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Moderna COVID-19 Vaccines Update

Moderna, Inc.

June 5, 2024

Vaccines and Related Biological Products Advisory Committee

Introduction

Frances Priddy, MD MPH

Executive Director, Clinical Development

Moderna, Inc.

Moderna Continues to Prepare and Evaluate New COVID-19 Vaccines as SARS-CoV-2 Variants Emerge

Moderna's Ongoing Commitment

- Monitor emerging Variants of Concern
- Develop new candidate vaccines
- Generate preclinical data
- Collect sera from vaccine recipients to assess cross neutralization of future variants
- Ensure manufacturing capabilities to rapidly respond to public health needs
- Prepared to supply new variant-containing vaccine as recommended

Recent Research Activities

- Currently licensed XBB.1.5 vaccine
  - Safety surveillance
  - Assessing real-world effectiveness
  - Evaluated cross neutralization against emerging variants
- Investigational JN.1-lineage vaccines (including JN.1 & KP.2)
  - Developed at risk
  - Generated preclinical data

Safety and Effectiveness of Moderna 2023-2024 (XBB.1.5) COVID-19 Vaccine

Safety of Moderna 2023-2024 (XBB.1.5) Vaccine in Adults

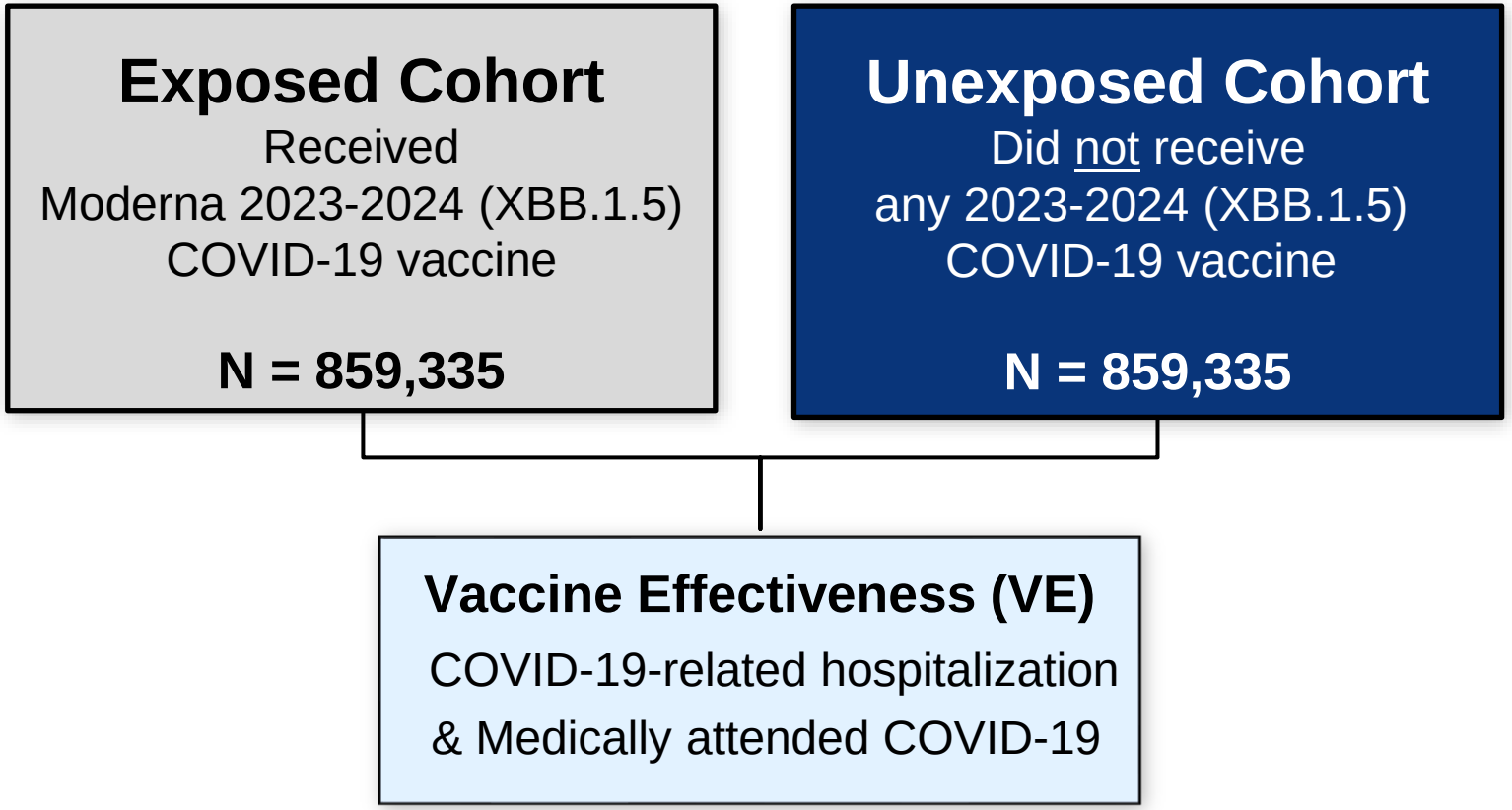
As of 03/17/24:

