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# Moderna COVID-19 Vaccines Update

Moderna, Inc.

May 22, 2025

Vaccines and Related Biological Products Advisory Committee

# Introduction

**Spyros Chalkias, MD**

Clinical Development

COVID-19 Vaccines

Moderna, Inc.

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

- 2nd leading cause of hospitalizations among respiratory viruses in US (*Oct 2024-Mar 2025, RESP-NET*)<sup>1</sup>
  - 250,000 - 410,000 hospitalizations reported (Oct 2024-May 2025)<sup>2</sup>
  - 30,000 - 50,000 COVID-19 deaths in US adults (Oct 2024-May 2025)<sup>2</sup>
    - 2024 summer surge observed with >15,000 additional deaths<sup>3</sup>
- ~73% of adults hospitalized in 2023/2024 with COVID-19 had not received the 2023/2024 variant vaccine<sup>1</sup>

1. ACIP Meeting April 15, 2025. <https://www.cdc.gov/acip/downloads/slides-2025-04-15-16/03-Havers-COVID-508.pdf>

2. CDC, Preliminary Estimates of COVID-19 Burden for 2024-2025; <https://www.cdc.gov/covid/php/surveillance/burden-estimates.html>, accessed 19MAY2025

3. [https://covid.cdc.gov/covid-data-tracker/#trends\\_weeklydeaths\\_select\\_00](https://covid.cdc.gov/covid-data-tracker/#trends_weeklydeaths_select_00), Accessed 16MAY2025

# Moderna Confirms the Safety and Effectiveness of Updated COVID-19 Vaccines Every Year

## Confirmation of Vaccine Safety and Effectiveness

- Assess the safety of Moderna COVID-19 vaccine through active and passive surveillance<sup>1</sup>
- Evaluate vaccine effectiveness (vaccinated vs. unvaccinated) in real world effectiveness studies (>900,000 persons/season over last 2 seasons)<sup>2,3,4</sup>
- Conduct clinical trials each year to assess safety, immunogenicity, and cross-neutralization against emerging variants<sup>5,6</sup>

## Development of Updated Vaccines as Virus Evolves

- Perform strain updates on COVID-19 vaccines as recommended by health authorities
- Generate data to inform agencies on strain selection and recommendations
- Develop candidate vaccines based on emerging SARS-CoV-2 variants
- LP.8.1 currently dominant variant in US and Europe
  - Evaluated in non-clinical studies
  - Manufacturing readiness complete



## **Effectiveness of Moderna 2024/2025 (KP.2) COVID-19 Vaccine**

# Moderna COVID-19 Vaccine’s Real-World Effectiveness Across Multiple Seasons and Variants

Age	Year	Vaccine	Dataset	Number Moderna Vaccinated	Days of Follow-up	Vaccine Effectiveness COVID-19 Related Hospitalizations (95% CI)
≥18 Years	2020-21	Primary Series	KPSC <sup>1</sup>	927,004	≤243	96% (96%, 97%)
	2021-22	Initial booster	KPSC <sup>2</sup>	431,328	≤90	89% (86%, 91%)
	2022-23	BA.4/BA.5	KPSC <sup>3*</sup>	290,292	~74	70% (64%, 75%)
			Veradigm <sup>4</sup>	859,335	63	60% (53%, 66%)
	2023-24	XBB.1.5	HealthVerity <sup>5</sup>	1,272,161	84	51% (48%, 54%)
			Optum <sup>6</sup>	884,425	111	58% (54%, 62%)

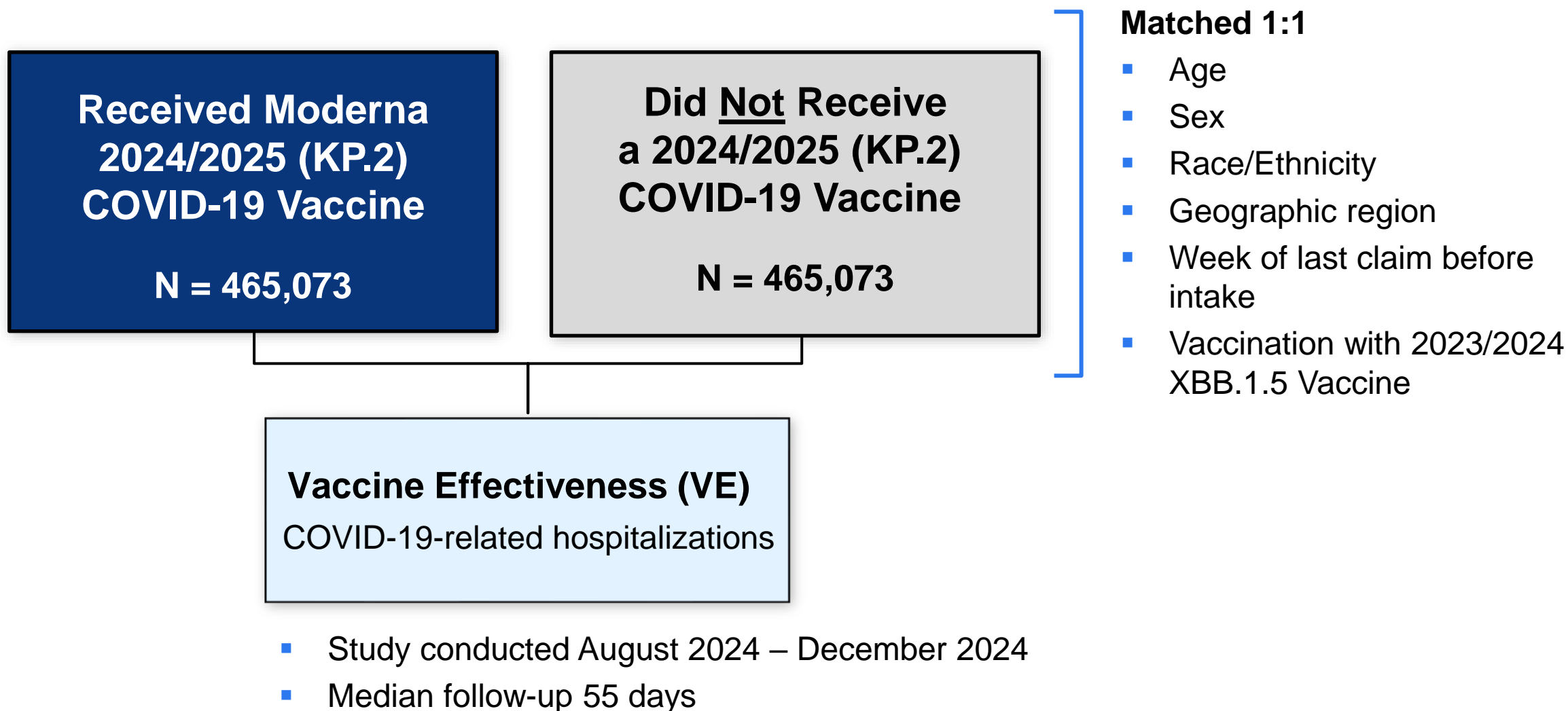
Moderna COVID-19 vaccines continue to offer protection against hospitalizations in the setting of increasing population-level immunity

