8%	11.8%
Native American	6.6%	6.7%
Asian	4.1%	4.2%
Native Hawaiian	0.3%	0.1%
Ethnicity: Hispanic/Latino	21.9%	21.9%
Medical Co-morbidities	37.2%	37.6%

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HIGH-LEVEL SAFETY SUMMARY THROUGH CROSS-OVER

SERIOUS AND SEVERE ADVERSE EVENTS WERE INFREQUENT AND BALANCED

	NVX-CoV2373 N=19,729	Placebo N=9,853
Any adverse event through Day 49	12.7%	11.5%
Any severe adverse event	1.2%	1.1%
Adverse Event of special Interest		
Potentially immune mediated	≤ 0.1%	≤ 0.1%
COVID-19 related	≤ 0.1%	≤ 0.1%
Serious Adverse Events	0.9%	1.0%
Deaths	0.05%	0.05%

Table 14.3.1.1

PRIMARY ENDPOINT: PCR-CONFIRMED MILD, MODERATE, OR SEVERE COVID-19 ILLNESS OCCURRING ≥7 DAYS AFTER SECOND DOSE IN BASELINE SERONEGATIVE PARTICIPANTS

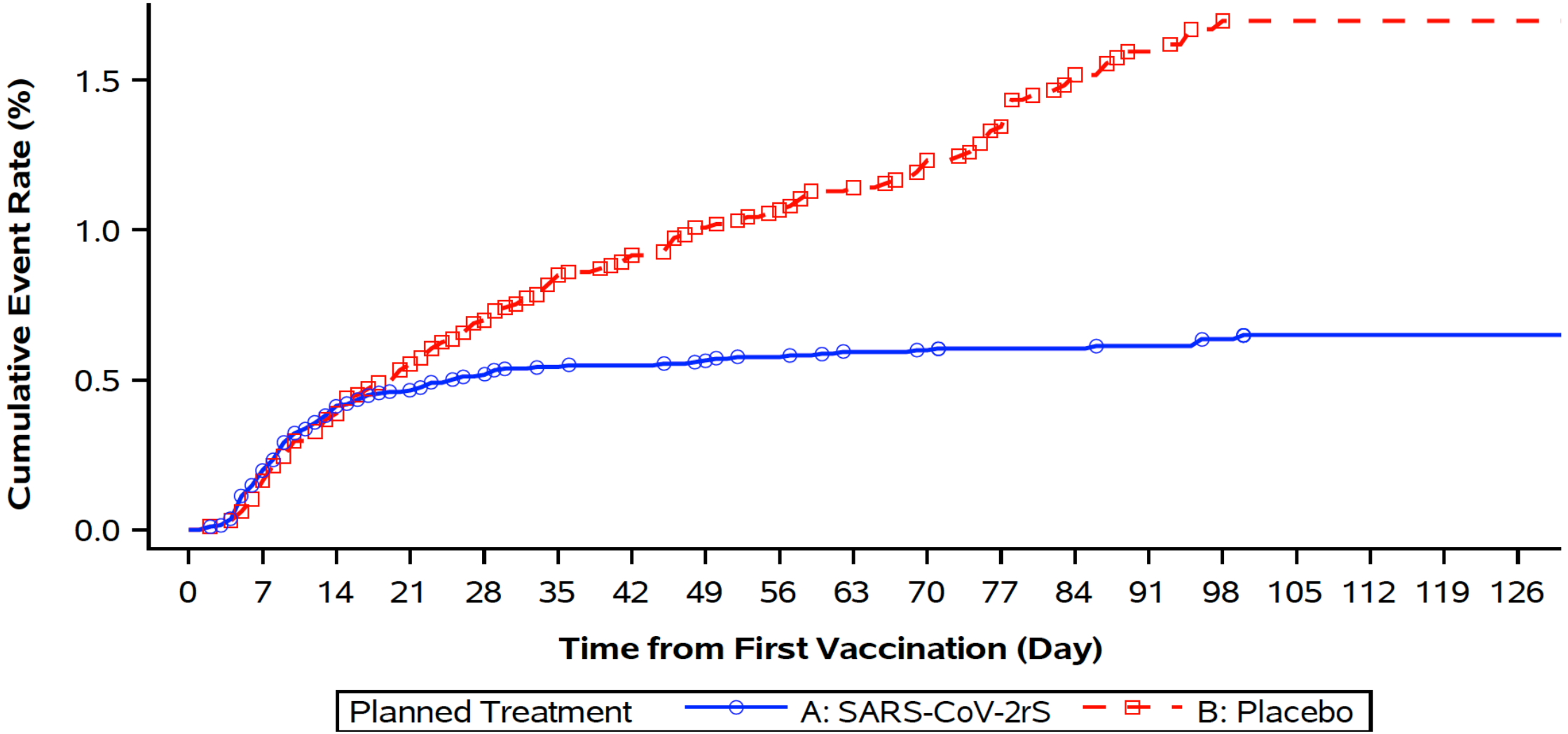
Primary endpoint: Efficacy against mild, moderate and severe COVID-19 illness		
	NVX-CoV2373 (n=17,312)	Placebo (n=8,140)
Total	**14**	**63**
Mild	*14*	*49*
Moderate	*0*	*10*
Severe	*0*	*4*
Vaccine Efficacy	**90.4%** (95% CI: 82.9; 94.6)	

- Statistical success criteria included lower bound of 95% CI >30%
- 61% of cases caused by Variants of Concern & Variants of Interest
- All break-through cases in vaccine group were mild

Per-Protocol Efficacy Analysis set: Table 14.2.1.1.1, 14.2.1.1.2

PCR-CONFIRMED MILD, MODERATE AND SEVERE DISEASE AFTER 1ST VACCINATION

VACCINE AND PLACEBO RATES SEPARATE PRIOR TO DOSE 2 (DAY 21)
NO EVIDENCE OF WANING EFFICACY THROUGH DAY 98



SECONDARY ENDPOINT: PCR-CONFIRMED MODERATE, OR SEVERE COVID-19 ILLNESS OCCURRING ≥7 DAYS AFTER SECOND DOSE IN BASELINE SERONEGATIVE PARTICIPANTS

Efficacy for Moderate and Severe cases		
	NVX-CoV2373 (n=17,312)	Placebo (n=8,140)
Total	**0**	**14**
Moderate	0	10
Severe	0	4
Vaccine Efficacy	**100%** (95% CI: 87.0; 100)	

- Post-hoc analysis for severe disease only VE = 100% (95% CI 34.8; 100)
- An additional 6 COVID Hospitalizations (including 1 death) occurred in the placebo group but were not included in the efficacy analysis because PCR samples were not evaluated in the central lab

Per-Protocol Efficacy Analysis set: Table 14.2.6.1.2

Secondary endpoint: primary efficacy analysis by age

>65 year-old cohort of inadequate size/attack-rate to establish efficacy

	< 65 years of age		> 65 years of age	
	NVX-CoV2373 (n=15,264)	Placebo (n=7,194)	NVX-CoV2373 (n=2,048)	Placebo (n=946)
Total	**12**	**61**	**2**	**2**
Vaccine Efficacy	**91.5%** (95% CI: 84.2; 95.4)		**57.5%** (95% CI: -487; 96.9)	

- Total number of >65 yo in per-protocol population diminished by unblinding to receive EUA vaccine
  - Unblinding in vaccine group 342/2048
  - Unblinding in placebo group 206/946

- UK Phase 3 study for adults >65 Years of age: VE = 88.9% (95% CI: 20.2; 99.7)
  - Placebo: 9/1957 **vs** NVX-C0V2373 1/1953

Table 14.2.1.1.4.1

VIROLOGIC CHARACTERIZATION OF CASES IN PER-PROTOCOL EFFICACY POPULATION

- A total of 77 cases were reported during the primary efficacy window

- Sequence data available for 61/77 (79.2%) endpoint case
  - Variants of Concern 35/61 (57.4%)
  - Variant of Interest 13/61 (21.3%)
  - Variants **not** of Concern/Interest 13/61 (21.3%)

