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2024-2025 COVID-19 Vaccine Formula: Pfizer/BioNTech Clinical and Preclinical Supportive Data

Vaccines and Related Biological Products Advisory Committee

June 5, 2024

Presentation Outline

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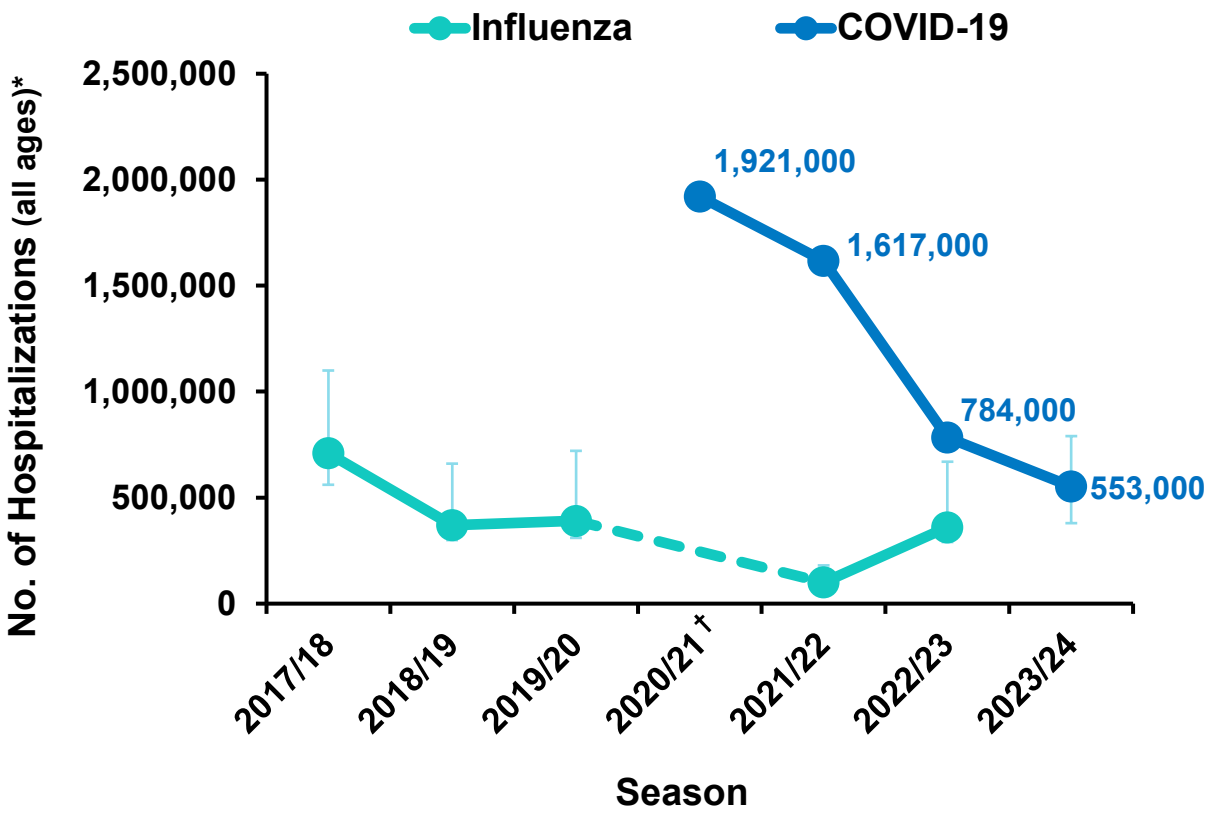
Real-World Evidence & Variant Epidemiology

Omicron XBB.1.5-Adapted Vaccine Clinical Humoral Immune Responses

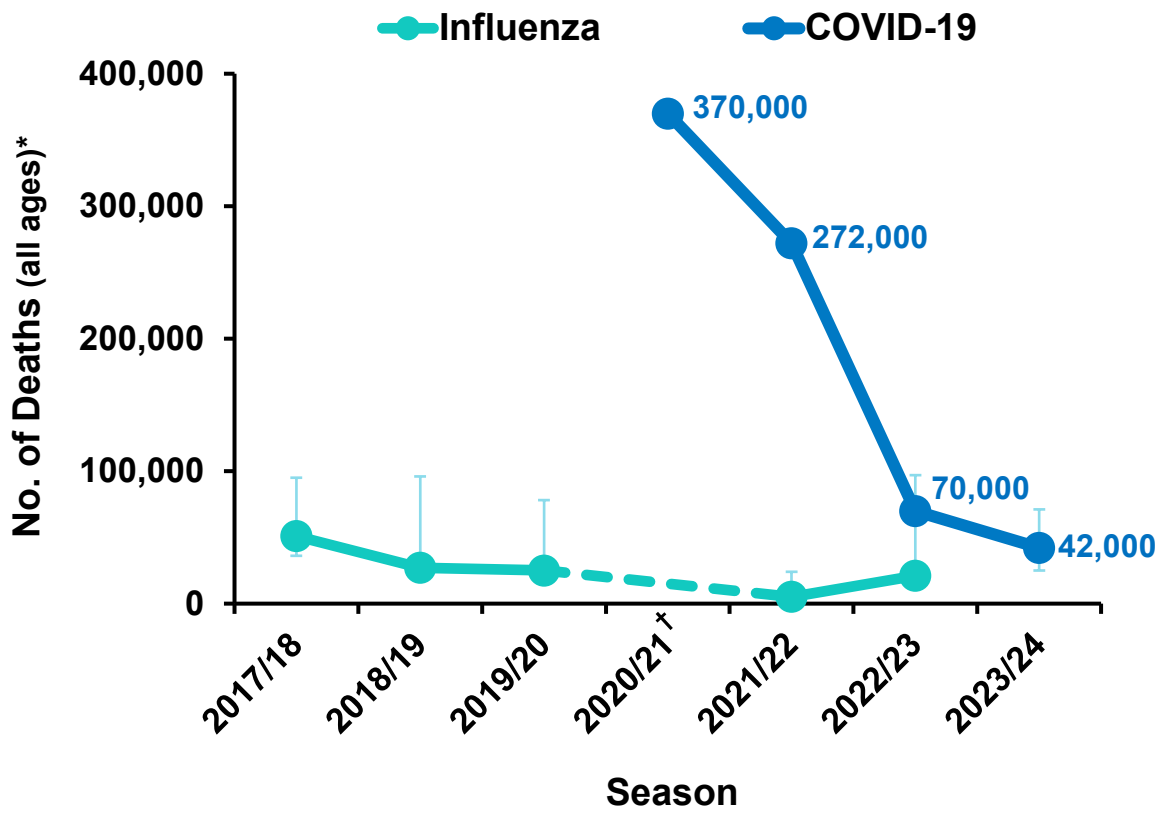
Preclinical Evaluation of Omicron JN.1 Lineage-Adapted Vaccines