CI: Confidence Interval; KPSC: Kaiser Permanente Southern California; Sources: 1. Florea, *PLoS One* 2022; 2. Florea, *Clin Infect Dis* 2023; 3. Tseng, *Nat Comms* 2023, \*This study included individuals ≥ 6 years of age (<1%); 4. Kopel, *Open Forum Infect Dis* 2024; 5. Wilson, *Infect Dis Ther* 2025; 6. Zheng, Moderna data on file, 2025



# Observational, Retrospective Cohort Study of Moderna's 2024/2025 (KP.2) Vaccine in Adults

*Veradigm Electronic Health Records Linked to Komodo Healthcare Claims*





# Effectiveness of Moderna 2024/2025 (KP.2) Vaccine

*Vaccinated August – December 2024; Median Follow-up 55 Days*

Age/Risk	Number of KP.2 Vaccine Recipients	Vaccine Effectiveness COVID-19 Related Hospitalizations (95% CI)
All Persons ≥18 Years	465,073	53% (35%, 66%)
≥18 Years and High Risk*	326,556	47% (25%, 62%)
≥50 Years	365,484	53% (35%, 66%)
≥65 Years	258,098	53% (34%, 67%)

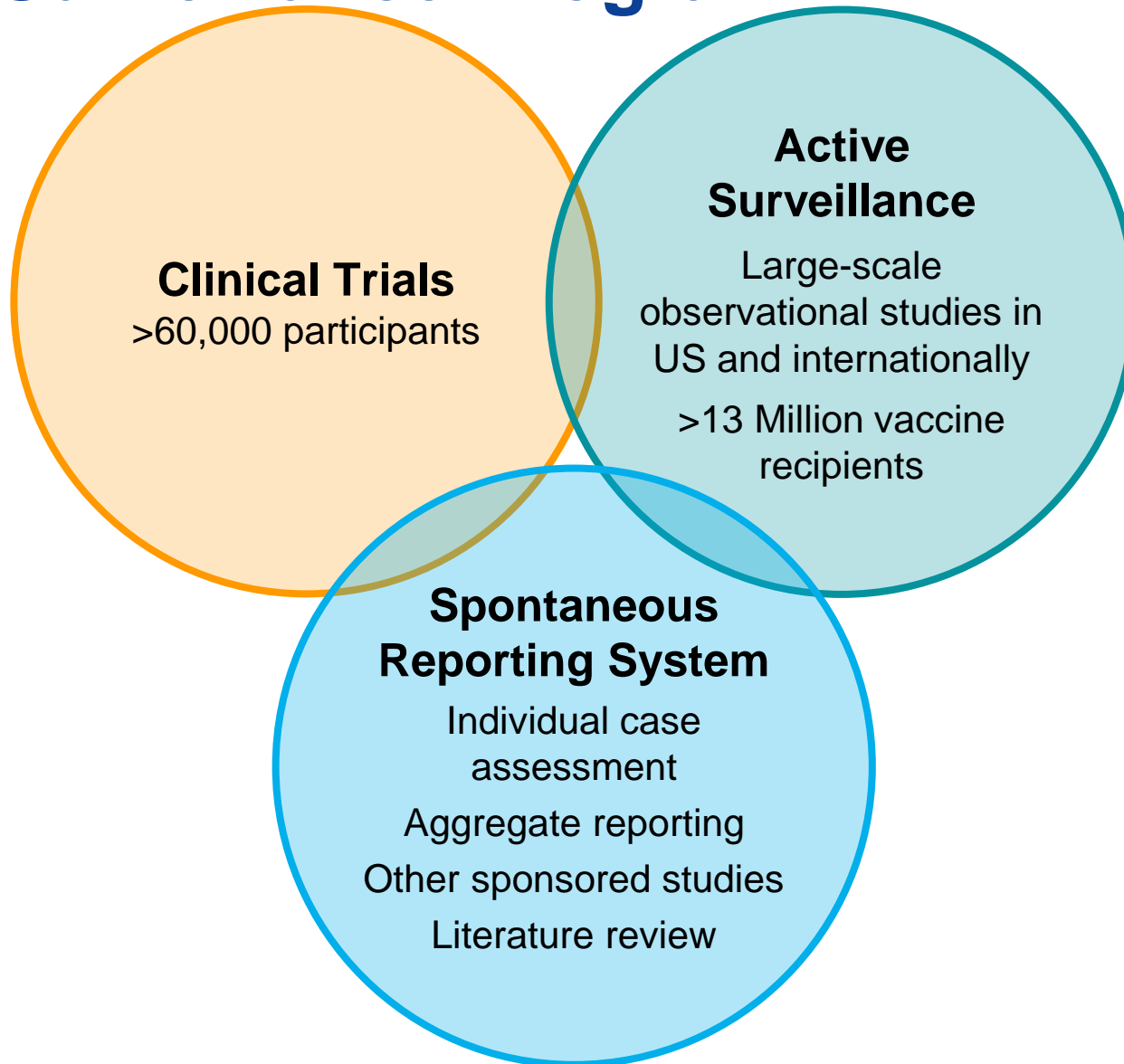
Moderna 2024/2025 (KP.2) vaccine provides additional protection against COVID-related hospitalizations in a population with pre-existing immunity

\*High risk defined by CDC: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html>  
Wilson A, *MedRxiv*, 2025



# Comprehensive COVID-19 Vaccine Safety Surveillance Program

# Moderna's Comprehensive COVID-19 Vaccine Safety Surveillance Program



- Ongoing systematic safety review<sup>1</sup>
- >1.8 billion doses distributed worldwide over the past 5 years
- Myocarditis/pericarditis remains very rare
  - Significantly lower rates since 2022/2023 season<sup>2,3</sup>
- Safety profile consistent across all approved Moderna COVID-19 vaccine compositions
- Benefit / risk continues to be favorable