- Variants of Concern 35/61
  - 31/61 (50.8%) identified as B.1.1.7 (*alpha,* UK)
  - 2/61 (3.3%) identified as B.1.351 (*beta,* South Africa)
  - 2/61 (3.3%) identified as P.1 (*gamma,* Japan/Brazil)

- Variants of Interest 13/61
  - 4/61 (6.6%) identified as B.1.429 (*epsilon,* USA/California)
  - 8/61 (13.6%) identified as B.1.526 (*iota,* USA/New York)
  - 1/61 (1.6%) identified as B.1.617.1 (*kappa,* India)
  - 1/61 (1.6%) identified as P.2 (*zeta,* Brazil)

Sequencing performed at University of Washington

KEY SECONDARY ENDPOINT: EFFICACY AGAINST VARIANTS NOT CURRENTLY CONSIDERED VARIANTS OF CONCERN OR VARIANTS OF INTEREST

Efficacy for viral isolates NOT currently considered Variants of Concern/Interest		
	NVX-CoV2373 (n=17,312)	**Placebo (n=8,140)**
Total	**0**	**13**
Mild	*0*	*10*
Moderate	*0*	*2*
Severe	*0*	*1*
Vaccine Efficacy	**100%** (95% CI: 85.8; 100)	

- Statistical success criteria included lower bound of 95% CI >30%
- Sequence not available for 16 cases 15 mild (7 in vaccine, 8 in placebo), and 1 severe in placebo

Per-Protocol Efficacy Analysis set: Table 14.2.2.1.1B, 14.2.2.1.2B

HIGH LEVELS OF EFFICACY MAINTAINED AGAINST VARIANTS OF CONCERN & VARIANTS OF INTEREST

Efficacy for viral isolates considered Variants of Concern/Interest		
	NVX-CoV2373 (n=17,312)	**Placebo (n=8,140)**
Total	**7**	**41**
Mild	*7*	*31*
Moderate	*0*	*8*
Severe	*0*	*2*
Vaccine Efficacy	**93.6%** (95% CI 83.5; 96.7)	

Variants of Concern 35/61
- 31/61 (50.8%) identified as B.1.1.7 (*alpha,* UK)
- 2/61 (3.3%) identified as B.1.351 (*beta,* South Africa)
- 2/61 (3.3%) identified as P.1 *gamma,* Japan/Brazil)

Variants of Interest 13/61
- 4/61 (6.6%) identified as B.1.429 (*epsilon,* USA/California)
- 8/61 (13.6%) identified as B.1.526 (*iota,* USA/New York)
- 1/61 (1.6%) identified as B.1.617.1 (*kappa,* India)
- 1/61 (1.6%) identified as P.2 (*zeta,* Brazil)

- Sequence not available for 16 cases 15 mild (7 in vaccine, 8 in placebo), and 1 severe in placebo

Per-Protocol Efficacy Analysis set: Table 14.2.5.1.1B 14.2.5.1.2B

STRAINS/ VARIANTS* IDENTIFIED, BY DISEASE SEVERITY

INCLUDES POST-HOC SEQUENCE

	NVX-CoV2373 (n=17,312)	Placebo (n=8,140)
Total	**14**	**63**
Mild Disease	*(4) B.1.1.7 UK* *(1) B.1.351 South Africa* *(2) B.1.526 New York* *(7) No Sequence*	*(20) B.1.1.7 UK* *(1) B.1.351 South Africa* *(2) P.1 Japan / Brazil* *(1) B.1.429 USA/California* *(5) B.1.526 USA/New York* *(1) B.1.617.1 India* *(1) P.2 Brazil* *(1) B.1* *(1) B.1.1* *(1) B.1.1.316* *(1) B.1.1.519* *(1) B.1.2* *(2) B.1.243* *(2) B.1.311* *(1) B.1.596* *(8) No Sequence*
Moderate Disease	0	*(6) B.1.1.7 UK* *(2) B.1.429 USA/California* *(2) B.1.2*
Severe Disease	0	*(1) B.1.1.7 UK* *(1) B.1.526 USA/New York* *(1) B.1.2* *(1) No Sequence*

Red: Variant of Concern
Orange: Variant of Interest
Green: Not VOC or VOI

Vaccine Efficacy (primary)
- **90.4%** (95% CI: 82.9; 94.6)

Non-VoI/VoC (key secondary)
- **100%** (95% CI: 85.8; 100)

Severe/Moderate (secondary)
- **100%** (95% CI: 87; 100)

VoI/VoC (exploratory)
- **92.6%** (95% CI: 83.6; 96.7)

Alpha (post-hoc)
- **93.6%** (95% CI: 81.7; 97.8)

- Based on US CDC classification
- Includes post-hoc sequences

FORREST PLOT FINAL ANALYSIS

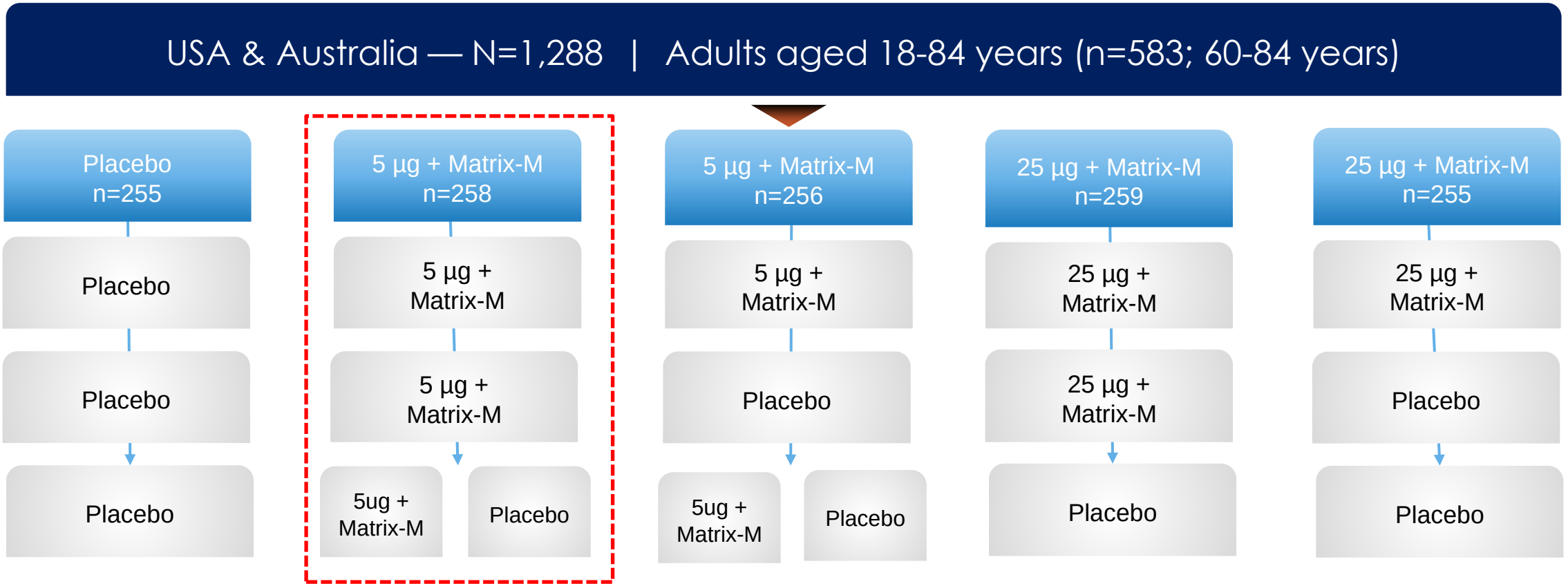
Parameter	NVX-CoV2373 *No. of Events/No. at Risk (%)*	Placebo	Vaccine Efficacy, % (95% CI)
Per-protocol population	14/17,312 (0.1)	63/8140 (0.8)	90.4 (82.9, 94.6)
Full analysis population	16/18,584 (0.1)	69/9144 (0.8)	89.3 (81.6, 93.8)
Subgroups			
Age			
Participants 18 to ≤64 years of age	12/15,264 (0.1)	61/7194 (0.8)	91.5 (84.2, 95.4)
Sex			
Male	5/9050 (0.1)	23/4131 (0.6)	90.9 (76.0, 96.5)
Female	9/8262 (0.1)	40/4009 (1.0)	90.0 (79.3, 95.1)
Race			
White	12/13,140 (0.1)	48/6184 (0.8)	89.4 (80.0, 94.4)
Black or African American	0/1893 (0.0)	7/905 (0.8)	100.0 (67.9, 100.0)
Non-White	2/4068 (< 0.1)	14/1911 (0.7)	93.6 (71.7, 98.5)
Ethnicity			
Hispanic or Latino	8/3733 (0.2)	11/1751 (0.6)	67.3 (18.7, 86.8)
Not Hispanic or Latino	6/13,538 (< 0.1)	52/6379 (0.8)	95.1 (88.5, 97.9)
Country			
US	14/16,294 (0.1)	62/7638 (0.8)	90.4 (82.8, 94.6)
Comorbidity status			
Yes	7/8109 (0.1)	34/3910 (0.9)	90.8 (79.2, 95.9)
No	7/9203 (0.1)	29/4230 (0.7)	89.9 (77.1, 95.6)
High-risk status			
Yes	13/16,493 (0.1)	62/7737 (0.8)	91.0 (83.6, 95.0)

