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Novavax Vaccine Regimens Addressing COVID-19

Novavax, Inc.

Vaccines and Related Biological Products Advisory Committee

January 26, 2023

Novavax Vaccine Regimens Addressing COVID-19

Filip Dubovsky, MD, MPH

Executive Vice President & Chief Medical Officer

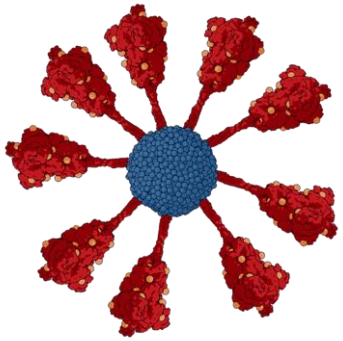
Novavax, Inc.

NVX-CoV2373 Overview

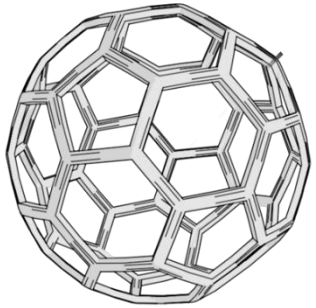
- Novavax prototype strain vaccine induces high levels of cross-reactive antibodies for forward-drift variants, including Omicron BA.5
  - Responses seen with both homologous and heterologous boosting
  - Prototype, omicron variant, and bivalent vaccine all perform comparably
- Prototype strain vaccine presents conserved neutralizing epitopes, resulting in cross-protective responses
- Lower neutralizing responses observed for BQ.1.1 and XBB.1 variants due to mutations in conserved epitopes
  - Antibody titers similar to those induced by bivalent mRNA vaccines
  - Titers likely associated with continued protection against severe outcomes
- Vaccine composition update expected to restore cross-reactivity for future forward drift variants

Novavax Vaccine Platform
Recombinant Protein Plus Matrix-M™

Recombinant protein particle



Matrix-M adjuvant



Novavax vaccine platform

Independent USG / NIH Analysis Correlates Anti-Spike IgG with Protection

- Analysis based on US/Mexico Phase 3 Study (90% efficacy)
- Majority (~80%) of cases attributed to variants of interest/concern
- Anti-spike IgG and pseudovirus neutralization titers correlated with protection against PCR-confirmed symptomatic SARS-CoV-2 infection
  - IgG antibody response correlated more strongly

IgG level (BAU/ml)	Estimate of VE (95% CI)
100	**65%** (23, 91)
1,000	**88%** (78, 94)
6,934	**95%** (88, 98)

Neutralizing Antibody Titer (IU_{50}/mL)	Estimate of VE (95% CI)
50	**76%** (50, 93)
100	**82%** (66, 93)
1,000	**93%** (85, 97)