- ~45 million doses of XBB.1.5 vaccine administered
- No new safety or medical topics of concern observed
- No change in the favorable benefit-risk assessment of the vaccine

Safety surveillance continues

Observational, Retrospective Cohort Study (Adults ≥18 Years) of Moderna's 2023-2024 (XBB.1.5) Vaccine in Adults

Veradigm Electronic Health Records Linked to Komodo Health Claims



Matched 1:1

- Age
- Sex
- Race
- Ethnicity
- Geographic region
- Week of last claim
- Prior bivalent COVID-19 vaccine (09/01/22 - 09/11/23)

- Study conducted September 2023 – December 2023
- Median follow-up 63 days

Kopel et al., *MedRxiv,* 2024

Effectiveness of Moderna 2023-2024 (XBB.1.5) Vaccine

Study 946 – Vaccinated Sept – Dec 2023; Median Follow-up 63 Days

Age/Risk	Vaccine Effectiveness (%, Confidence Interval)	
	COVID-19 Related Hospitalizations	Medically Attended COVID-19
≥18 Years	**60%** (53%, 66%)	**33%** (30%, 36%)
≥18 Years and High Risk*	**59%** (51%, 65%)	**35%** (31%, 38%)
≥50 Years	**61%** (54%, 67%)	**35%** (32%, 38%)
≥65 Years	**61%** (53%, 67%)	**39%** (35%, 42%)

Moderna 2023-2024 (XBB.1.5) vaccine provides protection against COVID-related hospitalizations and medically attended visits

Medically attended COVID-19 includes ED visits, urgent care visits, office visits, telemedicine visits, and laboratory results
*High risk defined by CDC: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html
Kopel et al, *MedRxiv,* 2024

Cross Neutralization of Moderna 2023-2024 (XBB.1.5) Vaccine against New Emerging SARS-COV-2 Variants in Adults