CONSISTENT EFFICACY ACROSS PHASE 3 STUDIES

	UK Phase 3	PREVENT-19
Overall Efficacy	**89.7%**	**90.4%**
"Matched" Strain Efficacy	**96.4%** Prototype	**100%** (Non-VoI/VoC)
Efficacy Against Variants	**86.3%** Alpha (B.1.1.7)	**93.6%** Alpha (B.1.1.7) **92.6%** VoI/VoC
Efficacy Against Severe Disease	**NS** (all 5 severe cases in placebo group)	**100%**

PHASE 2 STUDY DESIGN AND STATUS

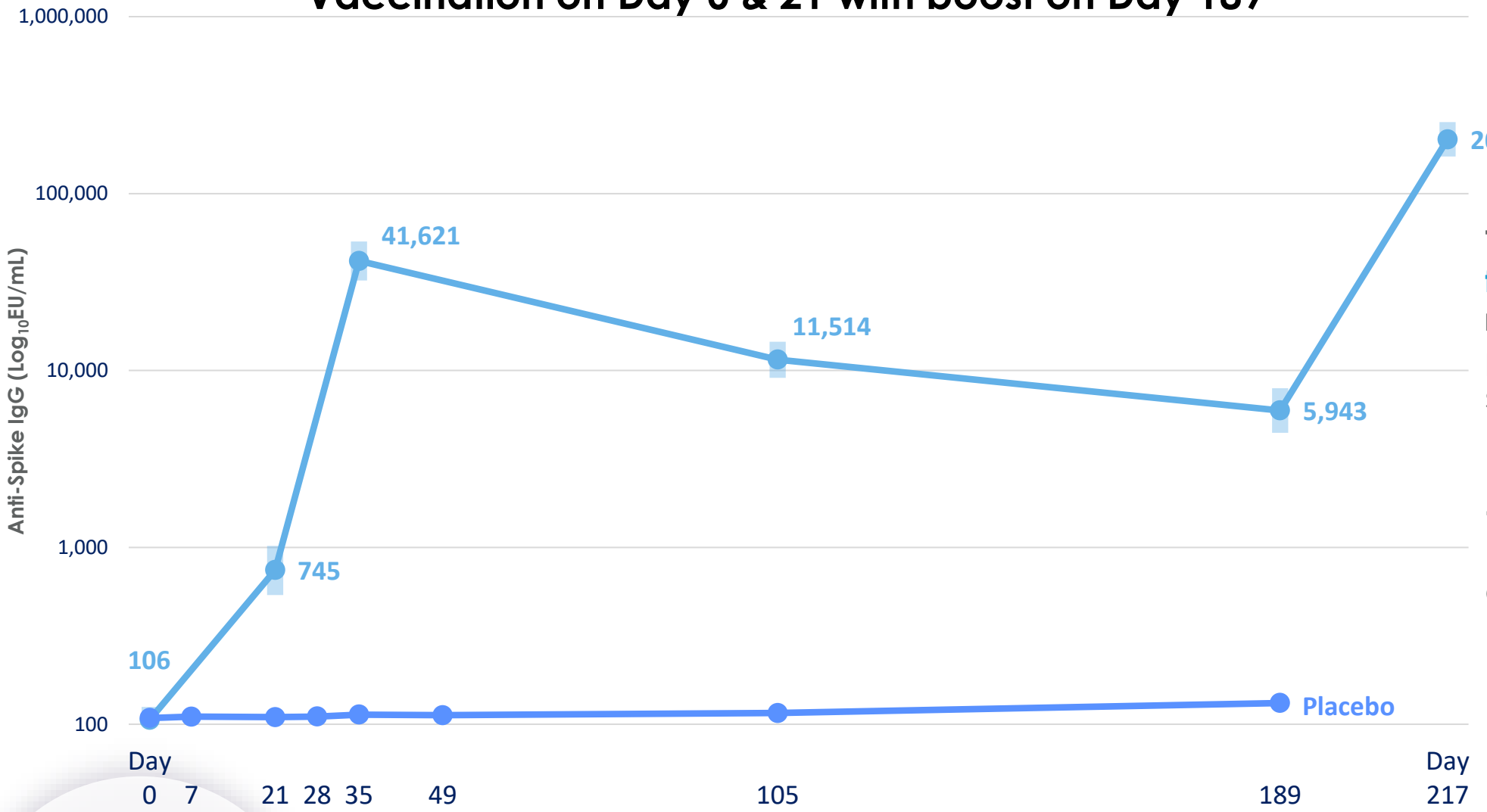
DAY 189 BOOST COMPLETE, IMMUNE RESPONSES EVALUATED ON DAY 217



Additional boosting administered on Day 357

Boosted antibody responses increase ~4.6 fold over peak response seen after 2 doses

Vaccination on Day 0 & 21 with boost on Day 189



Titers increased **~4.6-fold** compared to peak response seen after primary vaccination series.

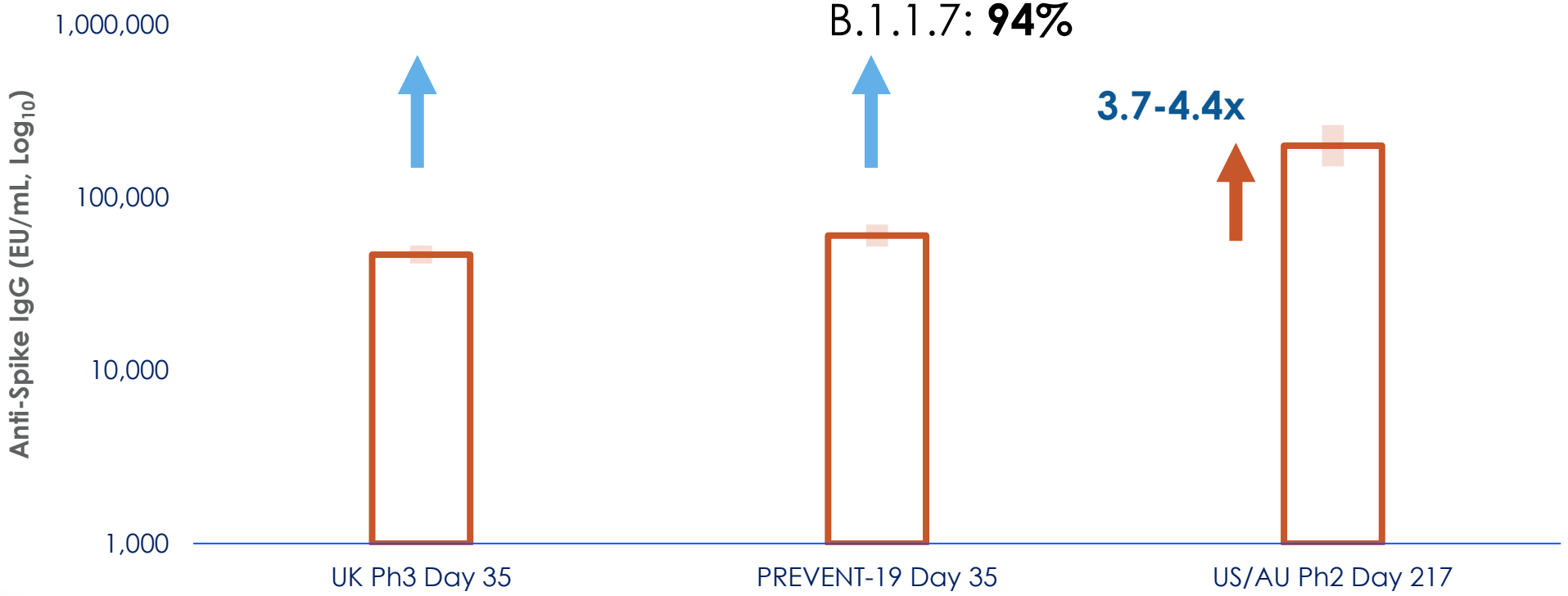
IgG titers increased ~3.9-fold in adults aged 18-59 & ~5.4-fold in adults aged 60-84.

