

Vaccines and Related Biological Products Advisory Committee Meeting

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Emergency Use Authorization (EUA) Application for NVX-CoV2373

Novavax, Inc.

Vaccines and Related Biological Products Advisory Committee

June 7, 2022

Emergency Use Authorization (EUA) Application for NVX-CoV2373

Filip Dubovsky, MD, MPH, FAAP

Executive Vice President & Chief Medical Officer
Novavax, Inc.



NVX-CoV2373: Well-Defined Vaccine Platform

**Recombinant protein vaccine,
naturally derived adjuvant**

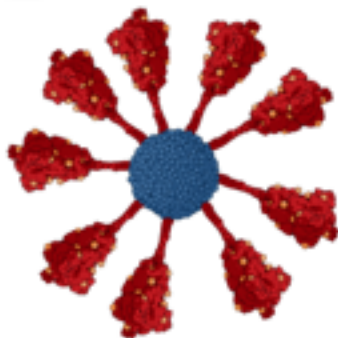
**Robust immunogenicity, high levels of efficacy against
mild, moderate, severe COVID-19**

**Favorable reactogenicity and positive benefit-risk profile
in large, diverse patient population**

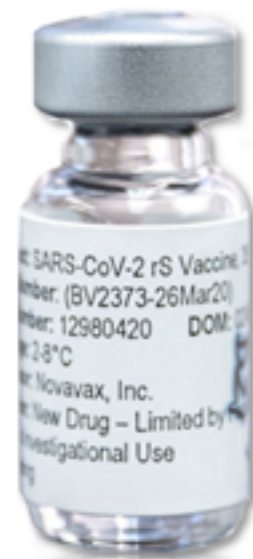
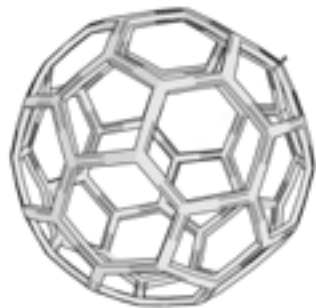
Novavax Vaccine Platform

Recombinant Protein Plus Matrix-M™

Recombinant protein



Matrix-M adjuvant



Novavax vaccine
platform

Recombinant Proteins Represent a Well-Understood Vaccine Platform

- Approved recombinant protein vaccines
 - Influenza
 - Hepatitis
 - Human Papillomavirus (HPV)
 - Meningococcal B (MenB)
 - Shingles
- Approved vaccines including saponin-based adjuvants
 - Malaria
 - Shingles

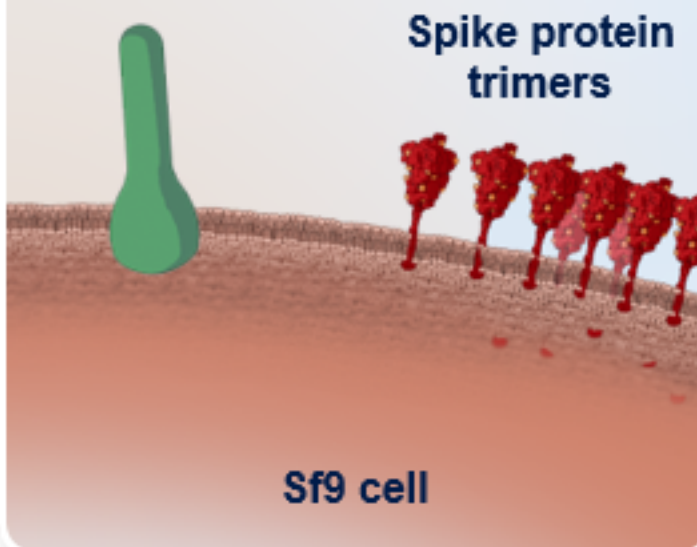
NVX-CoV2373 Antigen Full-Length Recombinant Spike Protein

1 SARS-CoV-2 spike gene inserted into insect virus



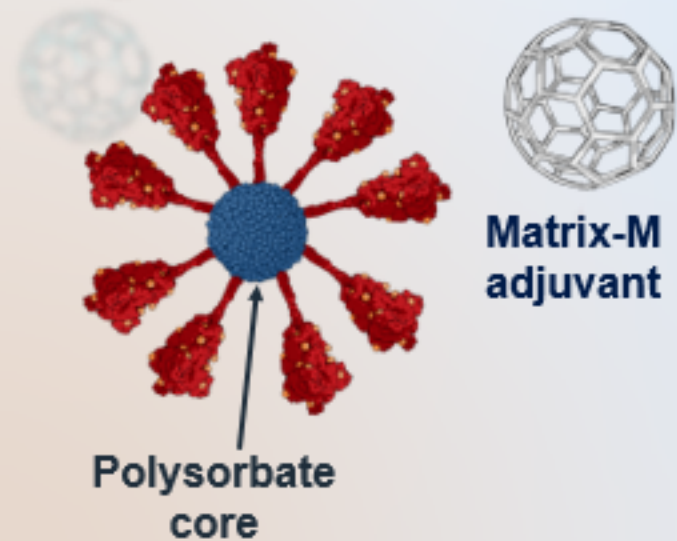
Baculovirus + Modified spike protein gene

2 Sf9 insect cell expressed protein trimers



Sf9 cell

3 Vaccine formation

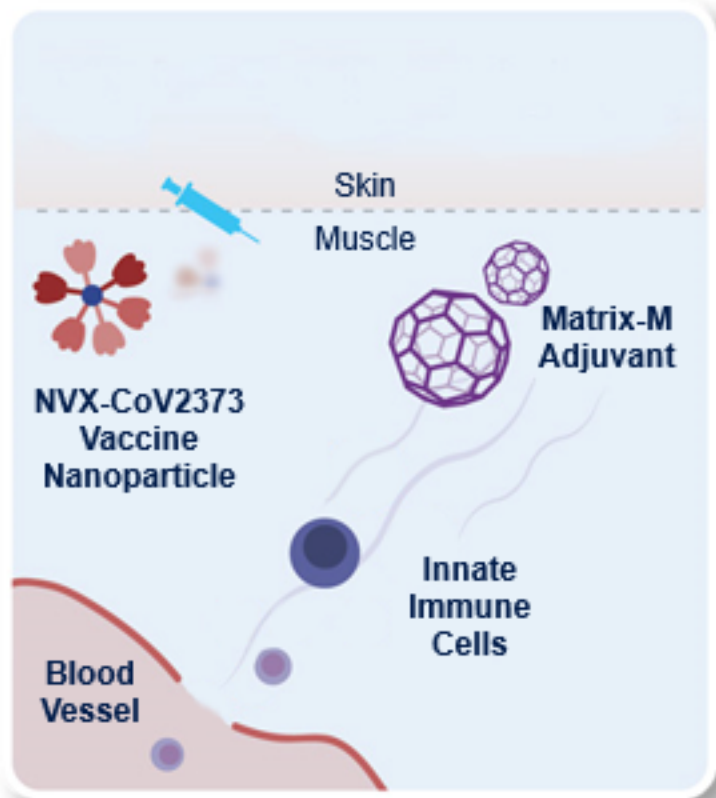


Polysorbate core

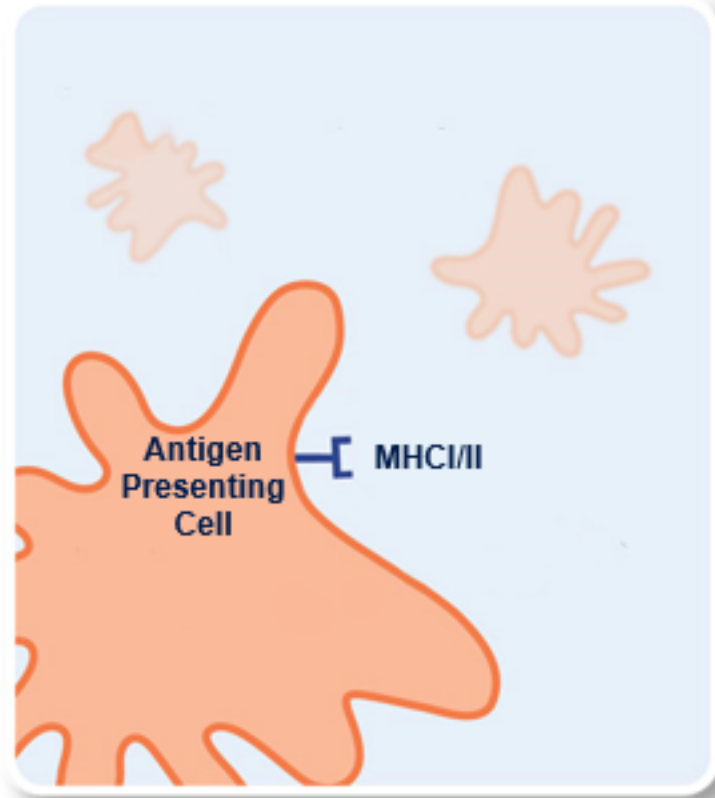
Matrix-M adjuvant

Matrix-M Increases Magnitude and Breadth of Immune Response

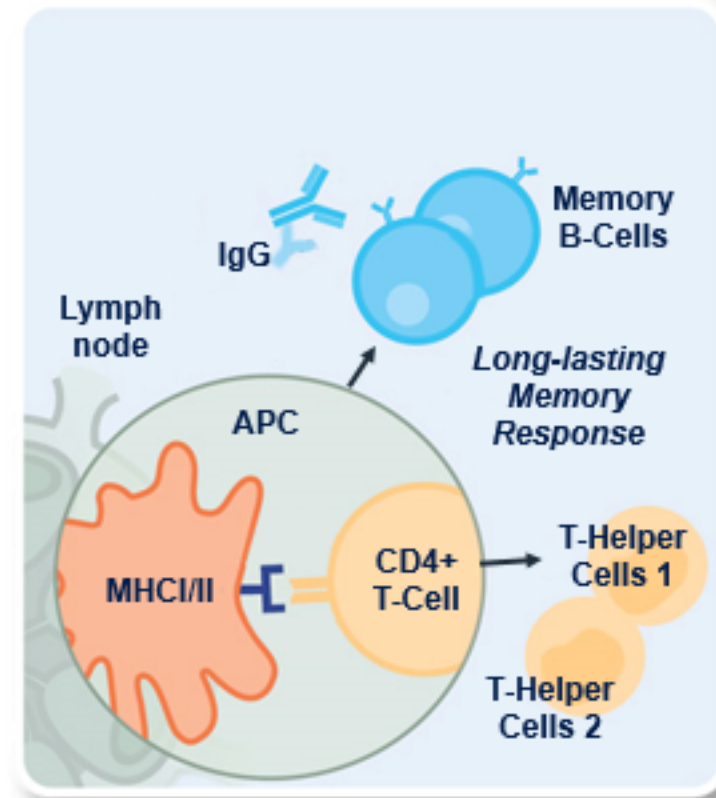
Recruitment and transient activation of innate immune cells



Rapid antigen delivery to and activation of antigen-presenting cells



Enhanced antigen presentation by MHC I and MHC II molecules in draining lymph nodes



NVX-CoV2373 Vaccine Presentation and Storage Supports Access and Ease of Use



Presentation

- 10-dose vials
- Preservative-free



Transportation & Storage

- Stable at 2 to 8°C



Dose Level & Regimen

- 5 µg antigen + 50 µg Matrix-M
- 2 doses given at least 21 days apart
- 0.5 mL intramuscular injection



Initial Indication

- \geq 18 years of age

NVX-CoV2373 Robust Clinical Development Program

PHASE 1-2 Study 101 (US/AU)

N = 131 (Ph. 1)
N = 1,288 (Ph. 2)

