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2025-2026 COVID-19 Vaccine Formula: Pfizer/BioNTech Supportive Data

Vaccines and Related Biological Products Advisory Committee

May 22, 2025

Presentation Outline

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Vaccine Research & Development
Pfizer Inc.

Evidence Supporting Vaccine Variant Updates

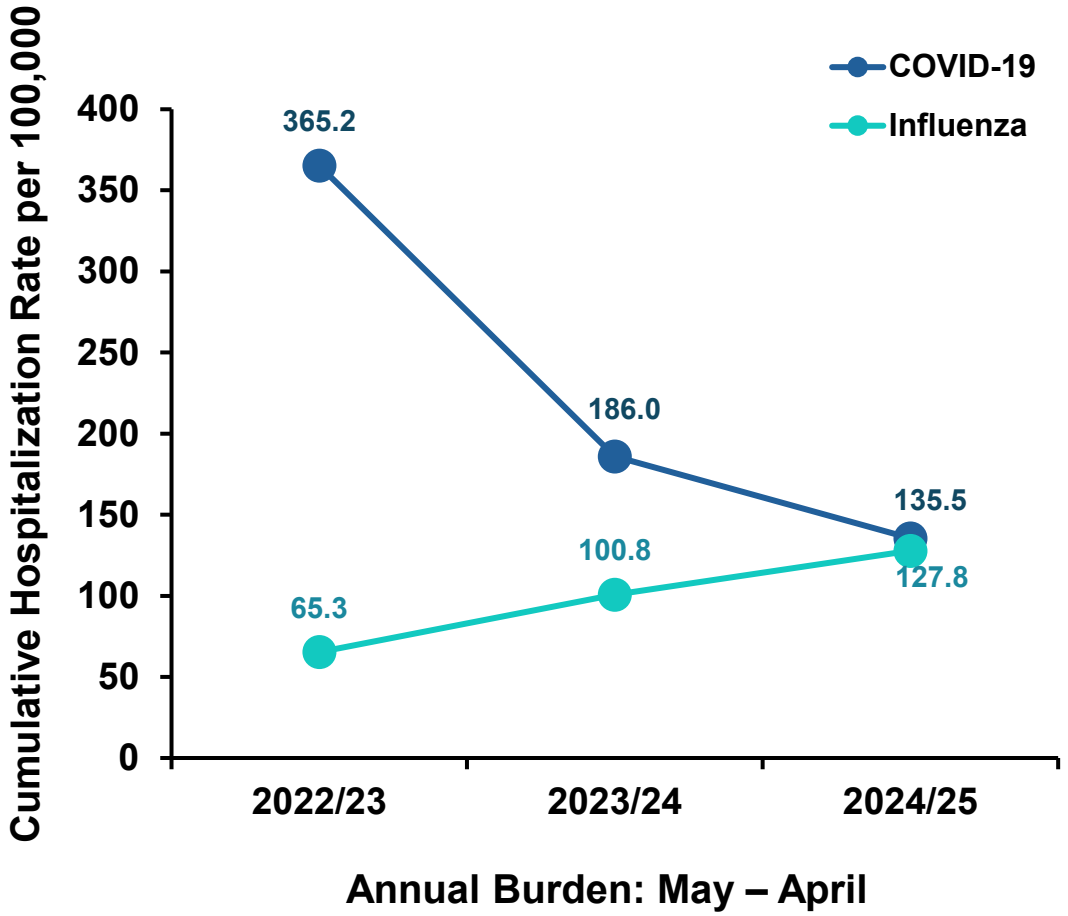
Real World Evidence and Variant Epidemiology

KP.2-Adapted Vaccine Clinical Immune Responses

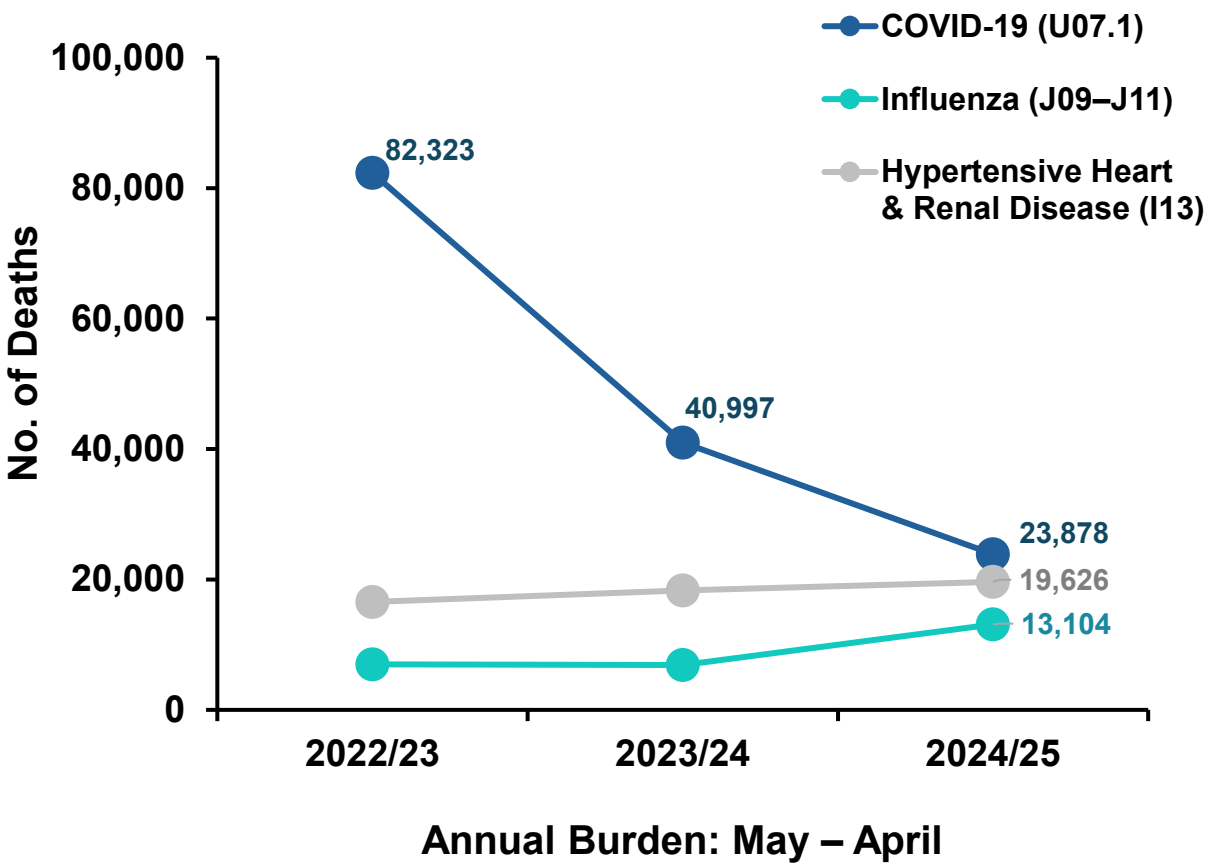
Preclinical Evaluation of LP.8.1-Adapted Vaccine

COVID-19 Still Causes Significant Morbidity and Mortality

Hospitalizations Associated with COVID-19 and Influenza in the US[1]



Deaths due to COVID-19, Influenza, and Hypertensive Heart & Renal Disease in the US[2]



1. Centers for Disease Control and Prevention. Respiratory Virus Hospitalization Surveillance Network (RESP-NET). Available at: https://www.cdc.gov/resp-net/dashboard/index.html. Accessed 14 May 2025.
2. Centers for Disease Control and Prevention. Provisional Mortality Statistics, 2018 through Last Week (CDC WONDER). Available at: https://wonder.cdc.gov/mcd-icd10-provisional.html. Accessed 14 May 2025.