Study 205J

Study Methodology

Study 205J

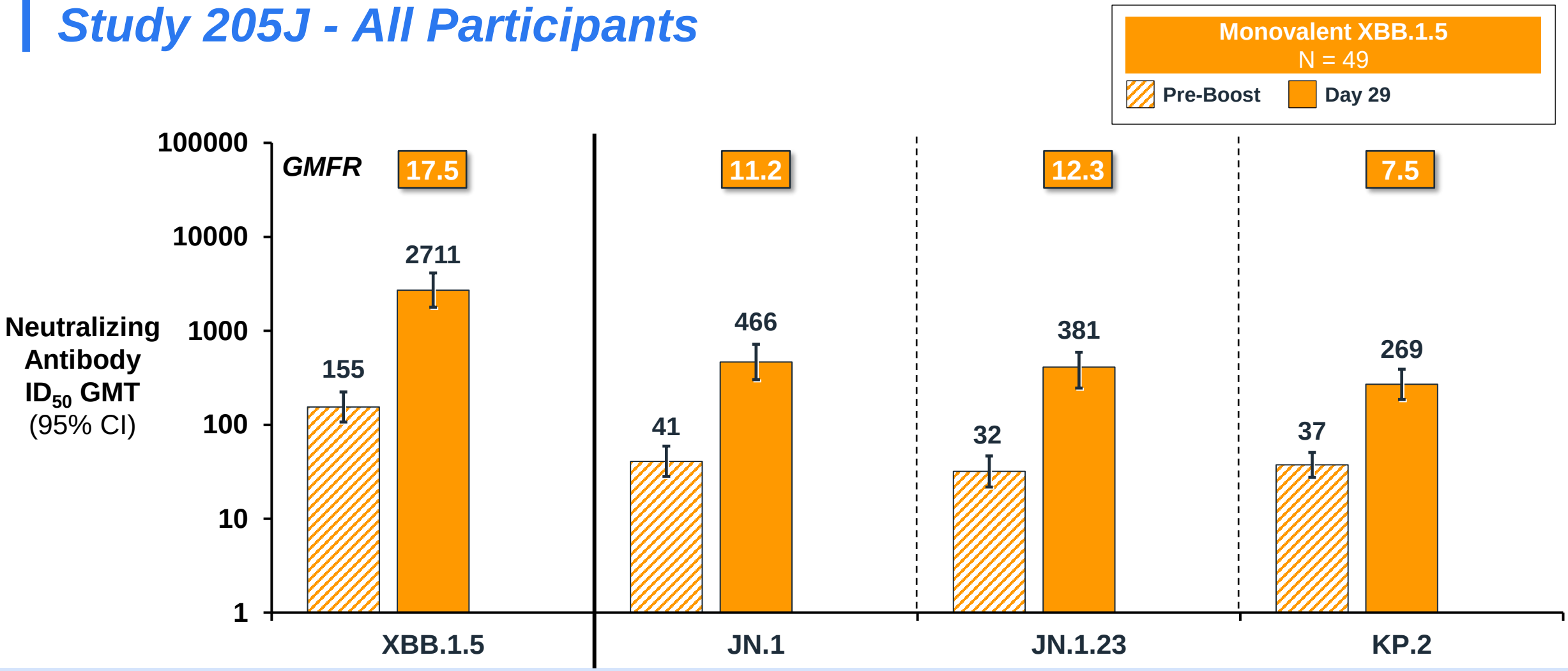
- 49 adults, ≥18 years old (mean 52 years)
- Received 5 doses of Moderna COVID-19 vaccine

4 Prior Vaccine Doses			Study Dose
1st & 2nd	3rd	4th	5th
mRNA-1273 100 µg	mRNA-1273 50 µg	Bivalent BA.4/BA.5 50 µg	XBB.1.5 50 µg

- 67% with evidence of prior SARS-CoV-2 infection prior to 5th dose
- Neutralization assessed Day 29 and Day 181 (6 months) post-vaccination with pseudovirus assay

Day 29 Neutralizing Antibody Against SARS-CoV-2 Variants (XBB and JN.1 variants) following 2023-2024 (XBB.1.5) Vaccine