Keech et al., NEJM, 2020; Formica et al., PLoS Medicine, 2021

- Established dose level in younger and older adults
- Confirmed need for adjuvant and 2 dose schedule
- Defined immunologic phenotype
- Assessed preliminary safety profile

PHASE 2a/b Study 501 (ZA)

N = 4,419

Shinde et al., NEJM, 2021

- Evaluated preliminary efficacy
- Defined safety profile
- Included participants with HIV

PHASE 3 Study 302 (UK)

N = 15,187

Heath et al., NEJM, 2021; Toback et al., The Lancet Res Med, 2021

- Established safety profile
- Established efficacy
- Evaluated safety with influenza vaccine

PHASE 3 Study 301 (US/MX)

Adults
N = 29,945
12 to < 18 years
N = 2,247

Dunkle et al., NEJM, 2021

- Established safety profile in US population
- Established efficacy in US population

High Levels of Protection Achieved with NVX-CoV2373

Overall Efficacy

90.4%

Medical Comorbidities

92%

Against Moderate and Severe Disease

100%

Matched Strain

97%

Non-Variants of Interest / Concern

Against Variants

94%

Alpha (B.1.1.7)

93%

All Vol / VoC

Circulating Variants During Study 301 (US/MX)

Study 301 (US/MX)

Variants of Concern (VoC)

Alpha (B.1.1.7)
Beta (B.1.351)
Epsilon (B.1.427/429)
Gamma (P.1)

Variants of Interest (VoI)

Delta (B.1.617.2)
Iota (B.1.526)
Kappa (B.1.617.1)
Zeta (P.2)

Non-variants

Original
(Wuhan-like) / D614G

NVX-CoV2373 Authorizations



World Health
Organization



European
Union



UK



India*



Switzerland



Japan†



South Korea



United Arab
Emirates



Bangladesh



Australia



The Philippines



Thailand*



Canada



New Zealand



Indonesia



Singapore

Status of Ongoing Clinical Development Program

- Study 301 adolescent results submitted to FDA for review
- Completion of safety follow-up from Phase 2-3 studies
- Continuation of pediatric evaluation
 - Adolescents (boosting)
 - School-age children and younger
- Clinical evaluation of variant vaccines for circulating SARS-CoV-2 variants
- Evaluation of homologous and heterologous boosting
- Post-authorization studies for effectiveness and safety monitoring

Agenda

Immunogenicity and Efficacy

Raburn Mallory, MD

Senior Vice President & Head of Clinical Development
Novavax, Inc.

Safety

Denny Kim, MD, MPH

Senior Vice President & Chief Safety Officer
Head of Global Vaccine Safety
Novavax, Inc.

Clinical Perspective

Gregory A. Poland, MD, FIDSA, MACP, FRCP

Mary Lowell Leary Emeritus Professor of Medicine
Distinguished Investigator of the Mayo Clinic
Director, Mayo Vaccine Research Group

Conclusion

Filip Dubovsky, MD, MPH, FAAP

Executive Vice President & Chief Medical Officer
Novavax, Inc.

Additional Responders

Mori Krantz, MD, FACP, FACC

Governor, American College of Cardiology
(Colorado Chapter)
Senior Cardiologist, Clario Inc.

Greg Glenn, MD

President, R & D
Novavax, Inc.

Henrietta Ukwu, MD, FACP

SVP, Chief Regulatory Officer
Novavax, Inc.

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Novavax, Inc.

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Lisa Dunkle, MD

VP, Global Medical Lead, Study 301
Novavax, Inc.

Immunogenicity and Efficacy

Raburn Mallory, MD

Senior Vice President & Head of Clinical Development
Novavax, Inc.



NVX-CoV2373 Demonstrated High Levels of Immunogenicity and Efficacy

- Induced high levels of neutralizing antibodies in both younger and older adults
- Showed high levels of efficacy in preventing COVID-19
- High level of efficacy for Variants of Concern / Variants of Interest
- Provided complete protection from moderate and severe COVID-19

NVX-CoV2373 Non-Clinical Results Supported Progressing to Clinical Development

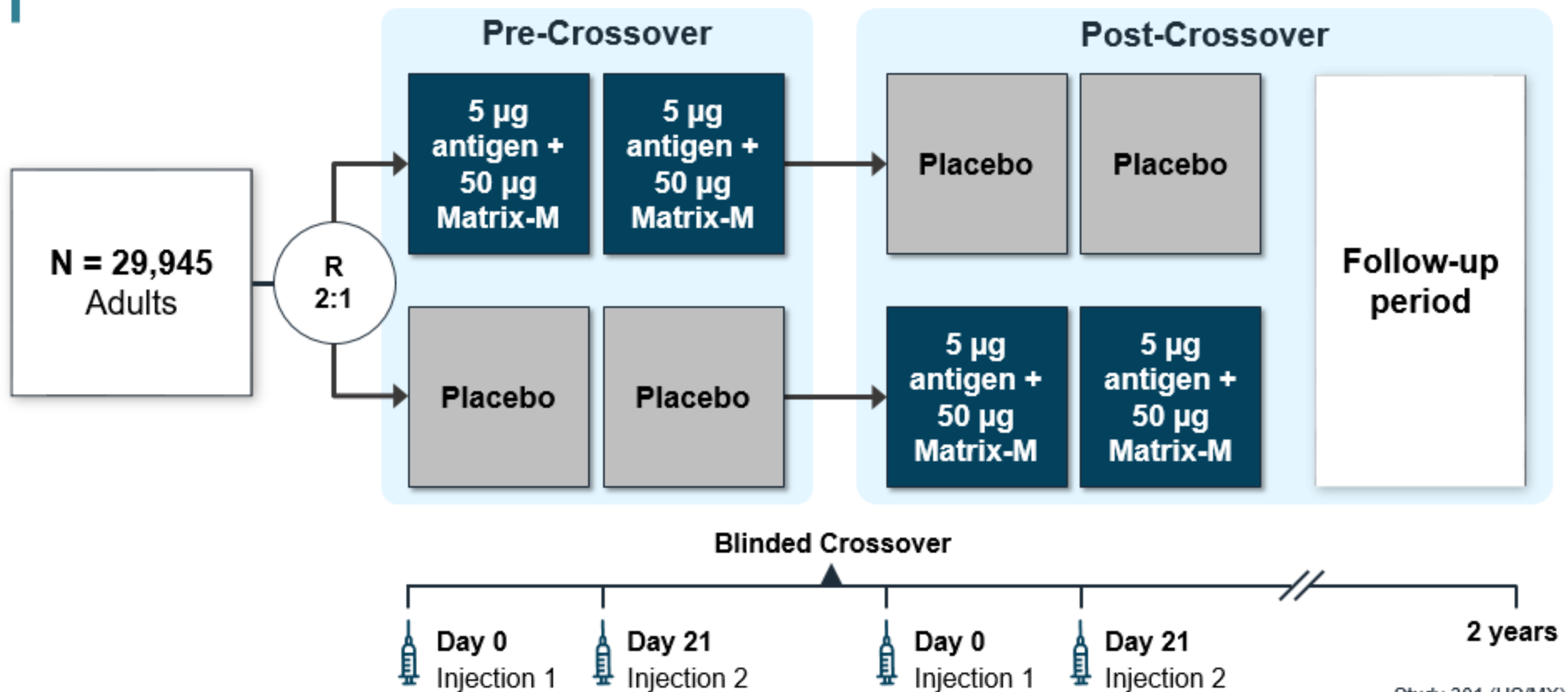
Types of studies	Key findings
Immunogenicity	<ul style="list-style-type: none"><li data-bbox="680 511 2308 639">▪ Induced anti-spike IgG, hACE2-binding inhibiting antibodies, and neutralizing antibodies<li data-bbox="680 654 2010 715">▪ Induced strong Th1-type CD4+ T-cell responses¹
Animal challenge	<ul style="list-style-type: none"><li data-bbox="680 833 2308 895">▪ Suppressed viral replication in both upper and lower airways<li data-bbox="680 909 1900 971">▪ No evidence of enhanced disease pathology
Toxicology	<ul style="list-style-type: none"><li data-bbox="680 1082 2308 1143">▪ No safety concerns identified in standard toxicology program<li data-bbox="680 1158 2175 1282">▪ No adverse findings in developmental and reproductive toxicology study

Study 301 (US/MX)

PREVENT-19

PRE-fusion protein subunit Vaccine Efficacy Novavax Trial – COVID-19

Study Design



Efficacy Endpoint Definitions

- **Primary:** first occurrence of PCR-confirmed symptomatic mild, moderate, or severe COVID-19 with onset ≥ 7 days after second dose in serologically negative participants at baseline
 - Primary statistical hypotheses for vaccine efficacy (VE)
 - Lower Bound 95% CI for VE $> 30\%$
- **Secondary:** first occurrence of PCR-confirmed moderate or severe COVID-19, as defined in primary endpoint

Variants Represented Most Detected Cases

Variant of Concern/Interest	% of Cases
	Study 301 (US/MX) (n = 75 cases)
Alpha ¹	53%
Iota ²	11%
Epsilon ¹	7%
Gamma ¹	4%
Beta ¹	3%
Delta ²	1%
Kappa ²	1%
Zeta ²	1%
Total	81%

1. Variant of Concern; 2. Variant of Interest

CDC: May 25, 2021

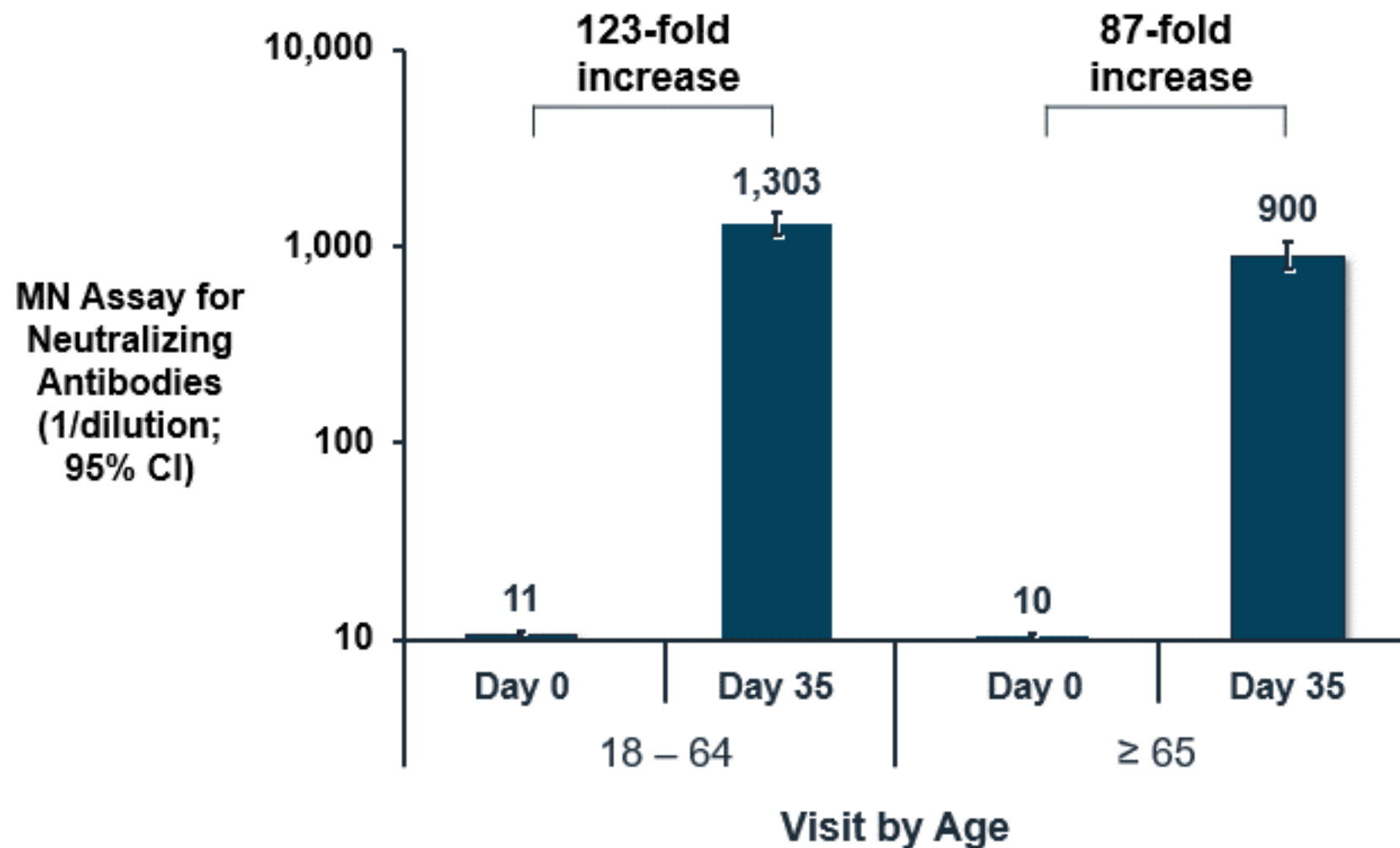
Study 301 (US/MX)