1. Urdaneta V. *Open Forum Infect Dis*, 2024

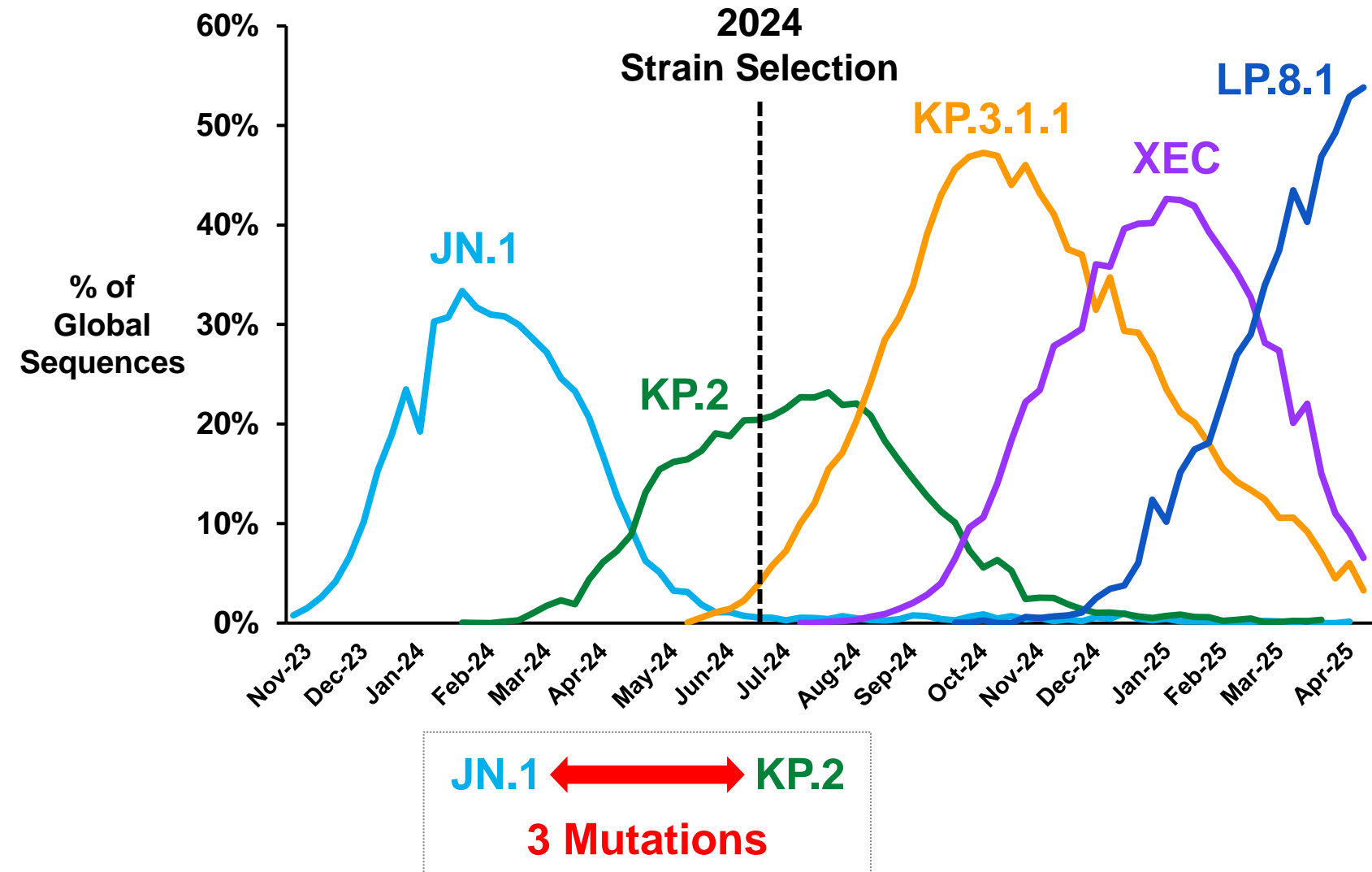
2. Shoaibi, A. *Vaccine*, 2023

3. Lloyd, P. C. *Drug Saf*, 2025

# **Cross Neutralization of Moderna 2024/2025 (KP.2 & JN.1) COVID-19 Vaccines Against New Emerging SARS-COV-2 Variants in Adults**