COVID-19 Vaccines Prevent Severe Illness and Deaths in US

BURDEN PREVENTED[1]	2023 – 2024 Seasonal	2023 – 2024 Annual
Hospitalizations	68,000	107,000
ICU Admissions	13,000	18,000
In-hospital Deaths	5,300	6,700

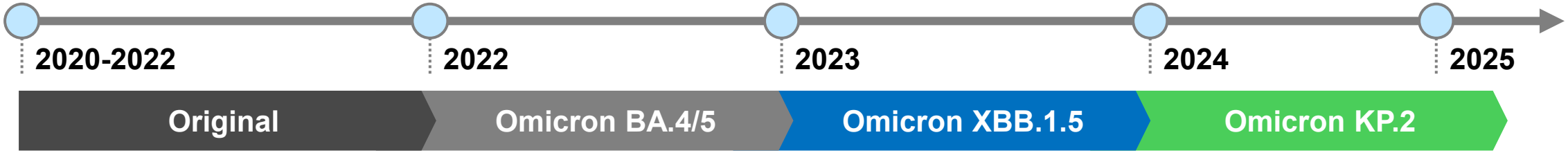
1. Wiegand et al. *Vaccine*. 2024. DOI: 10.1016/j.vaccine.2025.126808. Seasonal period defined October 2023 – April 2024; Annual period defined September 2023 – August 2024.
ICU = Intensive Care Unit

BNT162b2 Safety & Effectiveness Continuously Monitored by Pfizer/BioNTech

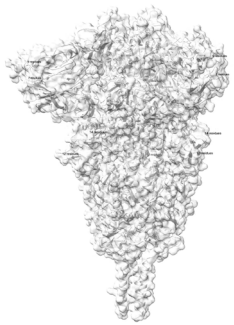
- **5 billion doses distributed globally since 2020 authorization**
- **22 clinical studies performed, enrolling > 70,000 participants**
  - >10,000 participants ≥ 65 years of age
  - >42,000 participants ≥ 18 to 64 years of age
  - >18,000 participants ≥ 6 months to 17 years of age
- **12 postmarketing safety studies evaluating safety in >60 million individuals**
- **Studies on 5 continents to monitor real-world effectiveness**

The BNT162b2 vaccine maintains a highly favorable benefit-risk profile

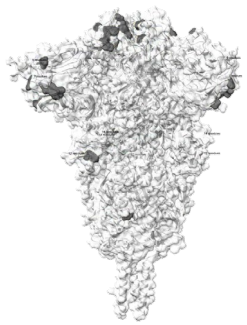
COVID-19 Variant-Adapted Vaccine Approvals Keeping Pace with Virus Evolution



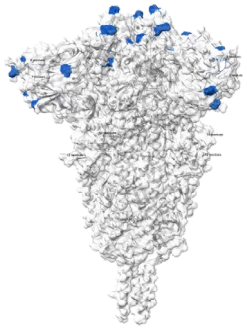
SARS-CoV-2 Spike Mutations[1]



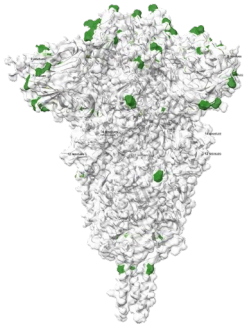
WT Spike



BA.4/5 Spike
(**34** mutations relative to WT)

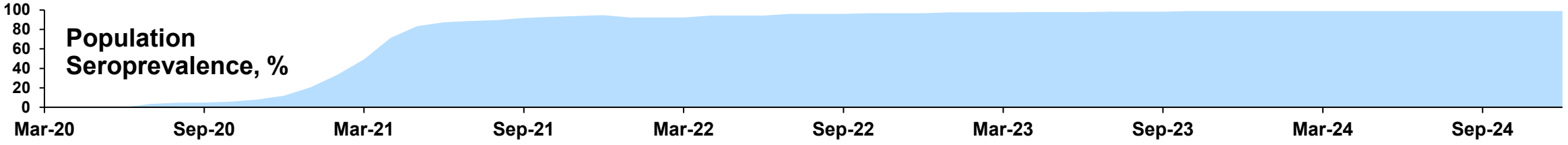


XBB.1.5 Spike
(**17** mutations relative to BA.4/5)



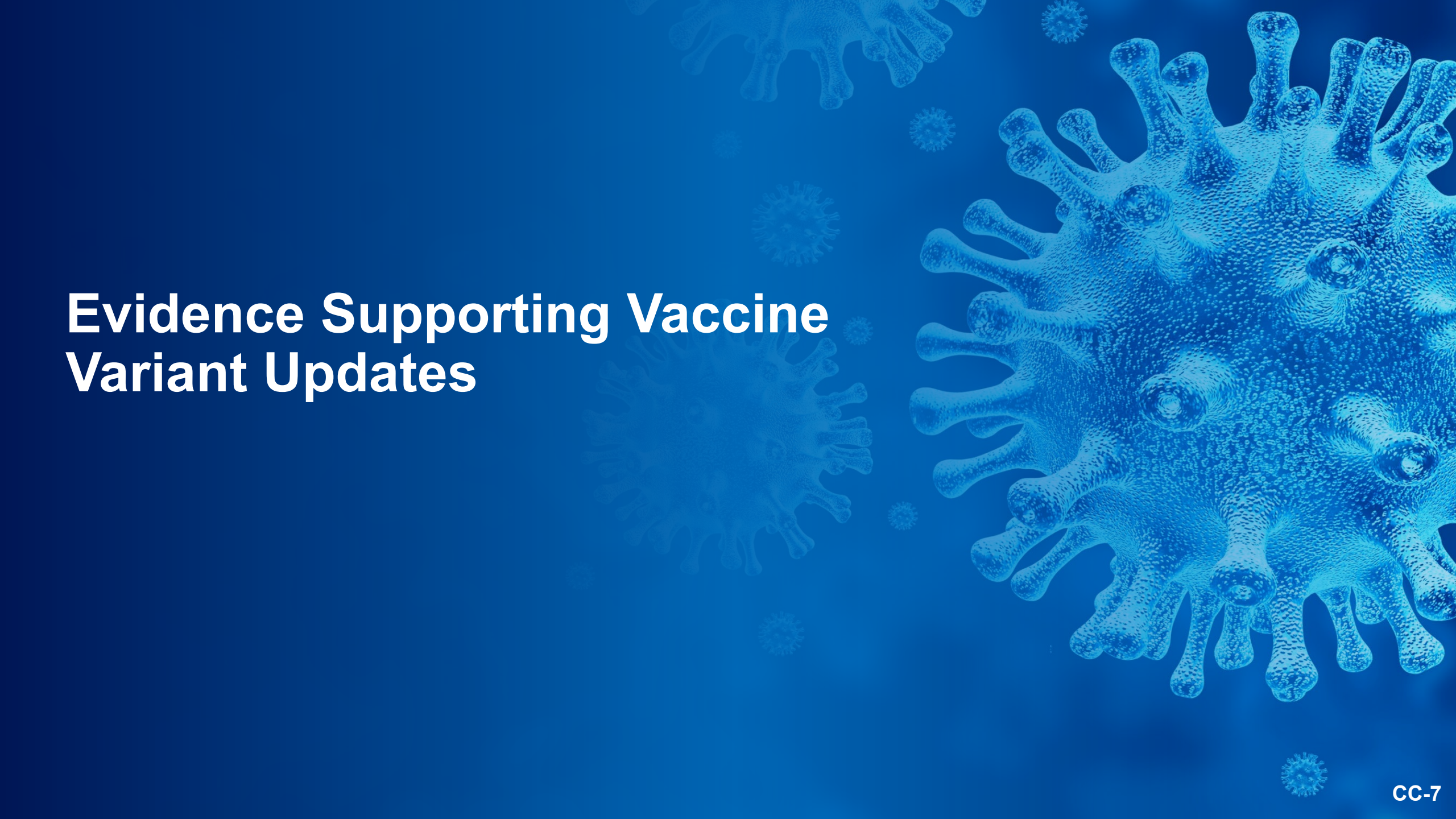
KP.2 Spike
(**38** mutations relative to XBB.1.5)