Seasonal COVID-19 Burden is Comparable to or Higher than Influenza

U.S. Hospitalizations[1-3]



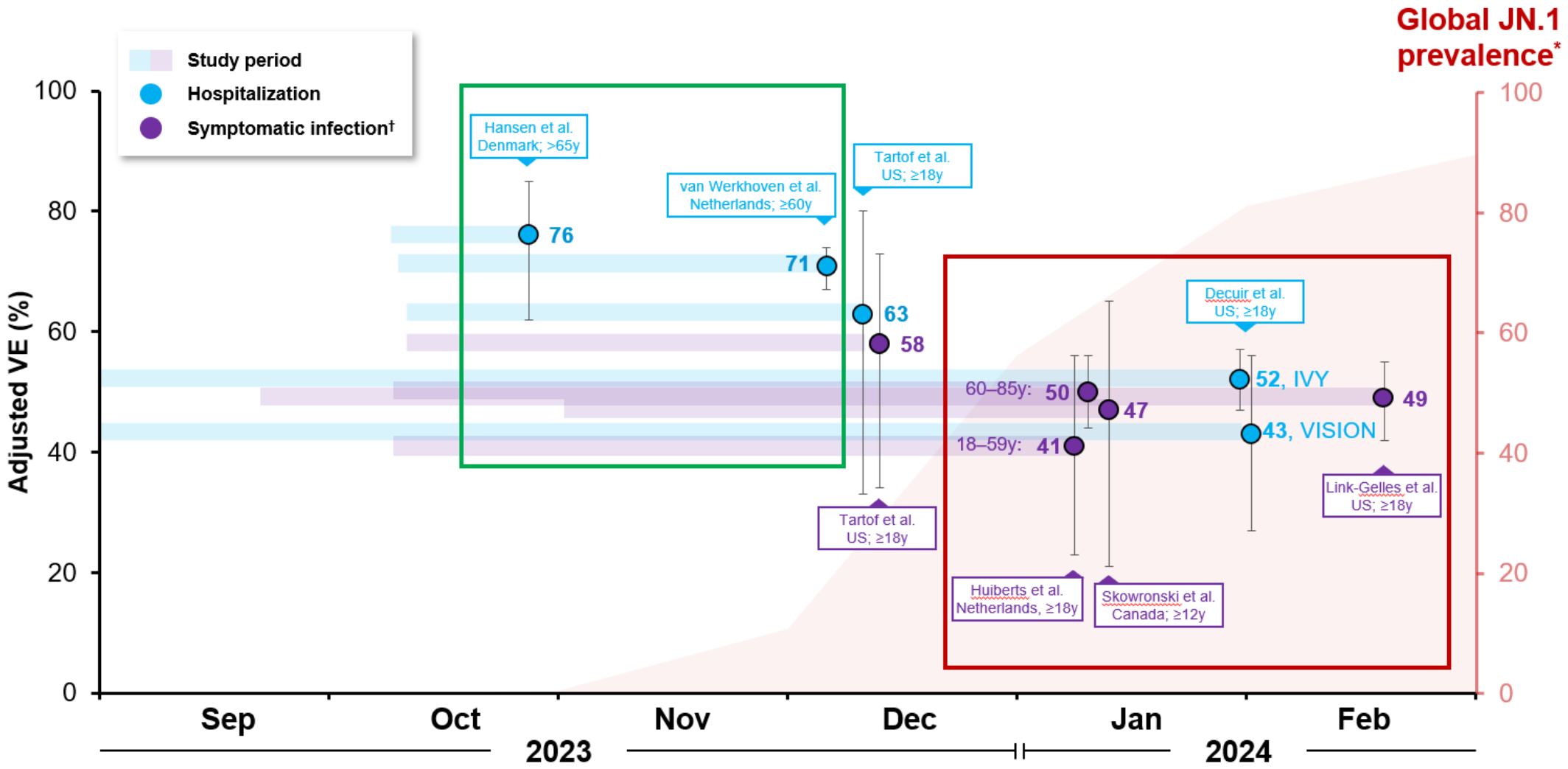
U.S. Deaths[2-4]



* Error bars represent 95% uncertainty intervals for influenza and are not listed for COVID-19 data.
† 2020-2021 season estimates are not available due to minimal influenza activity.

1. US Department of Health & Human Services. COVID-19 Reported Patient Impact and Hospital Capacity by State Timeseries (RAW). https://healthdata.gov/Hospital/COVID-19-Reported-Patient-Impact-and-Hospital-Capa/g62h-syeh/about_data
2. Centers for Disease Control and Prevention. Disease Burden of Flu. https://www.cdc.gov/flu/about/burden/index.html.
3. Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases (NCIRD). 2023-2024 U.S. Flu Season: Preliminary In-Season Burden Estimates. Accessed 2024 May 30. https://www.cdc.gov/flu/about/burden/preliminary-in-season-estimates.htm.
4. Centers for Disease Control and Prevention. COVID Data Tracker. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2024 May 30. https://covid.cdc.gov/covid-data-tracker.