Accepted for publication, (Fong et al., 2022) DOI: 10.1101/2022.06.22.22276362v1

Homologous Boosting

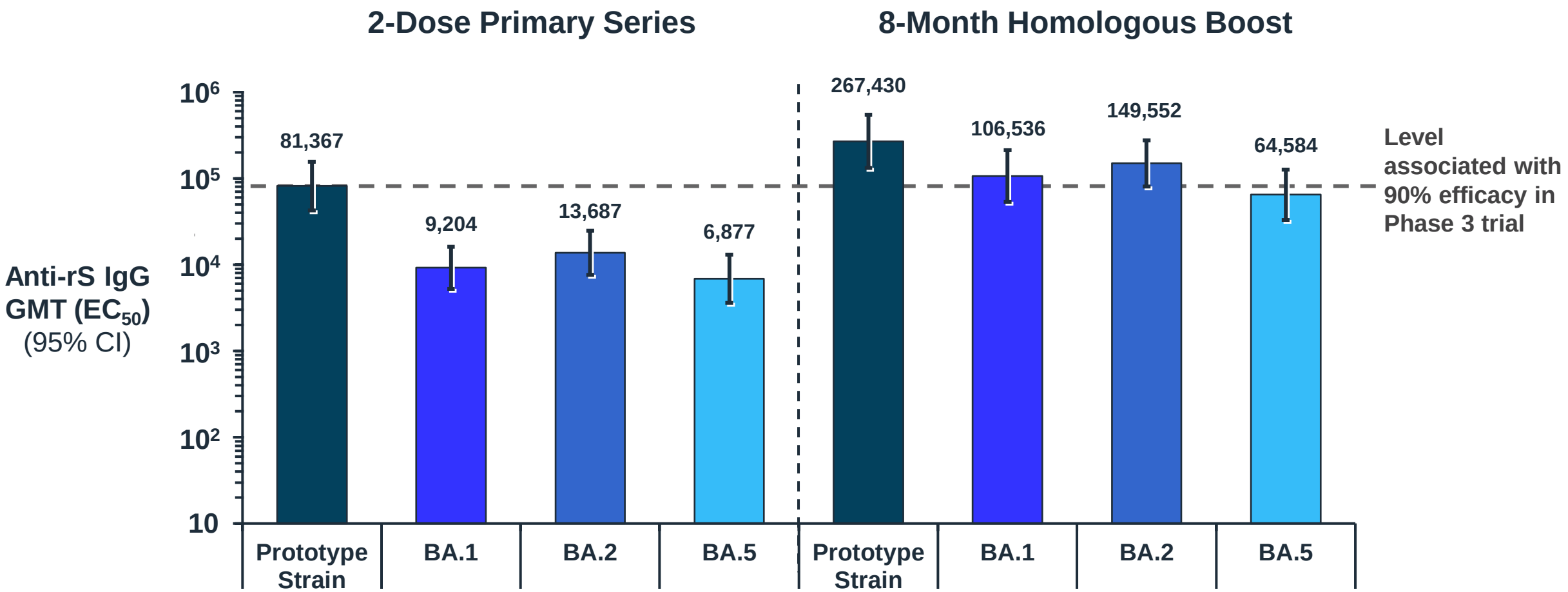
US / Mexico Adult Phase 3 Study

Participants received 2-dose primary series

Boosted 8 – 11 months after primary series

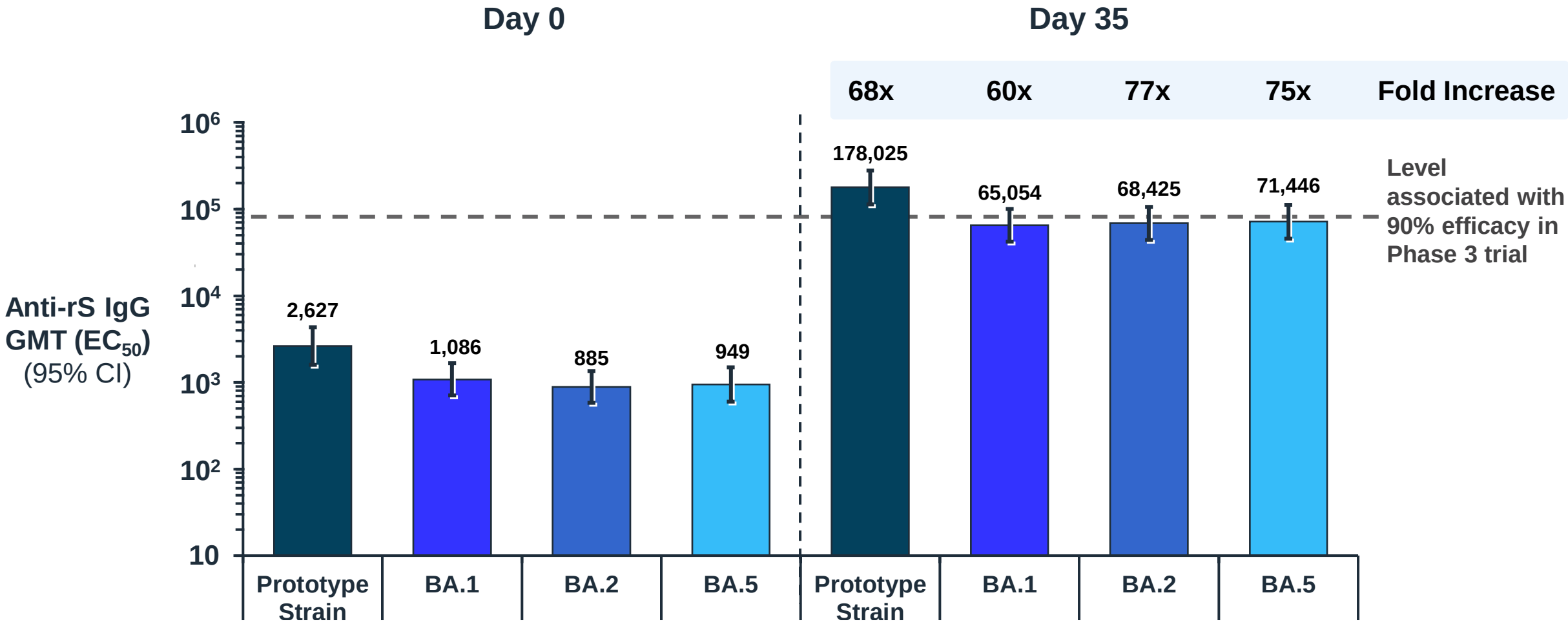
Robust IgG Titers Against Omicron Sub-variants Achieved with Boosting using Prototype Strain Vaccine

Median age 51 – 53 years; participants without evidence of infection



Robust IgG Titers Against Omicron Sub-variants After Primary Series in COVID-19 Infected Individuals

Median age 61 years (N = 30)