Demographics and Baseline Characteristics Well-Balanced

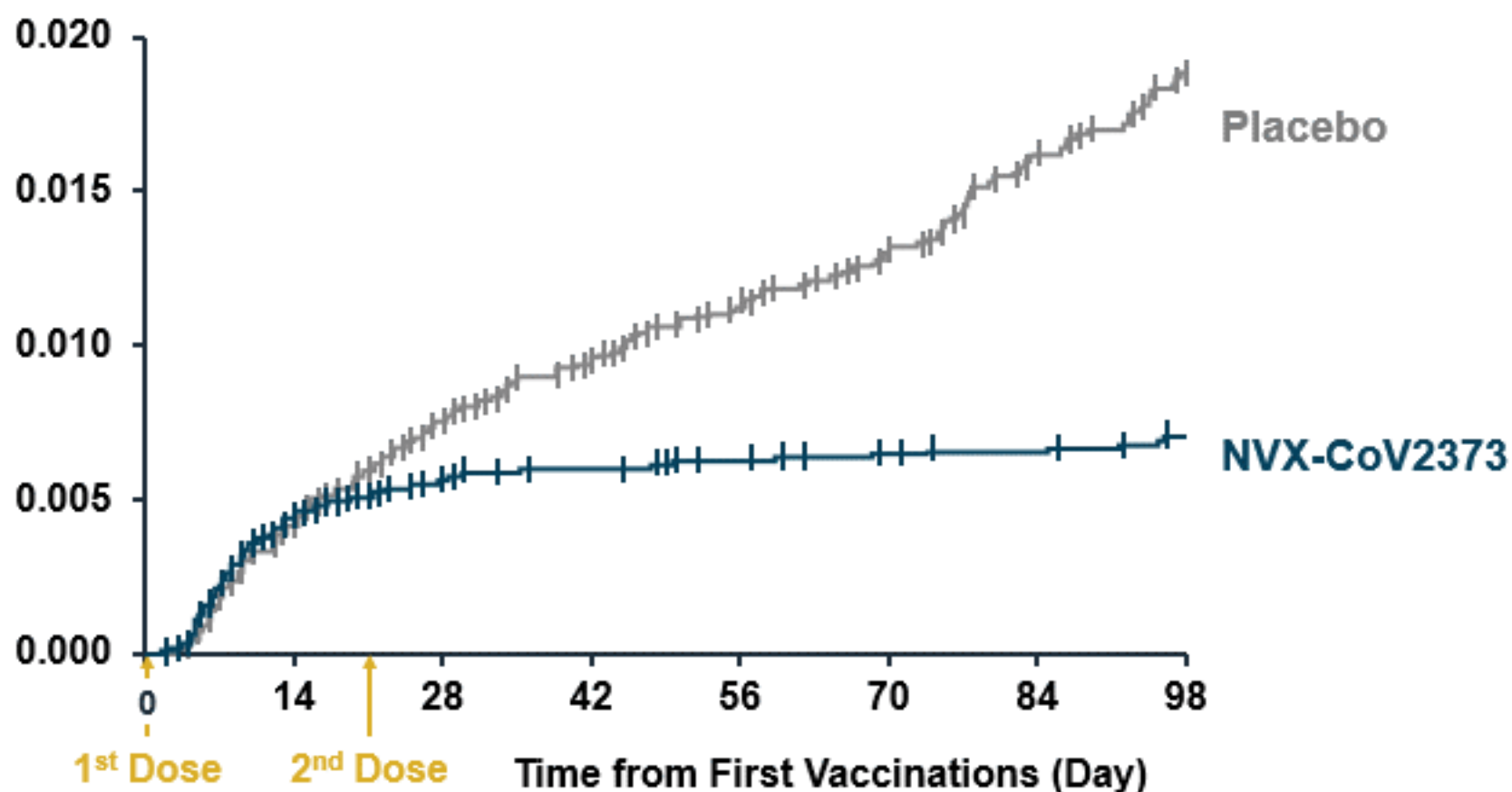
	NVX-CoV2373 (N = 19,735)	Placebo (N = 9,847)
US Mexico	94% 6%	94% 6%
Age (years) – median (range)	47 (18 – 95)	47 (18 – 90)
≥ 65 years	13%	13%
Female	48%	49%
Race		
White	75%	75%
Black/African American	12%	12%
American Indian or Alaska Native	7%	7%
Hispanic/Latino	22%	22%
BMI ≥ 30 kg/m²	37%	37%
High-risk*	95%	95%
SARS-CoV-2 seropositive	7%	7%

* Either ≥ 65 years with comorbidities or living or working conditions involving known frequent exposure to COVID-19 or densely populated circumstances

Robust Neutralizing Antibody Responses 14 Days After Second Dose



Efficacy and Durability of Two-Dose Regimen Demonstrated



N at risk		0	14	28	42	56	70	84	98
NVX-CoV2373		19,714	19,483	19,000	18,311	17,568	16,863	13,015	7,925
Placebo		9,868	9,720	9,410	8,773	8,082	7,482	5,654	3,445

NVX-CoV2373 Provides 90% Protection from Mild, Moderate, and Severe COVID-19

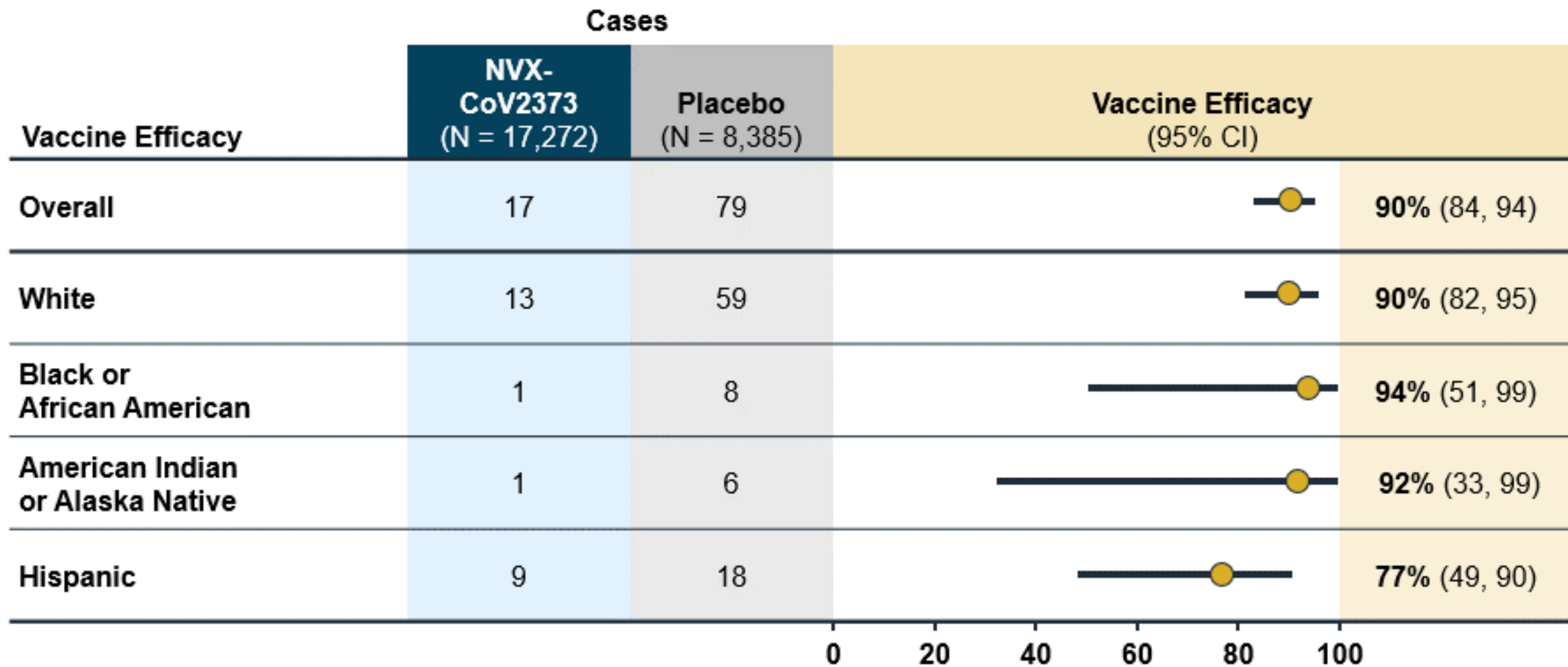
100% Protection Against Moderate / Severe Disease

	NVX-CoV2373 (N = 17,272)	Placebo (N = 8,385)
Cases	17 (0.1%)	79 (0.9%)
<i>Mild</i>	17	66
<i>Moderate</i>	0	9
<i>Severe</i>	0	4
Vaccine Efficacy Overall	90% (95% CI: 84, 94)	
Vaccine Efficacy Moderate/Severe	100% (95% CI: 85, 100)	