Study 205J - All Participants

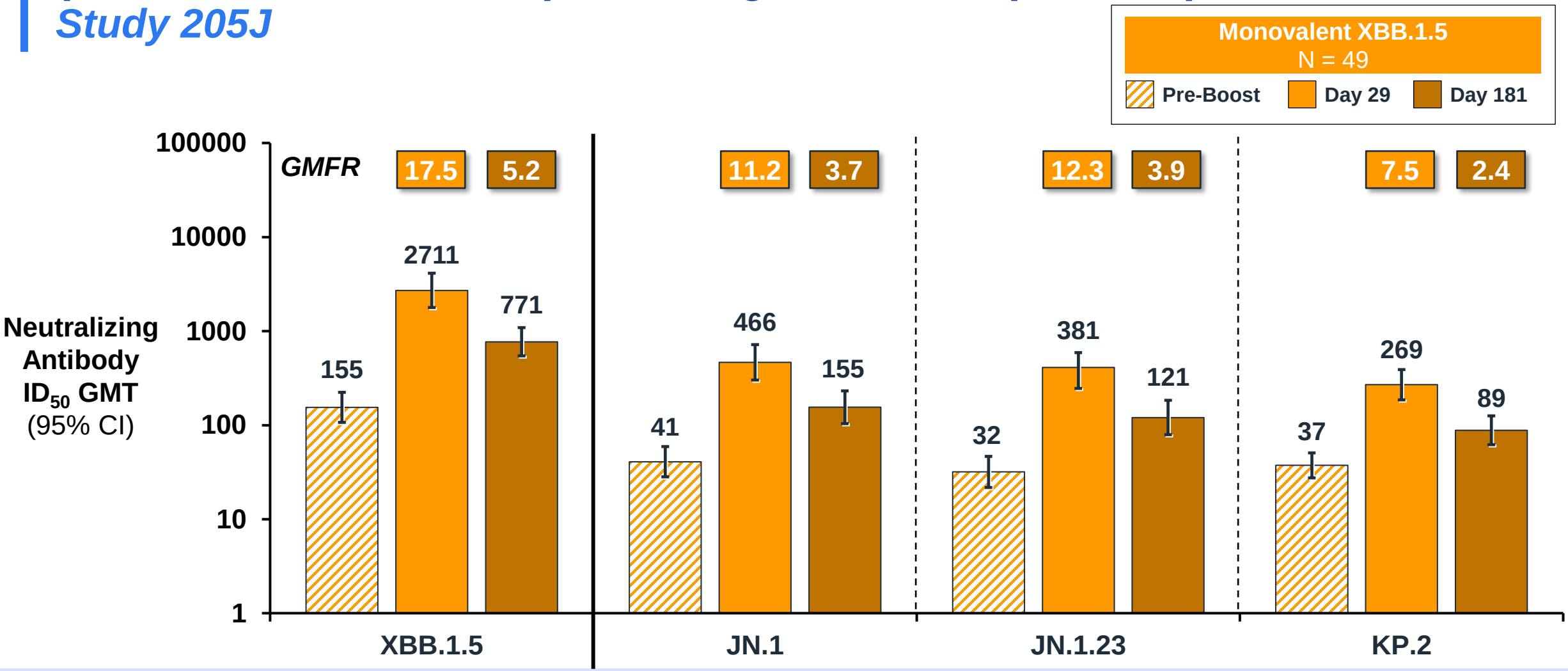


- Neutralizing antibody and cross protection reduced against JN.1 variants after XBB.1.5 vaccine
- Similar results regardless of prior infection status

GMFR from baseline

6 Month (Day 181) Neutralizing Antibody Against SARS-CoV-2 Variants (XBB and JN.1 variants) following 2023-2024 (XBB.1.5) Vaccine

Study 205J



- **Durable neutralizing responses for at least 6 months after XBB.1.5 vaccine**
- **Reduced response to JN.1 variants at all timepoints**

GMFR from baseline

Variant Monitoring, Risk Assessment, and Preclinical Assessment of Investigational New Variant Vaccines

Darin Edwards, PhD

Executive Director

COVID-19 Program Lead

Moderna, Inc.

Moderna's Current Genomic Surveillance and Risk Assessments

- JN.1 and its subvariants comprise 94% of sequences collected globally in May 2024[1]
  - JN.1 subvariants have become predominant
  - JN.1 continues to decline worldwide

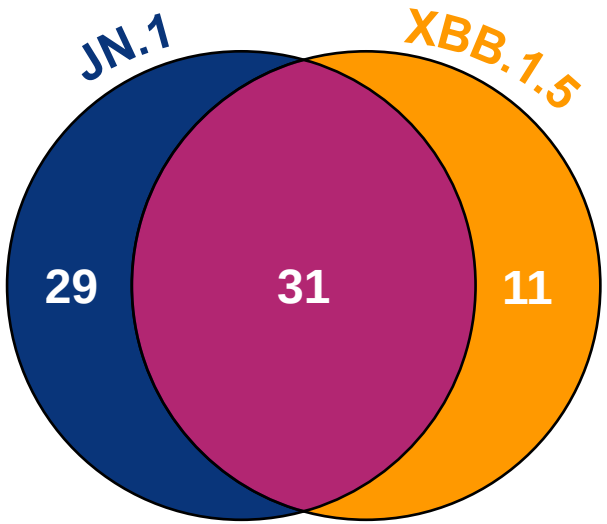
- JN.1 subvariants[1]
  - Subvariants with mutations in the spike receptor binding domain have recently increased in frequency
  - KP.2 is most commonly sequenced variant in the United States
  - KP.3 increasing rapidly worldwide

- Based on our current data, a JN.1 or KP.2 new variant vaccine is expected to provide protection against JN.1, KP.2, KP.3, and other JN.1 subvariants (JN.1.13.1, LA.2, and others)