novavax

BOOSTED ANTI-SPIKE IGG RESPONSES GREATER THAN OBSERVED IN PHASE 3 STUDIES

UK Phase 3 Efficacy
Prototype: **96%**
B.1.1.7: **86%**

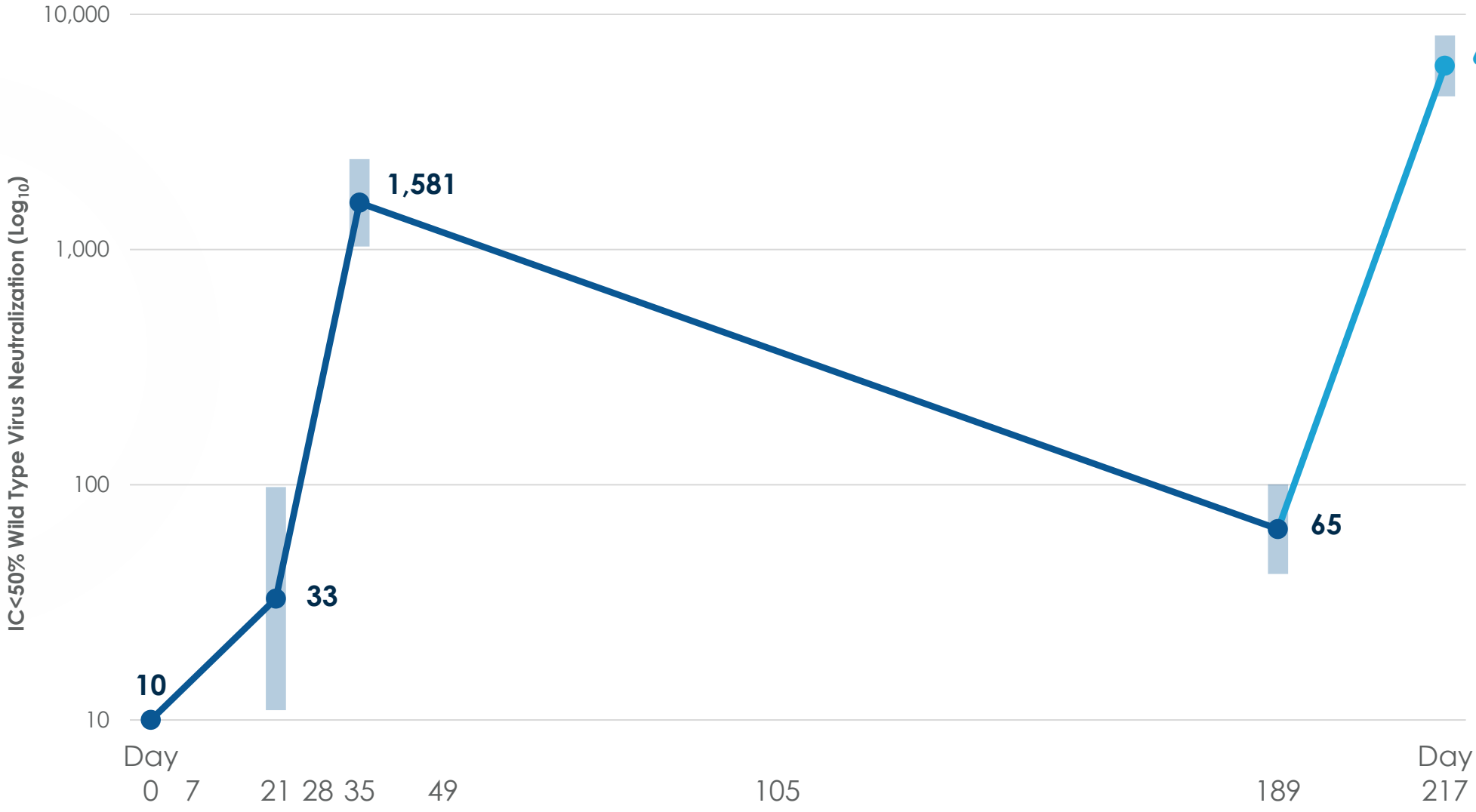
PREVENT-19 Efficacy
Non-VoI/VoC: **100%**
VoI/VoC: **93%**
B.1.1.7: **94%**



IgG Responses
with 95% CI

Increased Wild Type Neutralization Responses

Vaccination on Day 0 & 21 and boost on Day 189



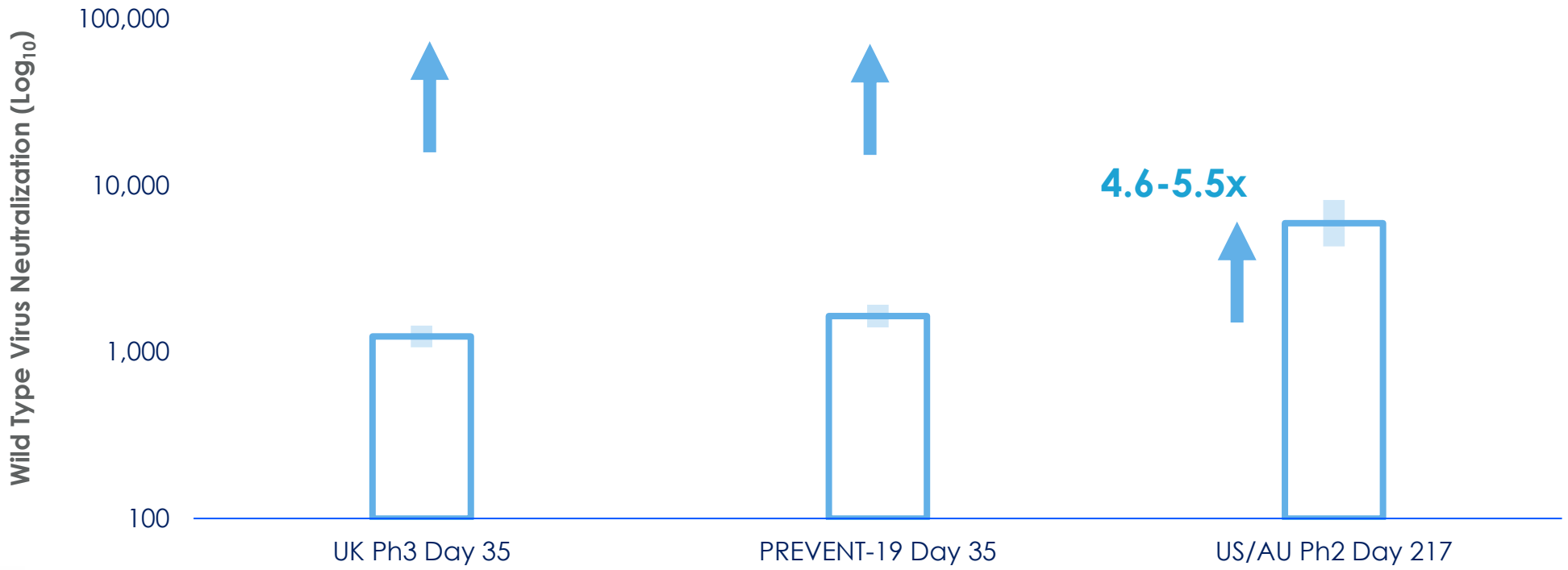
WT neutralization titers increased ~4.3-fold compared to peak response seen after primary vaccination series.