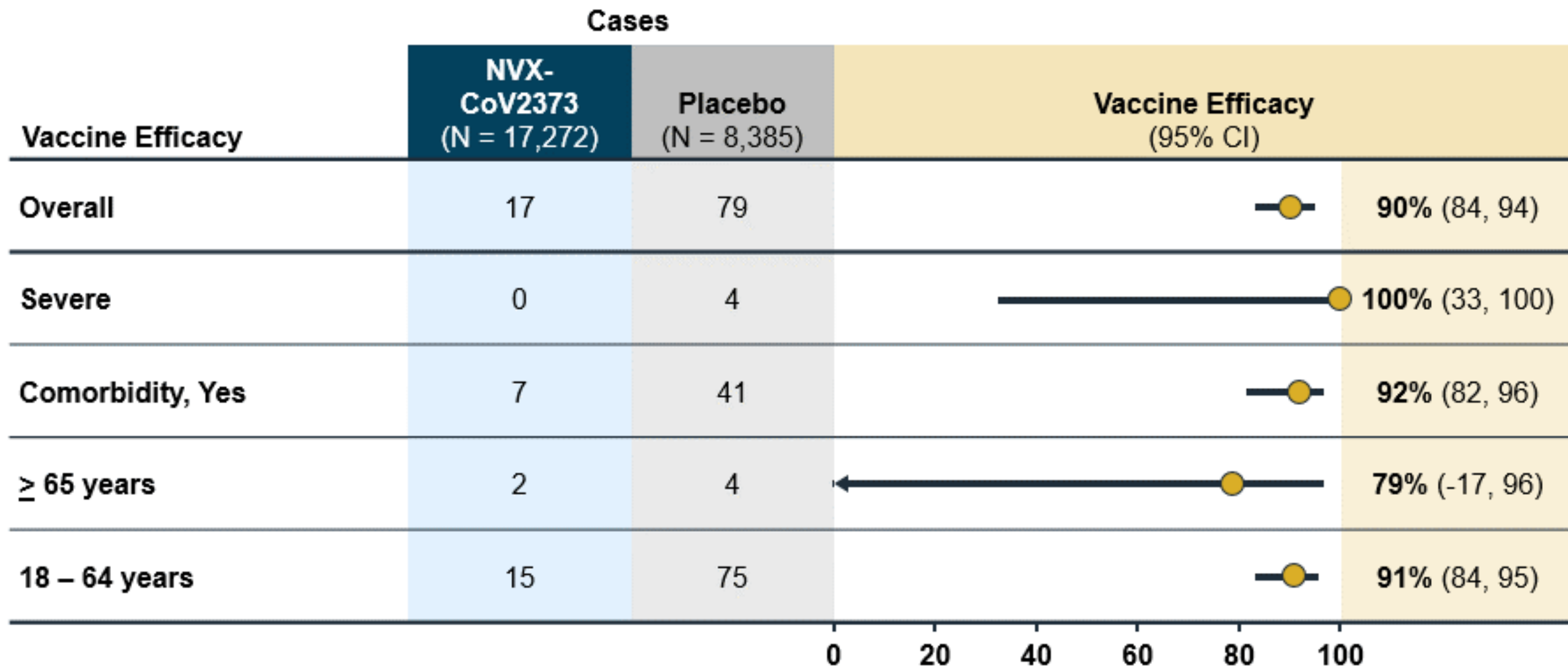
NVX-CoV2373 Efficacious Against Original Strain and Variants of Concern/Interest (VoC/VoI)

	PCR-confirmed VoC/VoI		All Other Strains	
	NVX-CoV2373 (N = 17,272)	Placebo (N = 8,385)	NVX-CoV2373 (N = 17,272)	Placebo (N = 8,385)
Cases	8 (< 0.1%)	53 (0.6%)	1 (< 0.1%)	13 (0.2%)
<i>Mild</i>	8	44	1	10
<i>Moderate</i>	0	7	0	2
<i>Severe</i>	0	2	0	1
Vaccine Efficacy Overall	93% (95% CI: 86, 97)		97% (95% CI: 74, 100)	

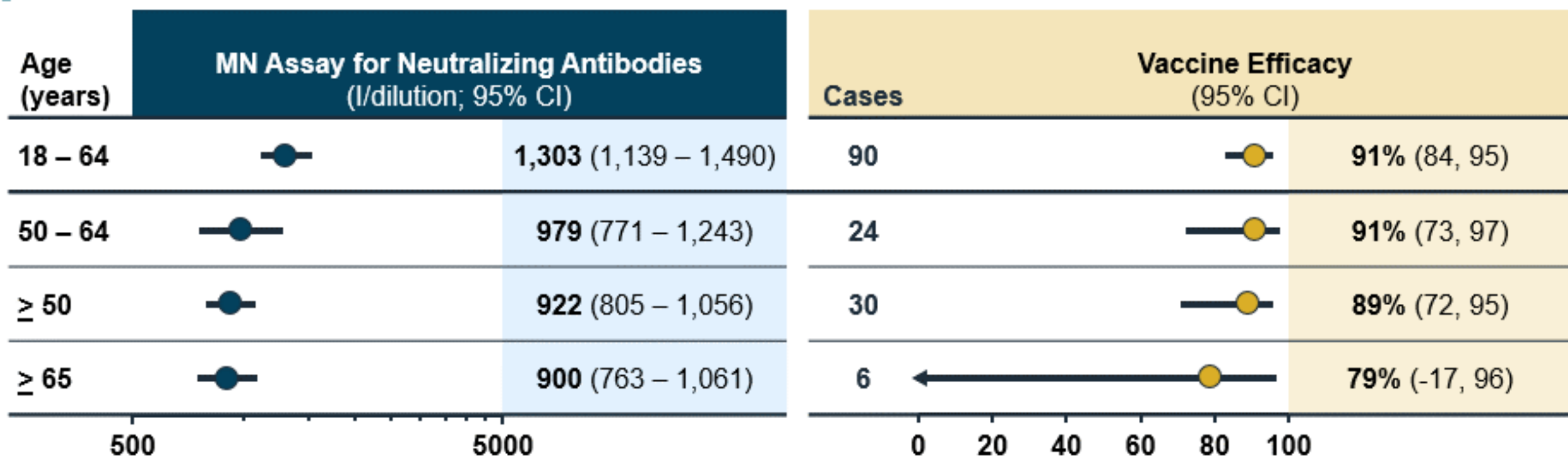
Consistent Efficacy Observed Across Subgroups



Consistent Efficacy Observed Across Subgroups



Robust Immunogenicity and Efficacy by Age



Study 301 (US/MX) Efficacy Summary: High Levels of Efficacy in Preventing COVID-19

- Exhibited high level of efficacy for Variants of Concern/Interest
- Provided complete protection from moderate and severe COVID-19
- Demonstrated consistently high efficacy across subgroups

Safety

Denny Kim, MD, MPH

Senior Vice President & Chief Safety Officer
Head of Global Vaccine Safety
Novavax, Inc.



~ 50,000 Participants Across 4 Studies

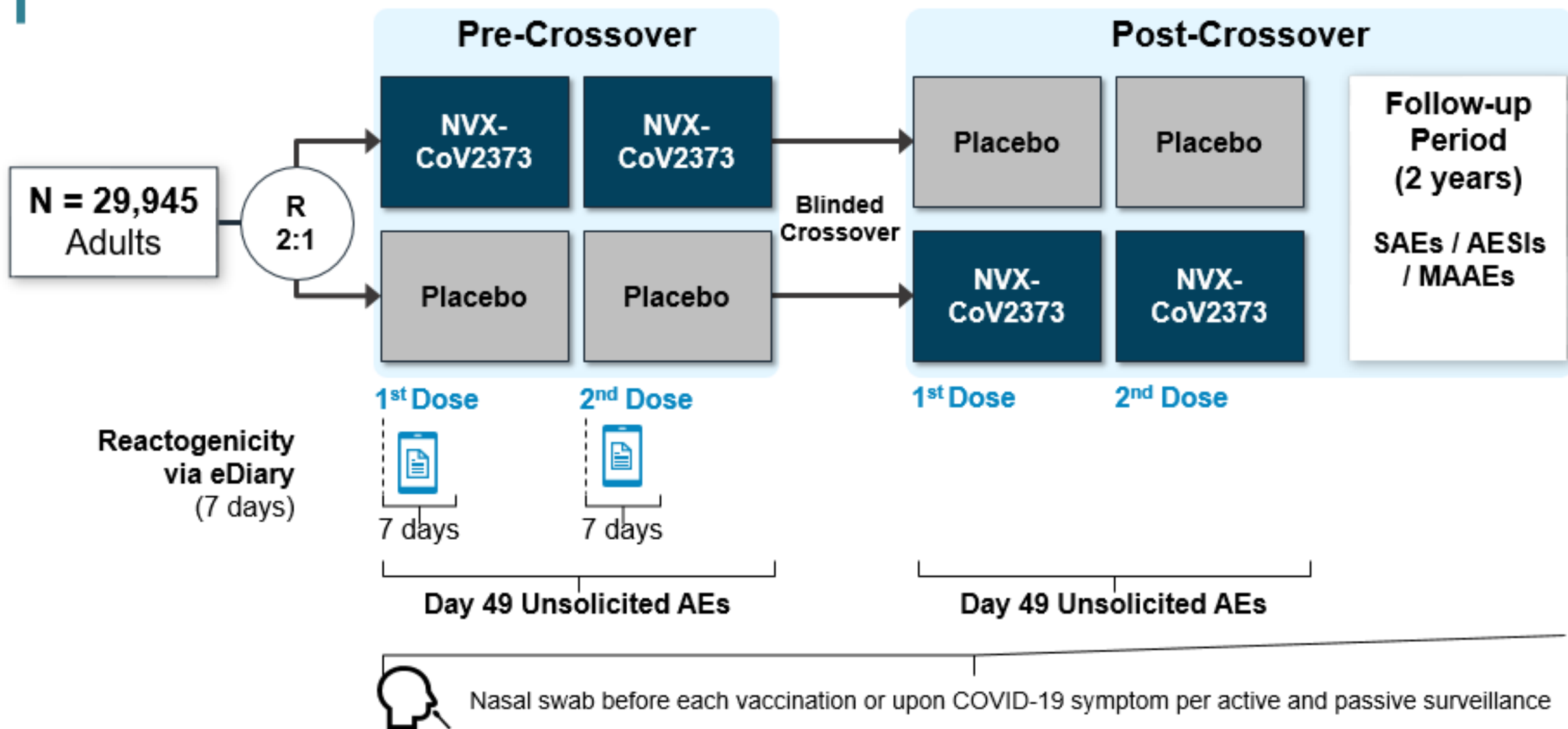
Pooled Safety Data Set

Study (Phase)	Country		NVX-CoV2373	Placebo	Total
Total			30,064	19,886	49,950
301 (Phase 3)	US & Mexico	Adult	19,735	9,847	29,582
302 (Phase 3)	UK	Adult	7,575	7,564	15,139
501 (Phase 2a/b)	South Africa	Adult	2,211	2,197	4,408
101 (Phase 1/2)	US & Australia	Adult	543	278	821

Safety Exposure: > 90 Days Median Post-Vaccination Follow-up and High Compliance

	NVX-CoV2373 (N = 19,735)	Placebo (N = 9,847)
Total follow-up, person-years	5,511	2,783
Median follow-up after 1st vaccination, days	92	89
Received 2 doses, n (%)	19,111 (97%)	9,416 (96%)