GISAID (as of May 31, 2024)

JN.1 Has Significant Antigenic Differences Compared to XBB.1.5

JN.1 vs. XBB.1.5



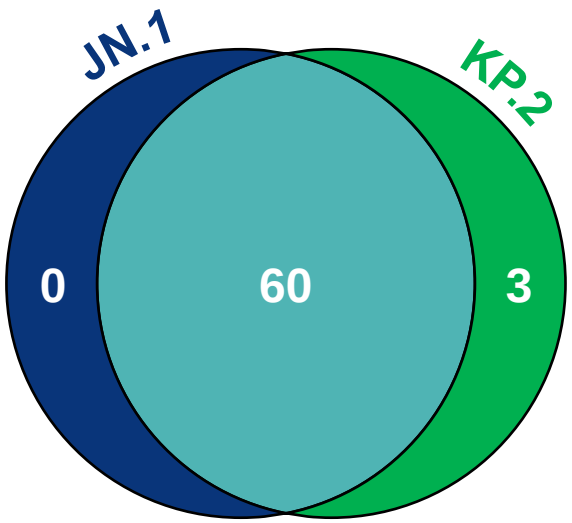
29 + 11 = 40 mutations

Antigenic differences between JN.1 and XBB.1.5 suggest an updated vaccine composition may be needed

Venn diagram generated via cov-spectrum

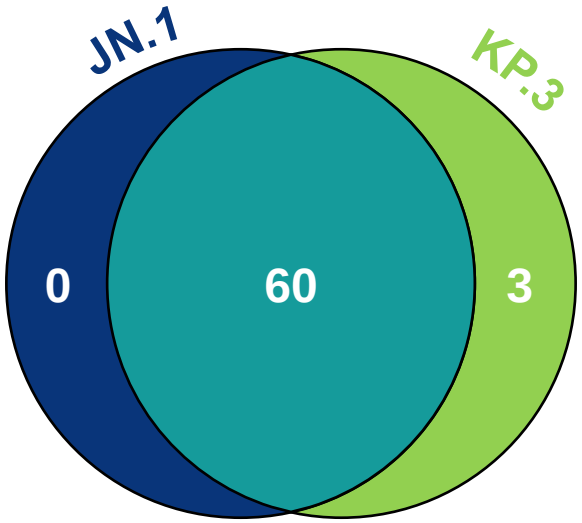
Minimal Antigenic Differences Between Circulating JN.1 Variants

JN.1 vs KP.2



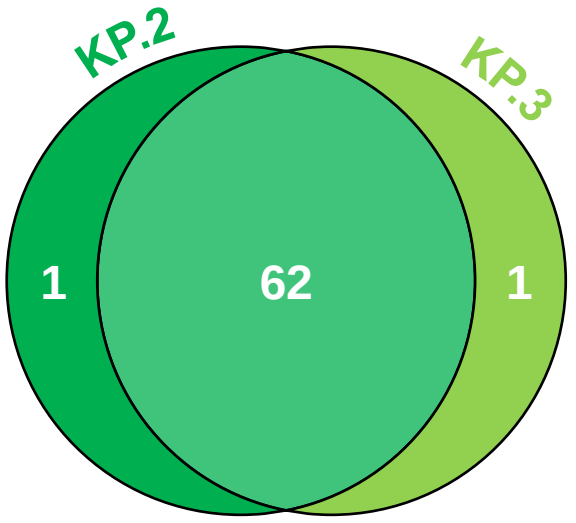
0 + 3 = 3 mutations

JN.1. vs KP.3



0 + 3 = 3 mutations

KP.2 vs KP.3



1 + 1 = 2 mutations

JN.1 or KP.2 vaccines are likely to cross-neutralize

Venn diagrams generated via cov-spectrum
KP.2 is alias for JN.1.11.1.2, KP.3 is alias for JN.1.11.1.3

Overview of Preclinical Studies to Assess Investigational JN.1 and KP.2 Vaccines

Preclinical Studies in Mice Comparing JN.1 or KP.2 Vaccine Candidates versus XBB.1.5 Vaccine