XBB.1.5 Vaccine Effectiveness Initially Robust, Decreased Over Course of 2023/2024 Season

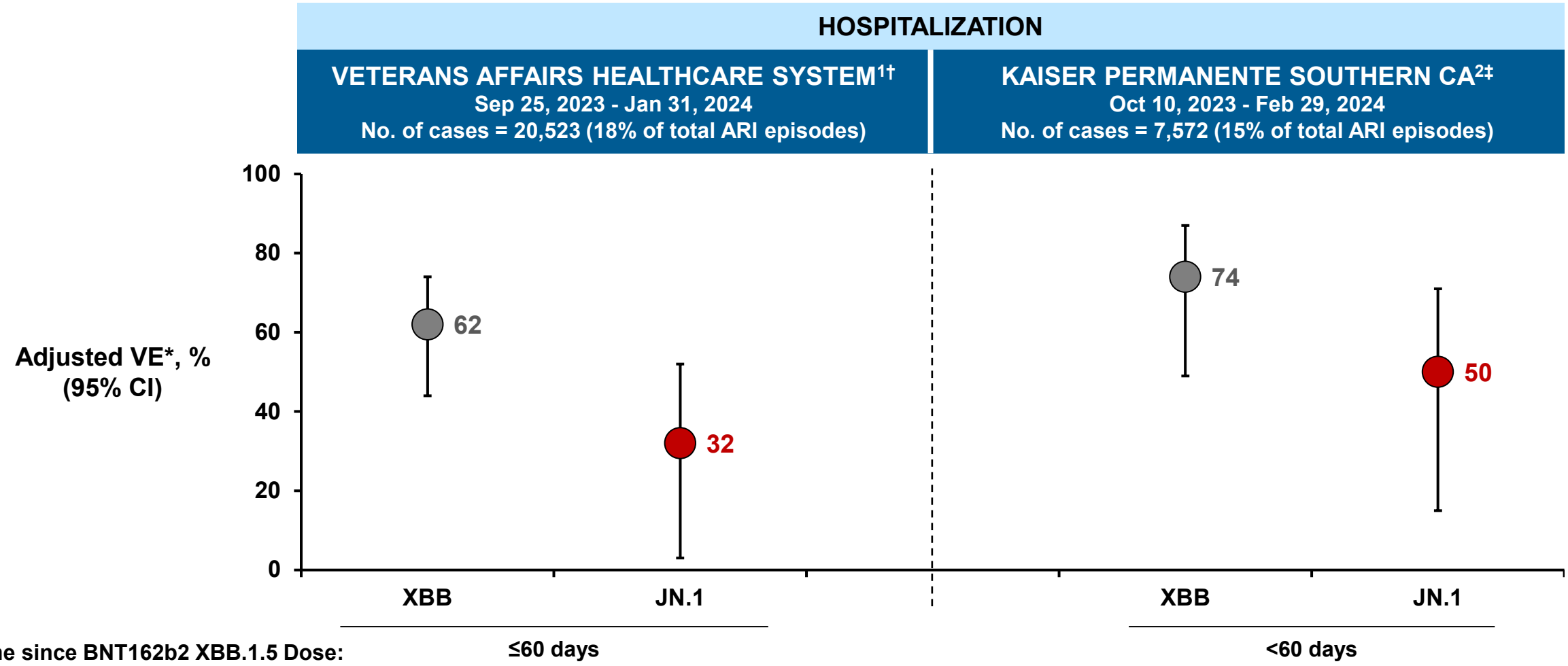


VE, vaccine effectiveness

*Historical data from: https://cov-spectrum.org. Accessed 2024 March 14. † Includes outcomes such as symptomatic infections, outpatient visits, and infections that were almost all symptomatic.

Hansen CH et al. Lancet Infect Dis 2024;24:e73-4; van Werkhoven CH et al. Euro Surveill 2024;29:pii=2300703; Tartof SY et al. medRxiv 2024; DeCuir J et al. MMWR 2024;73:180–188; Huiberts AJ et al. Euro Surveill 2024;29:pii=2400109; Skowronski DM et al. Euro Surveill 2024;29:pii=2400076; Link-Gelles R et al. MMWR 2024;73:77-83 and updated at ACIP

Vaccine Effectiveness Lower Against JN.1 Compared to XBB, When Controlling for Time Since Vaccination



ARI, acute respiratory infection; CA, California; CI, confidence interval; No., number; PCR, polymerase chain reaction; VE, vaccine effectiveness

* Compared to no receipt of any XBB vaccine.

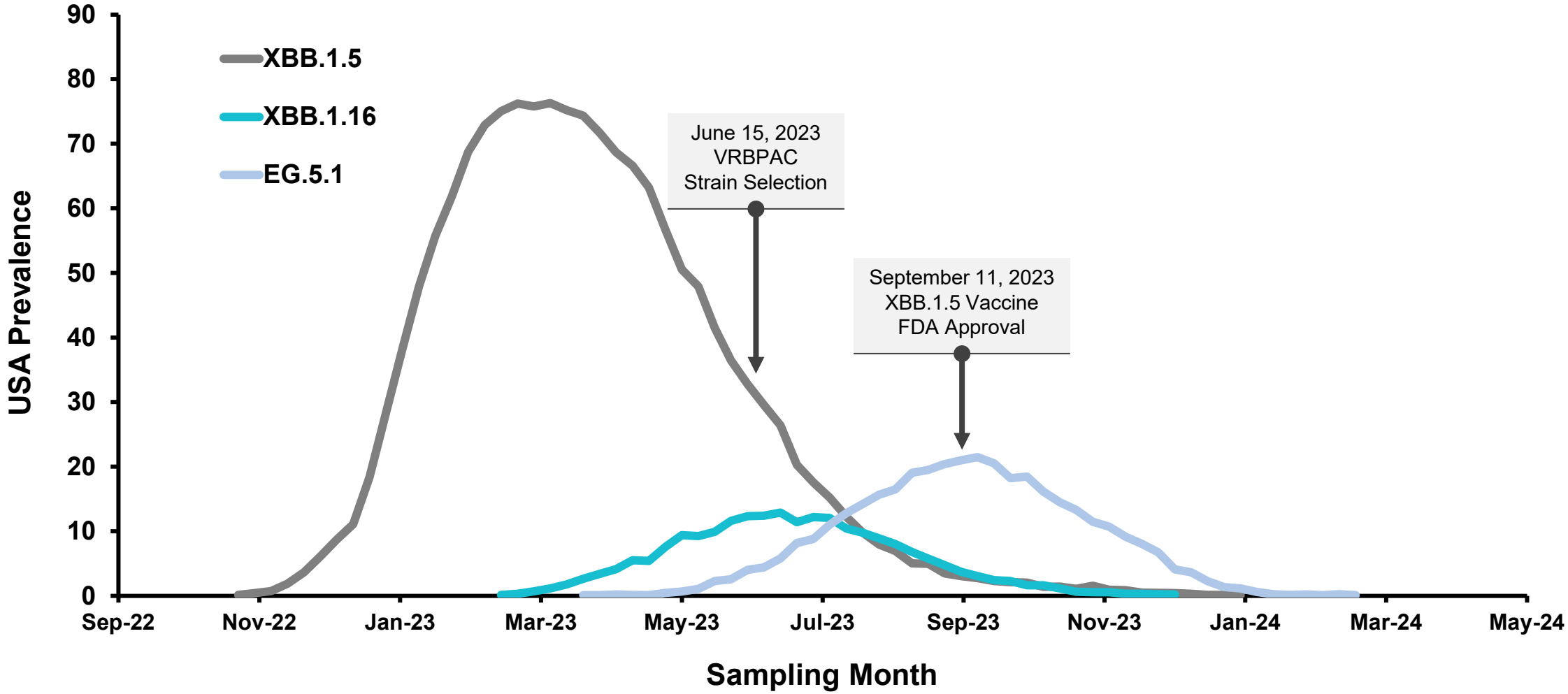
† Strain predominance periods defined as >80% prevalence of sequenced strains in the United States. The XBB period was defined as Sep 25 – Nov 30, 2023, and the JN.1 period was defined as Jan 1 – Jan 31, 2024.