Safety Follow-up





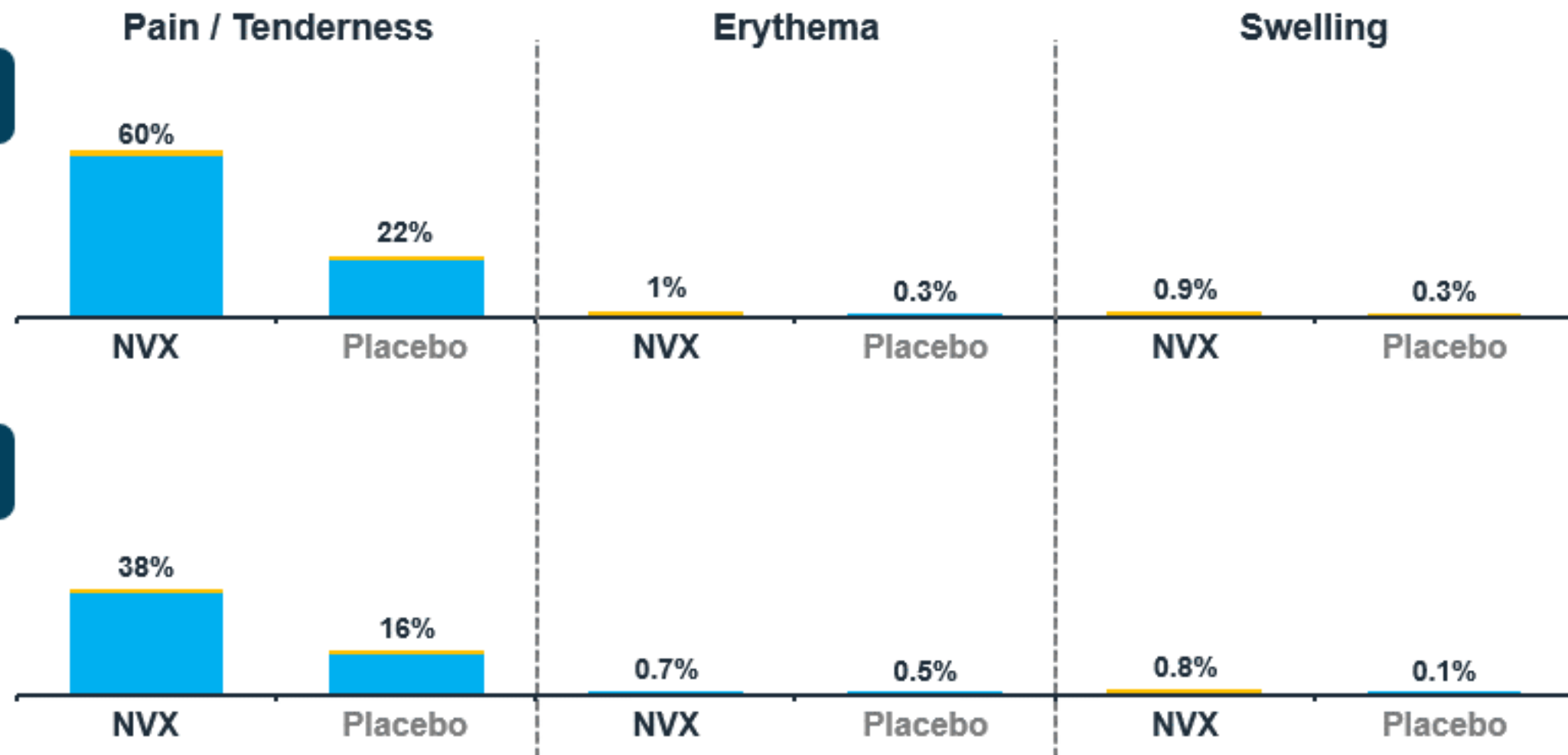
Study 301 (US/MX): Solicited Adverse Events

Collected via e-diary entries for 7 days following each vaccination

Dose 1 Local Events: Mostly Mild to Moderate, Resolved 1-2 Days

18 - 64
Years of Age

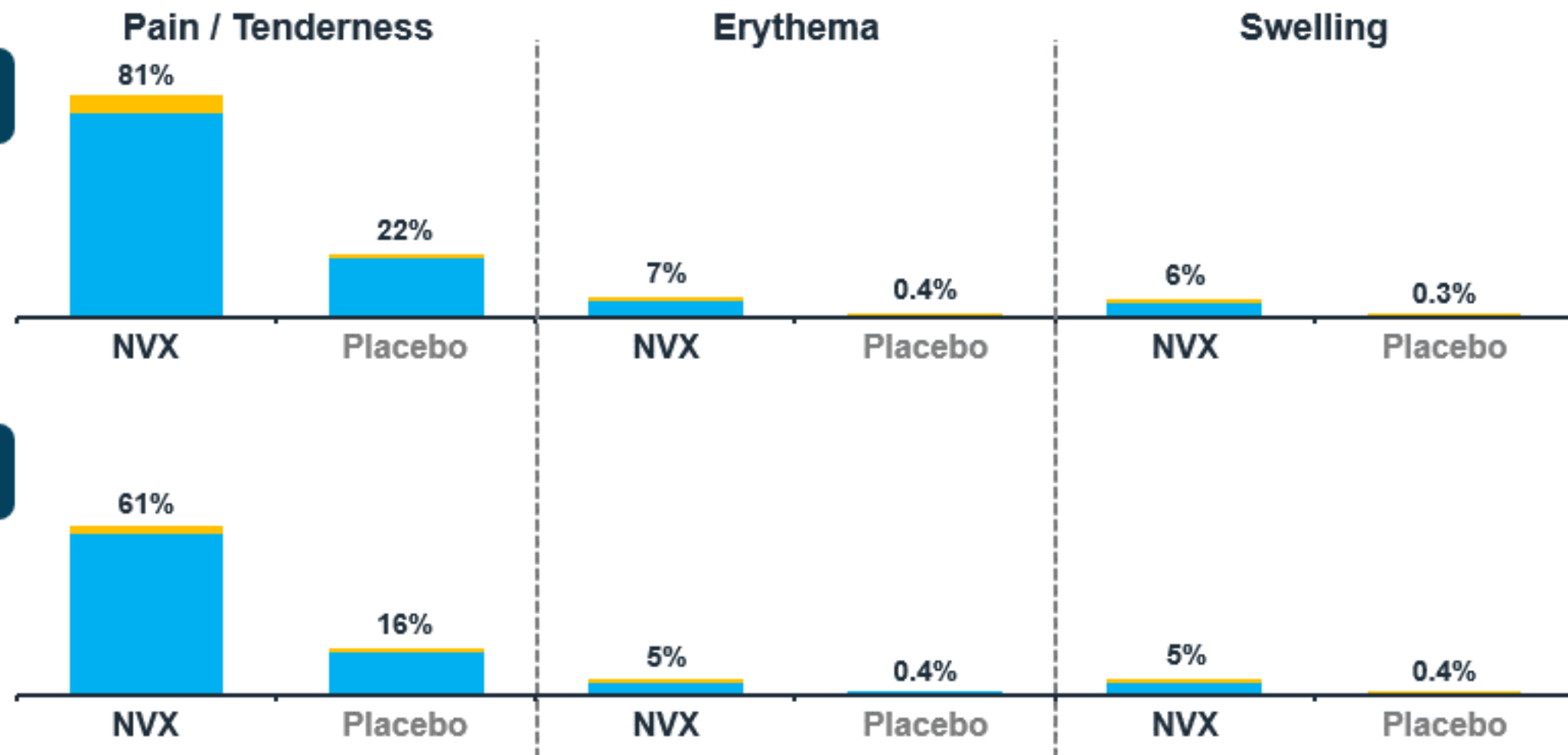
Grade 3+
Grade 1-2



Dose 2 Local Events: Mostly Mild to Moderate, Resolved in 1-2 Days

18 - 64
Years of Age

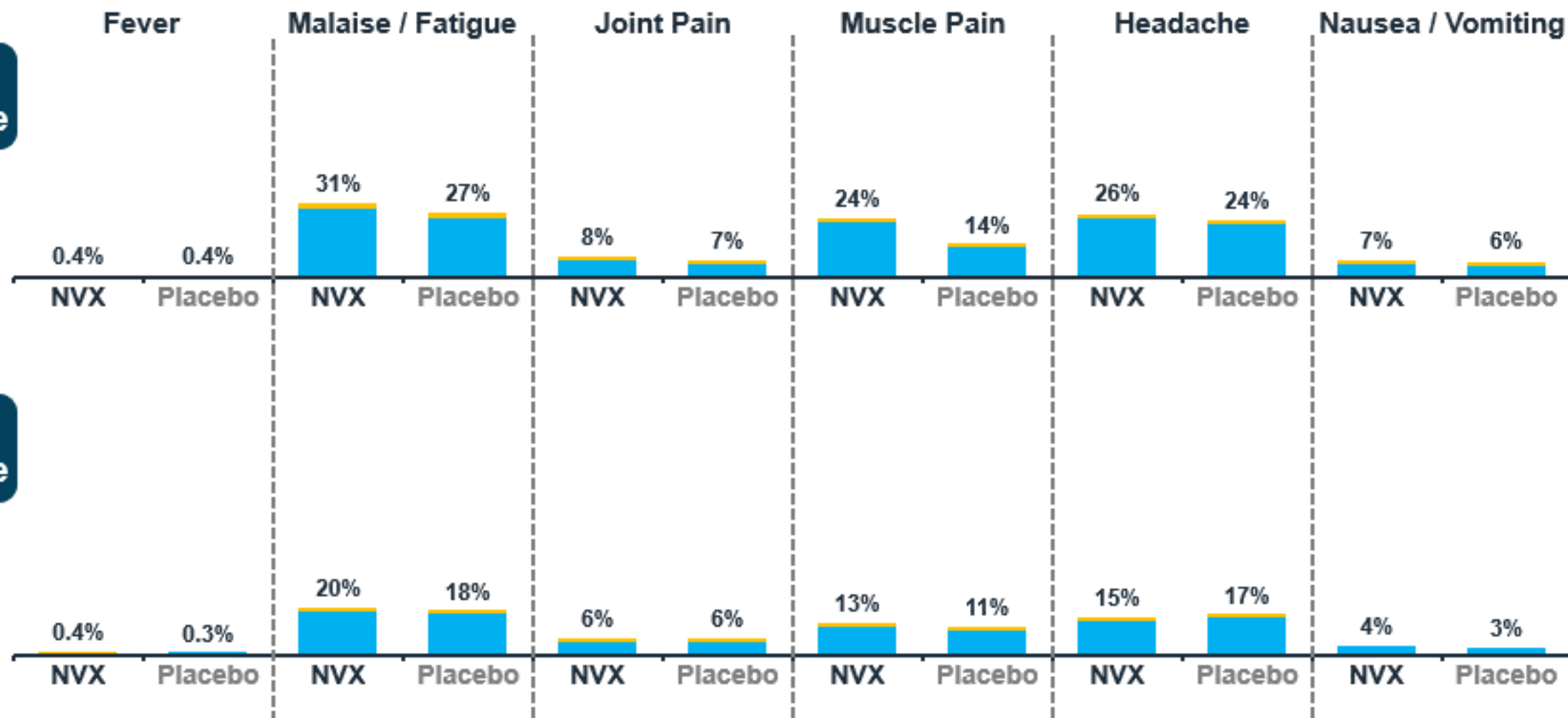
Grade 3+
Grade 1-2



Dose 1 Systemic Events: Most Mild to Moderate, Resolved 1-2 Days

18 - 64
Years of Age

Grade 3+
Grade 1-2



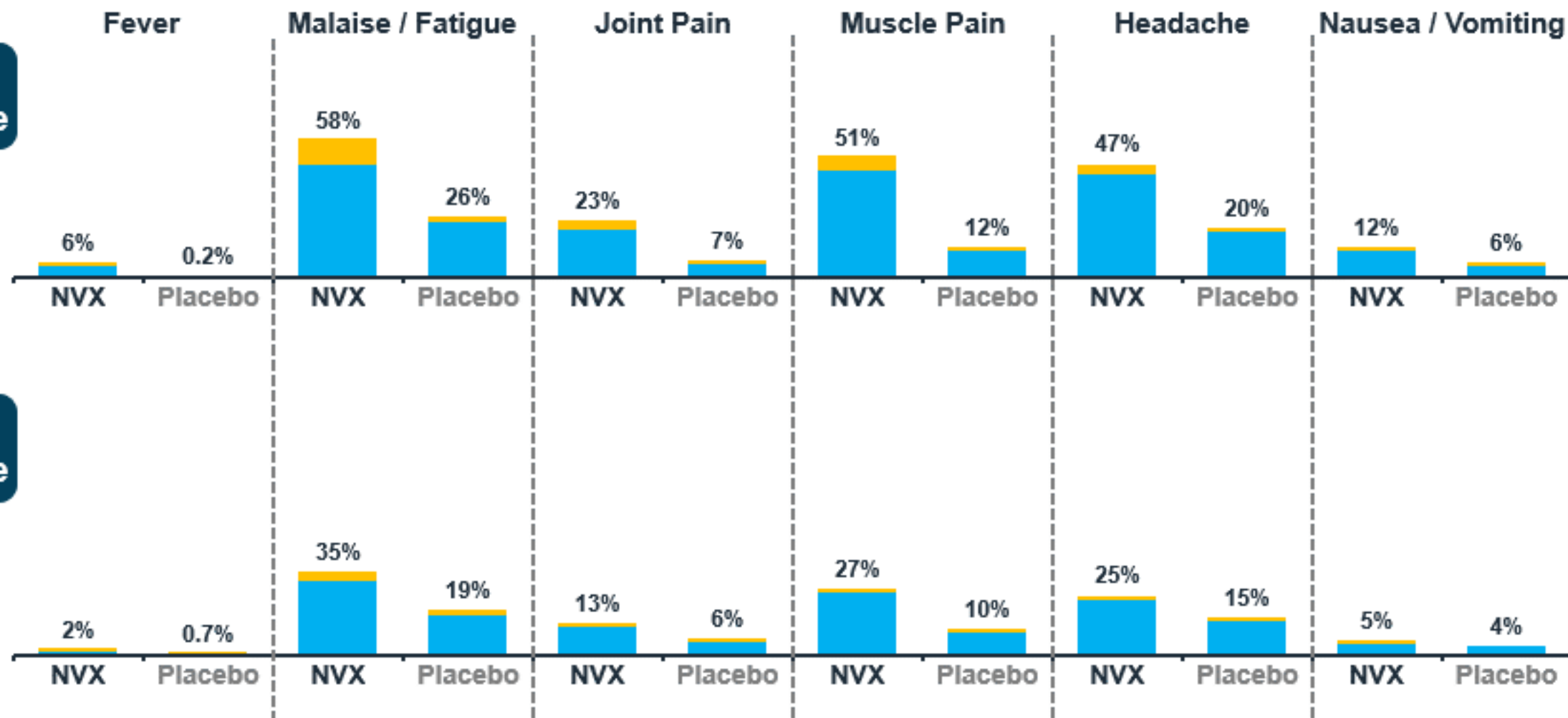
Includes events reported Day 0 to Day 6 post-vaccination; Grades based on FDA guidance