Primary Series

Antigen naïve mice

2 Doses of Monovalent JN.1 Vaccine

vs

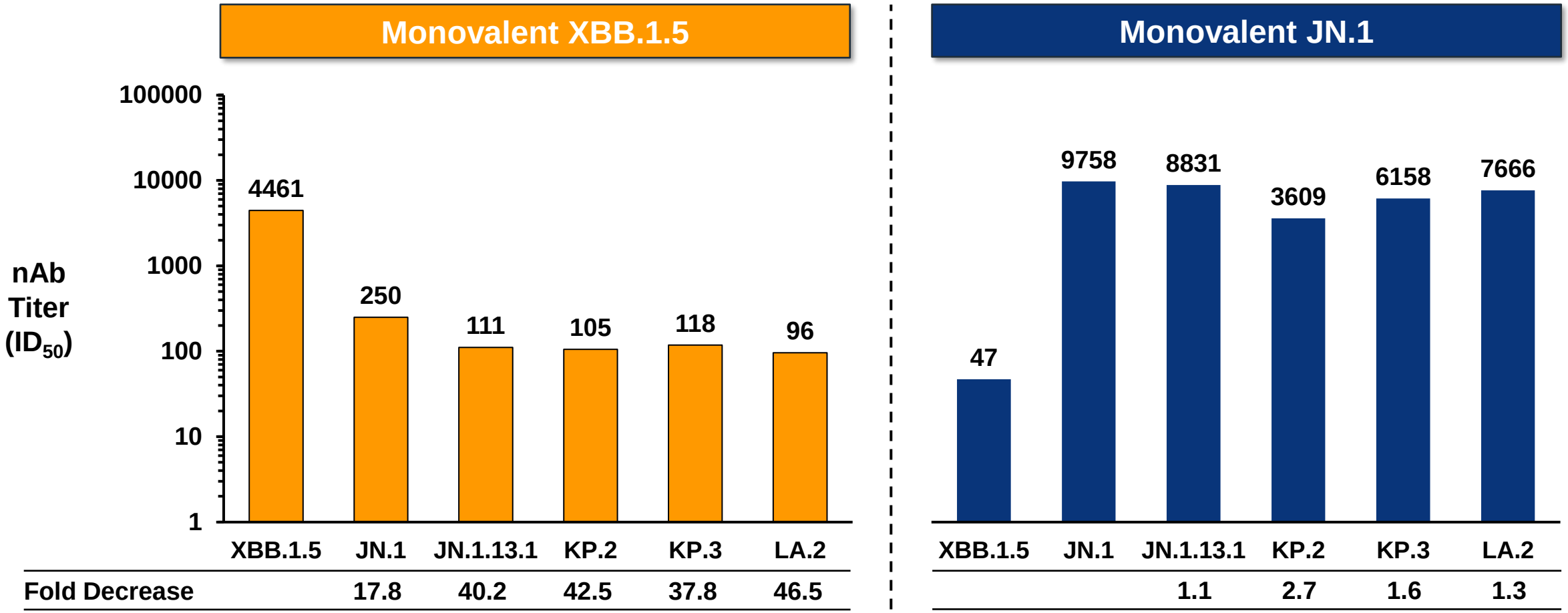
2 Doses of Monovalent XBB.1.5 Vaccine

Booster (3rd) Dose

Mice previously immunized with a 2-dose primary series of mRNA-1273

+ 1 Dose of Monovalent JN.1 Vaccine	+ 1 Dose of Monovalent KP.2 Vaccine
vs	vs
+ 1 Dose of Monovalent XBB.1.5 Vaccine	+ 1 Dose of Monovalent XBB.1.5 Vaccine

