Individuals using assistive technology may not be able to fully access the information contained in this file. For assistance, please call 800-835-4709 or 240-402-8010, extension 1. CBER Consumer Affairs Branch or send an e-mail to: ocod@fda.hhs.gov and include 508 Accommodation and the title of the document in the subject line of your e-mail.

Moderna COVID-19 Vaccines Update

Moderna, Inc.

May 28, 2026

Vaccines and Related Biological Products Advisory Committee

Introduction

Darin Edwards, PhD

COVID-19 Program Leader

Moderna, Inc.

Significant Burden of COVID-19 Disease in US (CDC Data)

- 2nd leading cause of hospitalizations in adults among respiratory viruses in US (Oct 2025-May 2026, RESP-NET)[1]
  - 120,000 - 250,000 hospitalizations (Oct 2025-May 2026)[2]
  - 13,000 - 41,000 COVID-19 deaths in US adults (Oct 2025-May 2026)[2]

- 65% of adults ≥65 years hospitalized with COVID-19 had no recorded 2024-25 vaccine dose[3]

1. Centers for Disease Control and Prevention. Respiratory Virus Hospitalization Surveillance Network (RESP-NET), https://www.cdc.gov/resp-net/dashboard/index.html, 15MAY2026
2. CDC, Preliminary Estimates of COVID-19 Burden for 2025-2026; https://www.cdc.gov/covid/php/surveillance/burden-estimates.html, accessed 15MAY2026
3. ACIP meeting June 25, 2025. https://www.cdc.gov/acip/downloads/slides-2025-06-25-26/02-MacNeil-COVID-508.pdf

Moderna's COVID-19 Vaccines Licensed in US

	mRNA-1273 (SPIKEVAX)	**mRNA-1283** (mNEXSPIKE)
Antigen Encoded	▪ **Full-length spike protein**	▪ **Linked receptor binding domain and N-terminal domains**
Licensed	▪ **January 2022**	▪ **May 2025**
Indications	▪ **≥65 years** ▪ **6 months – 64 years** with ≥ 1 CDC high-risk condition	▪ **≥65 years** ▪ **12 – 64 years** with ≥ 1 CDC high-risk condition

Prescribing Information for SPIKEVAX and mNEXSPIKE

Moderna Confirms the Safety and Effectiveness of Updated COVID-19 Vaccines and Prepares Vaccine Updates as SARS-CoV-2 Virus Evolves

Confirmation of Vaccine Safety and Effectiveness

- Assess the safety of Moderna COVID-19 vaccines through active and passive surveillance[1]
- Evaluate vaccine effectiveness in real world studies (>5.8 million vaccine doses since initial approval)[2-10]
- Conduct clinical trials to assess safety, immunogenicity, and cross-neutralization against emerging variants[11,12]

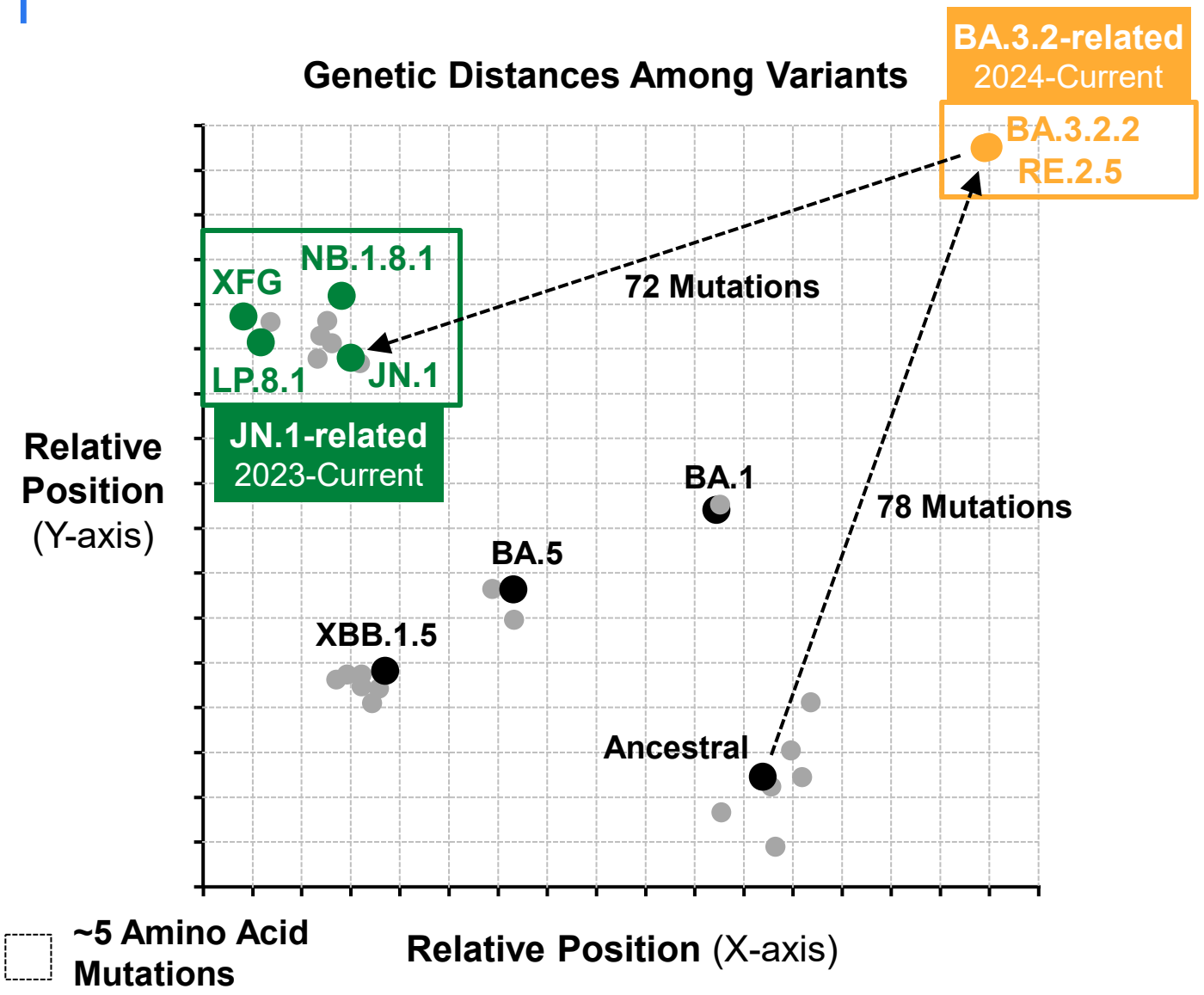
Develop and Evaluate New Variant Vaccines as Virus Evolves