‡ Strain determined using a hierarchical approach depending on available information: (i) whole genome sequencing (WGS), (ii) spike gene target failure, or (iii) periods of >80% sublineage predominance based on WGS data from US Health and Human Services Region 9. For (iii), cases were classified as XBB from Oct 10 – Dec 9, 2023, and as JN.1 from Jan 20 – Feb 29, 2024.

1. Caffrey et al. medRxiv. https://www.medrxiv.org/content/10.1101/2024.04.05.24305063v1 2. Tartof et al. medRxiv. https://www.medrxiv.org/content/10.1101/2024.05.04.24306875v1

XBB.1.5 Dominance Declining and XBB.1.16 Peaking at Time of June 2023 VRBPAC

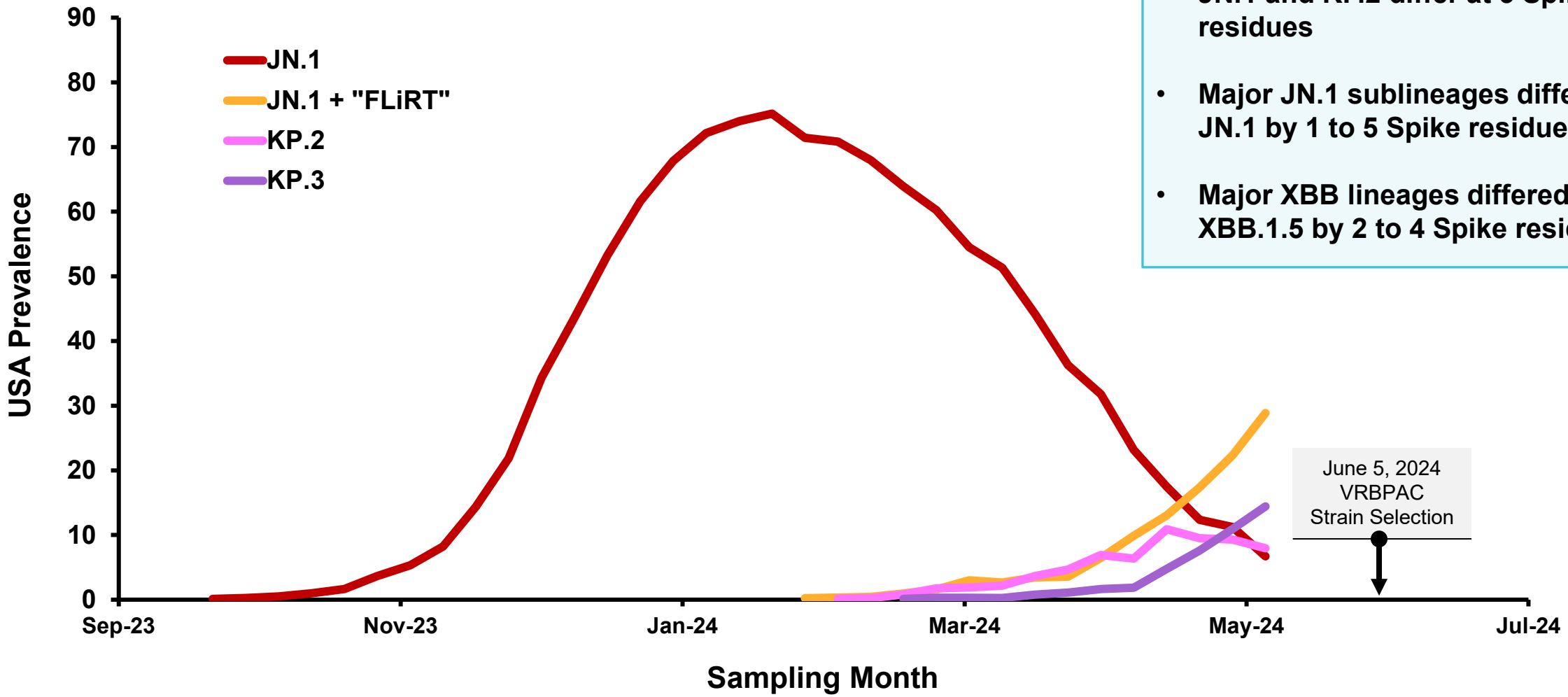
Trajectory of Emerging Variants Compared with Historic Dominant Variants



Source: GISAID - gisaid.org; data accessed/analysed/plotted within Pfizer, as of June 2, 2024. Each individual labelled lineage includes all sublineages with the same Spike protein amino acid sequence.