Homologous Boosting

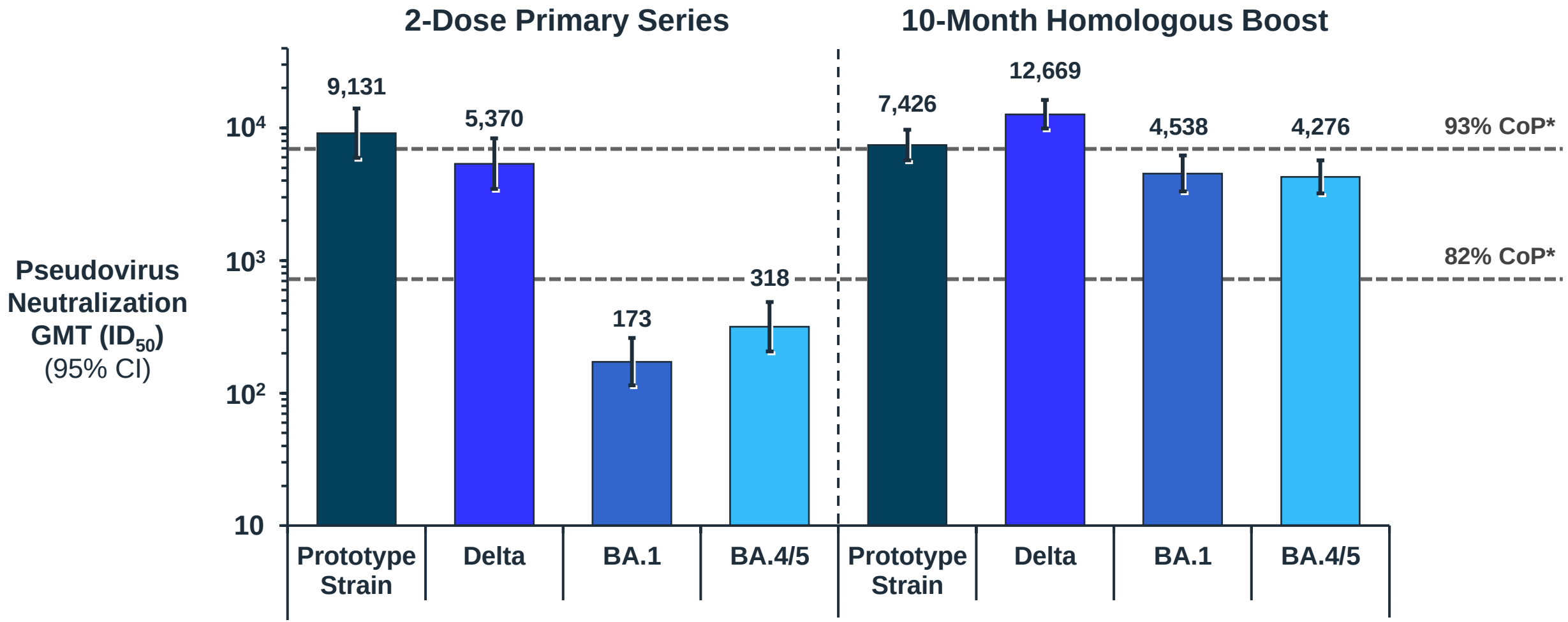
US Adolescent Phase 3 Study

Participants received 2-dose primary series

Boosted ~10 months after primary series

Robust Neutralization Responses in Adolescents After Boosting

12 – 17 years (N = 45)