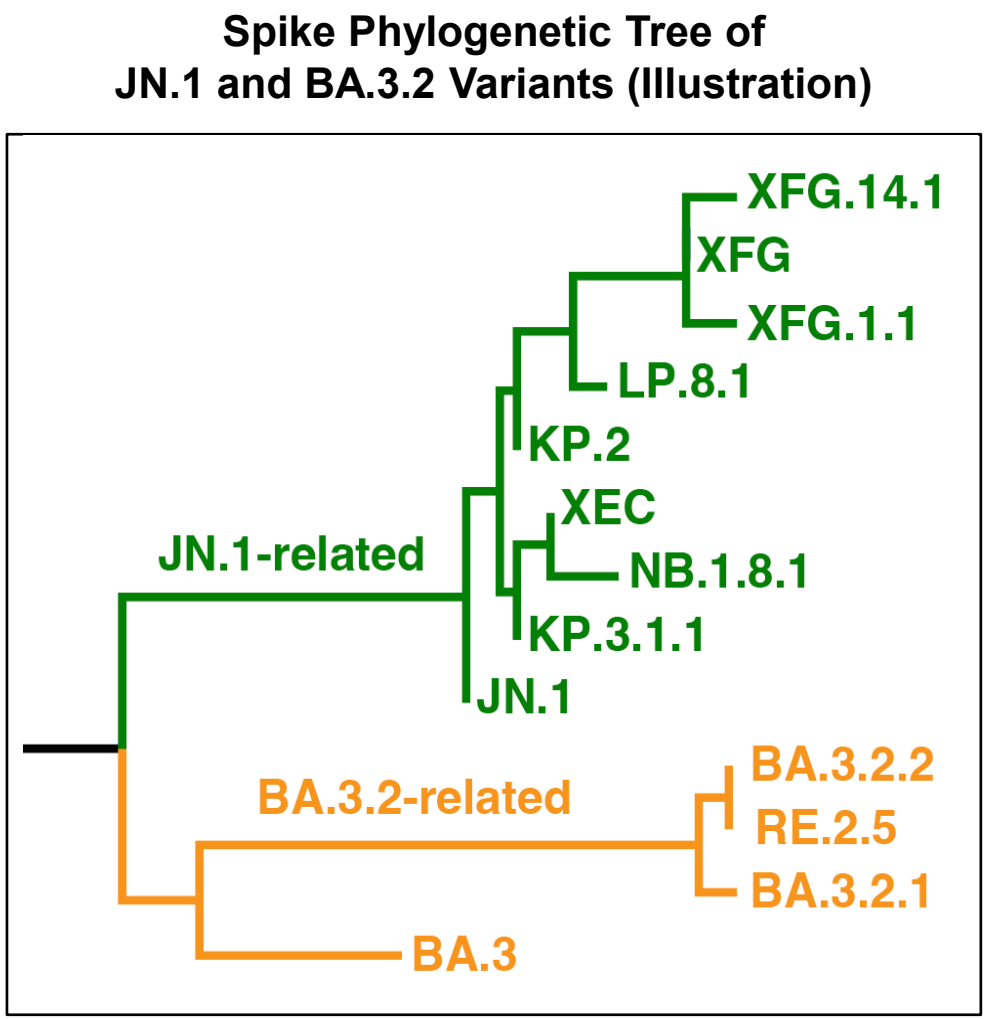
- Generate data to inform agencies on strain selection and recommendations
- Develop and evaluate candidate vaccines based on emerging SARS-CoV-2 variants
- Prepare to supply variant vaccine recommended by FDA

1. Urdaneta V *Open Forum Infect Dis.* 2024; 2. Kopel H *Open Forum Infect Dis.* 2024; 3. Wilson A *Infect Dis Ther.* 2025; 4. Ku *JH Vaccine* 2023; 5. Vicic N *Infect Dis Ther.* 2025; 6. Tseng HF Nat Commun 2023; 7. Zheng Z Vaccine X 2025; 8. Flores A *Clin Infect Dis* 2023; 9. Flores A *PLoS One*, 2022; 10. Kopel H *Open Forum Infect Dis* 2024; 11. Chalkias S, *New Engl J Med*, 2022; 12. Figueroa A *MedRxiv*, 2025

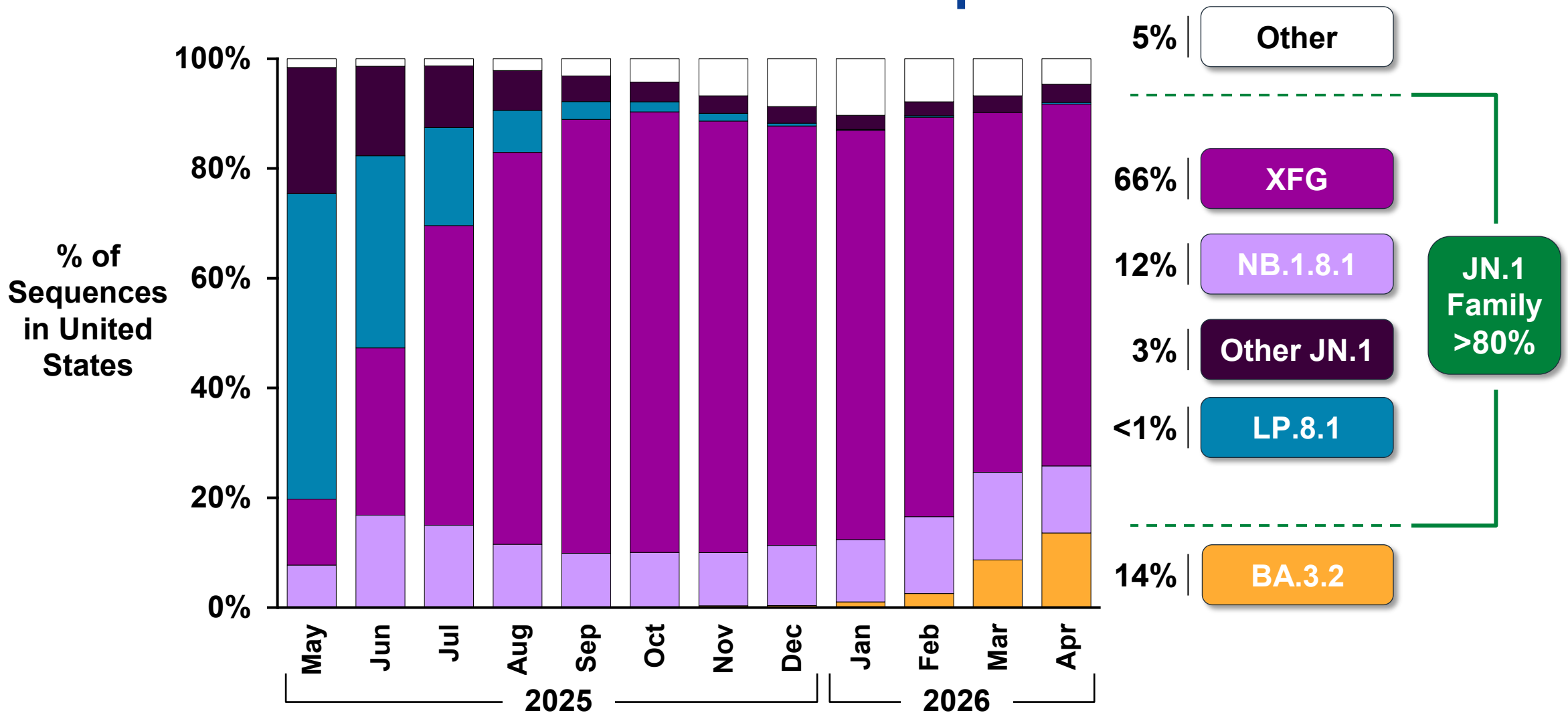
Current SARS-CoV-2 Variant Landscape in United States