Study 301 (US/MX)

Dose 2 Systemic Events: Most Mild to Moderate, Resolved 1-2 Days

18 - 64
Years of Age

Grade 3+
Grade 1-2



Includes events reported Day 0 to Day 6 post-vaccination; Grades based on FDA guidance

Study 301 (US/MX)



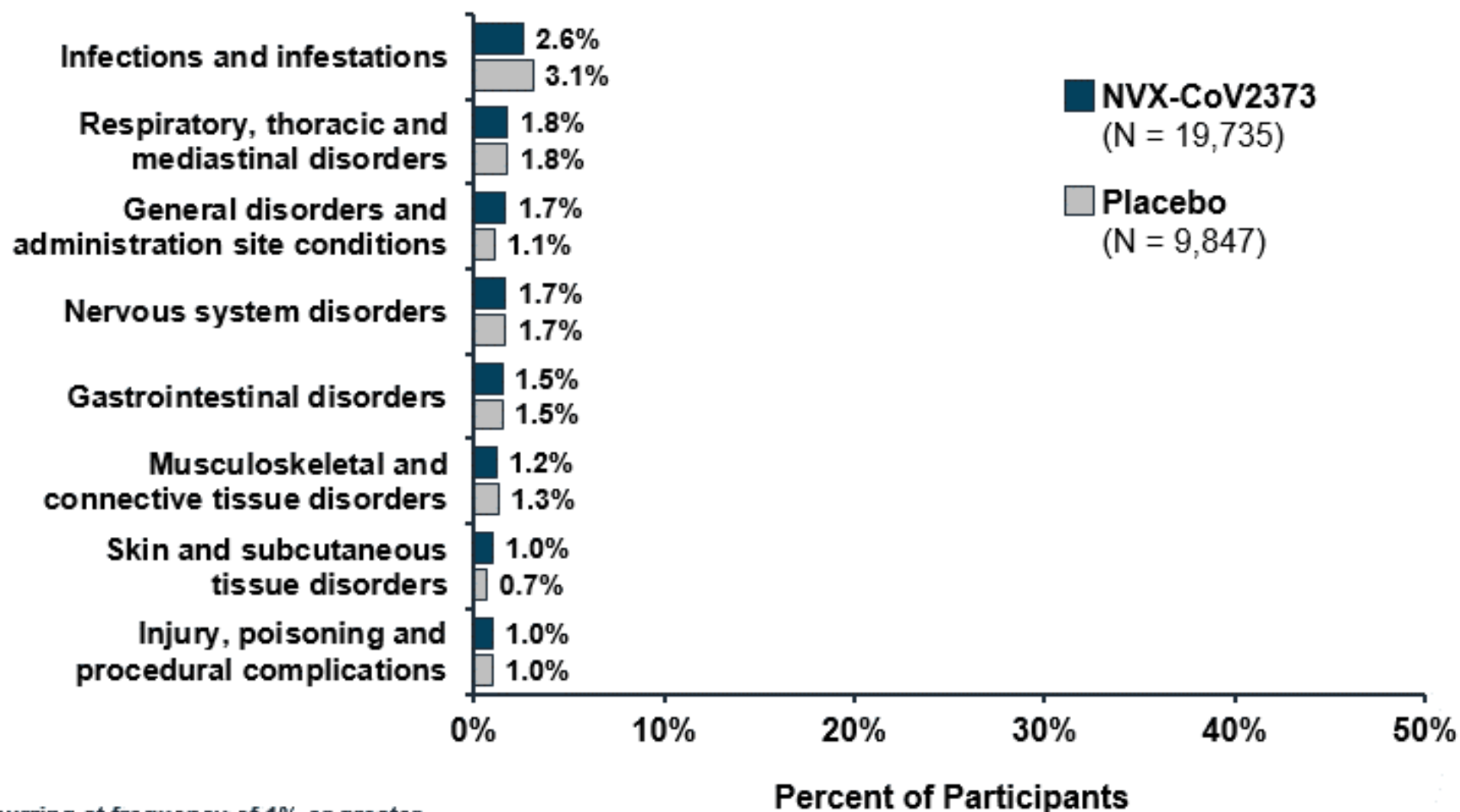
**Study 301 (US/MX):
Unsolicited Adverse Events**

Unsolicited AEs Comparable Between Groups

	Pre-Crossover		Post-Crossover	
	NVX-CoV2373 (N = 19,735)	Placebo (N = 9,847)	NVX-CoV2373 (N = 6,416)	Placebo (N = 15,298)
Any unsolicited AE (non-serious)	11.6%	11.2%	8.1%	5.6%
Severe AE (non-serious)	0.6%	0.4%	0.3%	0.1%
Medically-Attended AE (MAAE)	5.8%	5.7%	4.7%	4.0%
Potential Immune-Mediated Medical Condition (PIMMC)	0.2%	0.2%	0.2%	< 0.1%
Serious AE (SAE)	1.0%	1.1%	1.4%	1.2%
Death	< 0.1%	< 0.1%	< 0.1%	< 0.1%

Rate of AEs Similar and Low in Frequency Through Day 49

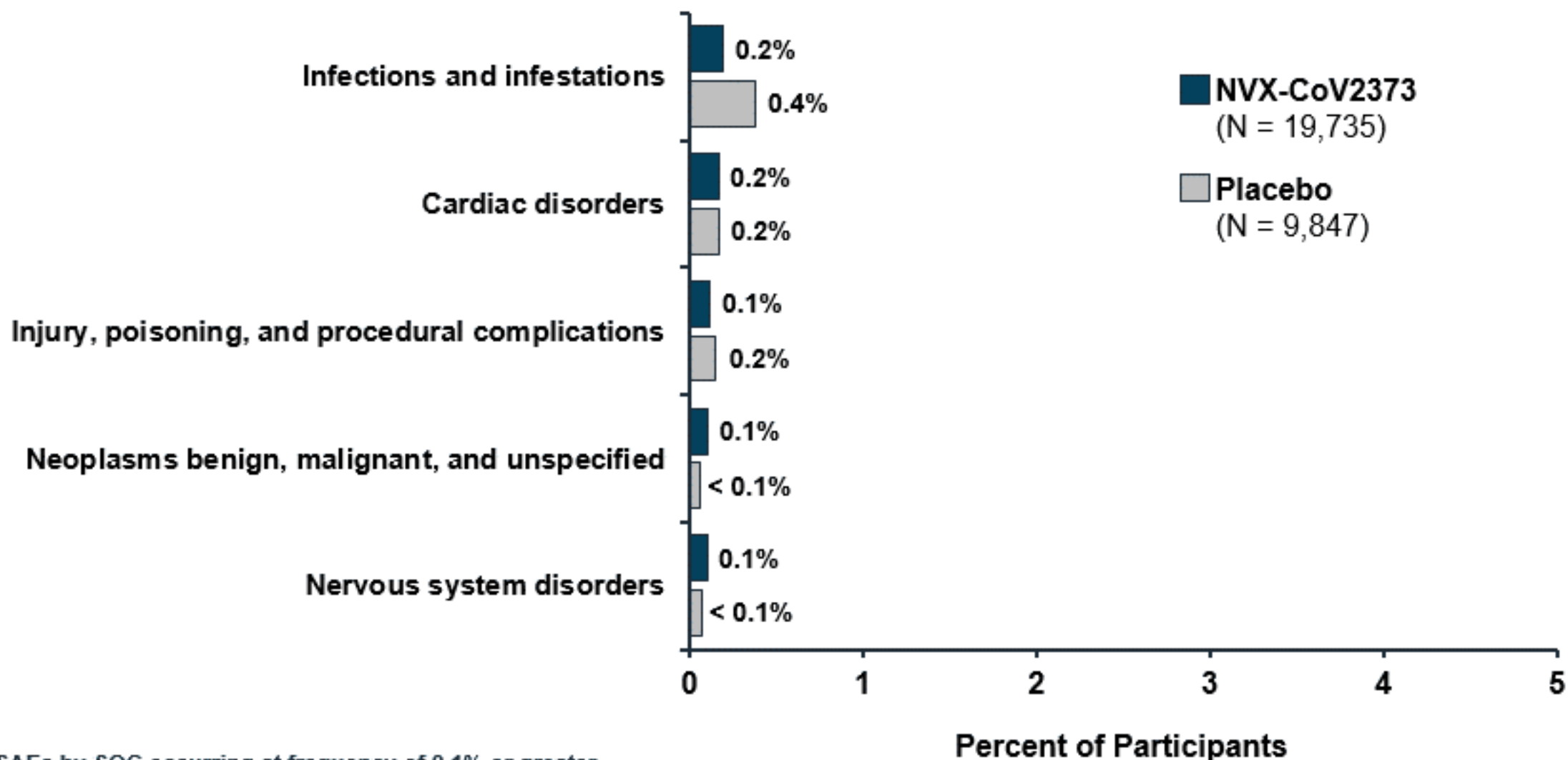
Day 0 – Day 49 (28 Days Post Dose 2)



Low Frequency of PIMMC, No Pattern Suggesting Association With Vaccination

Potential Immune-Mediated Medical Condition (PIMMC)	Pre-Crossover				Post-Crossover			
	NVX-CoV2373 (N = 19,735)		Placebo (N = 9,847)		NVX-CoV2373 (N = 6,416)		Placebo (N = 15,298)	
	n	%	n	%	n	%	n	%
Total	35	0.2%	19	0.2%	11	0.2%	15	< 0.1%
Neuropathy peripheral	3	< 0.1%	3	< 0.1%	0	0%	1	< 0.1%
Seizure	3	< 0.1%	2	< 0.1%	1	< 0.1%	1	< 0.1%
Bell's palsy	3	< 0.1%	1	< 0.1%	1	< 0.1%	2	< 0.1%
Uveitis	2	< 0.1%	2	< 0.1%	0	0%	0	0%
Rheumatoid arthritis	2	< 0.1%	1	< 0.1%	2	< 0.1%	1	< 0.1%
Thrombocytopenia	2	< 0.1%	1	< 0.1%	0	0%	2	< 0.1%
Basedow's disease	2	< 0.1%	0	0%	0	0%	0	0%
Ankylosing spondylitis	1	< 0.1%	0	0%	0	0%	2	< 0.1%