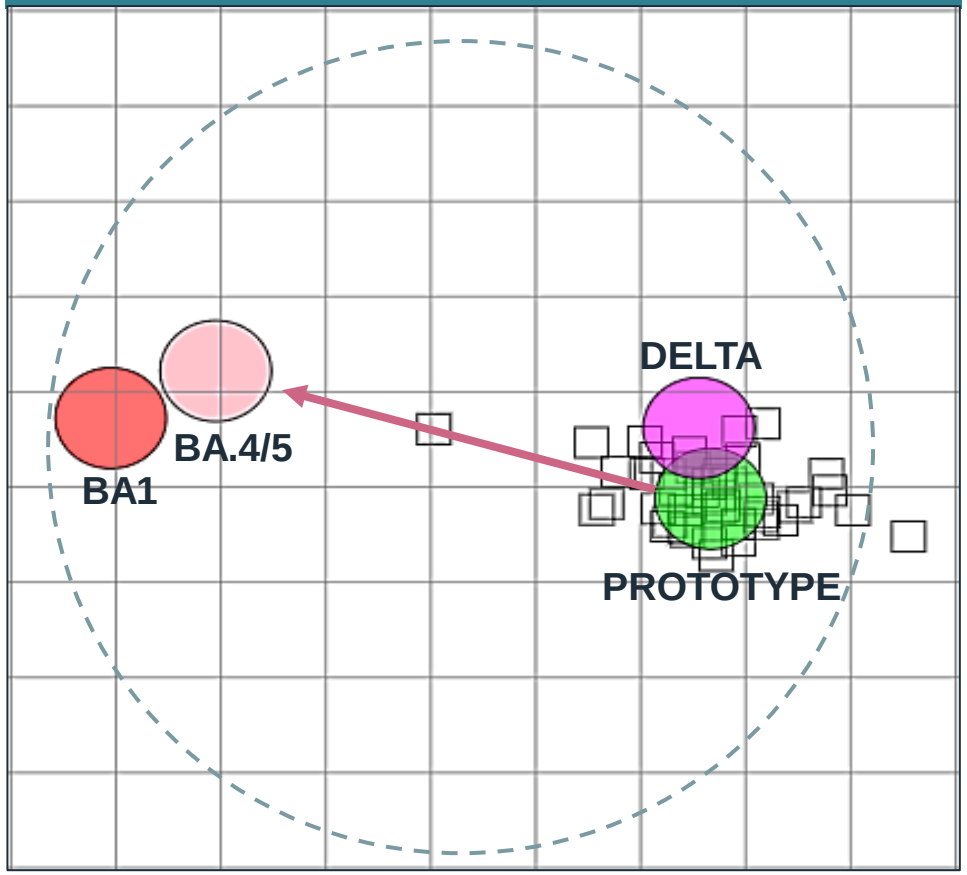


Validated assay conducted by Monogram includes randomly selected cohort

*Correlates of Protection inferred from Fong et al., 2022

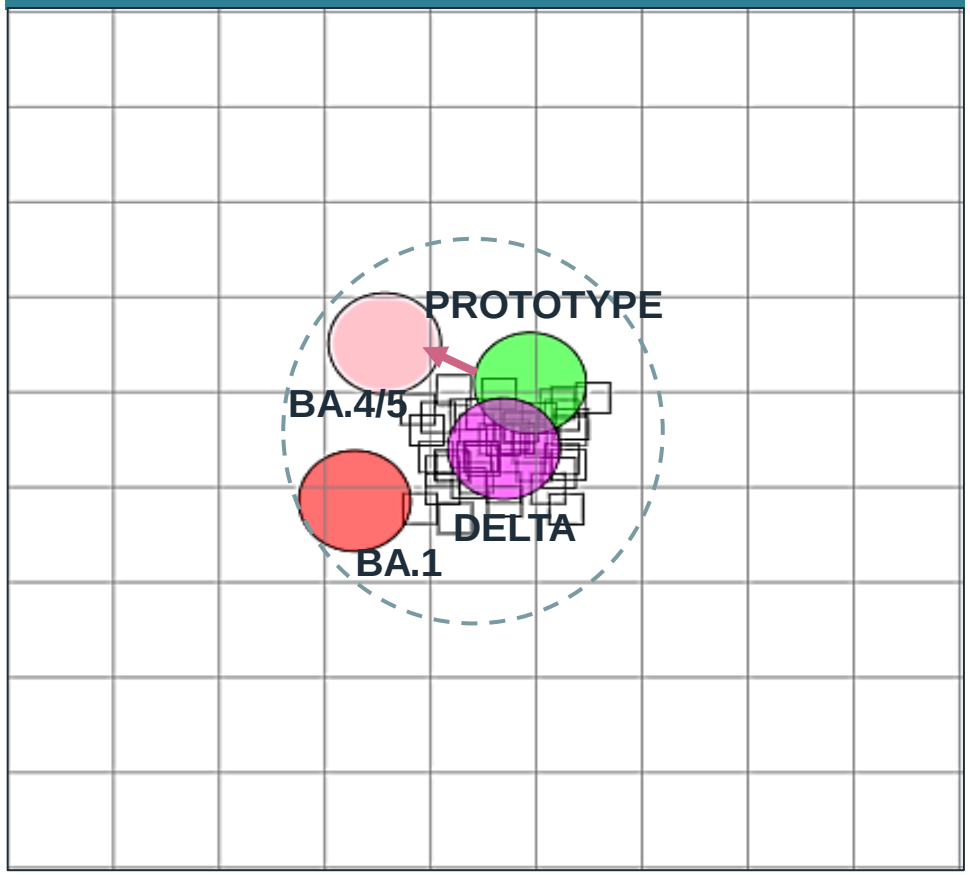
Antigenic Cartography of Pseudovirus Neutralization Responses for Adolescents

Primary : 2 Doses



Fold-Difference: Prototype → BA.4/5 = 28.8

Booster : 3 Doses



Fold-Difference: Prototype → BA.4/5 = 1.74

Note: each large square on the grid represents a 2-fold difference in neutralizing responses

Heterologous Boost

Study 311 (Australia)

Strain Change Study

Study Design: Boost with Either Prototype, BA.1, or Bivalent Vaccine

- Participants previously received 2 or 3 doses of mRNA vaccine
- 832 participants randomized to be boosted with different Novavax vaccines
  - Prototype strain
  - Omicron monovalent BA.1
  - Bivalent (Prototype + Omicron BA.1)
- Primary endpoint in individuals with 3 prior mRNA vaccine doses