Vaccine Effectiveness For Hospitalization[2-8]	32-97%	34-76%	32-74%	41-68%

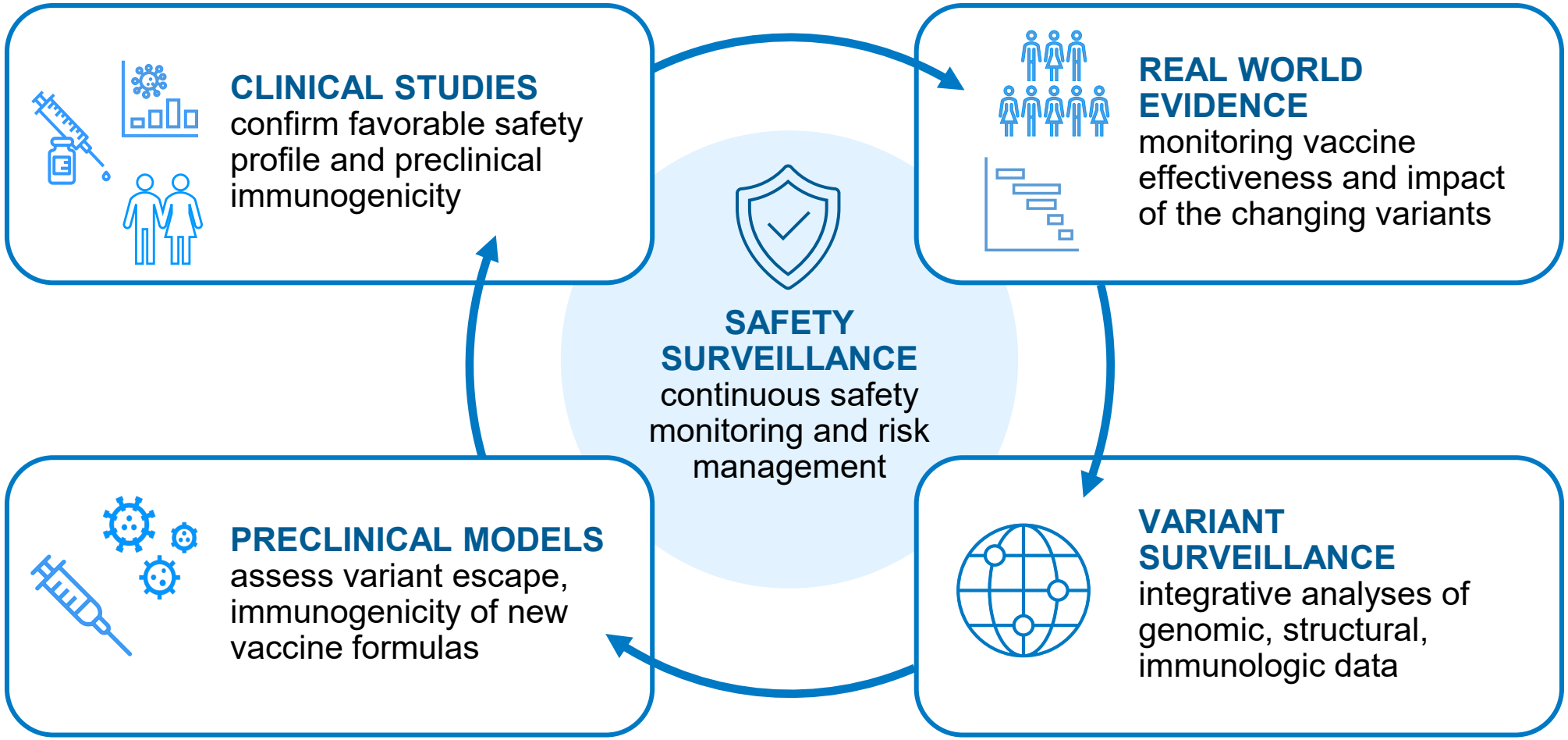


1. Pfizer internal analysis using data downloaded from GISAID - gisaid.org 2. Tartof et al. 2023. DOI: 10.1016/S2213-2600(22)00354-X 3. Tartof et al. 2022. DOI: 10.1016/j.lana.2022.100198 4. Tartof et al. 2023. DOI: 10.1016/S2213-2600(23)00306-5 5. Caffrey et al. 2024. DOI: 10.1016/j.lana.2022.100198 6. Tartof et al. 2024. DOI: 10.1093/ofid/ofae370 7. Pfizer data on file 8. Appaneal et al. 2025. DOI: 10.1038/s41467-025-59344-7

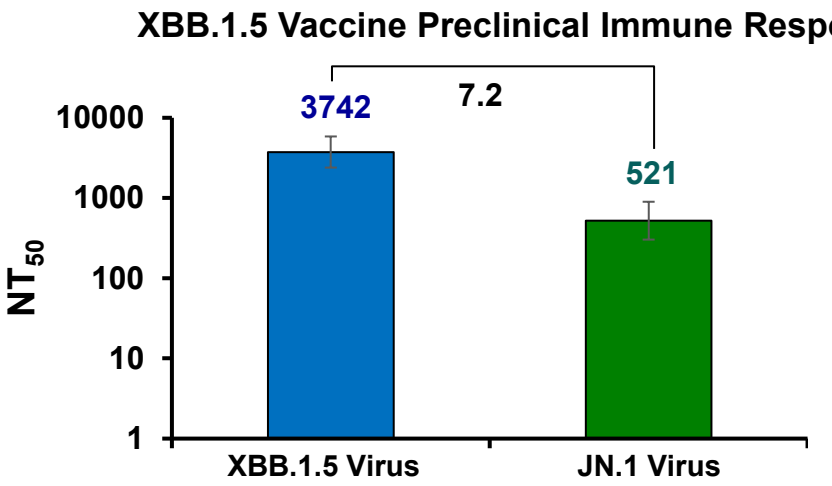
Evidence Supporting Vaccine Variant Updates

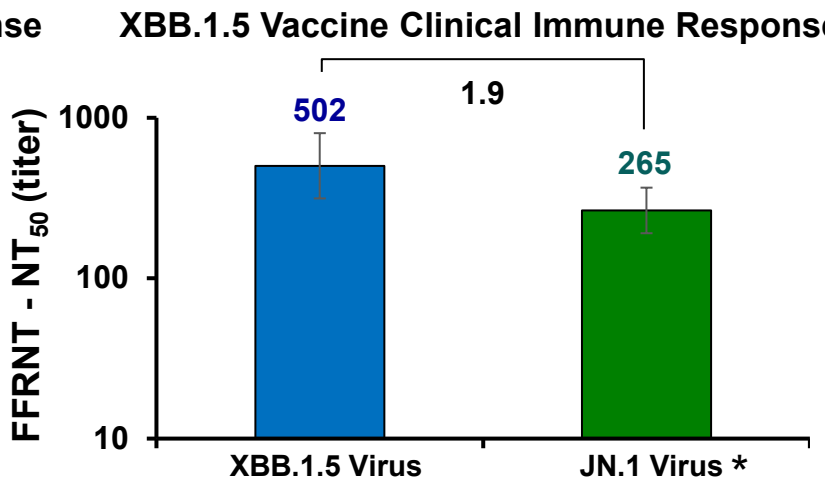


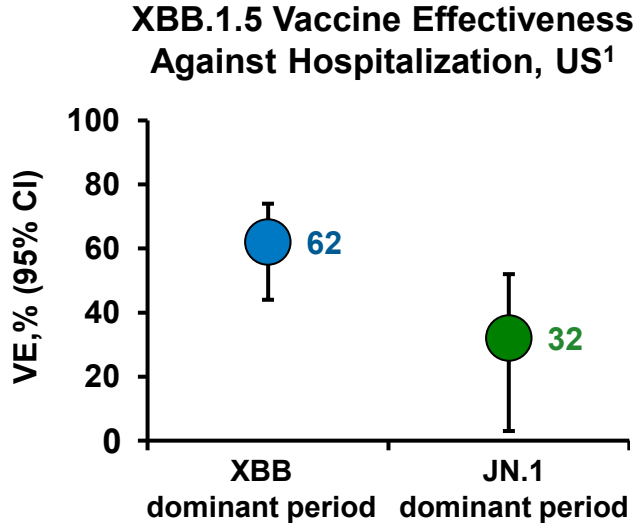
Pfizer/BioNTech's Multifaceted and Continual Process for Variant-Adapted Vaccine Evaluation