JN.1 Transitioning to Rise of Expanding Set of Closely Related Sublineages

- **JN.1 and KP.2 differ at 3 Spike residues**
- **Major JN.1 sublineages differ from JN.1 by 1 to 5 Spike residues**
- **Major XBB lineages differed from XBB.1.5 by 2 to 4 Spike residues**

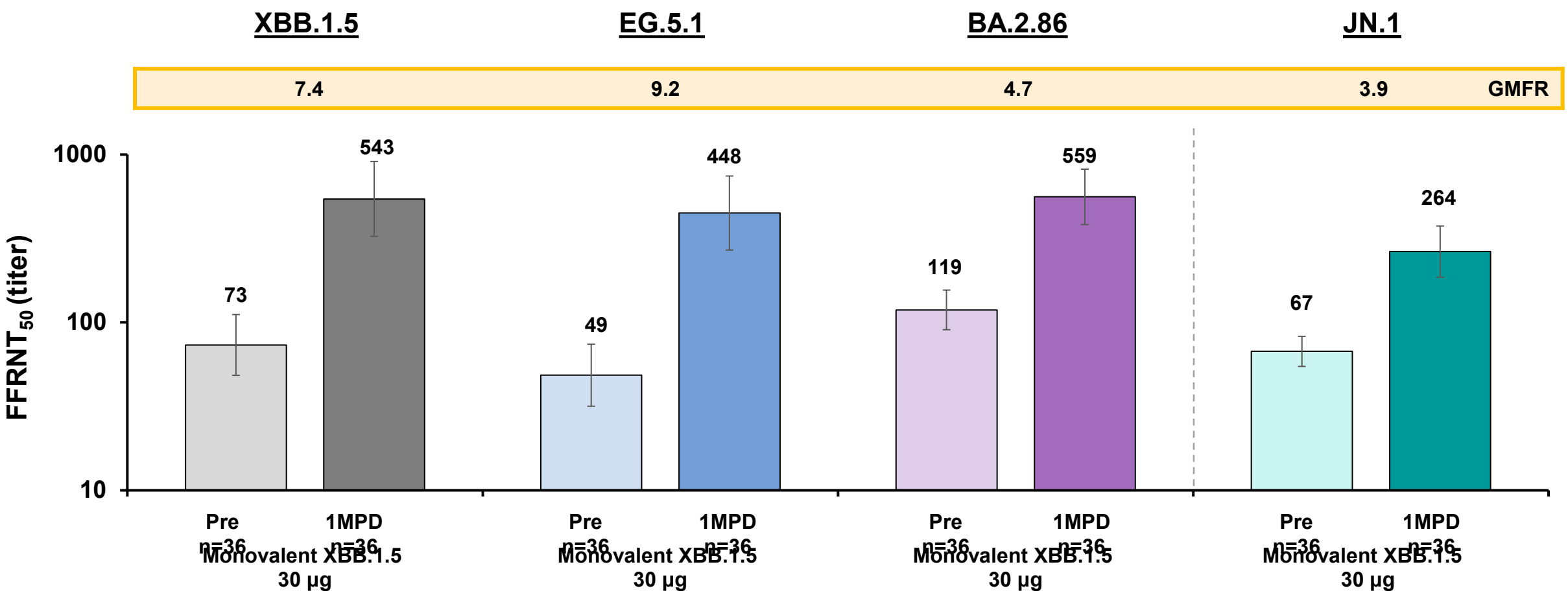


Source: GISAID - gisaid.org; data accessed/analysed/plotted within Pfizer, as of June 2, 2024. Each individual labelled lineage includes all sublineages with the same Spike protein amino acid sequence, except JN.1+"FLIRT curve does not contain KP.2. **JN.1+"FLiRT"** includes all JN.1 sublineages that contain S: R346T, F456L; **KP.2** contains S: R346T, F456L, V1104L; **KP.3** contains F456L, Q493E, V1104L.

XBB.1.5 Omicron-Adapted Vaccine Clinical Humoral Immune Response

Clinical Study: XBB.1.5 Vaccine Neutralizing Titers Maintain Against Variant Drift Until Emergence of Omicron JN.1

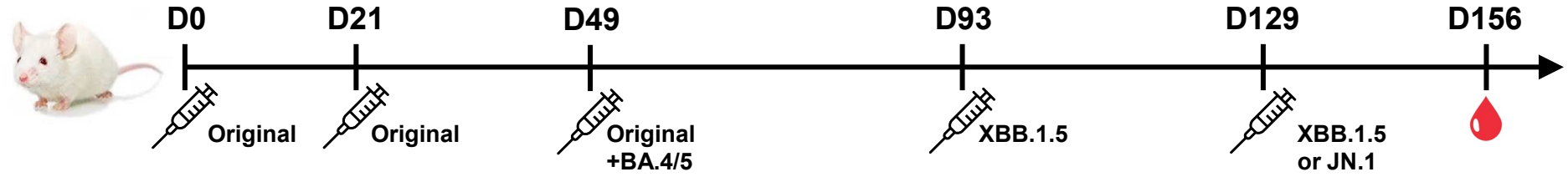
Evaluable Immunogenicity Population* – FFRNT Assay