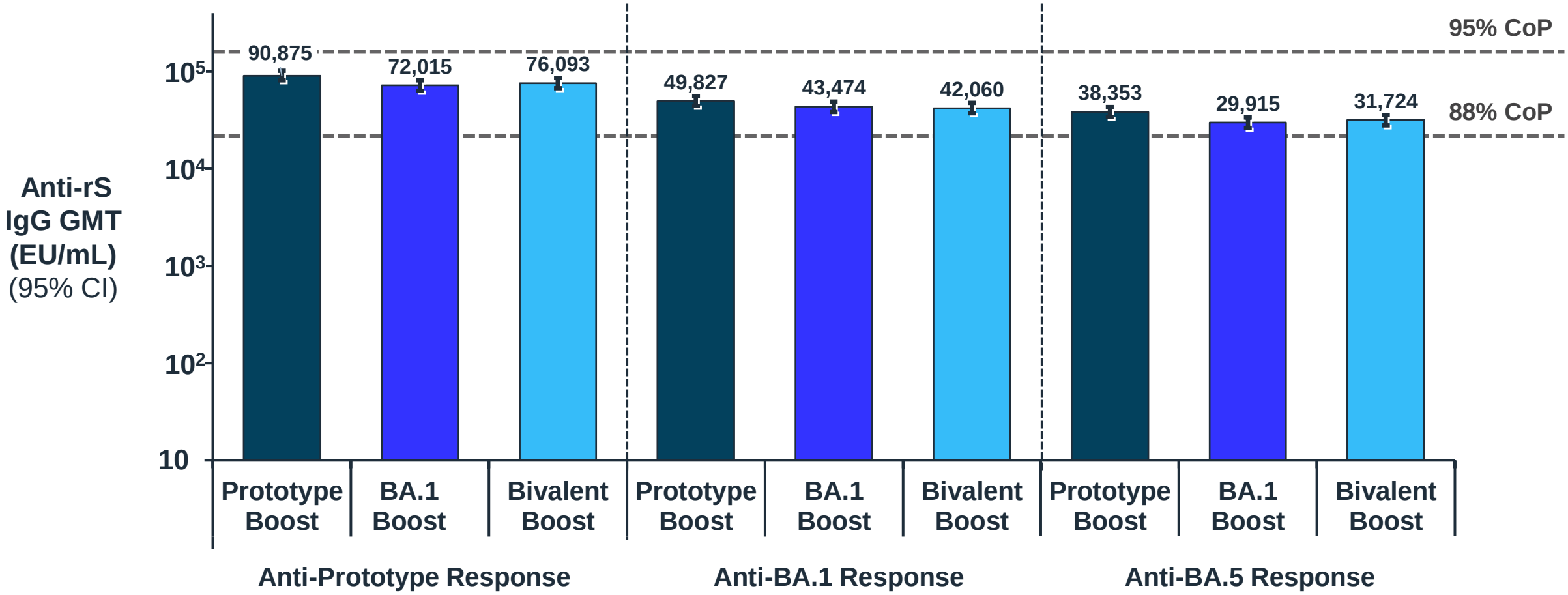
Demographics and Baseline Characteristics

Participants previously received 3 doses of mRNA vaccine

	BA.1 Vaccine (N = 258)	Prototype Strain Vaccine (N = 251)	Bivalent Vaccine (N = 240)
Age (years) – Median (range)	42 (18 – 64)	41 (18 – 64)	41 (18 – 64)
Female	54%	51%	55%
Race			
White	81%	78%	81%
Asian	14%	17%	15%
Other	3%	3%	3%
Previous Vaccine Pfizer x 3	77%	77%	73%
Previous Vaccine Pfizer x 2, Moderna	22%	21%	25%
Anti-N or PCR positive	51%	53%	51%
Median Interval to Boost (Days)	177	182	180

IgG Antibody Responses Similar at Day 14, Independent of Vaccine Formulation

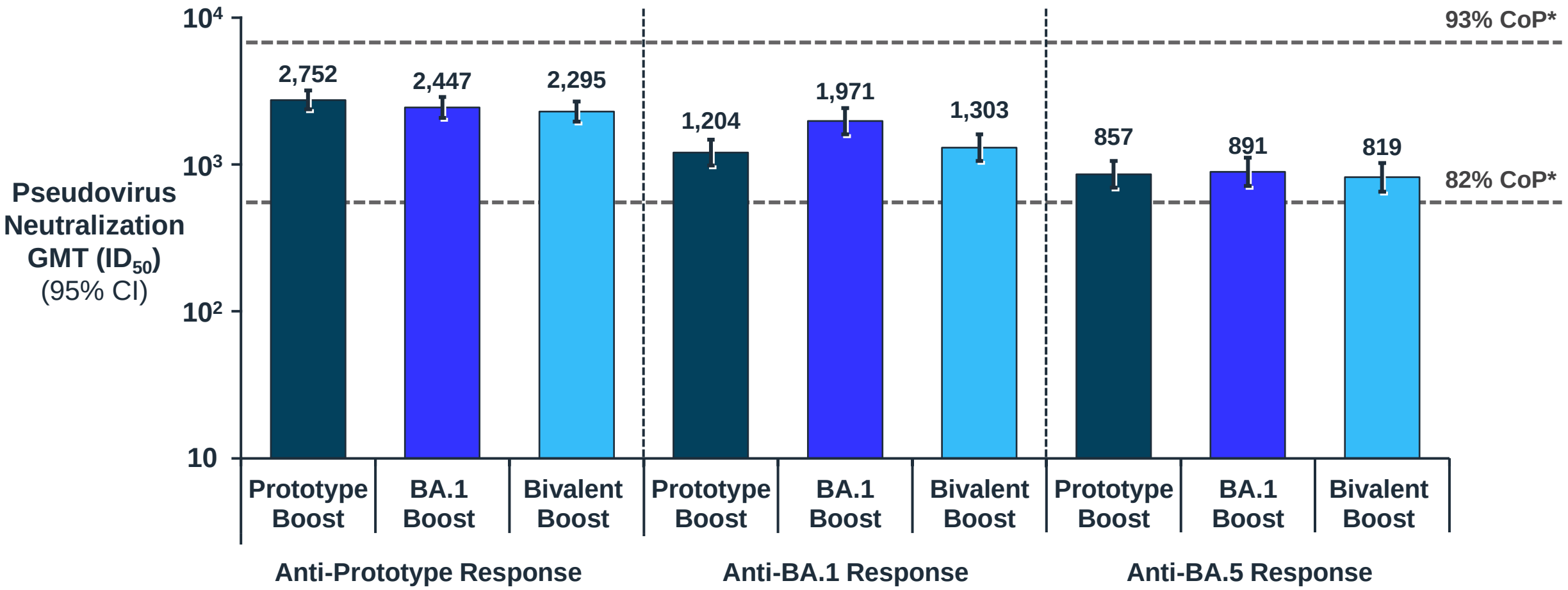
Primed with mRNA x 3 and boosted with Novavax prototype strain, BA.1, or bivalent vaccine