**Study 403**

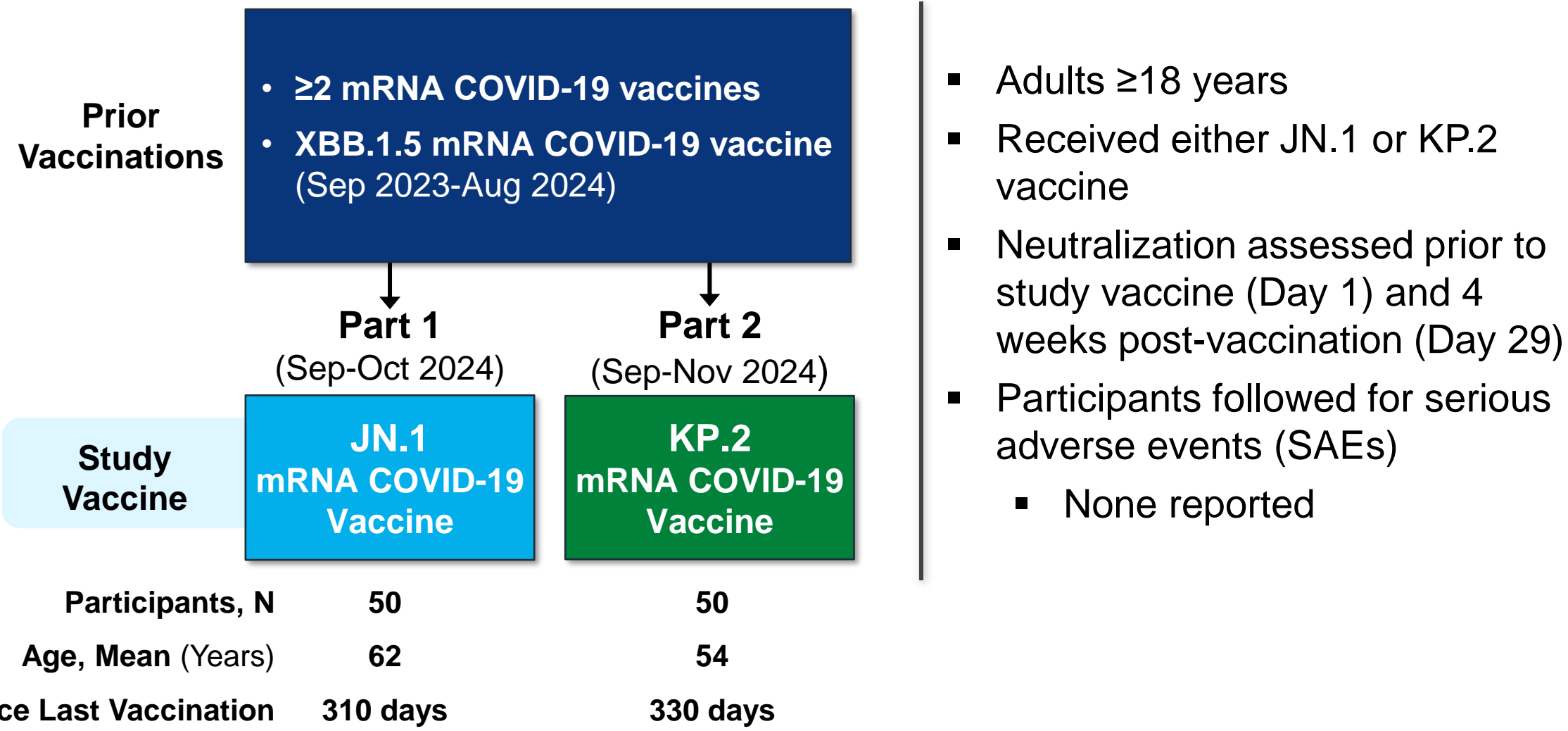
# Circulation of JN.1 and its Variants, 2024/2025



- JN.1 dominated early 2024, followed by KP.2
- KP.2 selected as 2024/2025 composition in US
- KP.2 better matches strains that subsequently emerged

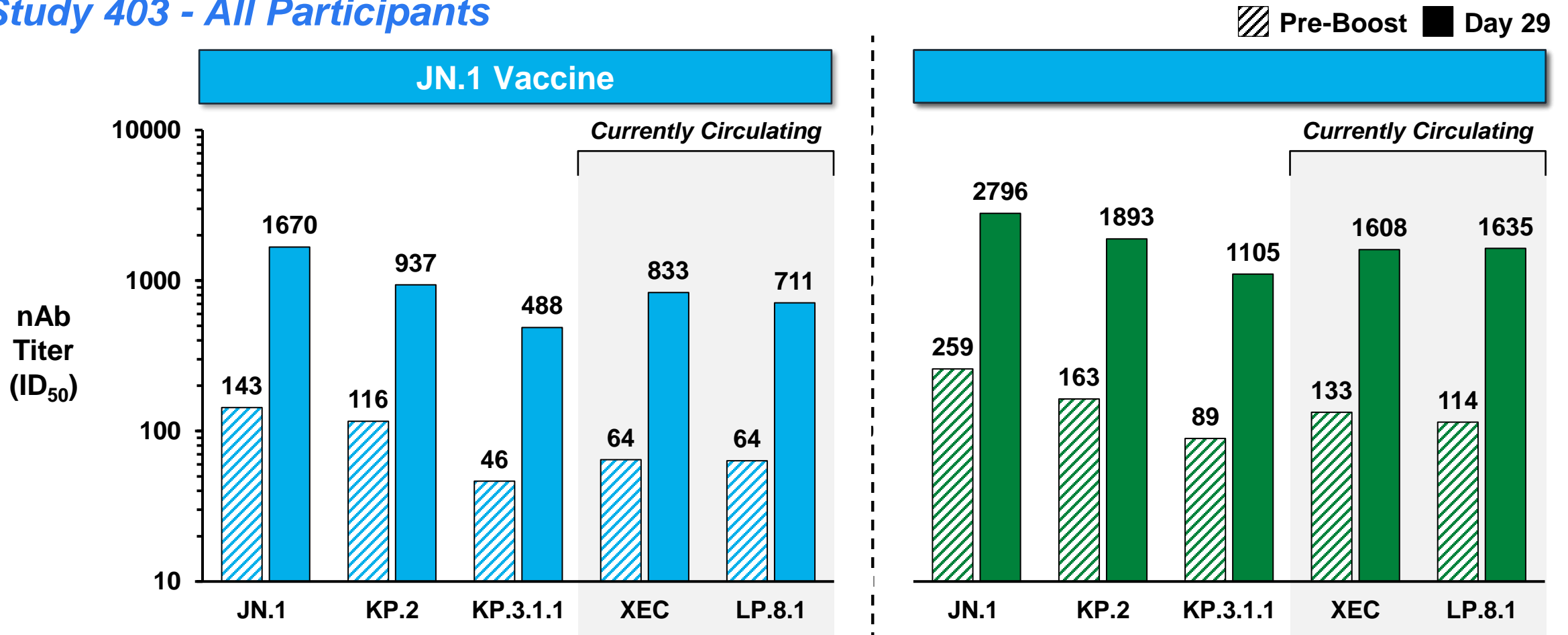
# Open-Label, Phase 3/4 Immunogenicity and Safety Study of Moderna JN.1 and KP.2 Vaccines

Study 403



# Day 29 Neutralizing Antibody Against JN.1 Variants following 2024/2025 (JN.1 or KP.2) Vaccine

*Study 403 - All Participants*



- Highest neutralization against matched variants; lower neutralization against circulating variants
- KP.2 vaccine elicited higher titers against currently circulating variants versus JN.1 vaccine