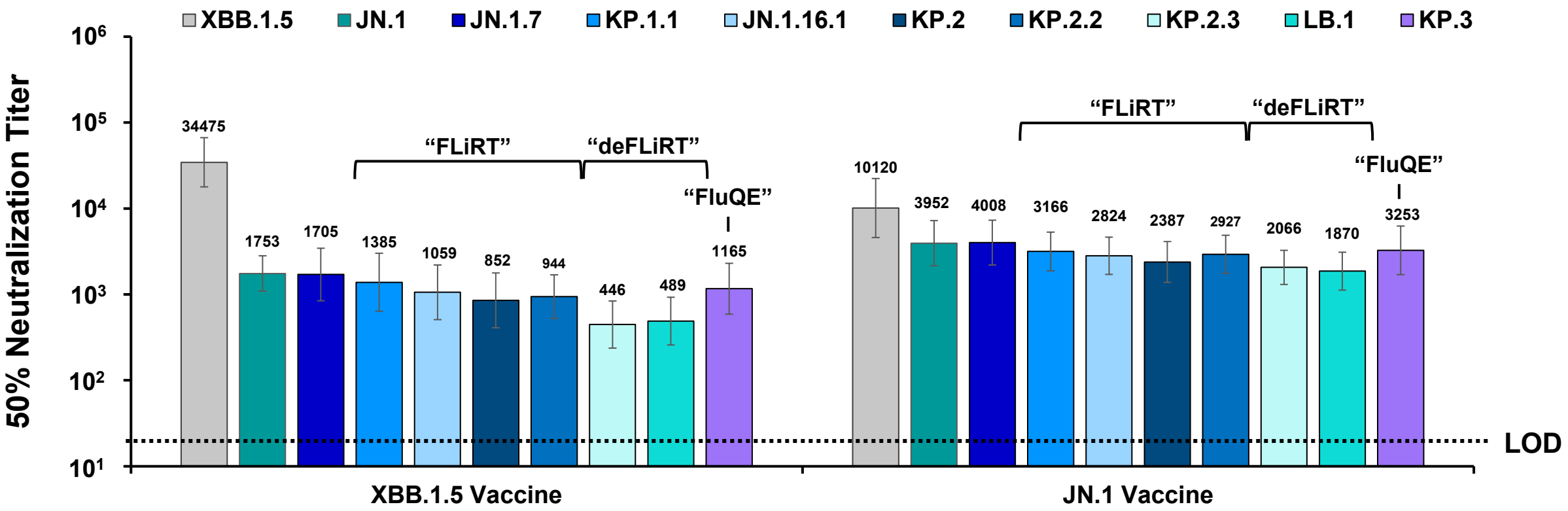


All participants were 18-55 years old; baseline seropositive for prior SARS-CoV-2 infection and had ≥ 3 mRNA COVID-19 vaccines with last vaccine being a bivalent (Original + Omicron BA.4/5) COVID-19 vaccine 150-365 days prior to enrolment.
GMFR = Geometric Mean Neutralizing Titer Fold Rise; Pre = Pre vaccination; 1MPD = 1 month post dose; FFRNT = fluorescent focus reduction neutralization test
XBB.1.5, BA.2.86 and EG.5.1 assays (grey, blue and purple bars) were run at a different time to JN.1 (green bars), which was also run with XBB.1.5, BA.2.86 (Neutralization titers and GMFRs were similar to those presented here).

Preclinical Evaluation of an Omicron JN.1 Adapted Vaccine

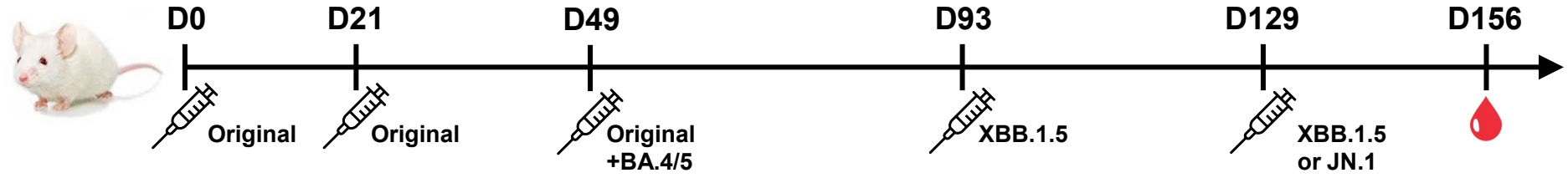
Vaccine-Experienced: 1 Month Post 5th Dose Neutralizing Responses Elicited by JN.1 and XBB.1.5 Vaccines

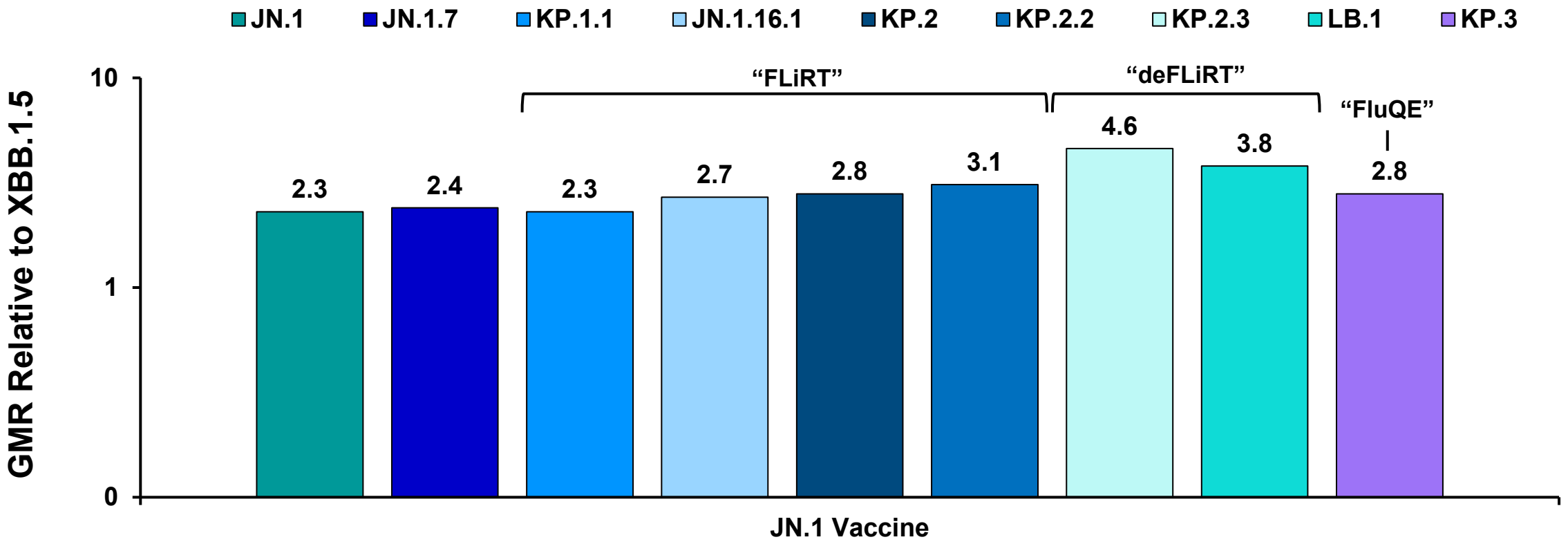




Pseudovirus neutralization assay; LOD = Limit of detection; the lowest serum dilution of 1:20.
N = 10 mice per vaccine group. Vaccine dose 0.5 µg.
"FLiRT" contains S: **F**456**L**, **R**346**T**; **"deFLiRT"** contains S: S31**del**, **F**456**L**, **R**346**T**; **"FLuQE"** contains S: **F**456**L**, **Q**493**E**