Neutralization titers increased ~3.7-fold in adults aged 18-59 & ~4.7-fold in adults aged 60-84.

BOOSTED MICRONEUTRALIZATION RESPONSES GREATER THAN OBSERVED IN PHASE 3 STUDIES

UK Phase 3 Efficacy
Prototype: **96%**
B.1.1.7: **86%**

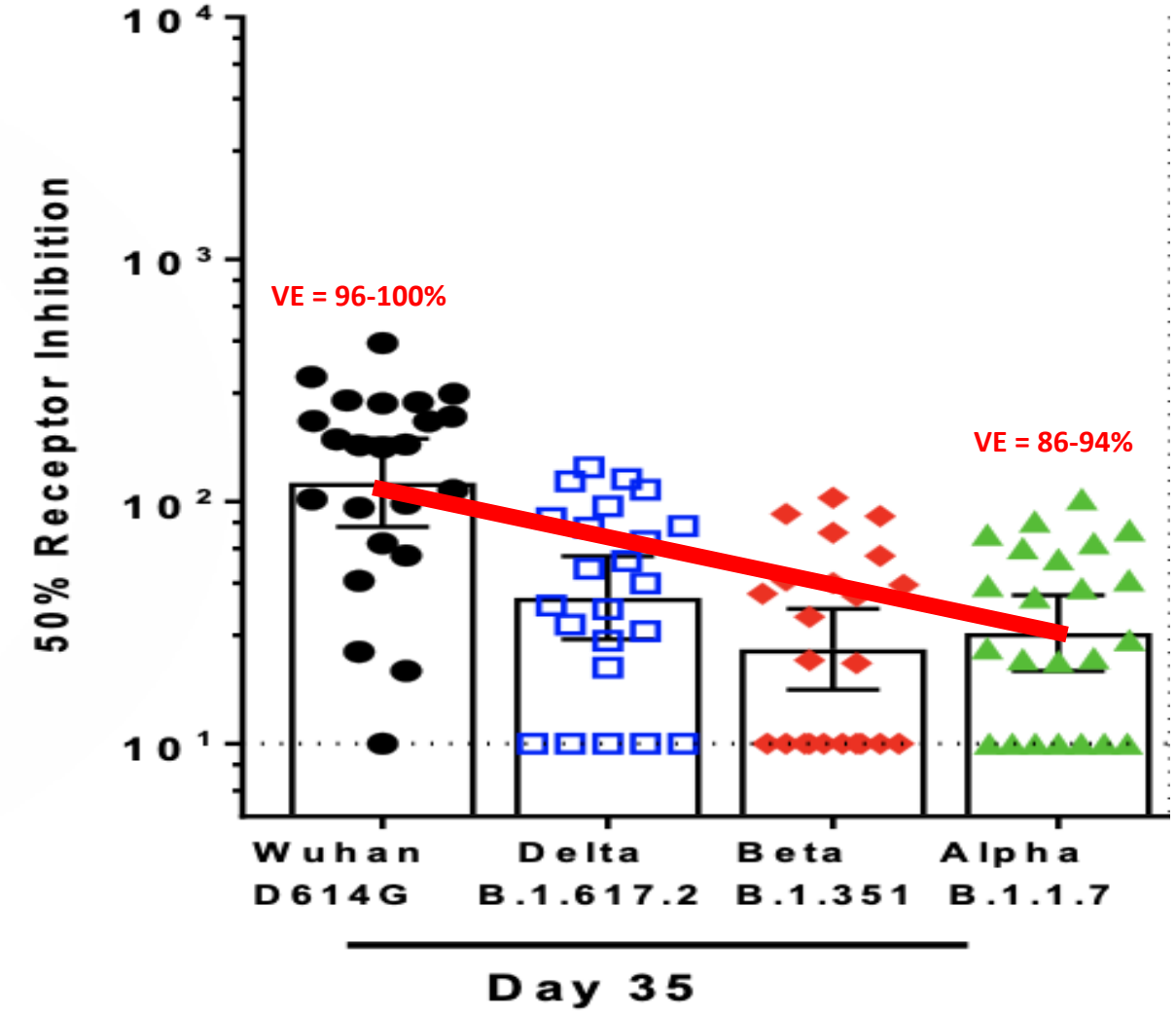
PREVENT-19 Efficacy
Non-VoI/VoC: **100%**
VoI/VoC: **93%**
B.1.1.7: **94%**



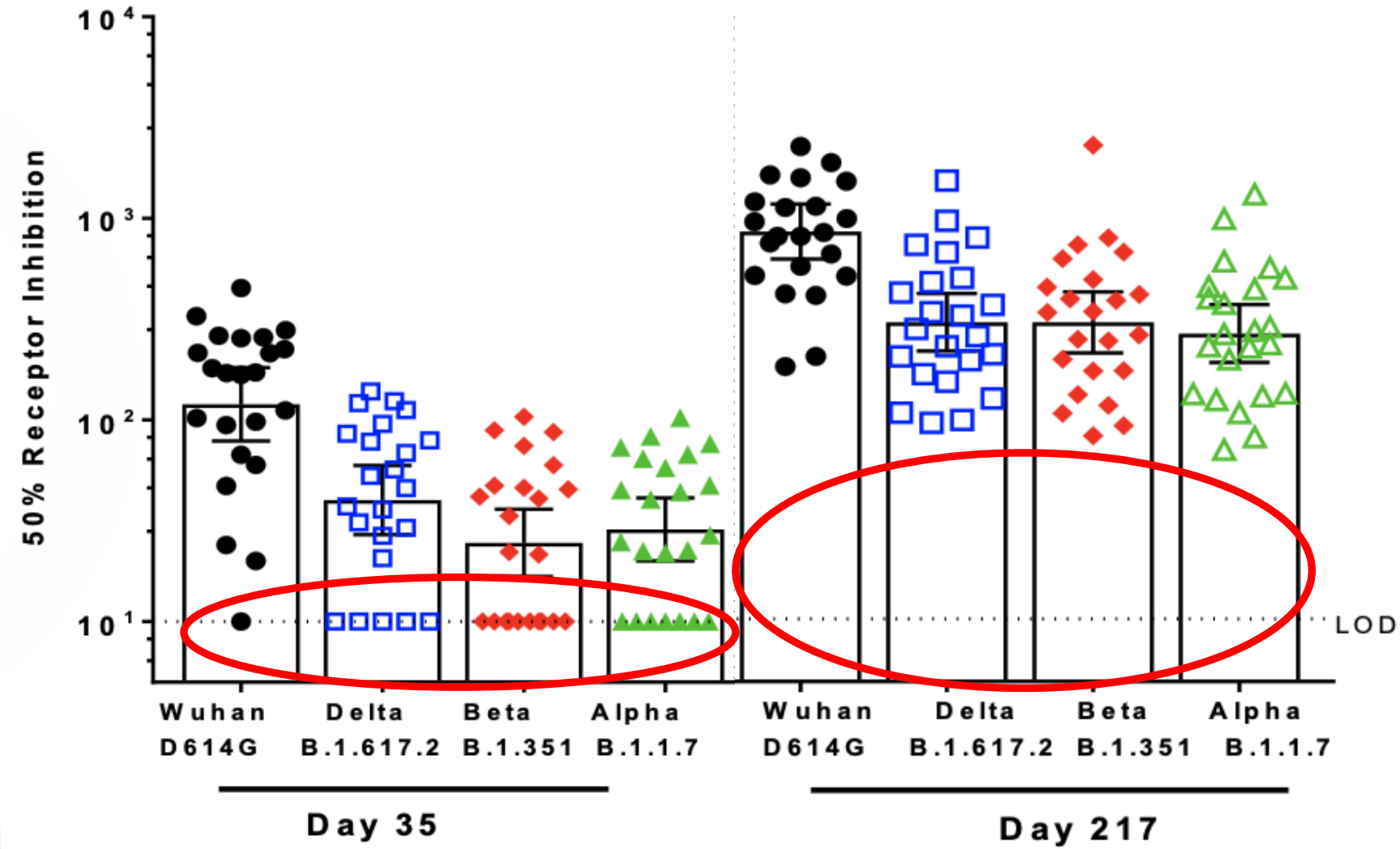
Microneutralization Responses
with 95% CI