JN.1- and BA.3.2-lineages are Co-circulating Globally





JN.1 Remains Dominant in US: XFG and Related JN.1 Variants Account for >80% of US Sequences



Analysis included all US SARS-CoV-2 sequences collected 5/1/25 – 4/30/26, Data retrieved from GISAID and analyzed at Moderna on 5/8/26; We gratefully acknowledge all GISAID contributors and submitting laboratories. Number of sequences/month ranged from 311 (4/26) – 9959 (8/25)
Other = other recombinants or variants that could not be classified into either JN.1 or BA.3.2 lineages

Modeling of Neutralization Titers Supports XFG Selection for Broad Coverage Across the Dominant JN.1 Family

Modeled Fold Reduction in ID_{50} Neutralization Titers

Vaccine	JN.1 Variants				BA.3.2 Variants	
	XFG	XFG.1.1	XFG.14.1	NB.1.8.1	BA.3.2.2	RE.2.5
LP.8.1	2.6	2.6	2.7	1.2	4.6	4.6
XFG	1.0	1.0	1.0	1.2	4.6	4.6
BA.3.2.2	2.6	2.6	2.7	1.1	1.0	1.0

<2 2–3.9 ≥4

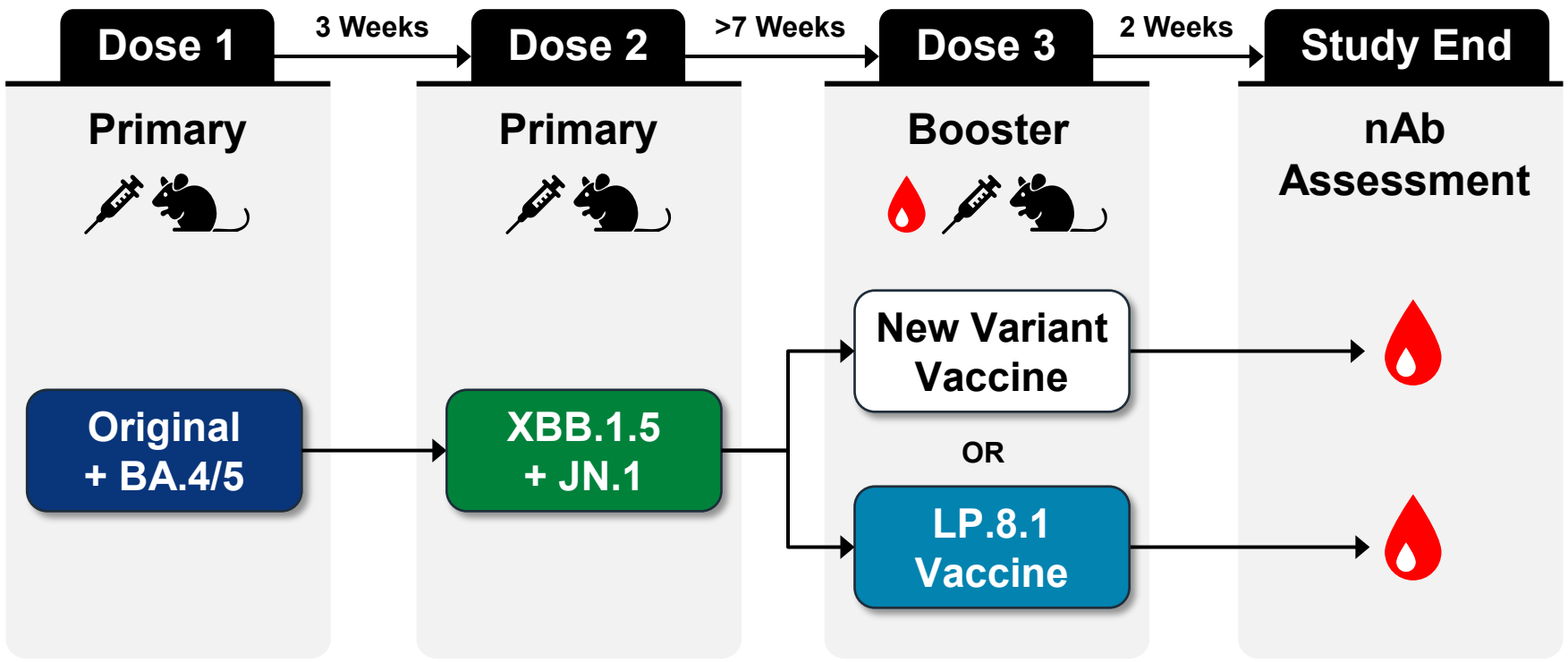
Fold Reduction Suggests Limited Immune Escape

Nasir et al. *J. Virol*, 2026

Overview of Preclinical Studies to Assess Investigational XFG or BA.3.2.2 Variant Vaccines