# **Variant Monitoring, Risk Assessment, and Preclinical Assessment of Investigational LP.8.1 Variant Vaccine**

**Darin Edwards, PhD**

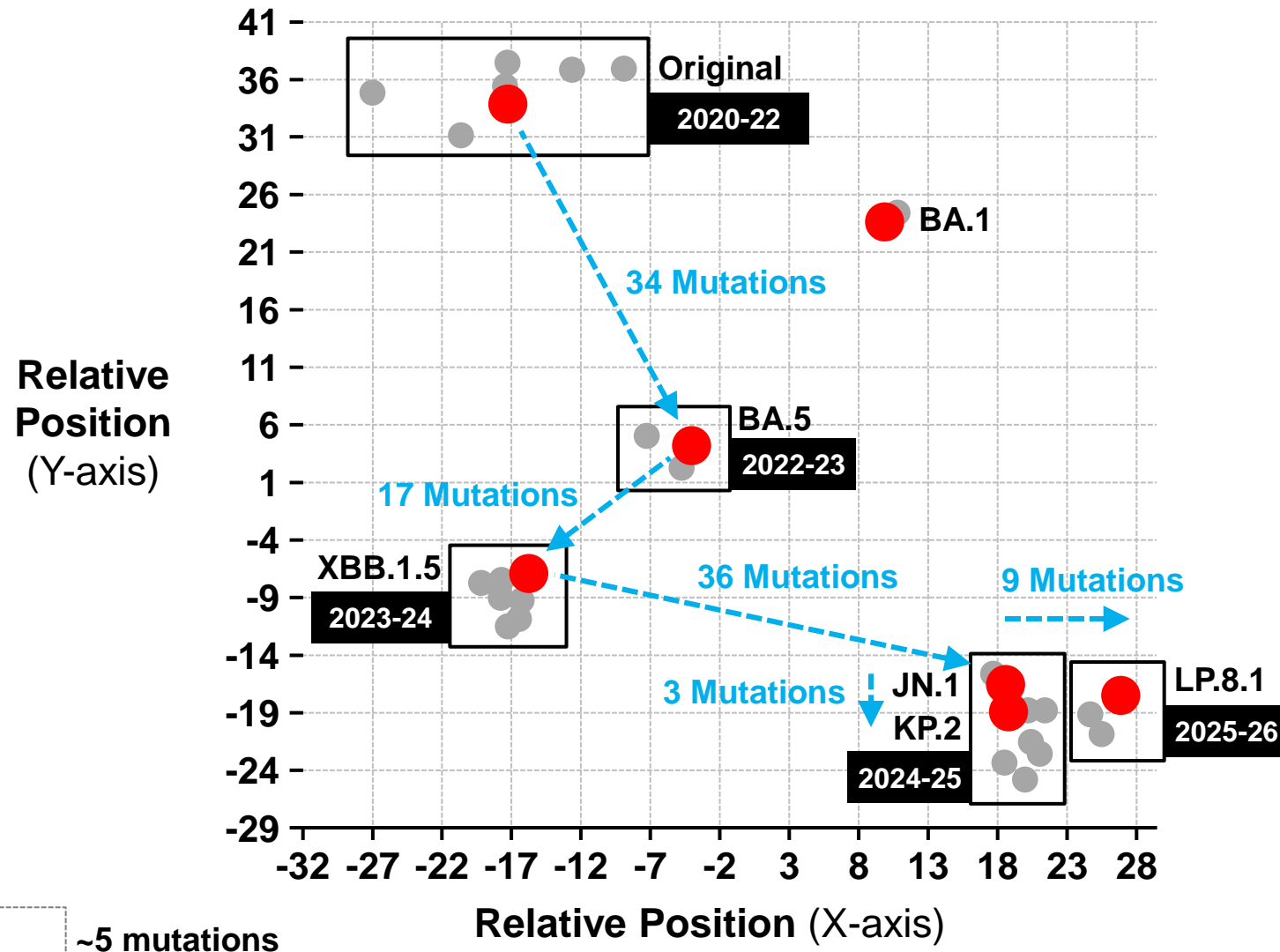
COVID-19 Program Leader

Moderna, Inc.



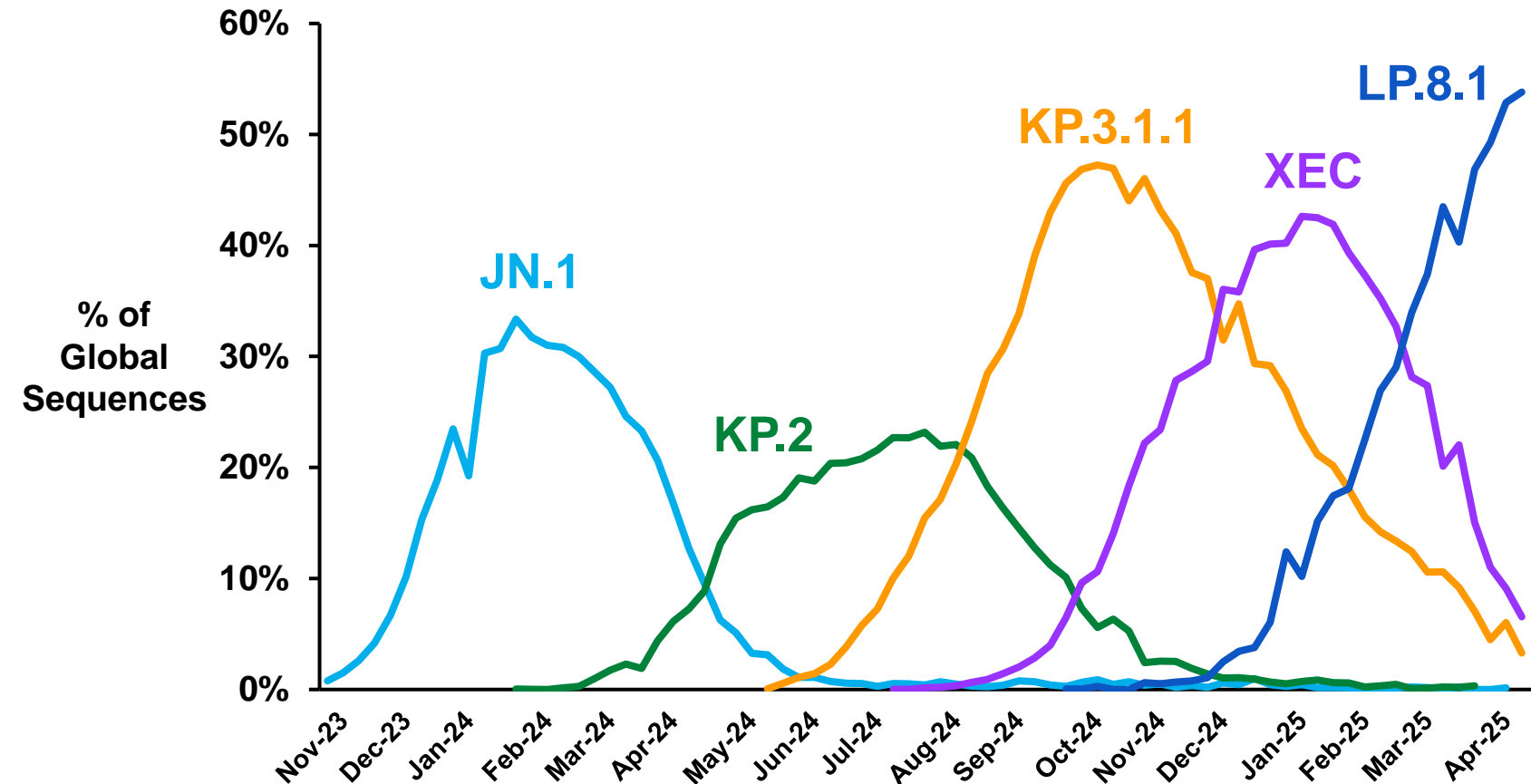
# Current Season Shows Stepwise Genetic Drift