Virus Evolution to New Variant Results in Immune Escape; Reducing Vaccine Effectiveness



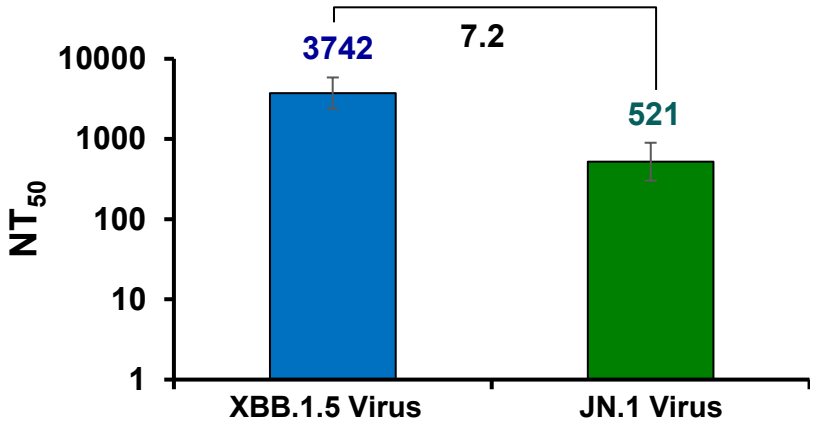




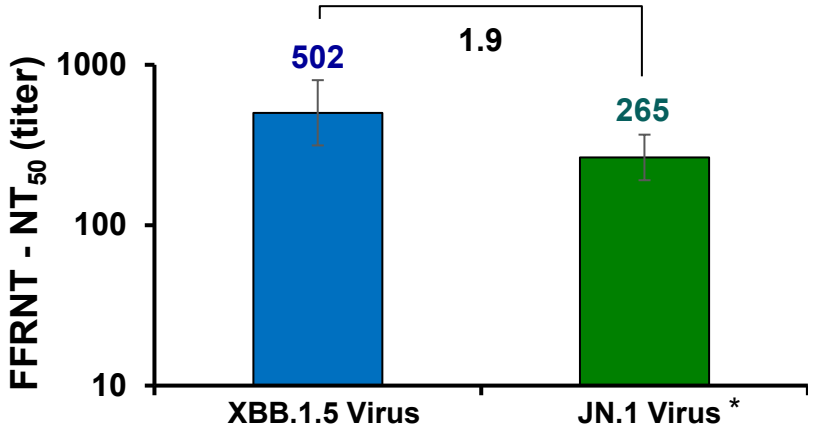
1. Caffrey et al. 2024. DOI: https://doi.org/10.1038/s41467-024-53842-w
* These data are generated from different subsets of participants in the same study (C4591054 SSA), and samples tested at different times

Virus Evolution to New Variant Results in Immune Escape; Updating Vaccine Provides Benefit

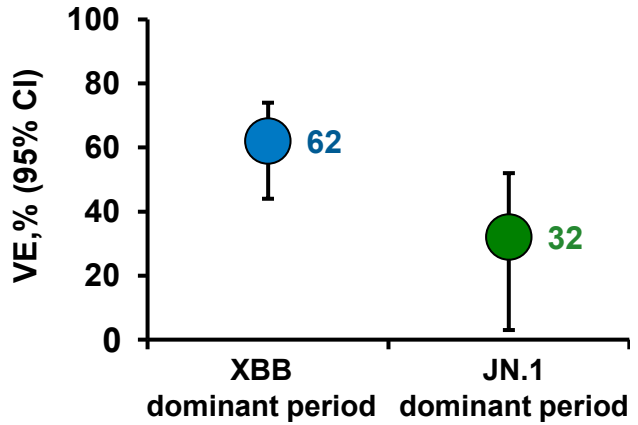
XBB.1.5 Vaccine Preclinical Immune Response



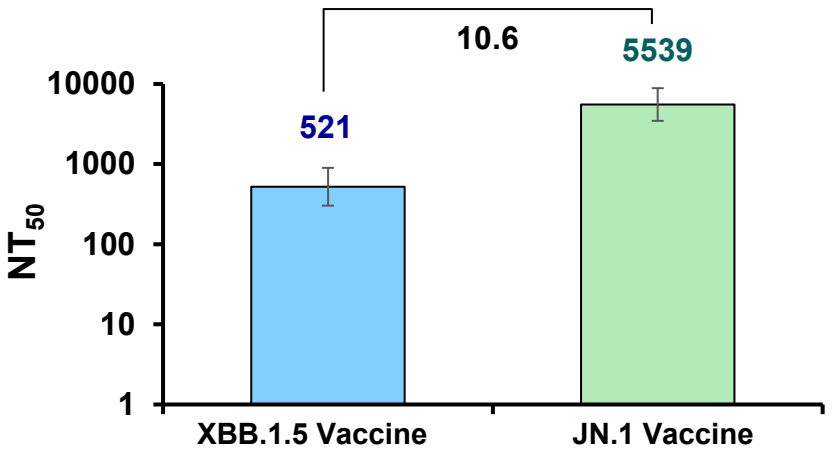
XBB.1.5 Vaccine Clinical Immune Response



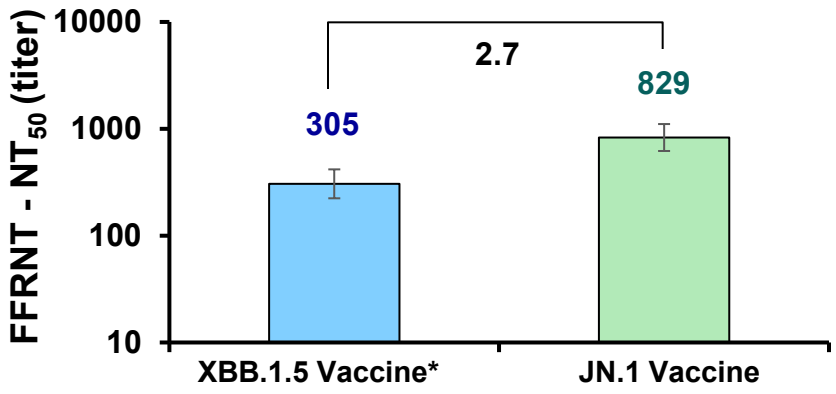
XBB.1.5 Vaccine Effectiveness Against Hospitalization, US[1]



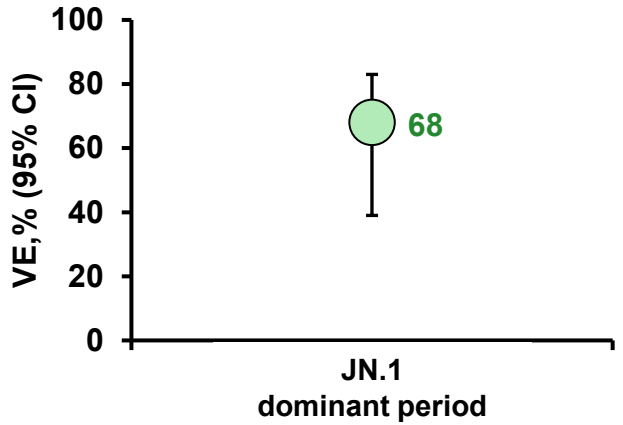
JN.1 Virus Neutralization in Preclinical Study