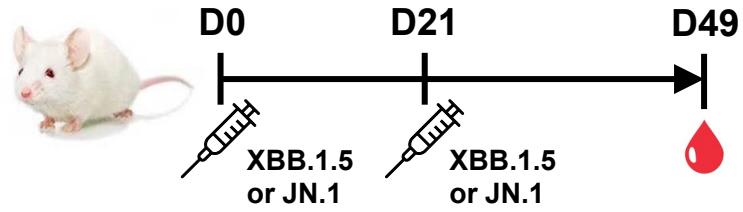
Vaccine-Experienced: Geometric Mean Ratios of JN.1 to XBB.1.5 Vaccine Neutralizing Titers at 1 Month Post 5th Dose

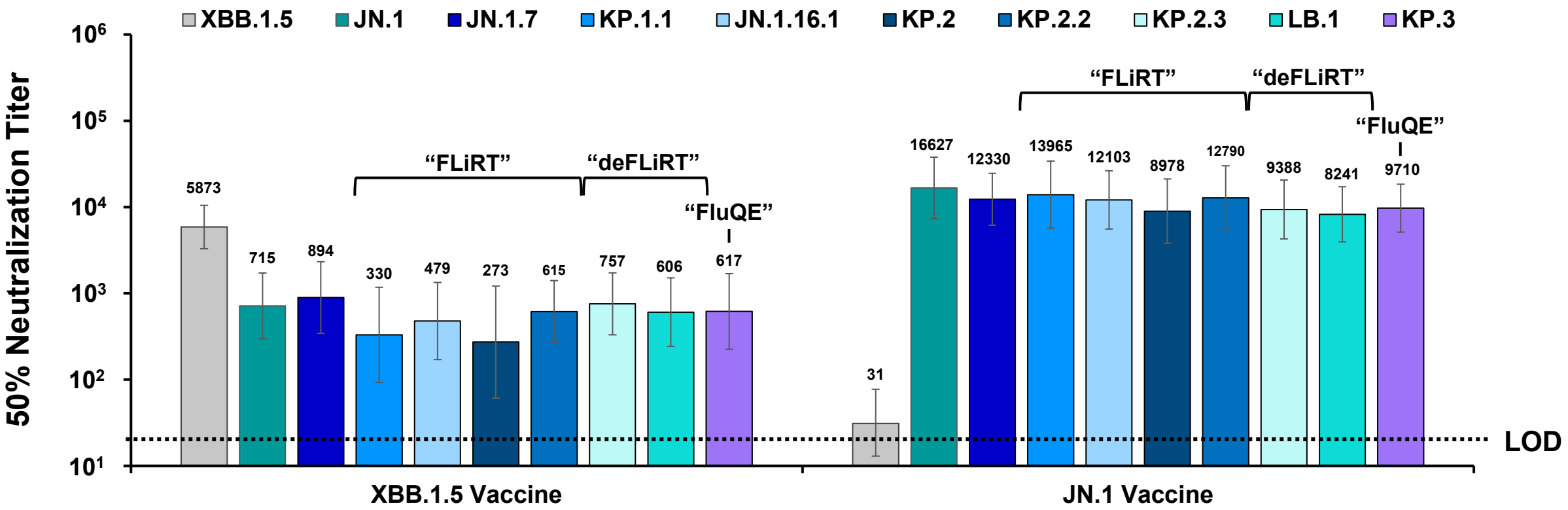




Pseudovirus neutralization assay.
N = 10 mice per vaccine group. Vaccine dose 0.5 µg.
"FLiRT" contains S: **F**456**L**, **R**346**T**; **"deFLiRT"** contains S: S31**del,** **F**456**L**, **R**346**T**; **"FLuQE"** contains S: **F**456**L**, **Q**493**E**

Vaccine Naïve: 1 Month Post 2nd Dose Neutralizing Responses Elicited by JN.1 and XBB.1.5 Vaccines

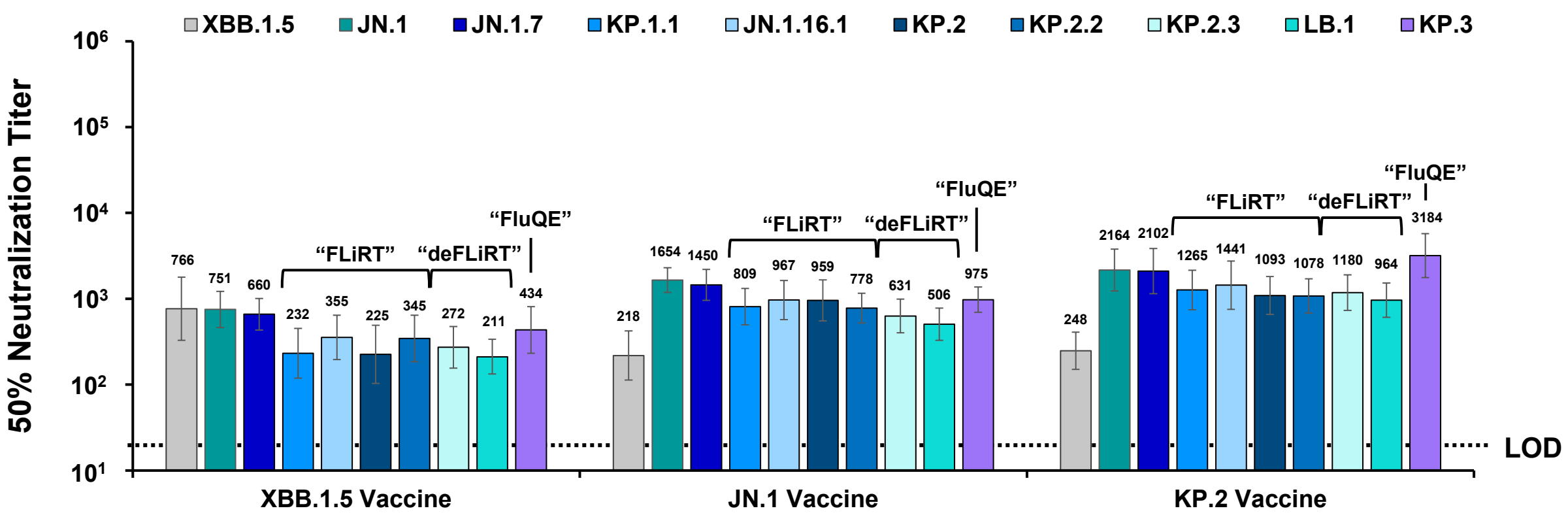




Pseudovirus neutralization assay; LOD = Limit of detection; the lowest serum dilution of 1:20.
N = 10 mice per vaccine group. Vaccine dose 0.5 μg.
"FLiRT" contains S: **F**456**L**, **R**346**T**; **"deFLiRT"** contains S: S31**del**, **F**456**L**, **R**346**T**; **"FLuQE"** contains S: **F**456**L**, **Q**493**E**