*Genetic Cartography: 2D Map of Spike Protein Differences Among Variants*



- **Prior seasons:** Major evolutionary jumps between vaccine strains (Original to ancestral to BA.5 to XBB.1.5 to JN.1)
- **Current season:** JN.1 lineage continues to evolve with LP.8.1 differing from JN.1 by 9 mutations

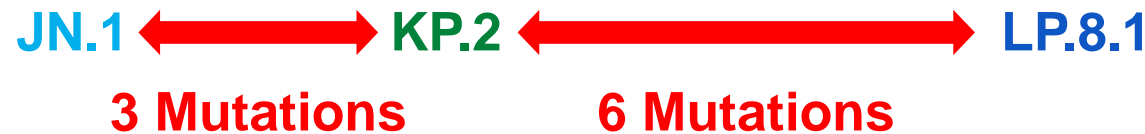
# LP.8.1 Highlights Continued Antigenic Drift from JN.1 in the Last 16 Months




## 2025

LP.8.1 is currently dominant and is further apart from:

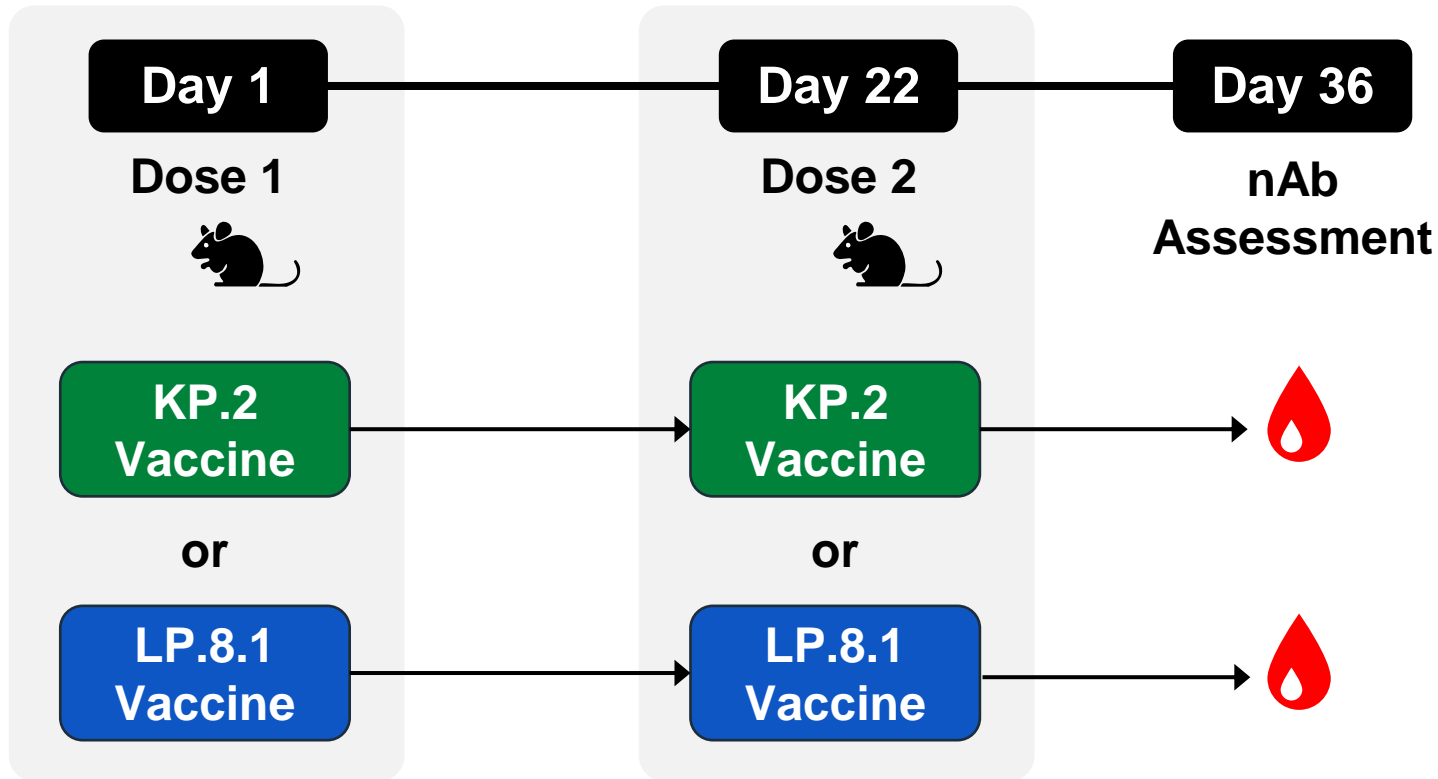
- KP.2 with 6 new Spike mutations
- JN.1 with 9 new Spike mutations
  - 2 new NTD glycans
  - 4 new RBD mutations