JN.1 Virus Neutralization in Clinical Study



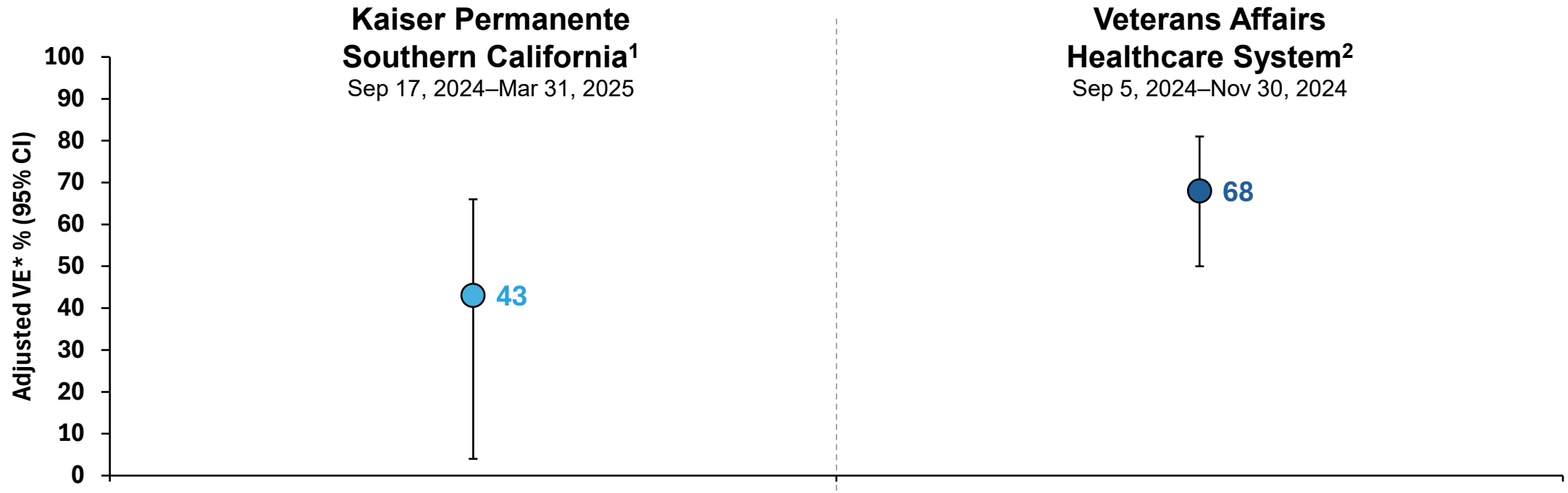
JN.1 Vaccine Effectiveness Against Hospitalization, EU[2]



1. Caffrey et al. 2024. DOI: https://doi.org/10.1038/s41467-024-53842-w 2. Volkman et al. *ESCMID*, 2025. Vienna, Austria.
* These data are generated from different subsets of participants in the same study (C4591054 SSA), and samples tested at different times

Real World Effectiveness and Variant Epidemiology

KP.2-Adapted Vaccine Provides Effectiveness Against Hospital Admission

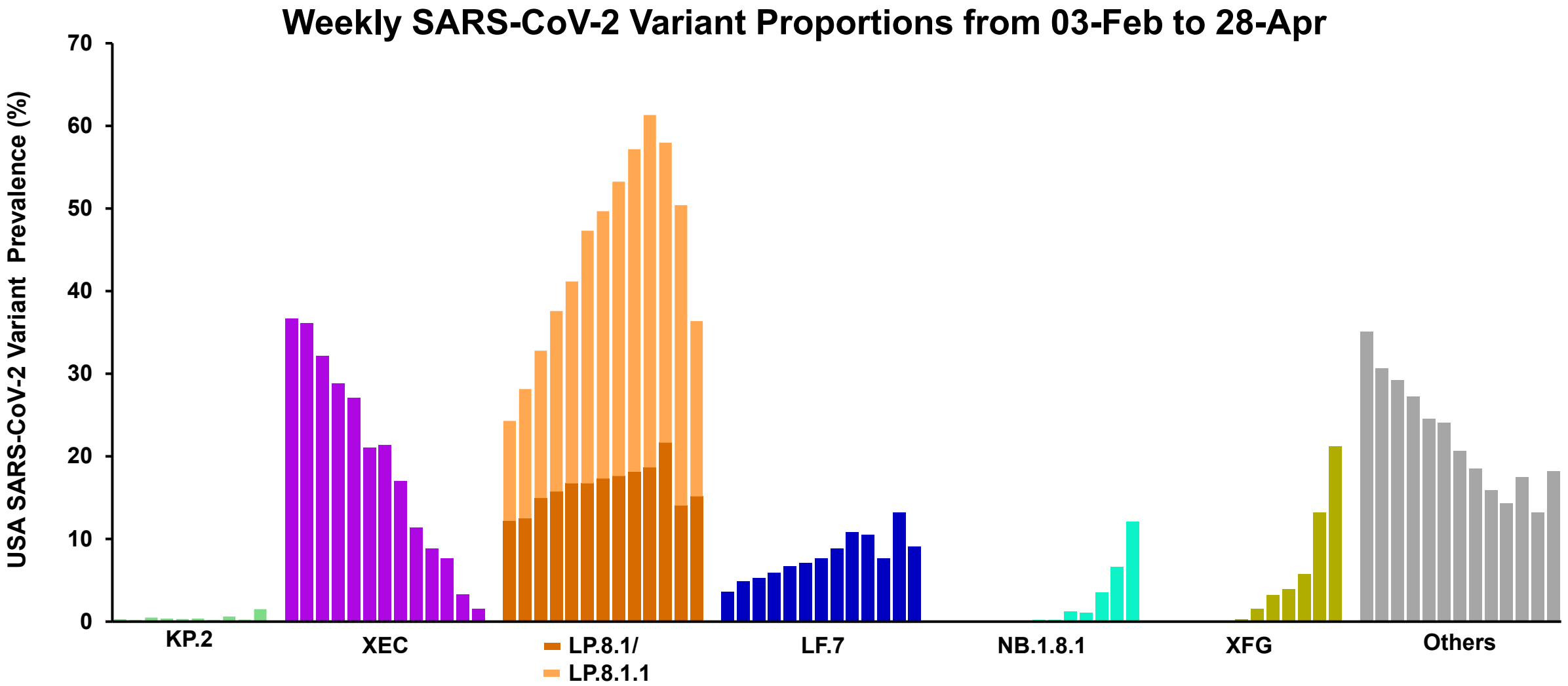


	Kaiser Permanente Southern California[1]	Veterans Affairs Healthcare System[2]
Design	Test-negative case-control	Test-negative case-control
Population	≥18y with ARI diagnosis and SARS-CoV-2 PCR test	≥18y with ARI diagnosis and SARS-CoV-2 PCR or RAT test
Median (IQR) age	53y (35 to 71)	68y (56 to 76)
Median (IQR) time since dose	88d (54 to 121)	30d (21 to 43)
Number of cases (%)	3,039 (5.1%)	7,224 (16.2%)

1. Pfizer data on file.
2. Appaneal, H.J. et al. Early Effectiveness of the BNT162b2 KP.2 Vaccine against COVID-19 in the US Veterans Affairs Healthcare System. Nature Communications. 2025. DOI: https://doi.org/10.1038/s41467-025-59344-7