Booster Series: Immunogenicity of XFG and BA.3.2.2 New Variant Vaccines vs Licensed LP.8.1 Vaccine in Variant-Experienced Mice

New Variant Vaccines Evaluated Using Both mRNA-1273 and mRNA-1283



Objective

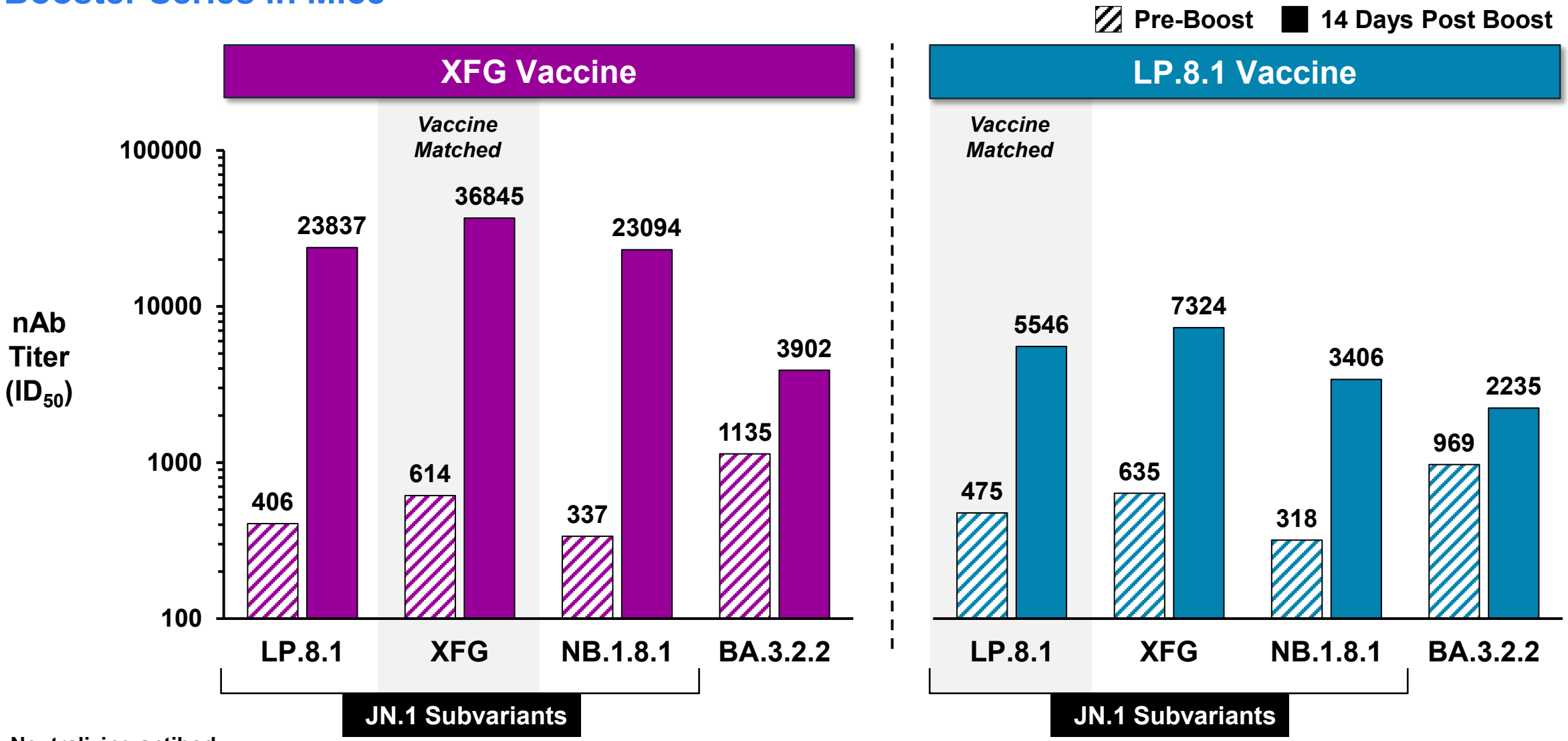
Compare booster response of licensed LP.8.1 vaccine versus investigational new variant vaccines against currently circulating strains

- mRNA-1273 and mRNA-1283 performed similarly across pre-clinical investigations
- Today's focus is on mRNA-1283

nAb – Neutralizing antibody
0.5µg dose 1 and 2; 1µg dose 3; n = 8-10 mice/group

mRNA-1283: XFG Vaccine Provides Higher Cross-Neutralization of JN.1 Subvariants than LP.8.1 with Similar BA.3.2.2 Neutralization