SAEs Occurred Infrequently, Similar Rates Across Treatment Arms



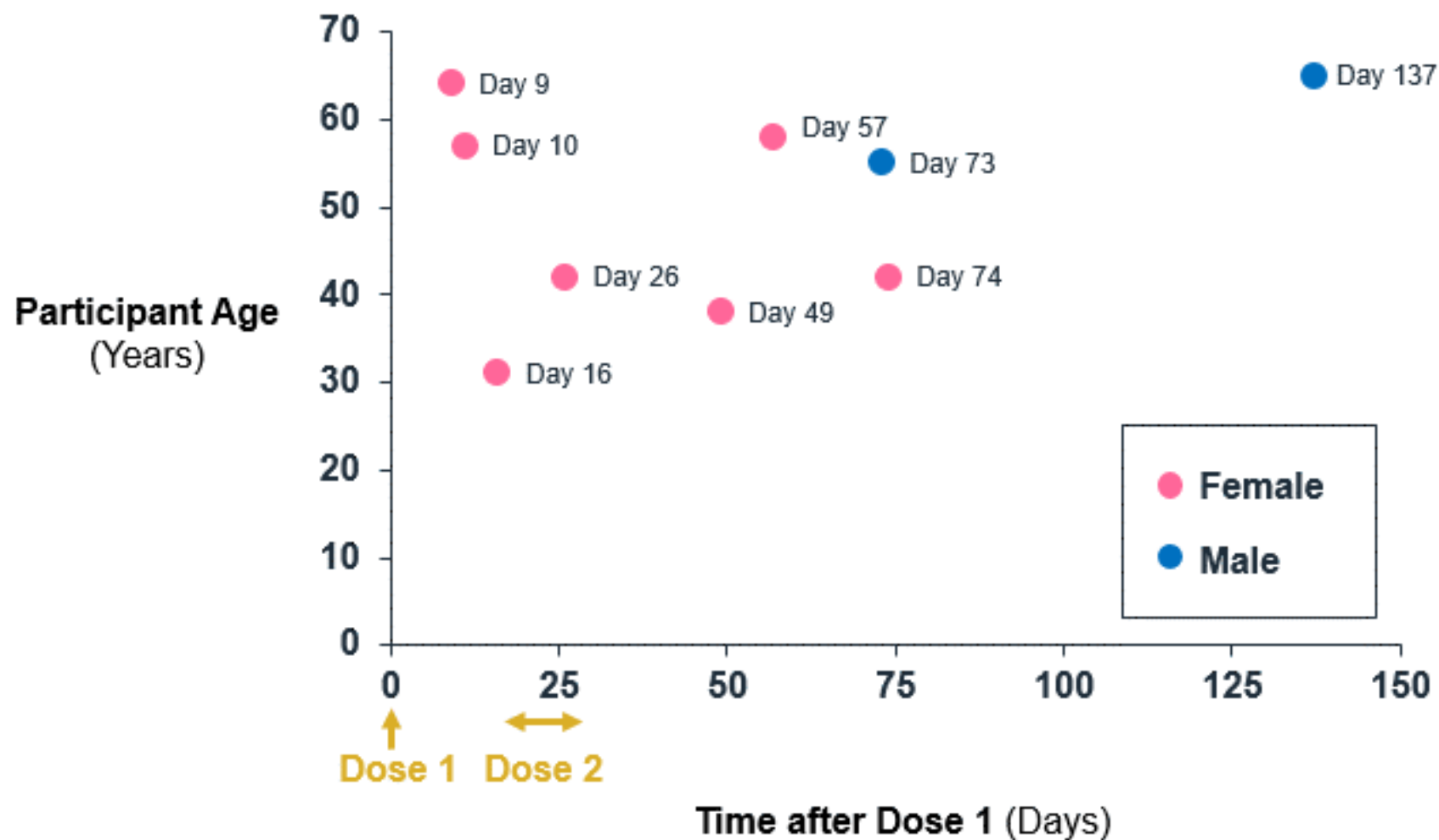


Cholecystitis

Cholecystitis: Weight of Evidence Does Not Suggest Causal Link

- **Cholecystitis / acute cholecystitis events (Study 301)**
 - NVX-CoV2373: 9 SAEs (0.05%) 0.16 / 100 PY
 - Placebo: 1 SAE (0.01%) 0.04 / 100 PY
 - Background rate¹ = 0.12 – 0.35 / 100 PY
- 1 case in Study 302; no cases in other Studies 501 and 101
- All events occurred in those with known risk factors for cholecystitis
- All participants had gallstones at time of event onset
- No additional findings from multiple SMQ analyses
- No clustering or temporal relation to treatment
- No post-authorization reports of cholecystitis

Cholecystitis Time to Onset





Myocarditis/Pericarditis

Myocarditis/Pericarditis Balanced During Placebo-Controlled Phase

- Placebo-controlled phase: NVX-CoV2373: 0.007% (2 cases); PBO: 0.005% (1 case)

Study	Treatment	Age	Sex	Time to onset	Dose	Comments
301	Placebo	31	F	72 Days	2 nd	Resolved without sequelae
301	NVX-CoV2373	67	M	28 Days	1 st	Severe COVID-19
302	NVX-CoV2373	19	M	3 Days	2 nd	Resolved without sequelae

Post-Crossover: Myocarditis/Pericarditis Occurred Within Expected Background Rates

- Post-crossover: Observed 3 cases/14,513 PY; expected background 1.6 – 4.6 cases¹

Study	Treatment	Age	Sex	Time to onset	Dose	Comments
301	NVX-CoV2373	16	M	2 Days	2 nd	Viral illness, resolved without sequelae
301	NVX-CoV2373	20	M	10 Days	1 st	Strep throat (ASO +), lost to follow up
302	NVX-CoV2373	60	F	8 Days	1 st	Respiratory tract infection, resolved without sequelae

Post-Authorization Myocarditis/Pericarditis

- 744,000 doses administered worldwide as of April 30, 2022
- Spontaneous reports from passive surveillance often have limited information
- 35 spontaneous reports of potential myocarditis or pericarditis
 - None met Brighton Collaboration definitive case definition
 - 1 probable myocarditis (47-year-old male, unknown time to onset)
 - 10 probable pericarditis
 - 7 males, 3 females; median age 42 years; 2-14 days time-to-onset from vaccination
 - 1 of 10 probable pericarditis cases with history of mRNA/pericarditis
- All probable cases originate from Australia (17% of total administration)

Ongoing Myocarditis/Pericarditis Surveillance

- Myocarditis/Pericarditis: Important Potential Risk
 - Careful monitoring post-authorization
- Targeted follow-up questionnaires
 - Brighton Collaboration case definition
- Monthly Summary Safety Reports (SSRs) submitted to Health Authorities
- Post-authorization safety studies

Clinical Development: Important Events of Interest

- No cases of anaphylactic reactions
- No cases of Thrombosis with Thrombocytopenia (TTS)
- 1 case of neuropathy meets Brighton Collaboration case definition criteria Guillain-Barré Syndrome (GBS) (*Study 302*)



Pregnancy

Pregnancy was an exclusion criterion

Pregnancy Outcomes for Women Vaccinated with NVX-CoV2373 Across Clinical Program

	Total NVX-CoV2373 (N = 147)	Time of Vaccination in Relation to Last Menstrual Period			
		Before (N = 105)	0-30 days after (N = 22)	> 30 days after (N = 9)	Unknown (N = 11)
Pregnancy outcome	136	99	19	8	10
Ongoing	56	51	1	3	1
Live birth	41	24	12	3	2
Miscarriage	25	18	4	1	2
Voluntary termination	13	6	2	1	4
Ectopic pregnancy	1	0	0	0	1
Stillbirth	0	0	0	0	0
Unknown	11	6	3	1	1

- Data do not indicate potential risk for mother or fetus



Vaccine Safety Will Be Monitored Following EUA

Plans and strategies to address potential safety concerns

Post-Authorization Pharmacovigilance

- Continue to investigate potential risks
- Supplement routine monitoring
 - Monthly Summary Safety Reports
 - Targeted follow-up questionnaires
 - Qualitative and quantitative reviews for signal detection

Planned Post-Authorization Studies

Study 401	Study 402	Study 403	Study 404	Study 405
Effectiveness	Safety	Effectiveness	Safety	Pregnancy
Against severe COVID-19 in Europe using COVIDRIVE	Using UK Clinical Practice Research Database	Using US Claims and/or Electronic Health Database	Using US Claims and/or Electronic Health Database	COVID-19 Vaccines International Pregnancy Exposure Registry

NVX-CoV2373 Safety Supports Positive Benefit Risk and Favorable Reactogenicity Profile

- **Placebo-Controlled, Pre-Crossover**
 - Well-characterized, exposure in > 30,000 recipients overall
 - Local and systemic events generally Grade 1-2, resolved in 1-2 days
 - Low rates of fever
 - Most AEs mild to moderate severity
- **Long-term follow-up, Post-Crossover (> 40,000 recipients)**
 - SAE rates low, comparable to placebo
 - Continue to monitor for potential risks



Clinical Perspective

Gregory A. Poland, MD, FIDSA, MACP, FRCP

Mary Lowell Leary Emeritus Professor of Medicine
Distinguished Investigator of the Mayo Clinic
Director, Mayo Vaccine Research Group