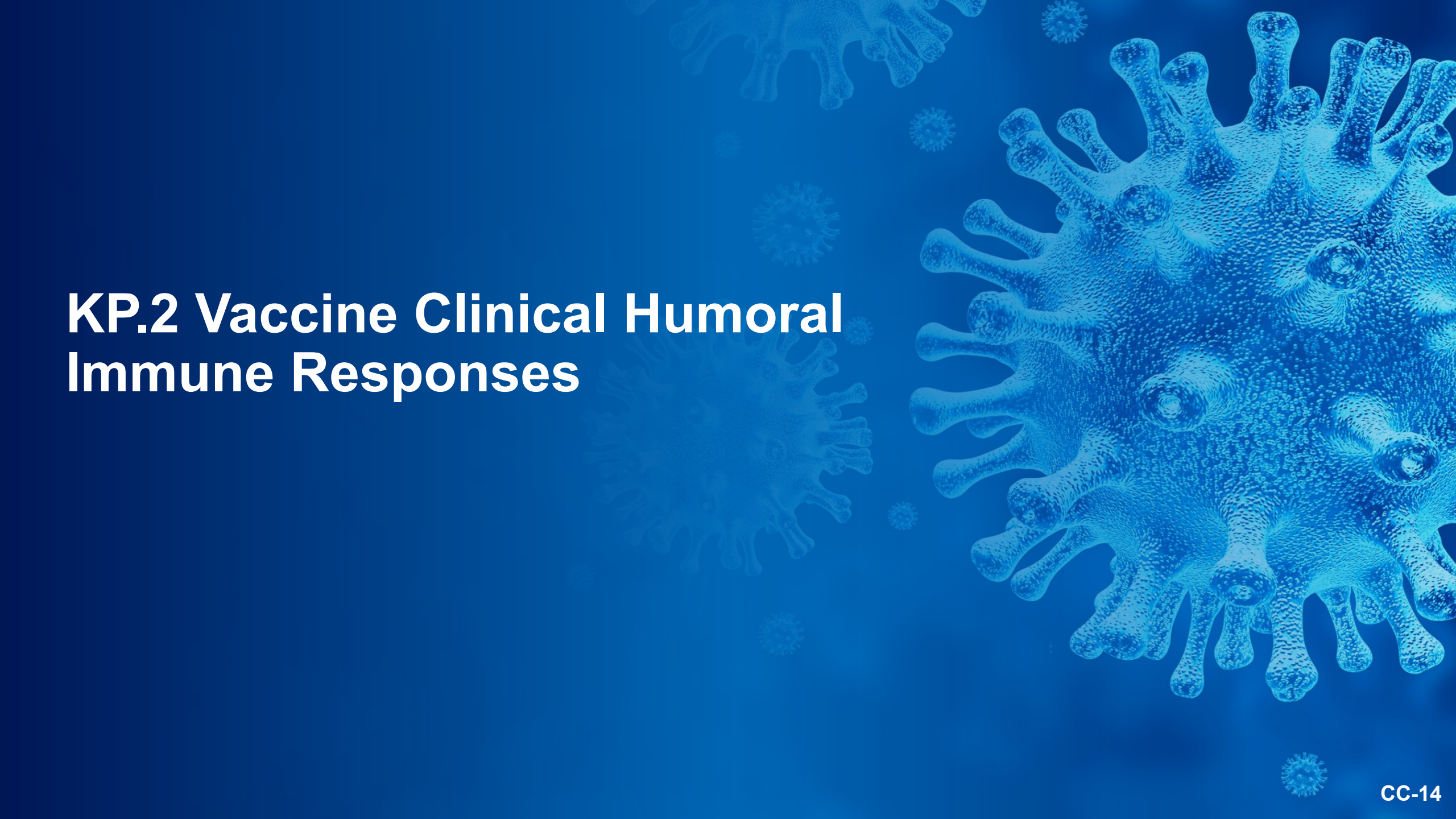
ARI, acute respiratory infection; CI, confidence interval; d, days; IQR, interquartile range; PCR, polymerase chain reaction; RAT, rapid antigen test; VE, vaccine effectiveness; y, years.
Vaccine Effectiveness (VE) Estimates are compared to no receipt of any 2024–2025 Covid-19 vaccine.

LP.8.1 is Dominant Variant; Emerging Variants Rise in Prevalence



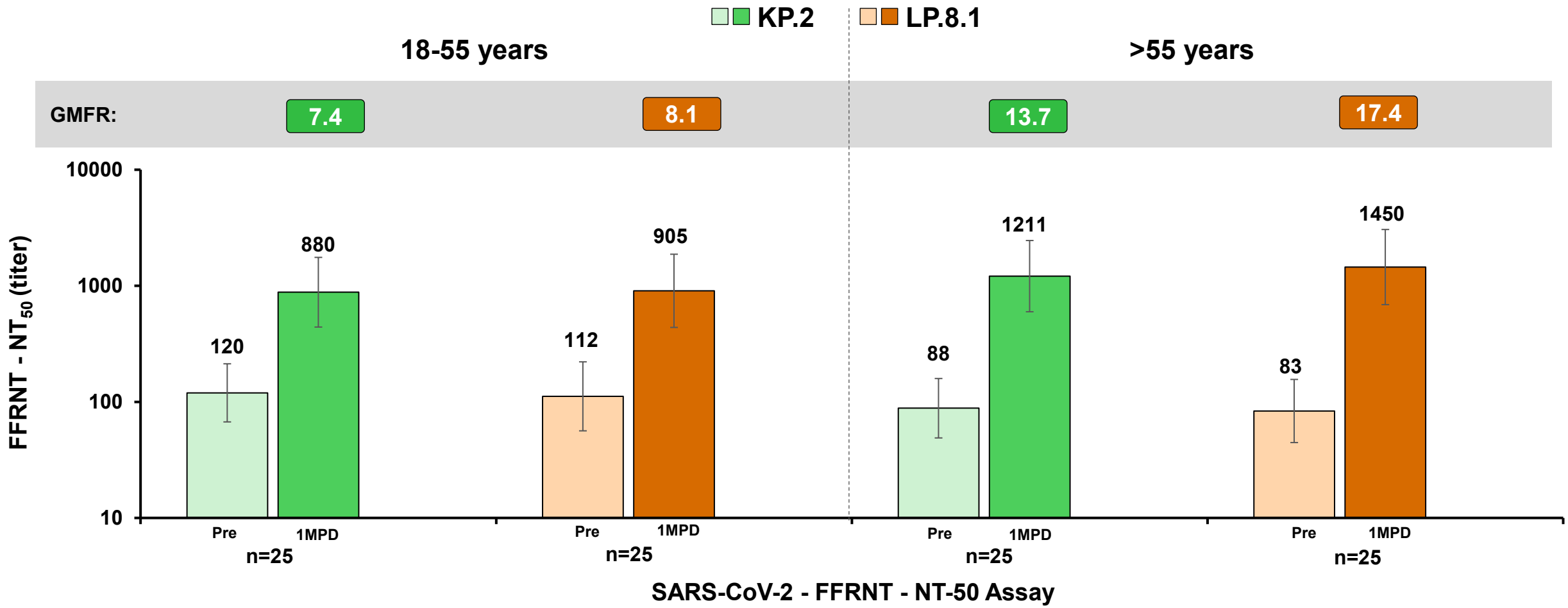
Source: GISAID - gisaid.org; data accessed/analysed/plotted within Pfizer, as of May 11, 2025. Each individual labelled variant includes all subvariants including those with the same Spike protein amino acid sequence. Each bar represents 1 week's variant prevalence data.