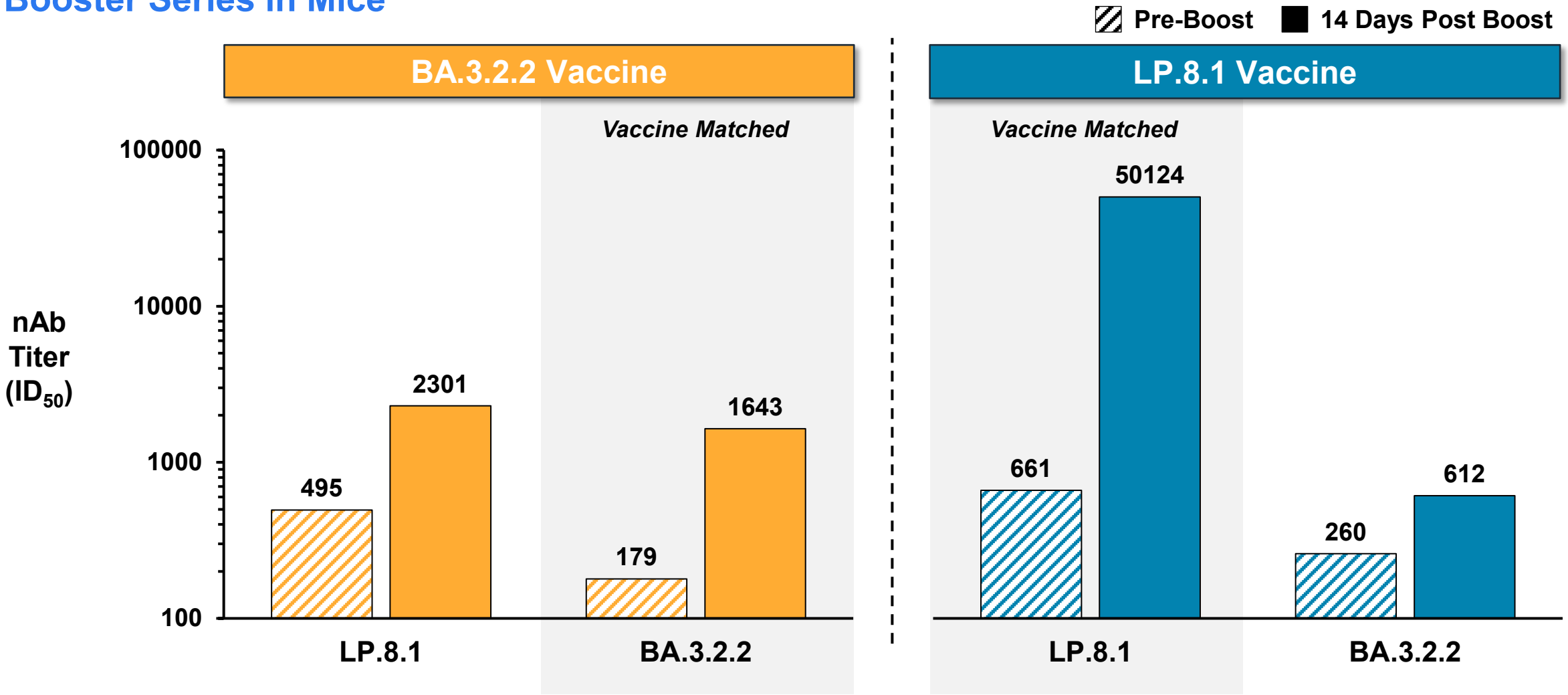
Booster Series in Mice



nAb – Neutralizing antibody
N = 8 mice/group

mRNA-1283: BA.3.2.2 Vaccine Neutralizes BA.3.2.2, Low Cross-Neutralization of LP.8.1

Booster Series in Mice



Not tested for XFG or NB.1.8.1
nAb – Neutralizing antibody
N = 10 mice/group

Summary – Preclinical Studies of XFG and BA.3.2.2 Investigational Vaccines

XFG Vaccine

- Strongly neutralized currently circulating JN-1 family variants, including XFG and NB.1.8.1
- Lower cross-neutralization of BA.3.2.2

BA.3.2.2 Vaccine

- Neutralized BA.3.2.2
- Low cross-neutralization of JN.1-lineage variants, including XFG

Real World Effectiveness of Moderna 2025/2026 LP.8.1 COVID-19 Vaccines (mRNA-1273 and mRNA-1283)

Rituparna Das, MD, PhD

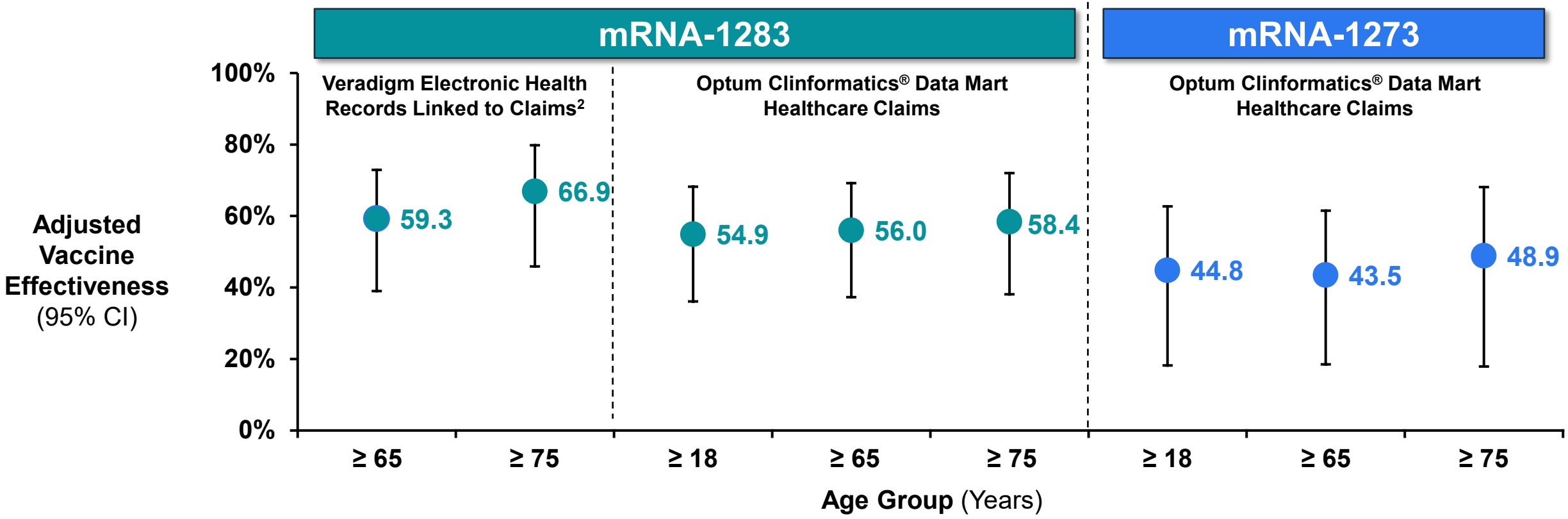
Senior Vice President

Clinical Development, Infectious and Rare Diseases

Moderna, Inc.

Moderna LP.8.1 Vaccines: Provided Strong Additional Protection Against COVID-19-Related Hospitalization

Routine Clinical Use in Adults



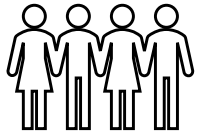
Study Design	Retrospective, Matched Cohort	Retrospective, Matched Cohort	Retrospective, Matched Cohort
Number of Adults	233,072/group[1]	354,753/group[1]	252,200/group[1]
Study Period	Aug 2025 – Jan 2026	Aug 2025 – Dec 2025	Aug 2025 – Dec 2025
Median Follow-up, Days (IQR)	69 (42, 95)	57 (27, 84)	61 (29, 85)

1. Equal number of vaccinated (group 1) and matched unvaccinated (group 2) in each study; 2. Vicic et al. medRxiv, 2026

Clinical Study Evaluating Immunogenicity and Safety of Moderna LP.8.1 Vaccines (mRNA-1273 and mRNA-1283)