*Correlates of Protection inferred from Fong et al., 2022.
Validated assays performed at Novavax Immunology includes all participants

Neutralization Titers Similar at Day 28, Independent of Vaccine Formulation

Primed with mRNA x 3 and boosted with Novavax prototype strain, BA.1, or bivalent vaccine



*Correlates of Protection inferred from Fong et al., 2022.
Validated assays performed at Monogram includes all participants

Heterologous Boost

Study 307 (US)

Lot-to-Lot Consistency Study

Study Design: Lot-to-Lot Consistency

- 911 participants with no history of COVID-19 in prior 4 months
- Prior to enrollment
  - 2 or 3 doses of COVID-19 vaccine with last dose > 6 months prior
- After enrollment
  - Boosted with 1 of 3 different lots of Novavax vaccine
  - Immunologic assessment at Day 28

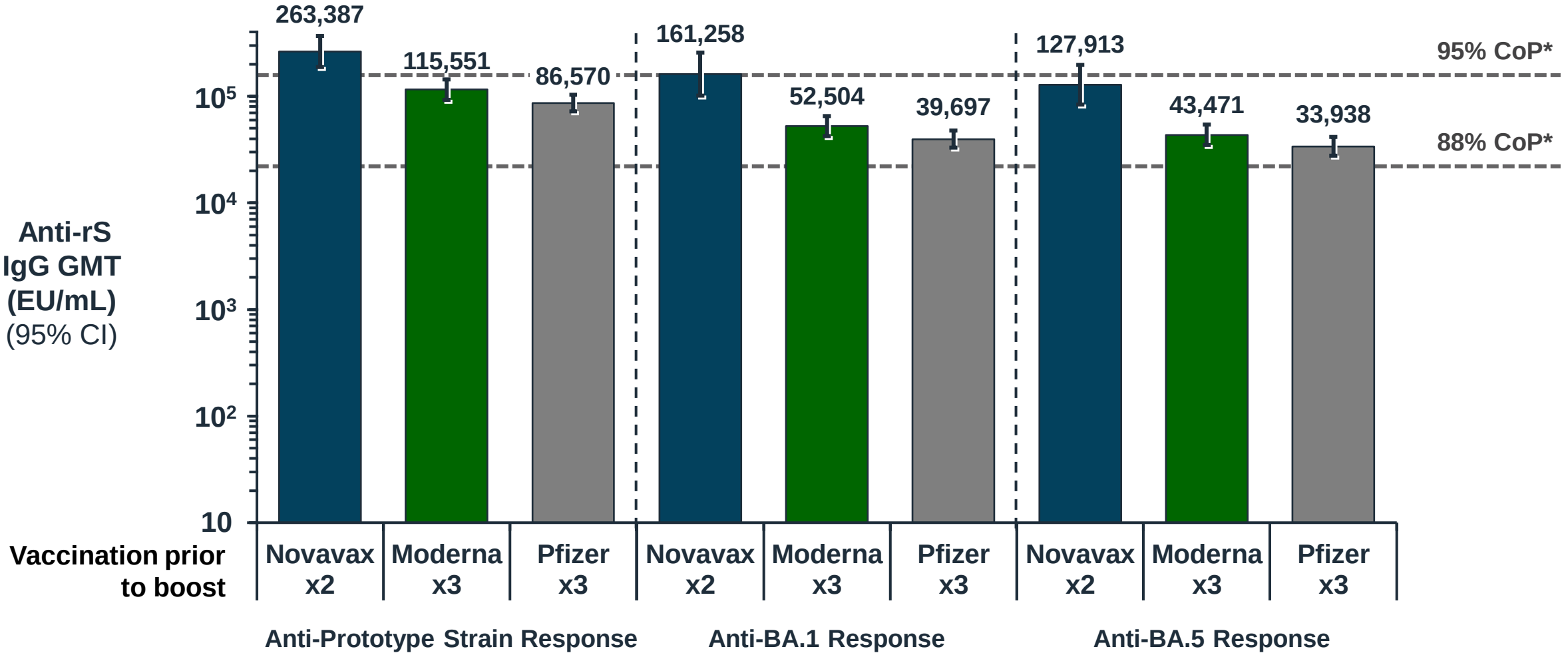
Demographics and Baseline Characteristics

	Novavax x 2 (N = 7)	Moderna x 3 (N = 59)	Pfizer x 3 (N = 59)
Age (years) – Median (range)	41 (25 – 46)	38 (19 – 49)	40 (18 – 49)
Female	43%	53%	78%
Race			
White	43%	86%	81%
Black or African American	29%	5%	10%
Asian	14%	5%	3%
Other	0%	3%	3%
Ethnicity Hispanic or Latino	0%	17%	17%
Median Interval to Boost (Weeks)	61	33	36

Includes all Novavax x 2 participants and randomly selected cohort of mRNA x 3 participants