Our Continuing Challenge

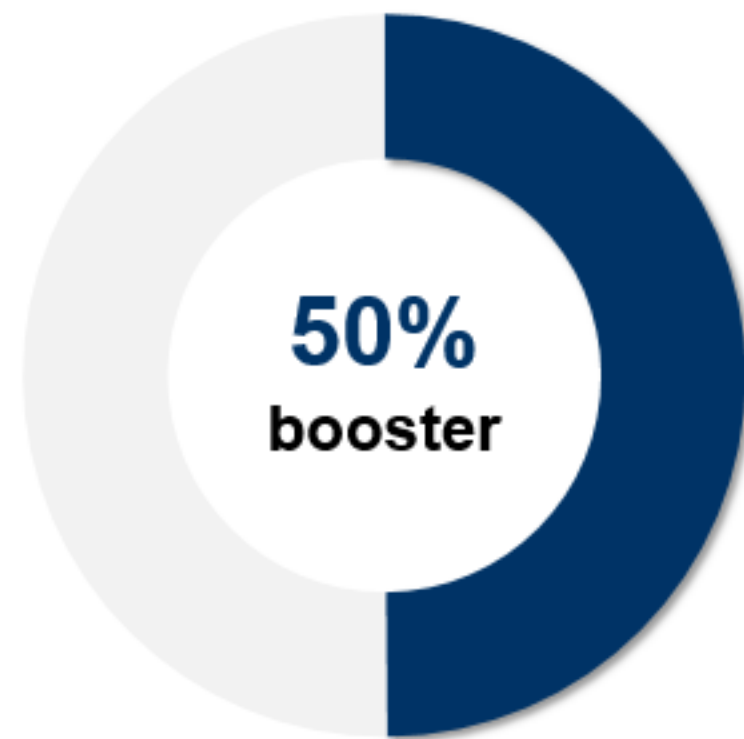
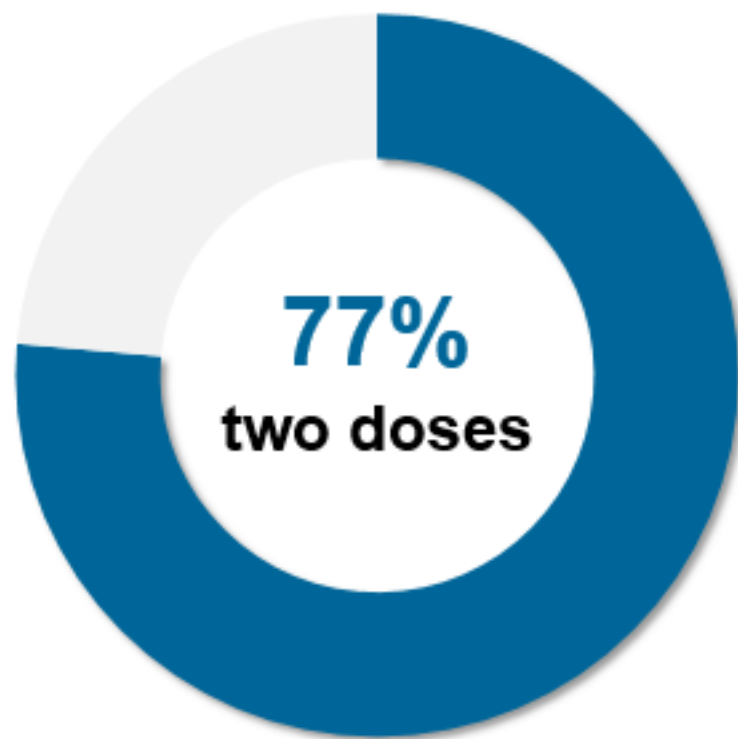
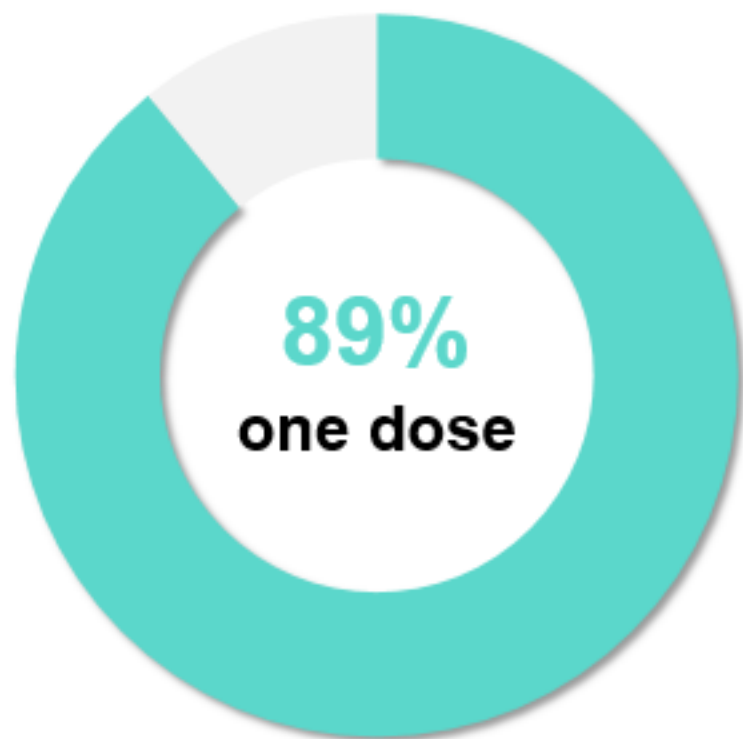
- SARS-CoV-2 challenges and re-challenges us
- Millions of Americans remain unvaccinated
- COVID-19 has long-term, multi-dimensional impacts
- Need for vaccines with different MoAs

Need Remains for Traditional Vaccine Option

73%

**of Americans want COVID-19 vaccines
from more traditional method**

Percentage of Vaccinated Americans ≥ 18 Years of Age



Benefit of Novavax Vaccine

- Immune-enhancing adjuvant = high efficacy, less reactogenicity
- Most AEs mild-to-moderate, resolved in 1 – 2 days
- Strong efficacy and safety in US/MX against numerous variants¹
- Similar efficacy and safety seen in published UK study^{2,3}

1. Dunkle et al., NEJM, 2021

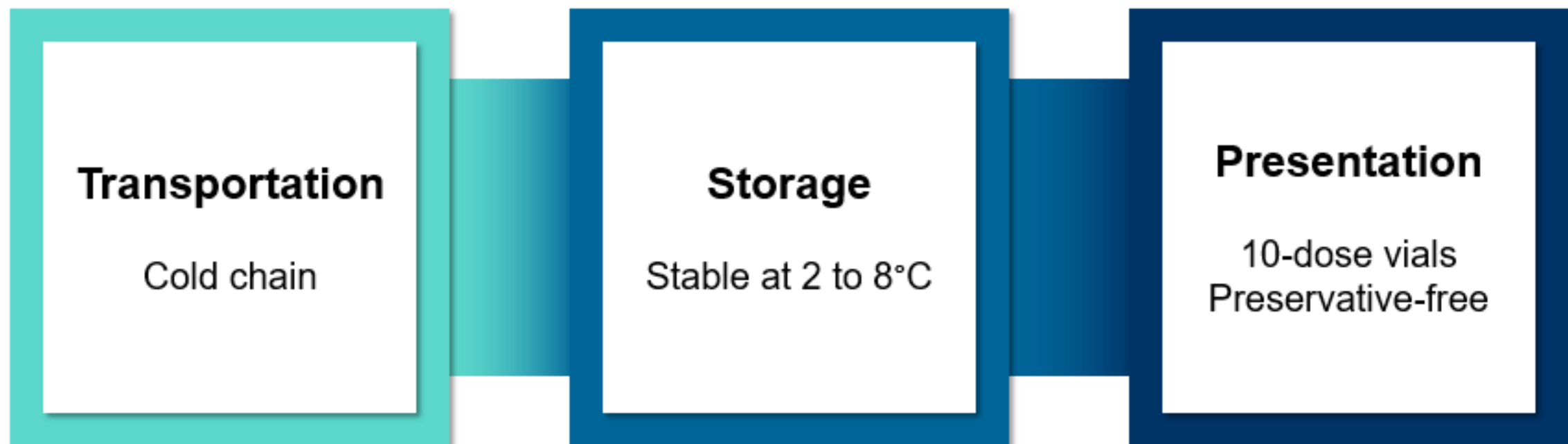
2. Heath et al., NEJM, 2021

3. Toback et al., The Lancet Res Med, 2021

Signals Broad Cross-Protection

- Robust antibody responses against multiple strains
- Clinical data from Phase 3 trials
- Important to have vaccine platform choices in a constantly evolving pandemic

NVX-CoV2373 Offers Increased Access and Ease of Storage



Immediate Health Impact on Unvaccinated Individuals

4x

greater risk of infection¹

23x

greater risk of hospitalization¹



20x

greater risk of dying¹

~ 300

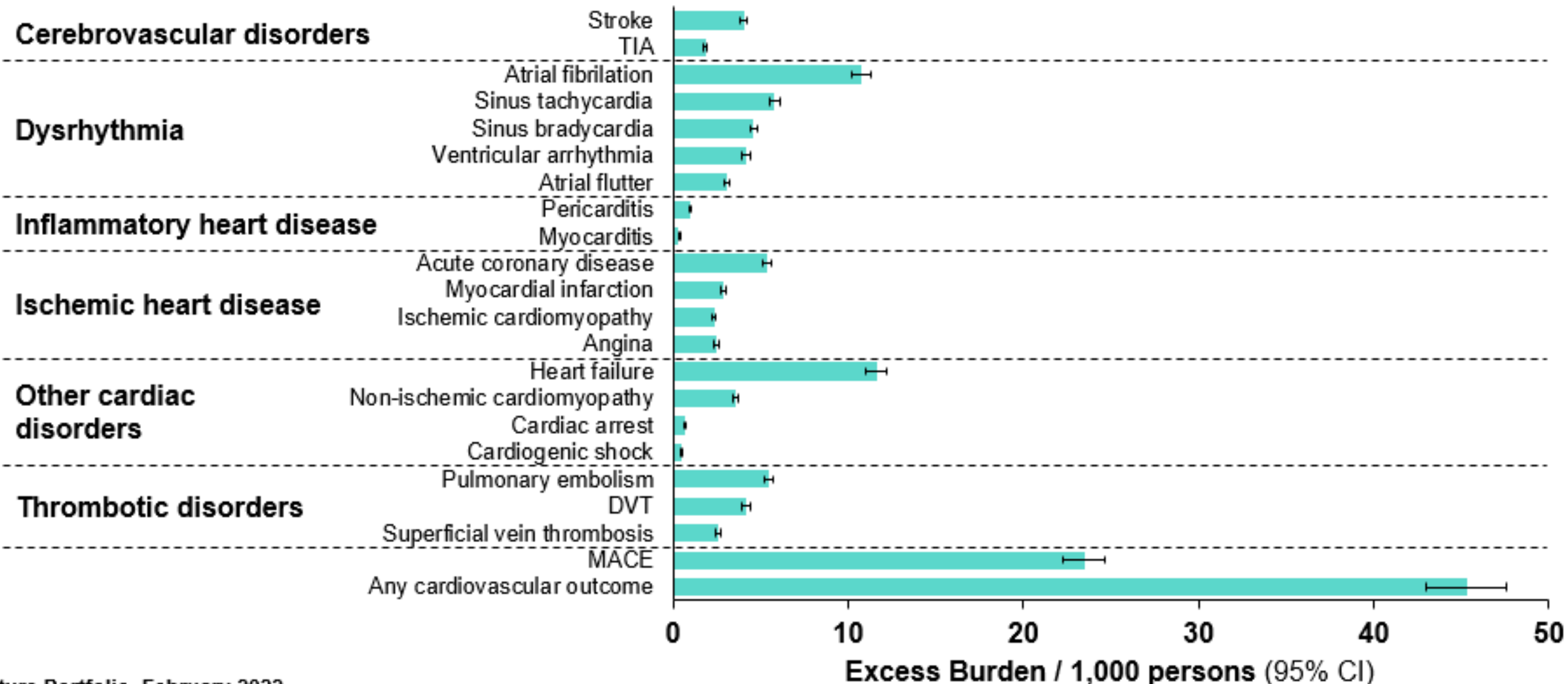
people die daily from
COVID-19 in US²

1. Danza et. al. 2022

2. CDC, May 31, 2022

Long-Term Impact on Individual & Public Health

Higher Risk of 20 Cardiovascular Conditions, With or Without Hospitalization



Mental Health Impact Following COVID-19 and Hospitalization

- ~ 60% more likely to experience anxiety and depression
- 46% more likely to have suicidal thoughts
- 34% more likely to develop opioid use disorders

NVX-CoV2373 Offers Benefits to Stakeholders

Patients / Providers

- **Efficacy**
- **Safety**
- **Tolerability**

Pharmacies / Distributors

- **Logistics of distribution, storage, and administration**

Employers

- **Encourage vaccination**

Policymakers

- **Ease of access**
- **Easy to explain to public**
- **Choice people want**

Our Opportunity Today

- Must remain proactive and vigilant in fight against COVID-19
- Authorization important for US and global health
- Goal: Right vaccine, for the right person, for the right purpose, at the right time
- More vaccine options fulfill goal of individualized care

Conclusion

Filip Dubovsky, MD, MPH, FAAP

Executive Vice President & Chief Medical Officer
Novavax, Inc.



Results from NVX-CoV2373 Development Program Support EUA in Adults 18 Years and Older

- Differentiated, well-understood recombinant protein platform
- 90% vaccine efficacy in Phase 3 Study 301 (US/MX)
- Favorable reactogenicity profile and safety data supporting a positive benefit-risk assessment
- Promises to be a useful tool to address the ongoing pandemic

Emergency Use Authorization (EUA) Application for NVX-CoV2373

Novavax, Inc.

Vaccines and Related Biological Products Advisory Committee

June 7, 2022