Two Single-Arm, Open-Label, Phase 3b/4 Immunogenicity and Safety Studies of Moderna LP.8.1 Vaccines (mRNA-1273 & mRNA-1283)

Studies 403, Part 3B & 401, Part 1B



- **Participants ≥ 12 Years**
- **Age Stratification**
  - 12 – 64 years with ≥1 risk factor
  - ≥ 65 years

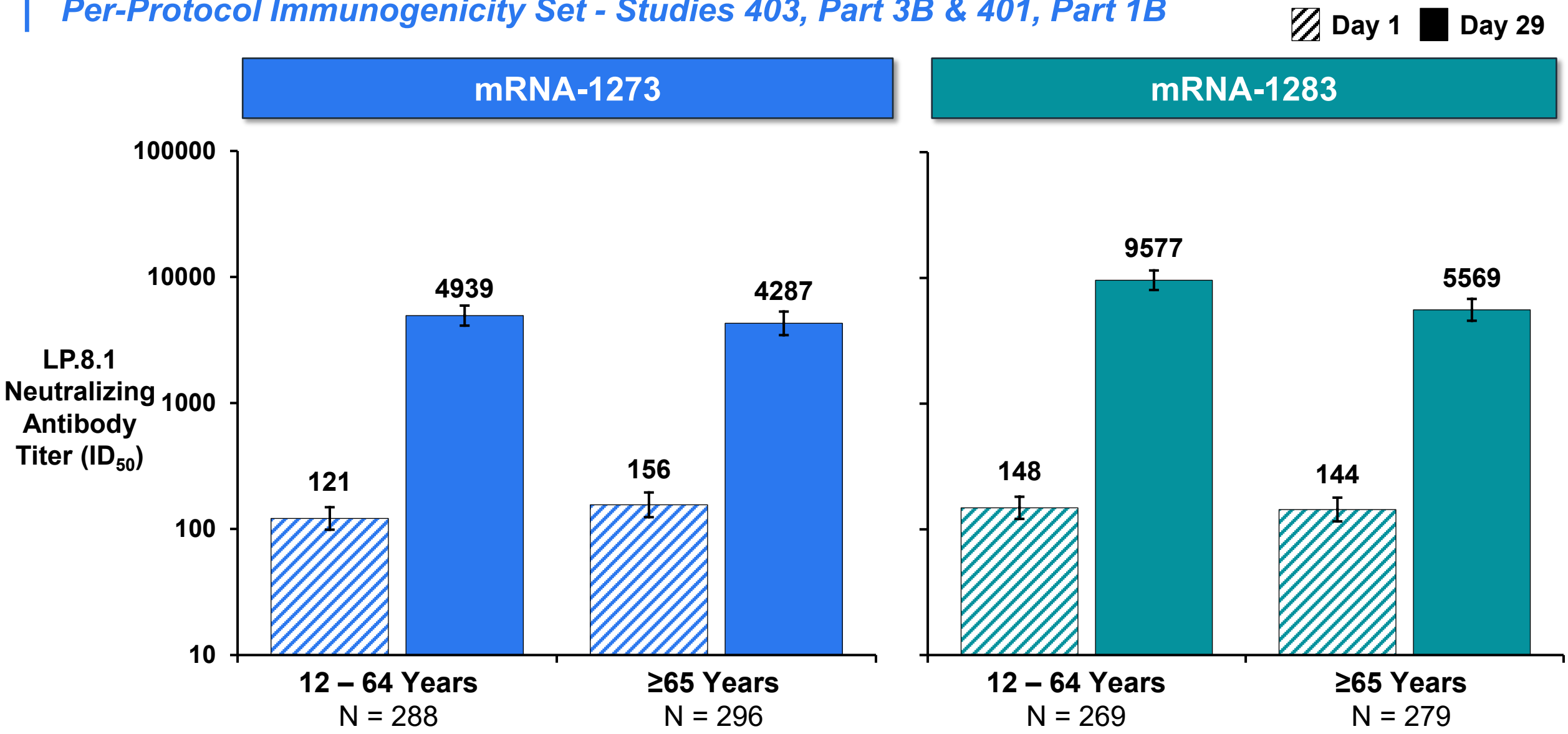
1 **Study 403** (Part 3B) **N = 661** → **mRNA-1273 (LP.8.1 variant) 50 µg**

2 **Study 401** (Part 1B) **N = 657** → **mRNA-1283 (LP.8.1 variant) 10 µg**

- Neutralization against matched variant (LP.8.1) assessed prior to study vaccine (Day 1) and 4 weeks post-vaccination (Day 29)
- Participants followed for safety for the duration of study
  - No vaccine-related serious adverse events reported

Moderna LP.8.1 Vaccines: Significantly Increased LP.8.1 Neutralizing Antibody Responses at Day 29