Functional hACE2 Inhibition Responses against variants were observed after primary vaccination

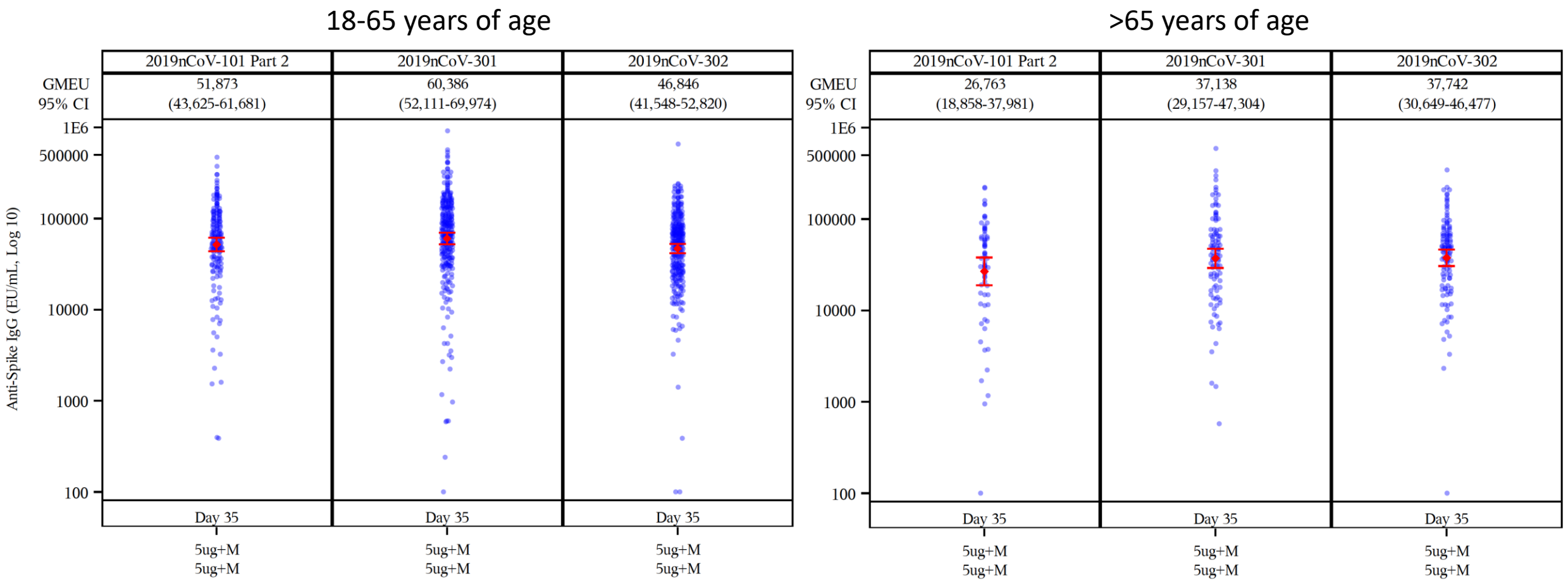
High levels of efficacy were observed in Phase 3 studies against Wuhan (96-100%) and alpha (86-94%) suggesting observed immune responses against delta and beta may be efficacious



After boosting ALL participants developed high levels of functional hACE2 responses against all variants