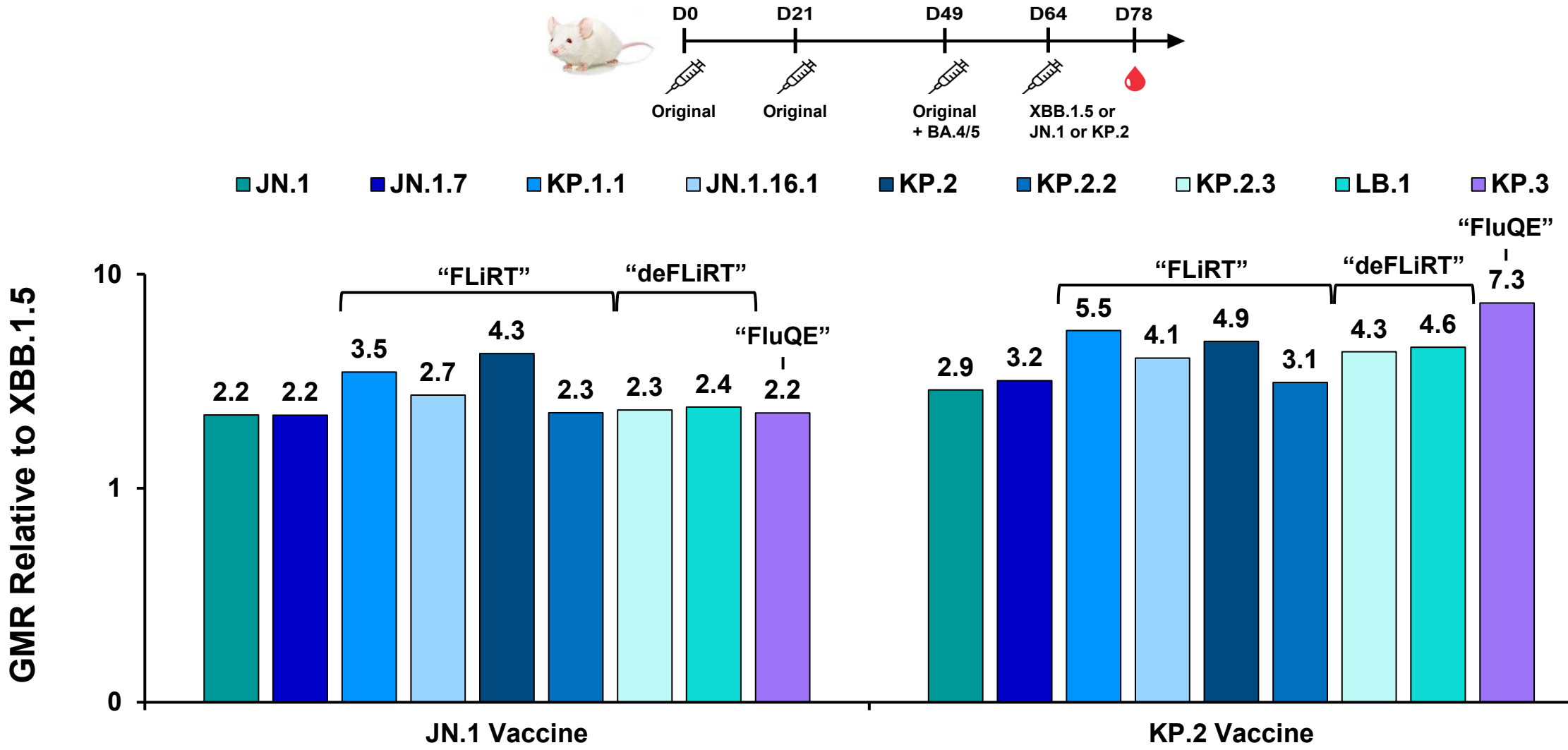
Preclinical Evaluation of an Omicron KP.2-Adapted Vaccine

Vaccine-Experienced: 2 Weeks Post 4th Dose Neutralizing Responses Elicited by XBB.1.5, JN.1 and KP.2 Vaccines



Pseudovirus neutralization assay; LOD = Limit of detection; the lowest serum dilution of 1:20.
N = 10 mice per vaccine group. Vaccine dose 0.5 µg
"FLiRT" = S: **F**456**L**, **R**346**T**; **"deFLiRT"** = S: S31**del, F**456**L**, **R**346**T**; **"FLuQE"** = S: **F**456**L**, **Q**493**E**

Vaccine-Experienced: Geometric Mean Ratio of JN.1 and KP.2 Vaccine Responses Compared to XBB.1.5 Vaccine Responses, 2 Weeks Post 4th Dose



Pseudovirus neutralization assay; LOD = Limit of detection; the lowest serum dilution of 1:20.
N = 10 mice per vaccine group. Vaccine dose 0.5 µg
"FLiRT" = S: **F**456**L**, **R**346**T**; **"deFLiRT"** = S: S31**del, F**456**L**, **R**346**T**; **"FLuQE"** = S: **F**456**L**, **Q**493**E**

Conclusions

Summary Evidence Supports a JN.1 Lineage Vaccine Update for the 2024/2025 Season

- XBB.1.5 vaccine had robust effectiveness against XBB lineages that declined against JN.1
- JN.1 sublineages are dominant, with minimal antigenic differences within family, mirroring observations for XBB lineages relative to XBB.1.5
- JN.1- and KP.2-adapted vaccines confer improved neutralizing responses over XBB.1.5 vaccine against broad panel of emerging variants

- Prepared to initiate supply of either JN.1 vaccine or KP.2 vaccine immediately upon approval

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