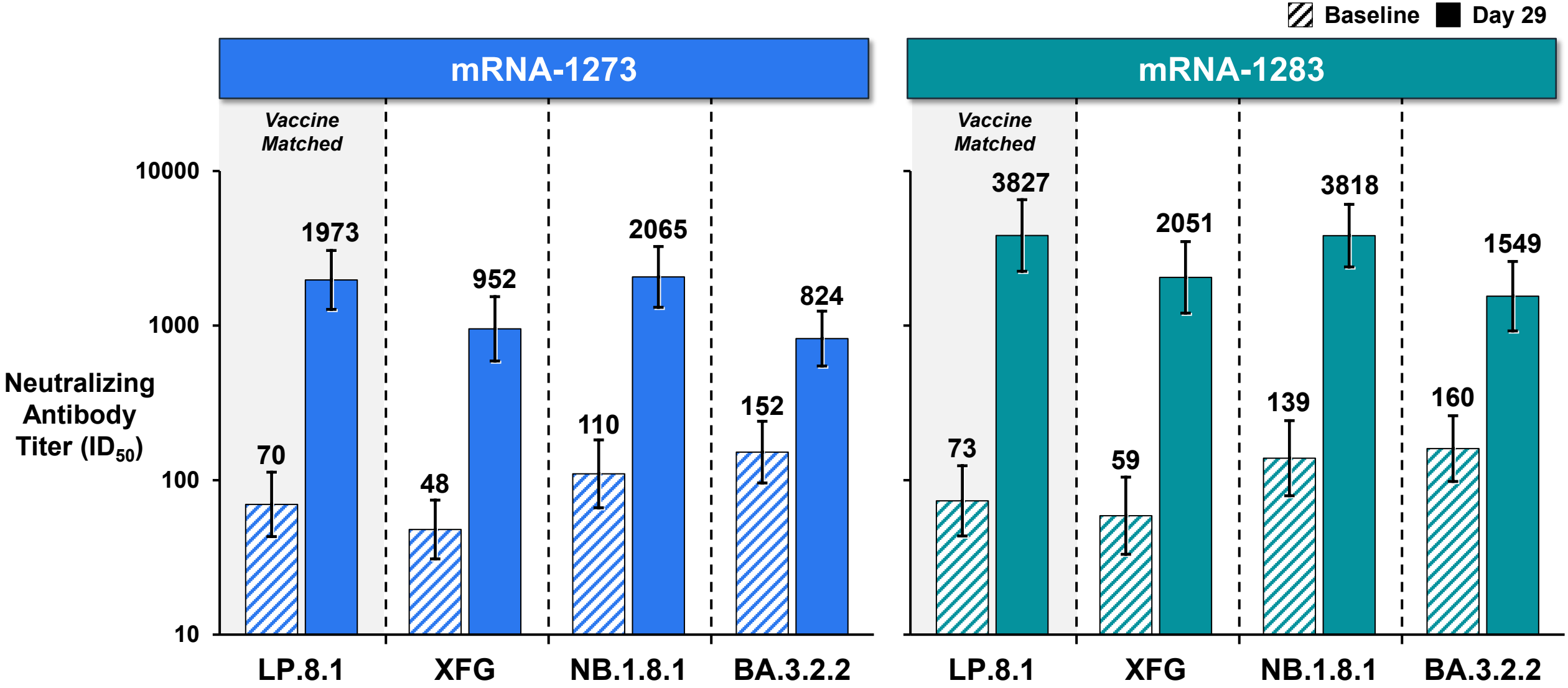
Per-Protocol Immunogenicity Set - Studies 403, Part 3B & 401, Part 1B



Clinical Studies Evaluating Cross Neutralization of Moderna Licensed LP.8.1 and Investigational BA.3.2.2 COVID-19 Vaccines

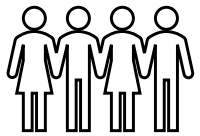
Moderna LP.8.1 Vaccines: Reduced Neutralization Observed Against XFG and BA.3.2.2

Studies 403, Part 3A & 401, Part 1A: Exploratory Analysis in a Subset of Participants (N = 51-56)



Single-Arm, Open-Label, Phase 3b/4 Immunogenicity and Safety Study of Investigational mRNA-1273 BA.3.2.2 Vaccine

Study 403, Part 5



Participants ≥ 18 Years

- 18 - 64 years with ≥1 risk factor
- ≥ 65 years

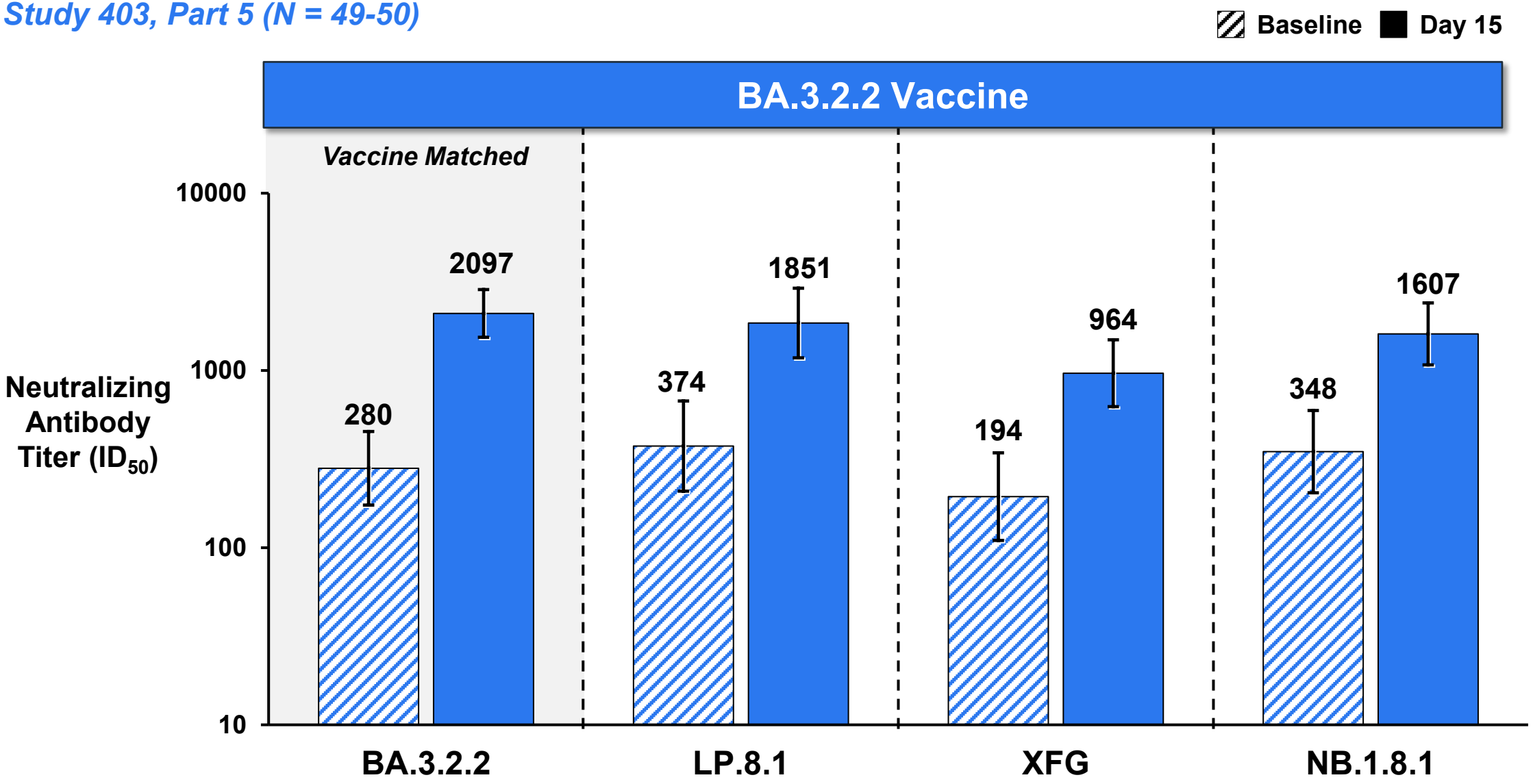
N = 50

→ **mRNA-1273 (BA.3.2.2 variant) 50 µg**

- Neutralization against circulating variants (BA.3.2.2, LP.8.1, XFG, NB.1.8.1) assessed prior to study vaccine (Day 1) and 2 weeks post-vaccination (Day 15)
- Participants followed for safety for the duration of study
  - No vaccine-related serious adverse events reported