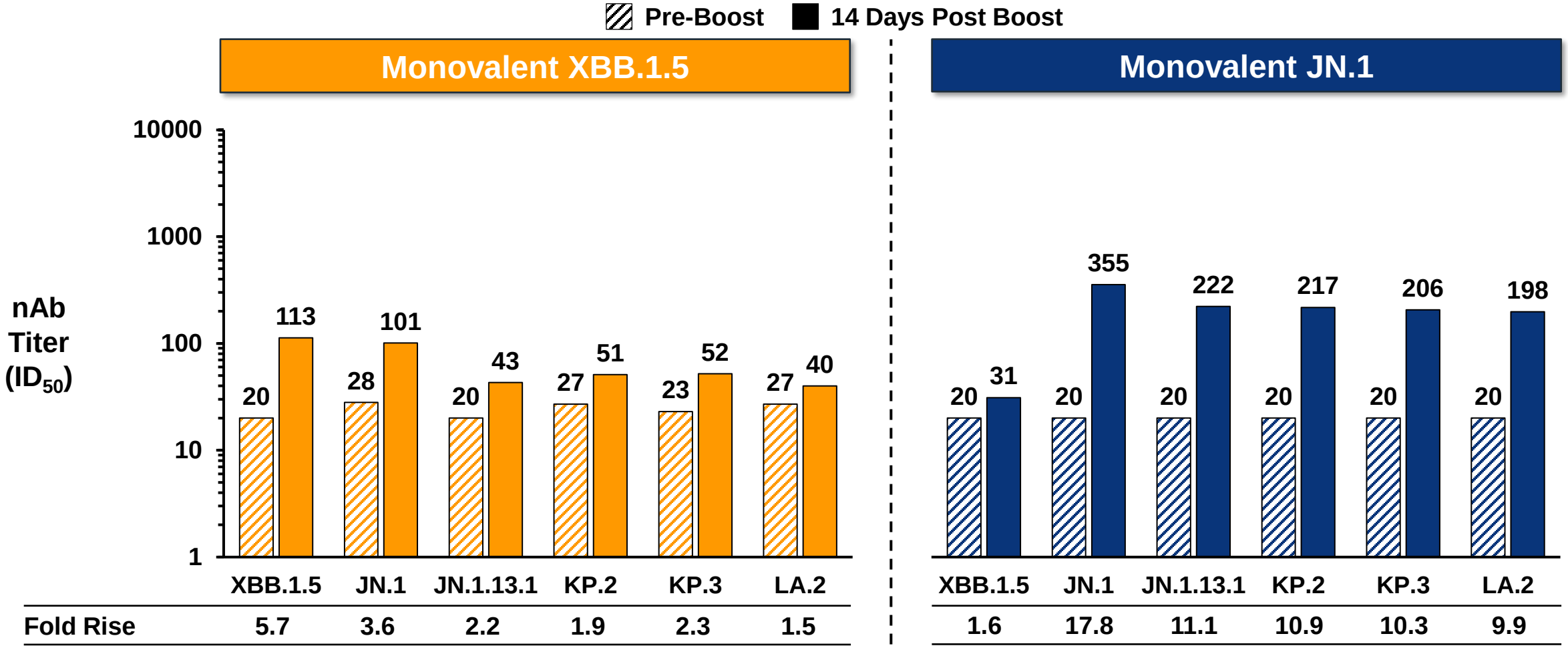
Neutralizing Antibody Titers in Mice 14 Days after Primary Series of XBB.1.5 Vaccine or JN.1 Vaccine



Monovalent JN.1 vaccine effectively neutralizes JN.1 and cross-neutralizes subvariants of JN.1 (KP.2, KP.3, etc)