KP.2 Vaccine Clinical Humoral Immune Responses



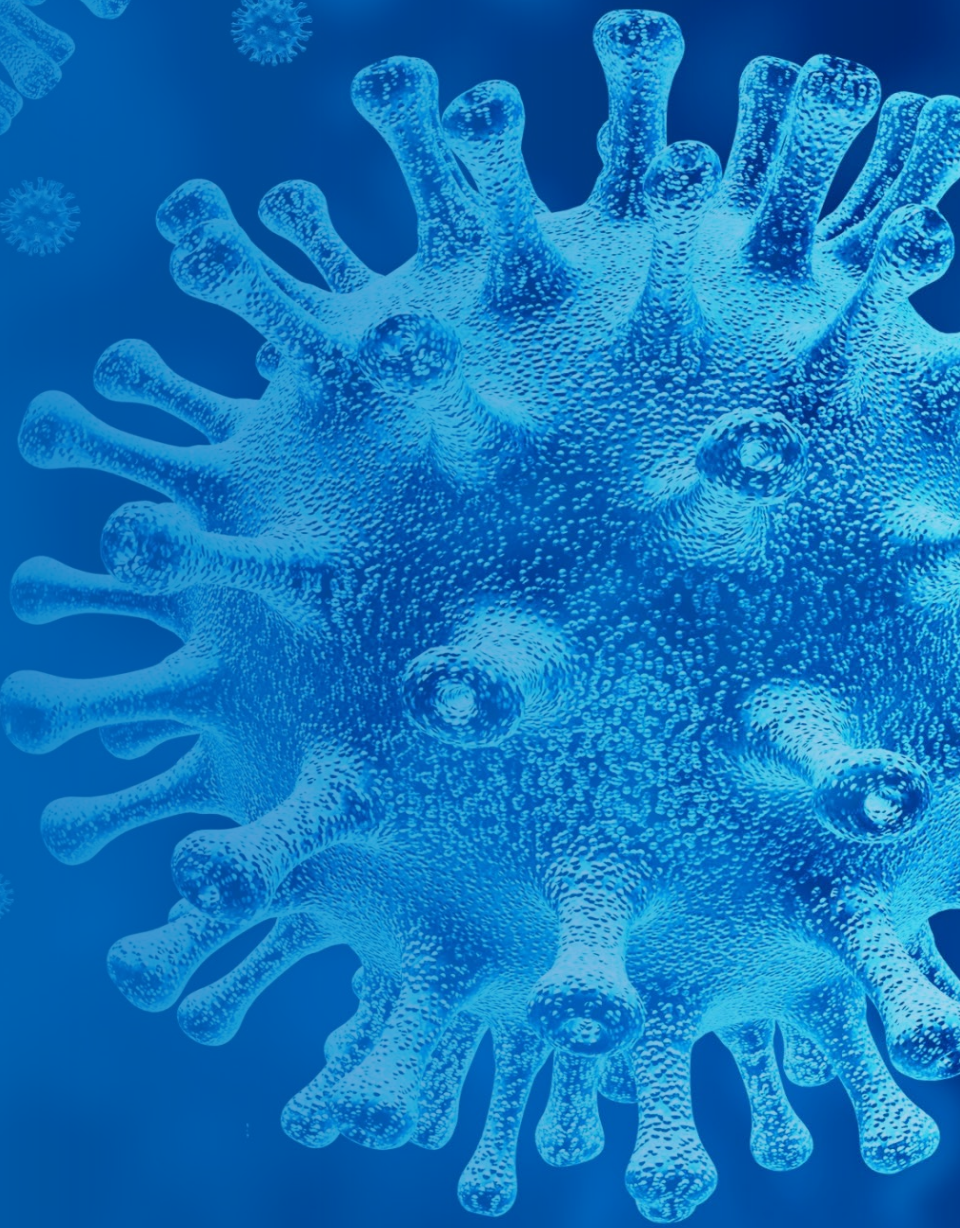
Clinical Trial: KP.2-Adapted Vaccine Elicits Robust Neutralizing Responses Against KP.2 and LP.8.1 Variants

Evaluable immunogenicity population – KP.2 Adapted Vaccine

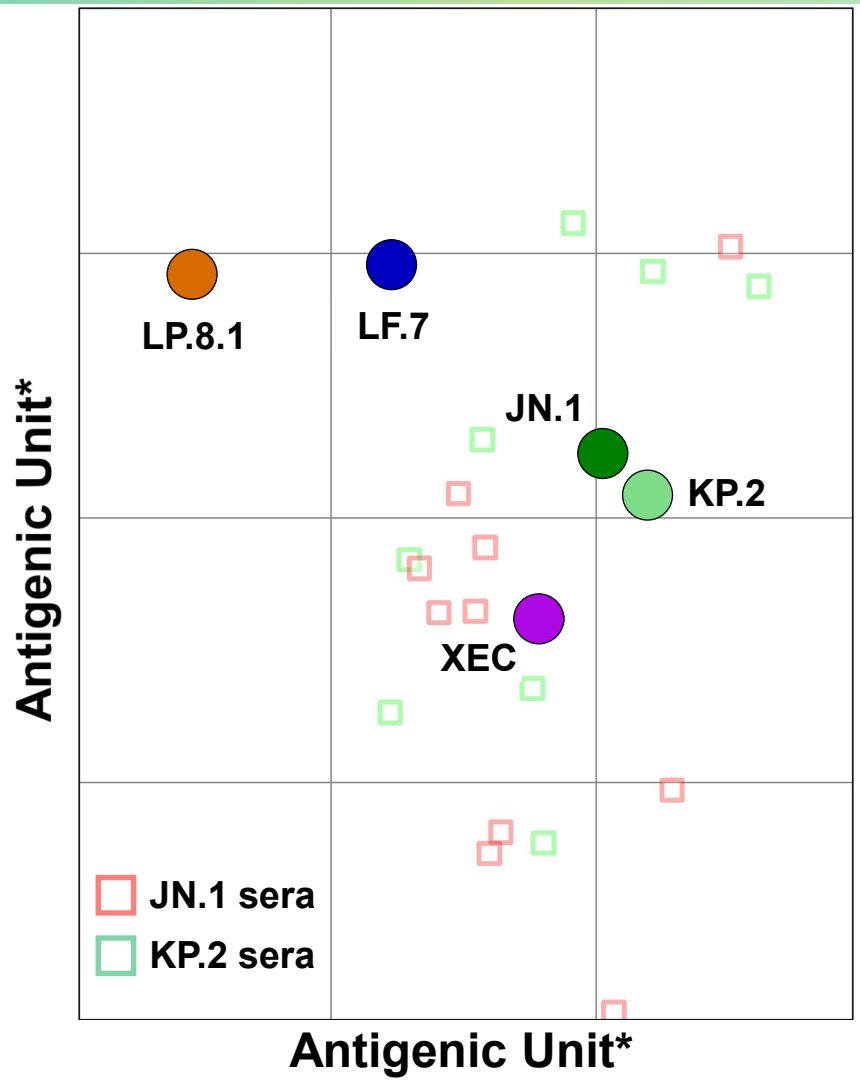


All participants were ≥18 years old; vaccine naïve or vaccine experienced with last COVID-19 vaccine being administered at least 150 days prior to enrollment.
GMFR = Geometric Mean Neutralizing Titer Fold Rise; Pre = pre-vaccination; 1MPD = 1-month post-vaccination; FFRNT = fluorescent focus reduction neutralization test