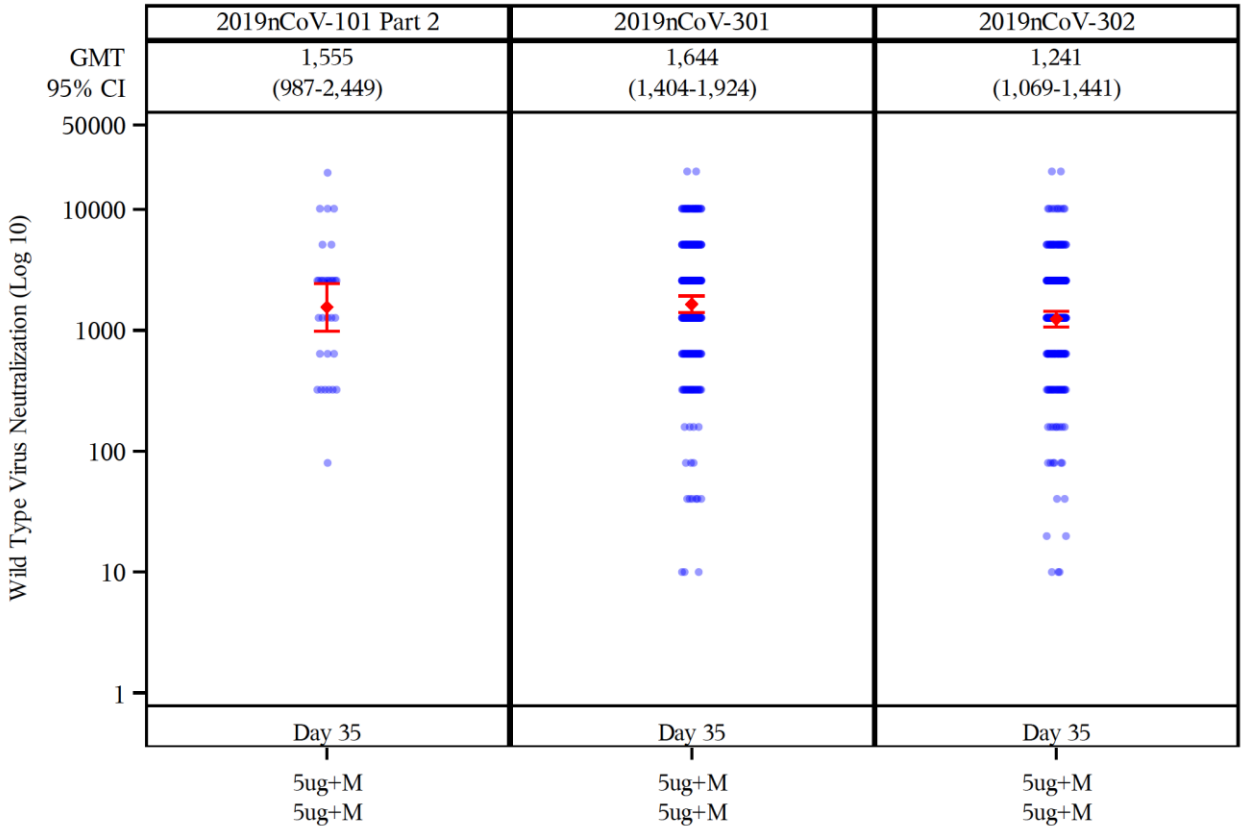


DAY 35 ANTI-SPIKE IGG RESPONSES ACROSS STUDIES BY AGE

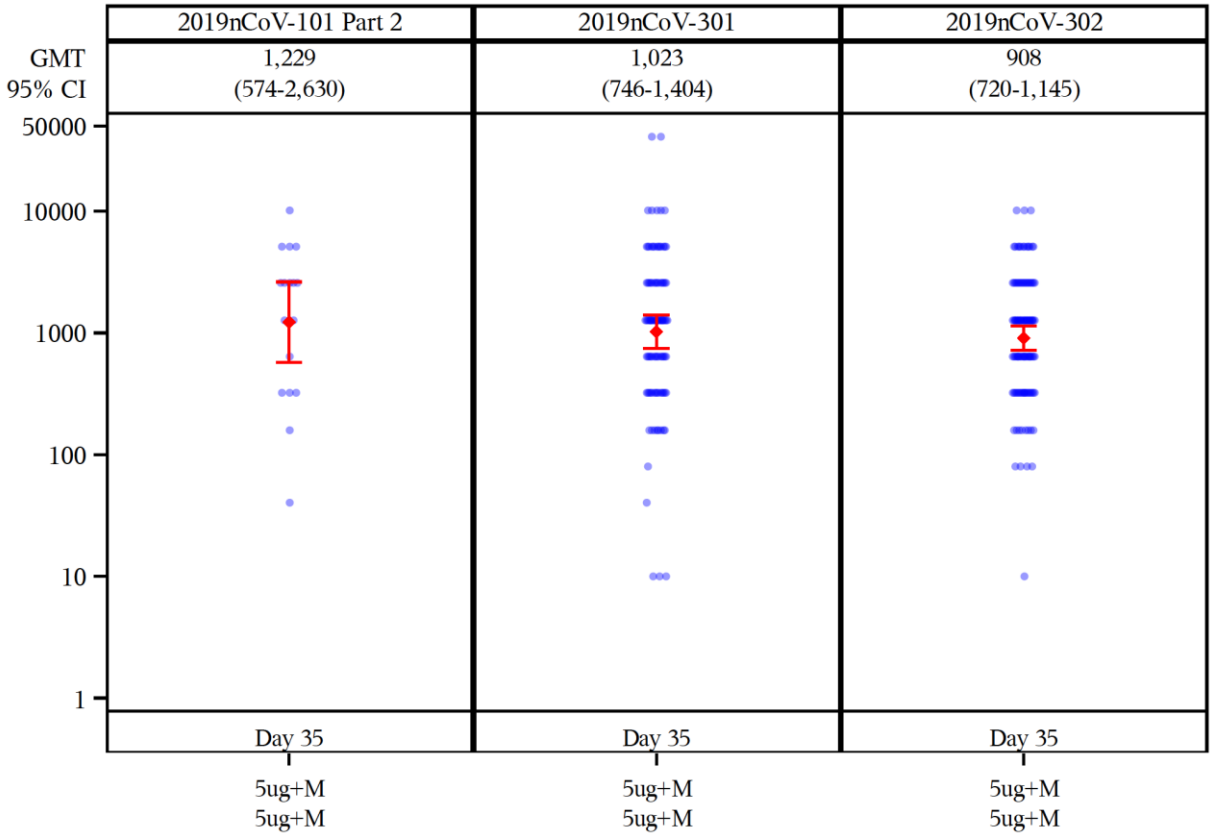


DAY 35 WILD-TYPE NEUTRALIZATION RESPONSES BY AGE

18-65 years of age

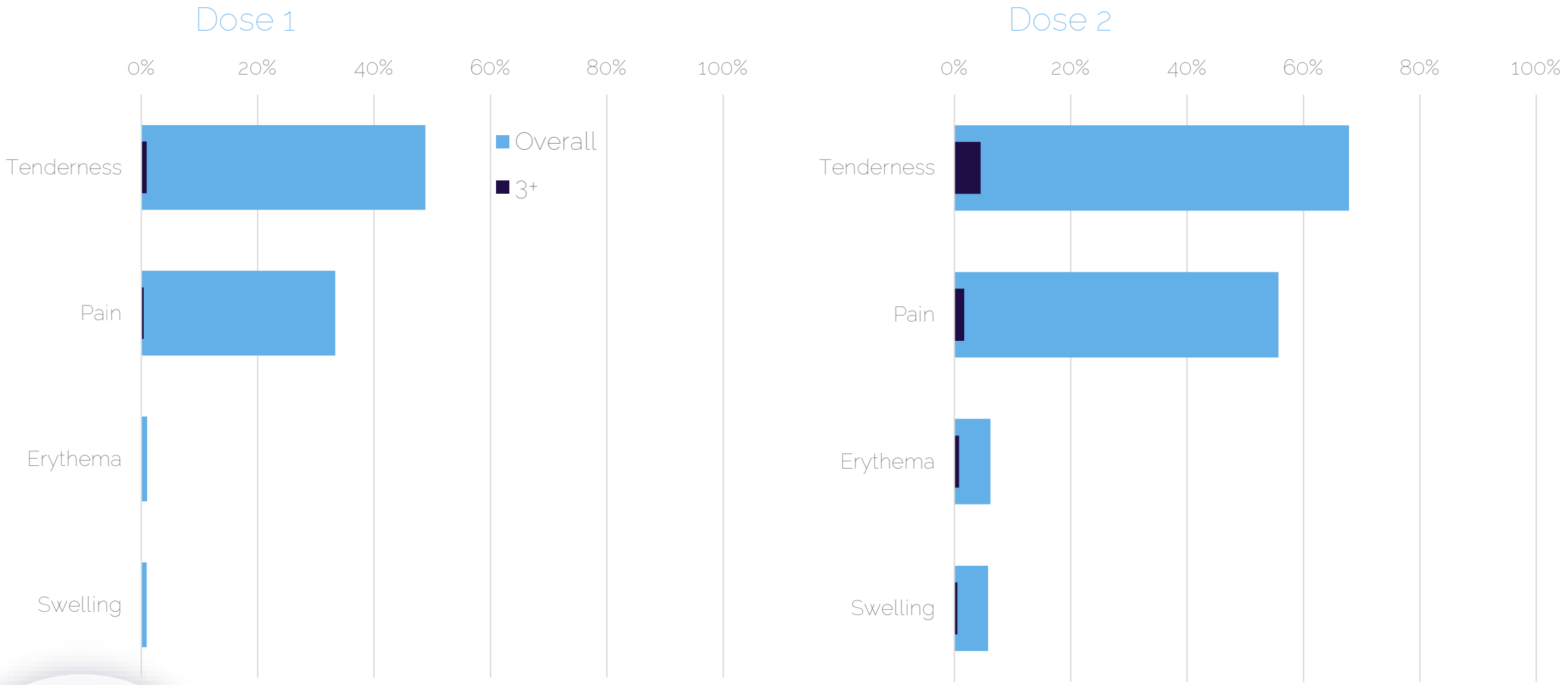


>65 years of age



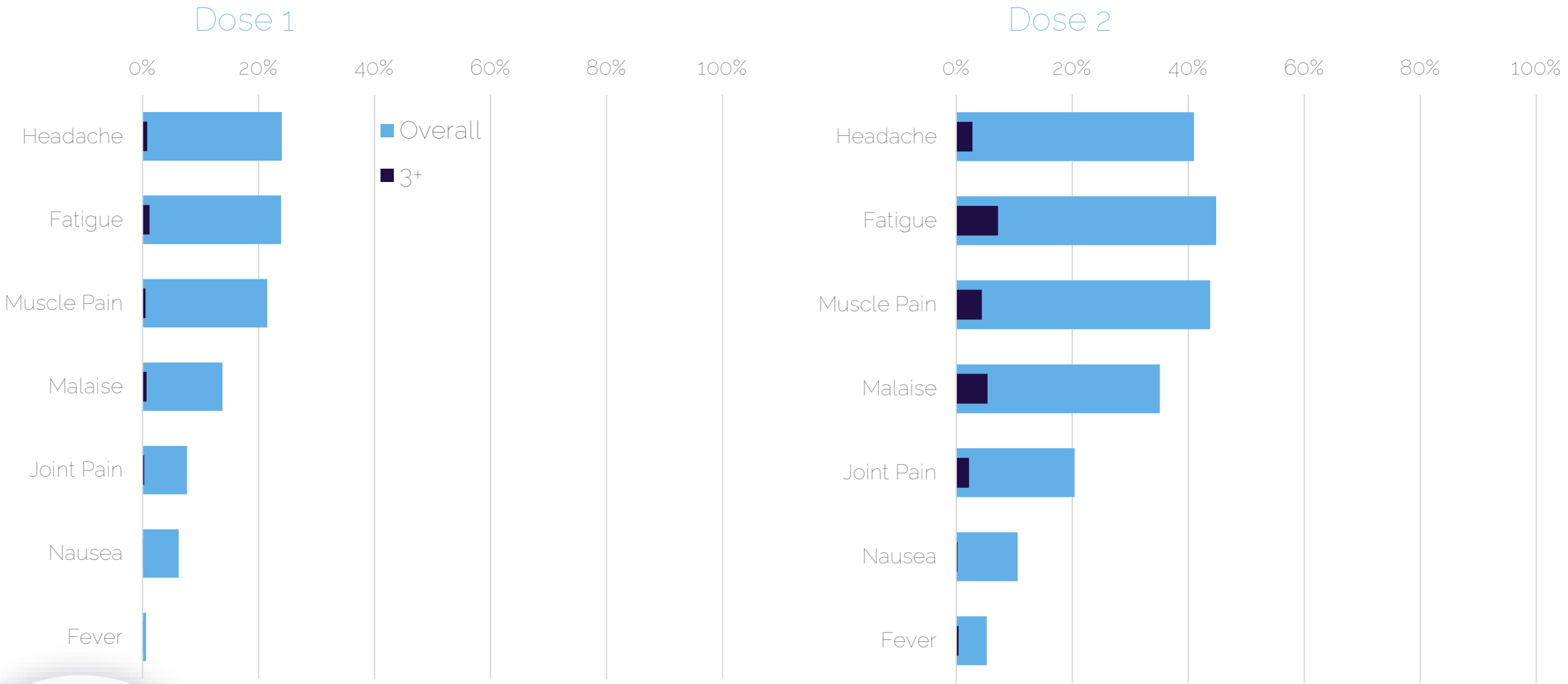
LOCAL: MAJORITY " NONE" OR " MILD"

Integrated safety across NVX-CoV2373 development



SYSTEMIC: MAJORITY " NONE" OR " MILD"

Integrated safety across NVX-CoV2373 development



Draft Adverse Reactions from Nuvaxovid Clinical Trials

System Organ Class	Very common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1,000 to < 1/100)	Rare (≥ 1/10,000 to < 1/1,000)	Very rare (< 1/10,000)	Not known (cannot be estimated from the available data)
Blood and lymphatic system disorders			Lymphadenopathy			
Nervous system disorders	Headache					
Gastrointestinal disorders	Nausea or vomiting[a]					
Skin and subcutaneous tissue disorders			Rash Erythema Pruritus Urticaria			
Musculoskeletal and connective tissue disorders	Myalgia[a] Arthralgia[a]					
General disorders and administration site conditions	Injection site tenderness[a] Injection site pain[a] Fatigue[a] Malaise[a,b]	Injection site redness[a,c] Injection site swelling[a] Pyrexia[a] Chills Pain in extremity	Injection site pruritis			

a Higher frequencies of these events were observed after the second dose.
b This term also included events reported as influenza-like illness
c This term includes both injection site redness and injection site erythema (common).

NUVAXOVID COVID-19 PROTEIN VACCINE RISK MANAGEMENT PLAN V0.4

(SUBMIT TO EMA 14 DEC 2021)

Safety Concerns	Pharmacovigilance (PV) Activities	Risk Minimization Measures
Important Identified Risks: None	Not applicable	Not applicable

Important Potential Risks
• Vaccine-associated enhanced disease (VAED), including vaccine associated enhanced respiratory disease (VAERD)
• Anaphylaxis
• Myocarditis and pericarditis
	Routine PV +
	• Targeted follow up questionnaires (2)
	  • Vaccine-associated enhanced disease (VAED), including vaccine associated enhanced respiratory disease (VAERD)
	  • Anaphylaxis
	• Signal Management, AESIs monitoring
	• Monthly summary safety reports; PSUR every 6 months
	• Traceability + Vaccine Reminder Cards
	
	Additional PV activities
	• Clinical Trials (4 safety)
	• Non-interventional studies (2 PASS + 1 pregnancy registry + 2 effectiveness studies)
		Routine Risk Minimization Measures
		• SmPC + PL
		
		Additional Risk Minimization Measures
		• None

Missing Information • Use in pregnancy and while breast feeding • Use in immunocompromised patients • Use in frail patients with co-morbidities (e.g. chronic obstructive pulmonary disease (COPD), diabetes, chronic neurological disease, cardiovascular disorders) • Use in patients with autoimmune or inflammatory disorders • Interaction with other vaccines • Long term safety	Routine PV + • Signal Management, AESIs monitoring • Monthly summary safety reports; PSUR every 6 months • Traceability + Vaccine Reminder Cards Additional PV activities • Clinical Trials (4 safety) • Non-interventional studies (2 PASS + 1 pregnancy registry + 2 effectiveness studies)	Routine Risk Minimization Measures • SmPC + PL Additional Risk Minimization Measures • None