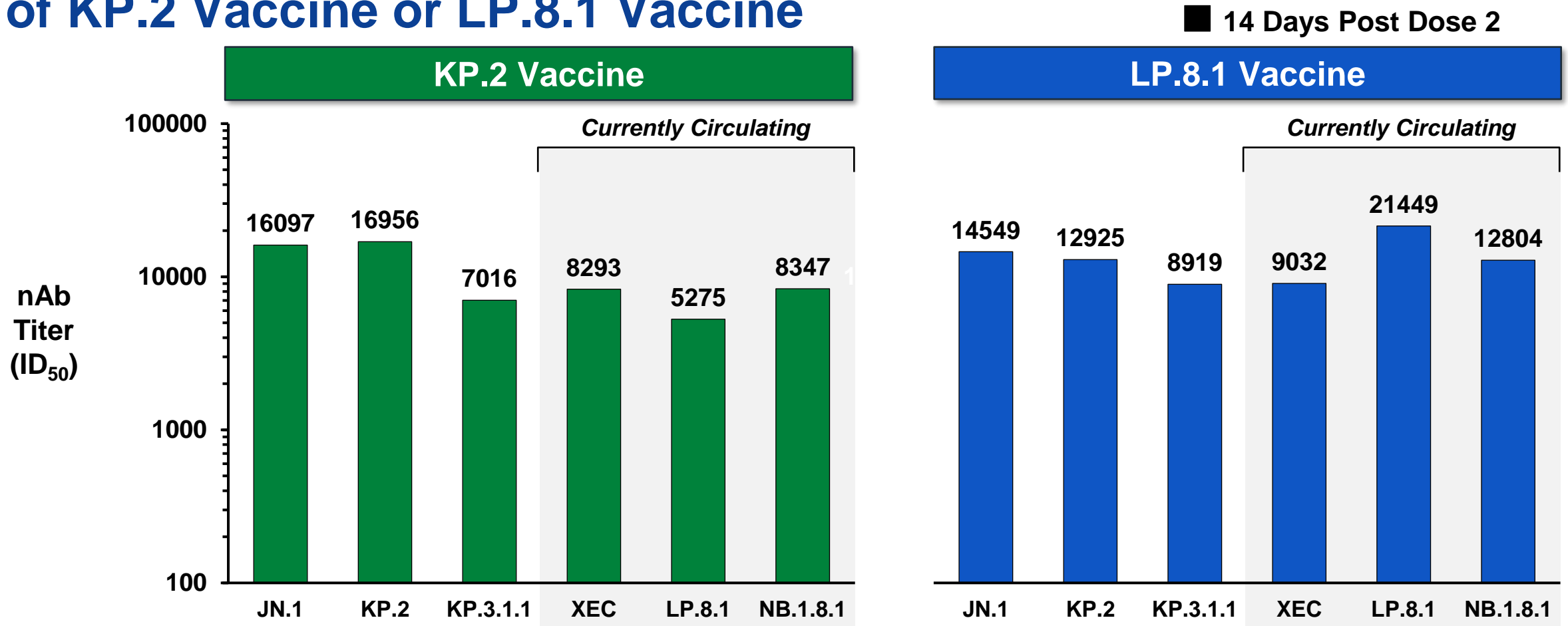
# Overview of Preclinical Studies to Assess Investigational LP.8.1 Variant Vaccine

# Primary 2-Dose Immunization Series: Immunogenicity of LP.8.1 or KP.2 Variant Vaccine in Naïve Mice



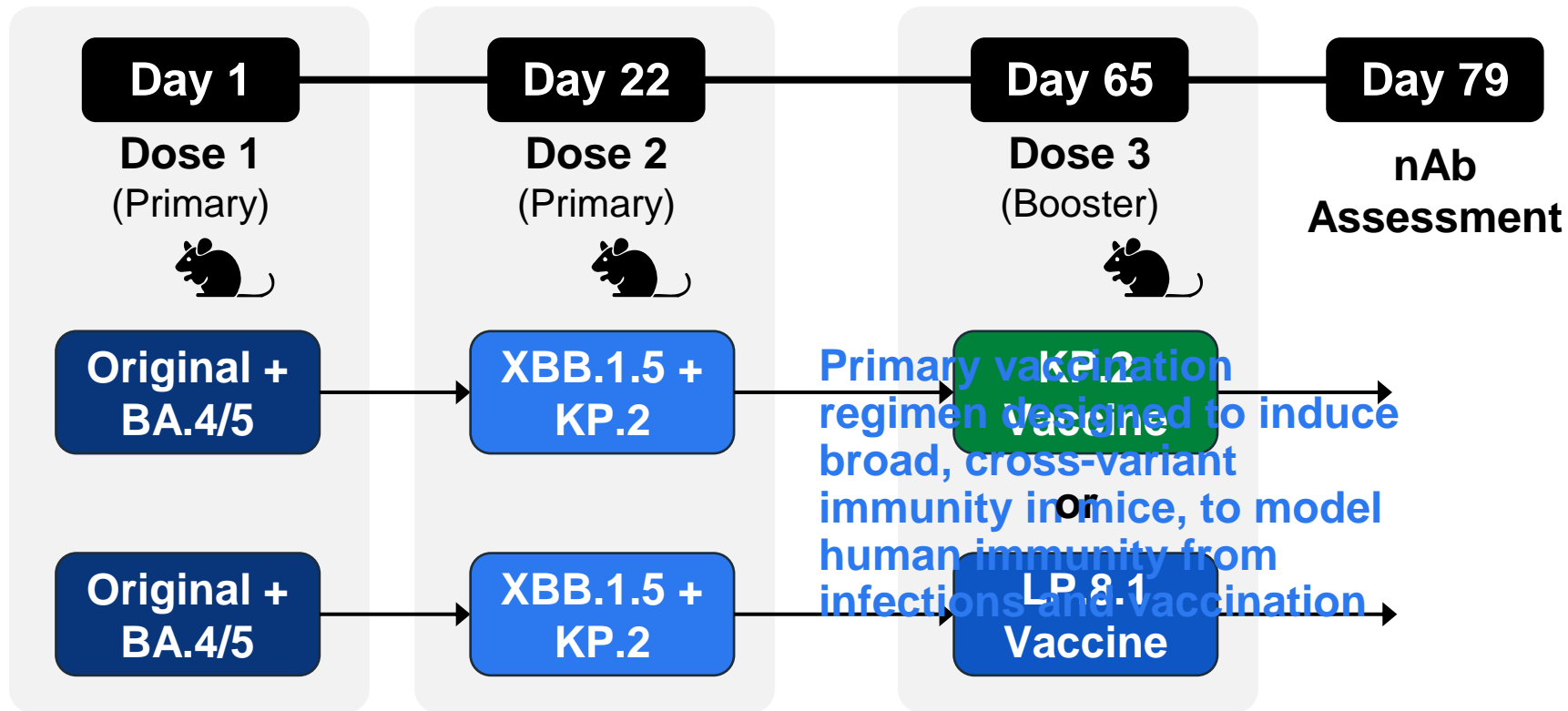
- **Objective**  
Assess currently approved vaccine composition and new variant vaccine against currently circulating variants
- **Immunogenicity**  
Neutralization of JN.1, KP.2, KP.3.1.1, XEC, LP.8.1, NB.1.8.1