1µg dose, D1 and D22, n = 8 per group

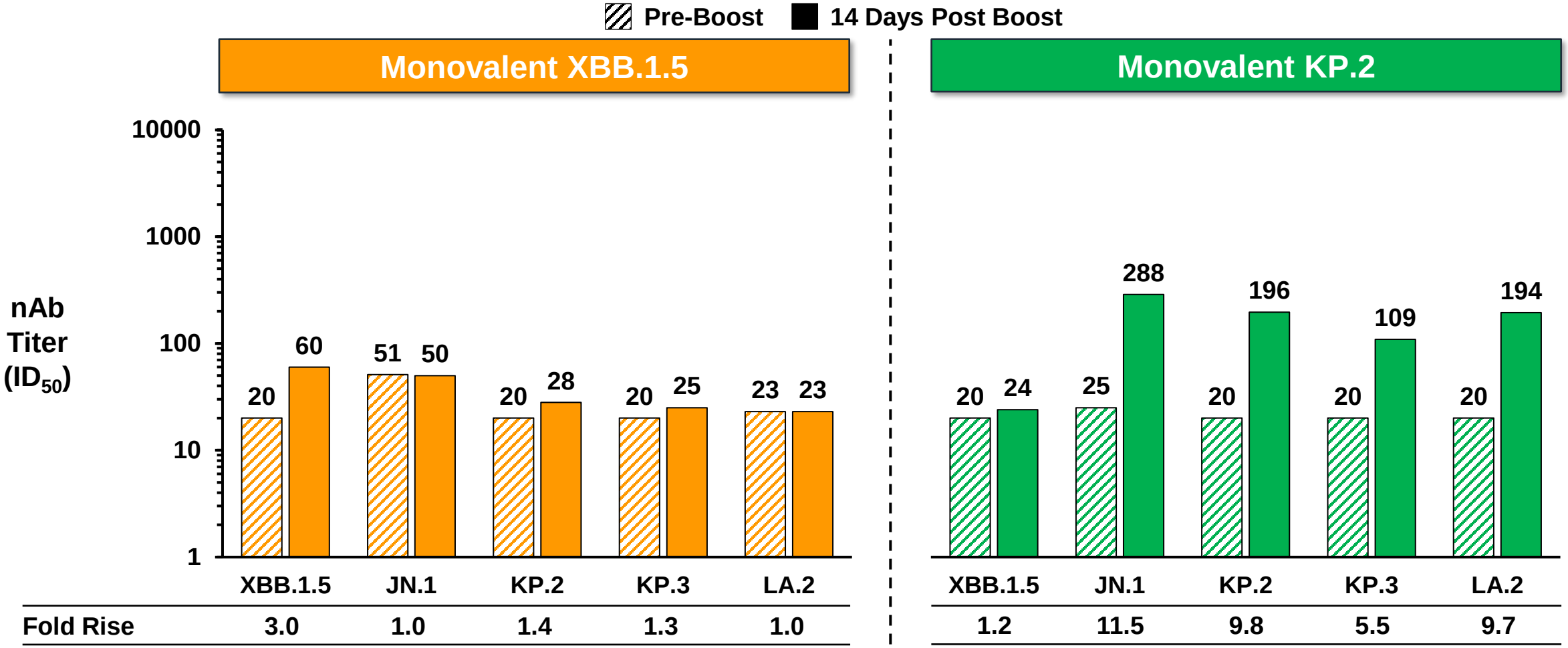
Neutralizing Antibody Titers in Mice 14 Days after Booster (3rd) Dose of XBB.1.5 Vaccine or JN.1 Vaccine



Monovalent JN.1 vaccine effectively increases neutralization of JN.1 and cross-neutralizes JN.1 subvariant viruses

0.5 µg dose of mRNA-1273, D1 and D22; 1 µg of either JN.1 or XBB.1.5 on D91, n=8 per group

Neutralizing Antibody Titers in Mice 14 Days after Booster (3rd) Dose of XBB.1.5 Vaccine or KP.2 Vaccine



Monovalent KP.2 vaccine effectively increases neutralization of KP.2 and cross-neutralizes other JN.1 subvariants

0.5 µg dose of mRNA-1273, D1 and D22; 1 µg of either KP.2 or XBB.1.5 on D42, n=8 per group

Summary of Pre-Clinical Data

- Data suggest that both a JN.1 and a KP.2 new variant vaccine increase neutralization against JN.1, KP.2, KP.3, and other currently circulating JN.1 subvariants
- Moderna is prepared to:
  - Submit for approval either a JN.1 or KP.2 new variant vaccine dossier
  - Supply the US market by mid-August, 2024

Conclusions

Summary

Currently Licensed 2023-2024 Vaccine (XBB.1.5)	▪ Moderna mRNA Vaccine (XBB.1.5) effective against COVID-19 during the period when XBB was predominant ▪ No new safety concerns identified; vaccine continues to be well tolerated
Preclinical and Clinical Studies of JN.1 and KP.2 Vaccines	▪ Pre-clinical data suggest a JN.1 or KP.2 vaccine is more immunogenic against currently circulating JN.1 subvariants than the licensed XBB.1.5 vaccine ▪ Small clinical trial with the selected new variant vaccine will be conducted post licensure to allow testing against future variants
Moderna's Vaccine Preparedness	▪ Moderna is prepared to supply either a JN.1 or KP.2 new variant vaccine in the US by mid-August 2024, if recommended by FDA

THANK YOU to Our Study Collaborators, Investigators, and Participants

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