Pregnancies in NVX-CoV2373 Trials: Descriptive analysis, Outcomes and Follow-up Status

155 pregnancies have been reported across the clinical program

- 46 pregnancies occurred in women exposed to placebo only prior to pregnancy
- 109 pregnancies occurred in women exposed to active vaccine at any time point prior to pregnancy

- Ongoing n=78
  - Approximately 51 pregnancies are ≥20 weeks gestation, based on estimated date of delivery
- Live births n=27
- Spontaneous abortions n= 21
  - Placebo 5/46 (10.8%)
  - Active vaccine 16/109 (14.7%)
  - No losses occurred within 14 days following vaccination
  - Spontaneous pregnancy loss in the general population 14-22% [1]
- Voluntary terminations n=16
- Unknown n=11
- Ectopic pregnancy n=2

#1: Antiretroviral Pregnancy Registry Steering Committee. Antiretroviral Pregnancy Registry Interim Report for 1 January 1989 through 31 January 2021. Wilmington, NC: Registry Coordinating Center; 2021. Available from URL: www.APRegistry.com

Planned Post-Authorization Studies

5 planned post-authorization studies

- 2019nCoV-401 = Novavax COVID-19 Vaccine Effectiveness Against Severe COVID-19 in Europe using COVIDRIVE platform
- 2019nCoV-402 = Post-Authorization Safety Study using the Clinical Practice Research Database (CPRD) in the UK
- 2019nCoV-403 = Post-Authorization Effectiveness Study Using a Claims and/or Electronic Health Database in the US (Using Aetion Evidence Platform and HealthVerity data sources)
- 2019nCoV-404 = Post-Authorization Safety Study Using a Claims and/or Electronic Health Database in the US (Using Aetion Evidence Platform and HealthVerity data sources)
- 2019nCoV-405 = COVID-19 Vaccines International Pregnancy Exposure Registry (C-VIPER); ClinicalTrials.gov: NCT04705116)

Conclusions

- NVX-CoV2373 has demonstrated high levels of efficacy in 2 separate Phase 3 studies
  - Efficacy consistent in numerous subgroup analyses performed including age, underlying comorbidities or high-risk status
  - Efficacy demonstrated for Alpha and Beta variants as well as for Variants of Interest / Variants of concern that circulated during conduct of US/Mexico Phase 3 study
- A booster dose given at 6-months robustly increased antibody responses to both the original Wuhan strain and the more recent Alpha, Beta and Delta variants
- The vaccine was safe and well-tolerated with a reactogenicity profile that compares favorably to approved vaccines
  - No important identified risks in the pre-licensure safety database
- Can be stored and transported at standard refrigerator temperatures
- Overall considered to have a positive benefit: risk ratio with a well-balanced safety and efficacy profile