# Neutralizing Antibody Titters in Mice 14 Days after Primary Series of KP.2 Vaccine or LP.8.1 Vaccine



- KP.2 vaccine has highest titers against JN.1 and KP.2, both of which no longer circulate, and reduced neutralization against currently circulating variants, including LP.8.1
- LP.8.1 vaccine neutralizes LP.8.1 and cross-neutralizes subvariants of JN.1

# Booster Dose Immunization Series: Immunogenicity of LP.8.1 or KP.2 Variant Vaccine in Variant-Experienced Mice



## Authorized / Approved Vaccines

- **Original:** Dec 2020 – Aug 2022
- **BA.4/5:** Aug 2022 – Sep 2023
- **XBB.1.5:** Sep 2023 – Aug 2024
- **KP.2:** Aug 2024 - Current

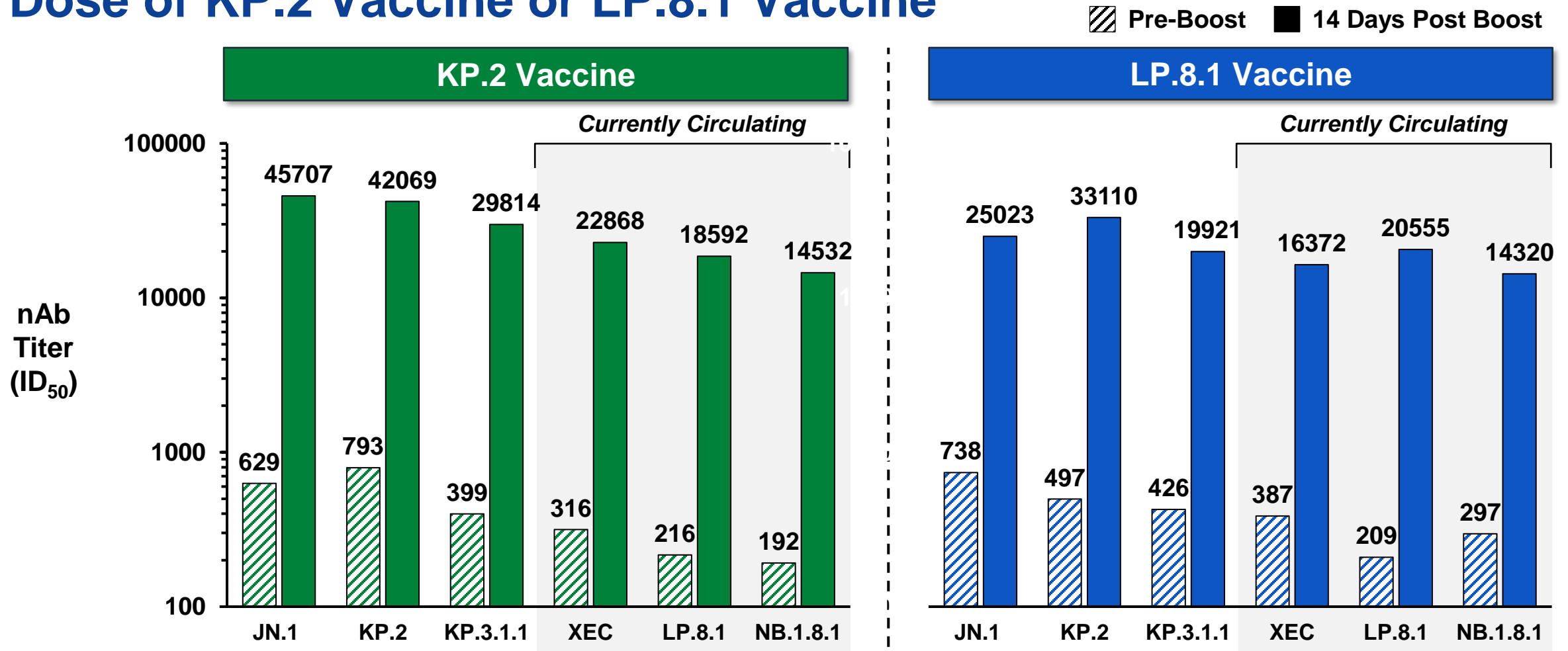
## Objective

Assess cross-neutralization of strain-matched and circulating variants after 3<sup>rd</sup> dose of currently approved vaccine (KP.2) vs investigational variant vaccine (LP.8.1)

## Immunogenicity

Neutralization of JN.1, KP.2, LP.8.1, XEC, KP.3.1.1, NB.1.8.1

# Neutralizing Antibody Titters in Mice 14 Days after Booster (3rd) Dose of KP.2 Vaccine or LP.8.1 Vaccine



- KP.2 and LP.8.1 vaccines cross-neutralize JN.1 sub-variants in variant-experienced animals
- LP.8.1 vaccine more immunogenic than KP.2 vaccine against LP.8.1

# Conclusions

Jacqueline Miller, MD

Chief Medical Officer

Moderna, Inc.



# Summary

## Safety and Effectiveness (2024/2025)

- Moderna 2024/2025 (KP.2) demonstrated significant real-world effectiveness in setting of increasing population-level immunity
- Clinical data showed robust neutralization against matched variants
- Safety profile consistent with all approved Moderna COVID-19 vaccine compositions
- Benefit / risk profile continues to be favorable

## Annual Strain Selection

- KP.2 vaccine elicited higher titers against more recent strains versus JN.1 vaccine
- LP.8.1 currently dominant in US
- LP.8.1 vaccine candidate neutralized circulating strains in preclinical studies
- If current trends continue, LP.8.1 vaccine is likely to better match emerging variants

## 2025/2026 Readiness

- Prepared to supply FDA recommended vaccine by mid-August 2025
- Clinical trial with selected 2025/2026 vaccine composition will be conducted post licensure
- Moderna will continue to monitor vaccine safety and effectiveness

# **THANK YOU to Our Study Collaborators, Investigators, and Participants**

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