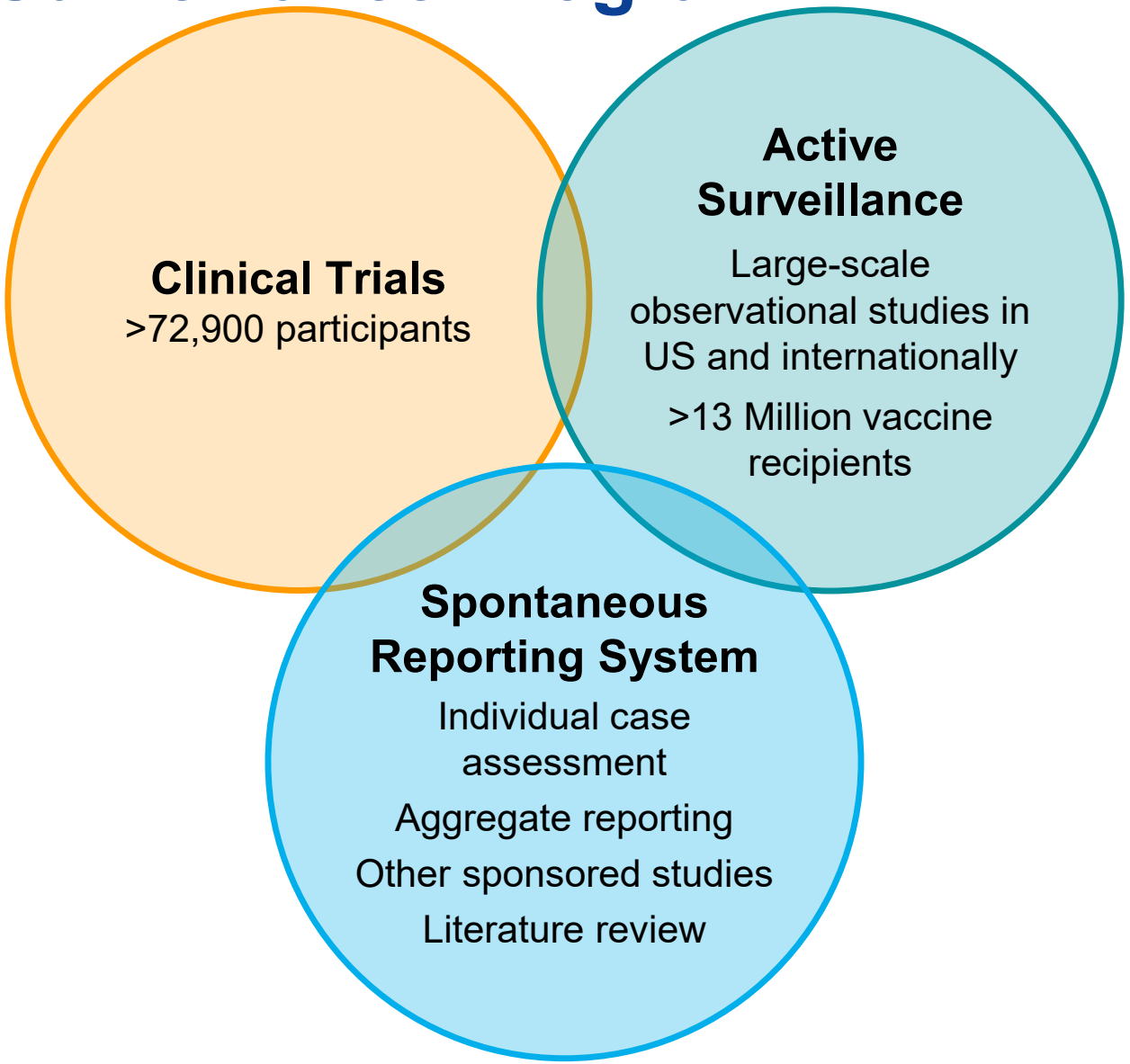
mRNA-1273 BA.3.2.2 Vaccine: Reduced Neutralization Observed Against LP.8.1, XFG, and NB.1.8.1

Study 403, Part 5 (N = 49-50)



COVID-19 Vaccines Safety Surveillance Program

Moderna's Comprehensive COVID-19 Vaccine Safety Surveillance Program



- Ongoing systematic safety review[1]
- >1.9 billion doses distributed worldwide over the past 6 years
- Myocarditis/pericarditis remains very rare
  - Significantly lower rates since 2022/2023 season[2-4]
- Safety profile consistent across all approved Moderna COVID-19 vaccines
- Benefit / risk continues to be favorable

1. Urdaneta V. *Open Forum Infect Dis,* 2024
2. Shoaibi, A. *Vaccine*, 2023
3. Lloyd, P. C. *Drug Saf,* 2025
4. Meyer S. Advisory Committee on Immunization Practices, June 2025

Summary

Summary

Safety and Effectiveness of 2025/2026 LP.8.1 Vaccines

- Effectiveness demonstrated across 3 real-world studies
- **LP.8.1 vaccine** neutralizes LP.8.1, lower cross neutralization of XFG & BA.3.2.2
- Safety profile consistent with approved Moderna COVID-19 vaccines
- Benefit-Risk profile continues to be favorable

2026/2027 Annual Strain Selection

- XFG variant dominant in US with BA.3.2 co-circulating at low levels
- **BA.3.2.2 vaccine** increases BA.3.2.2 neutralization, lower cross-neutralization of XFG
- **XFG vaccine** elicited higher titers against JN.1 family variants vs BA.3.2.2 vaccine
- Evidence supports a monovalent XFG vaccine as best option for 2026-2027

2026/2027 Readiness

- Prepared to supply recommended vaccine composition by mid-August 2026
- Moderna continues to monitor vaccine safety and effectiveness
- Clinical and pre-clinical data will be provided for emerging variants

THANK YOU to Our Study Collaborators, Investigators, and Participants

- All investigators
- Study site personnel
- Laboratories
- Most importantly, the individuals who participated in these trials