Novavax Prototype Strain Booster Provides Robust Breadth of Immunity

All Dosing Regimens Boosted with Novavax Prototype Strain Vaccine



*Correlates of Protection inferred from Fong et al., 2022.
Validated assays performed at Novavax Immunology Lab includes all participants

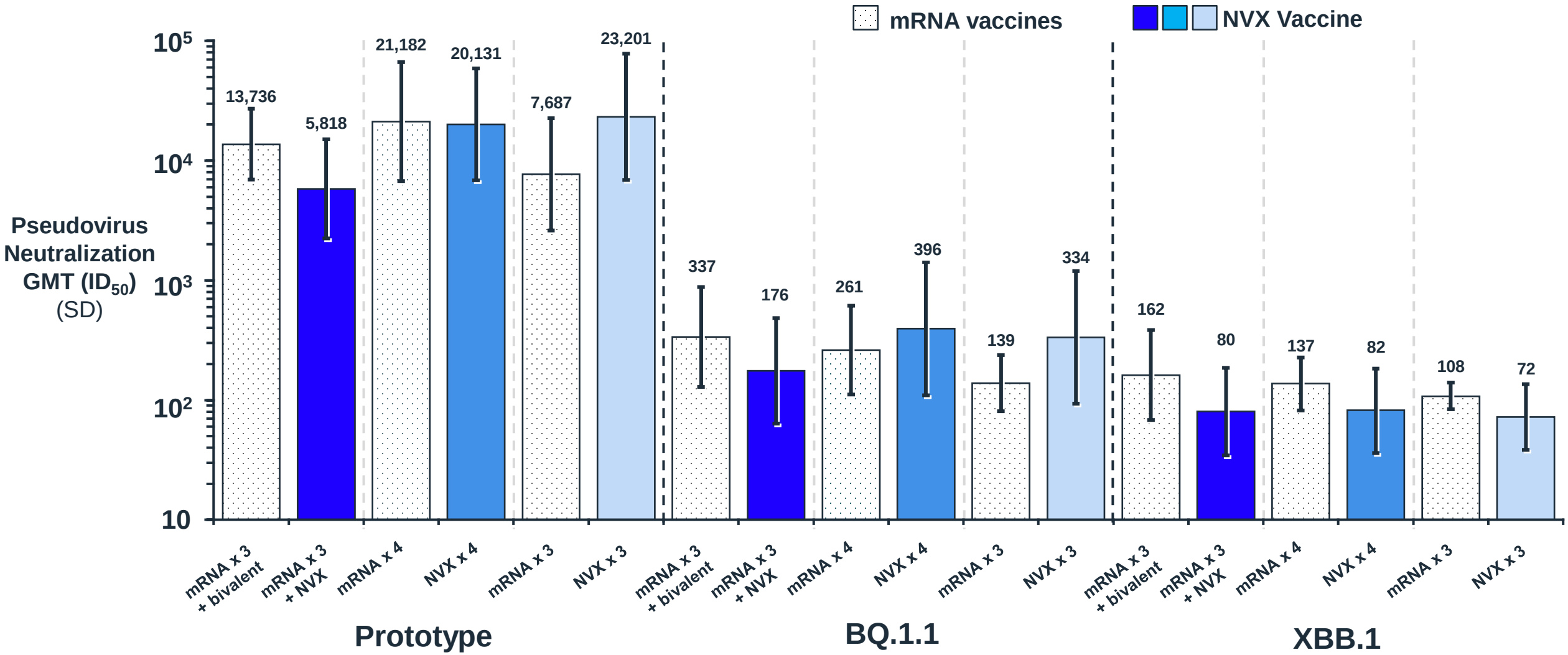
Pseudovirus Neutralization Assay for Prototype, BQ.1.1 and XBB.1

Performed at Columbia University

Dr David Ho Laboratory

Pseudovirus Neutralization Responses Observed for BQ.1.1 and XBB.1 (Seronegative Participants*)

GMT levels similar across all boosting regimens

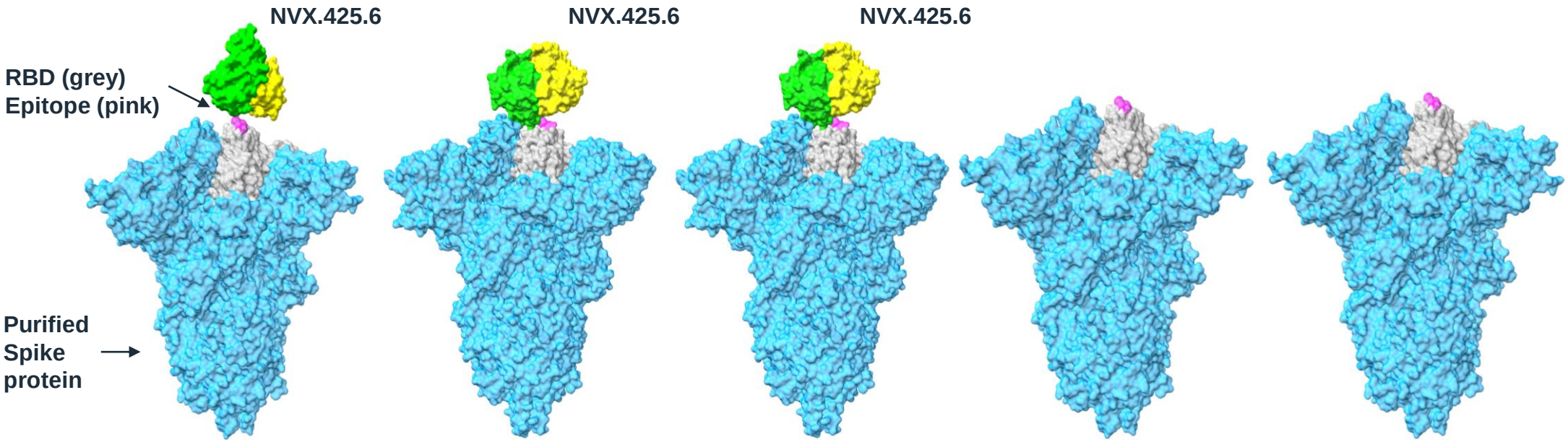


Data from Wang et al., 2022 and unpublished

*Seronegative defined as anti-N negative as per testing in Dr. Ho's lab

Structure - Function Analysis

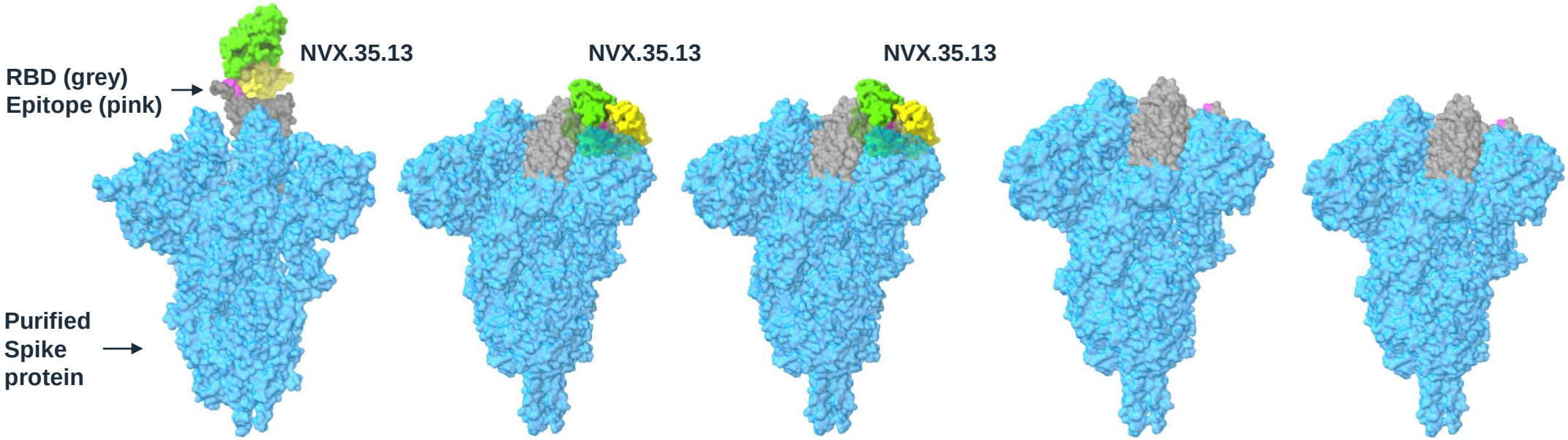
Mutations in Conserved RBD Epitope Impact Monoclonal Antibody Binding and Neutralization



NVX.425.6	Prototype Strain	BA.2	BA.5	BQ.1.1	XBB
Epitope RBD Mutations	None	None	None	K444T	K445P, G446S
Neutralization (ng/mL)	7.3	7.3	59	> 10,000	> 10,000

RBD = receptor binding domain

Mutations in Conserved RBD Epitope Impact Monoclonal Antibody Binding and Neutralization



NVX.35.13	Prototype Strain	BA.2	BA.5	BQ.1.1	XBB
Epitope RBD Mutations	None	None	None	F486V	F486S
Neutralization (ng/mL)	9.8	9.8	> 10,000	> 10,000	> 10,000

RBD = receptor binding domain

Novavax Vaccine Regimens Addressing COVID-19

- Novavax adjuvanted recombinant protein vaccine induces high levels of broadly neutralizing antibody and polyfunctional Th1-biased CD4+ response
- Conserved epitopes across variants appear to be biological basis for maintaining broad protective immune responses
- Homologous and heterologous boosting with prototype induces relevant responses to variants where conserved epitopes are maintained
- Monovalent and bivalent vaccines perform comparably
- Novavax prototype strain vaccine induces immune responses similar to available bivalent mRNA vaccines
- Vaccine composition update expected to induce protective immune responses for newly emerging forward drift variants

Novavax Future Composition and Strain Change

- Breadth of immune response against future-drift variants makes Novavax technology an appealing choice for future annual vaccination campaigns
- Boosting data indicate comparable performance to currently available vaccines
- Prepared to deliver recommended monovalent or bivalent vaccines for the 2023/24 vaccination season
- Follow influenza model
  - Strain recommendation by end of Q1
  - Recommendation should allow for antigenically-like strain
  - Approach allows for vaccine release and distribution

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