Preclinical Evaluation of an Omicron LP.8.1-Adapted Vaccine

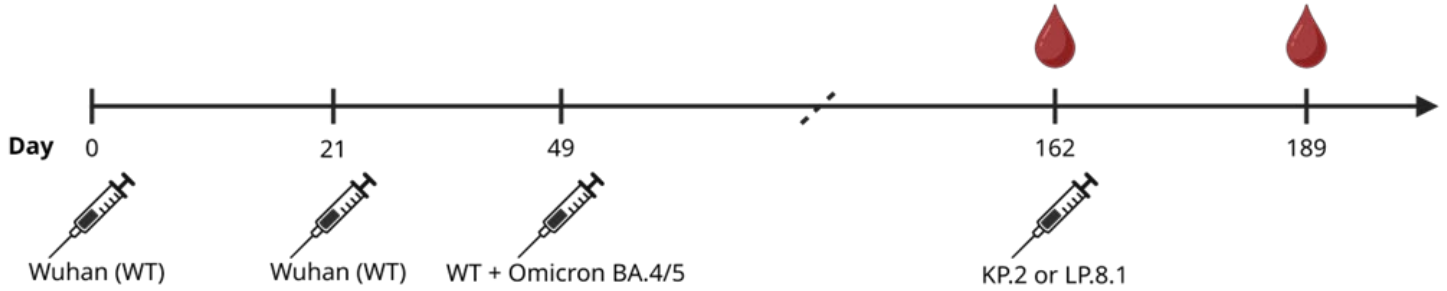


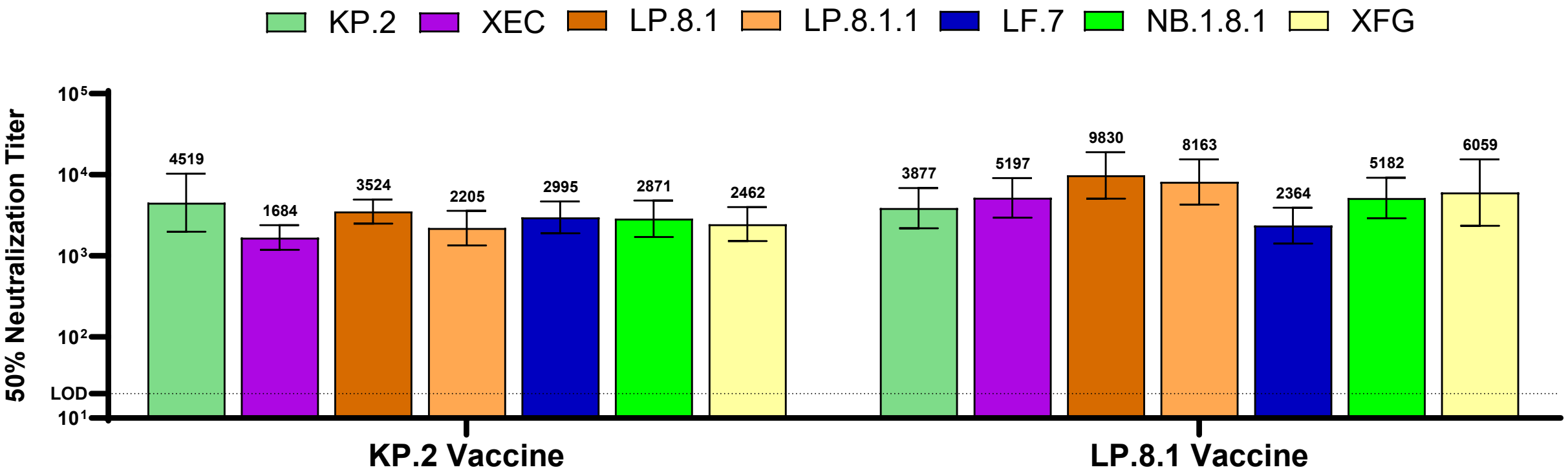
Recent JN.1 Subvariants Exhibiting Greater Antigenic Drift



*Each box represents 1 antigenic unit = 2-fold difference in neutralization titer.
Antigenic map generated in Racmacs package in R using 2000 optimizations, with the minimum column basis parameter set to “none.”
Generated from pseudovirus neutralization titers elicited by JN.1- and KP.2-adapted vaccines administered as a primary series to naïve mice.

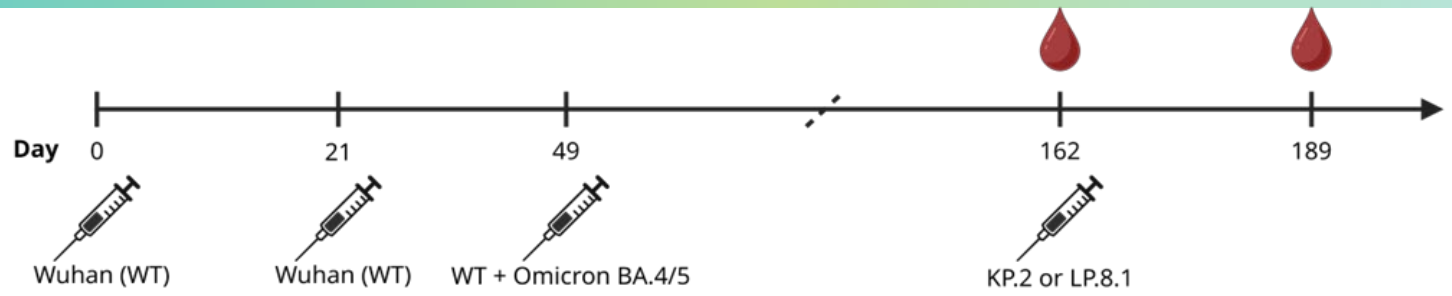
LP.8.1 Vaccine Elicits Broadly Cross-Reactive Neutralizing Responses in Vaccine-Experienced Mice

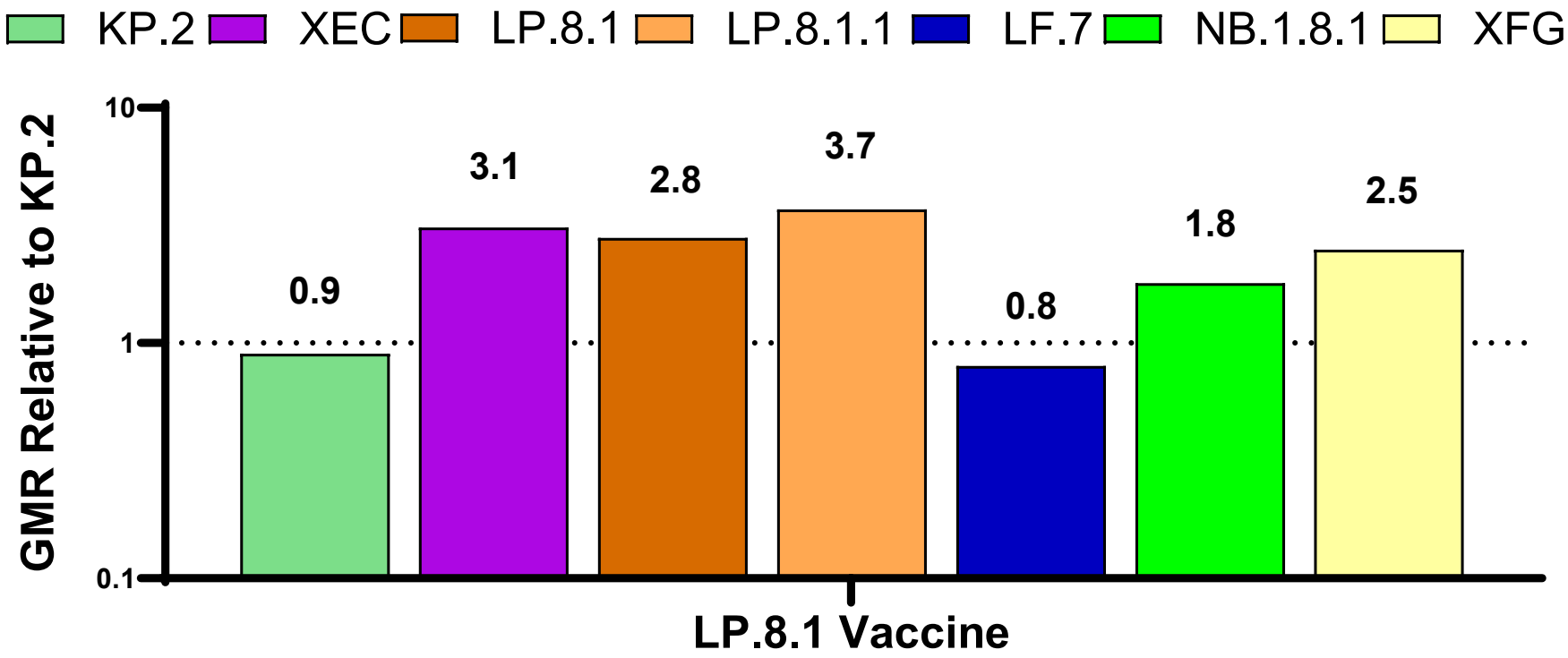




Neutralization titers measured by pseudovirus neutralization assay.
N = 10 mice per vaccine group. Vaccine dose 0.5 μg.

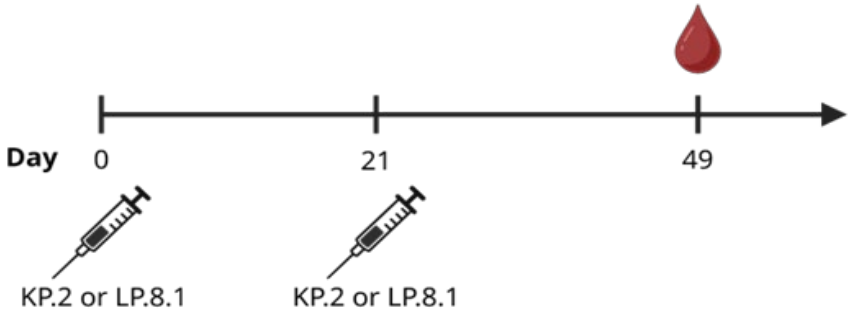
LP.8.1 Vaccine Elicits Improved Neutralization Compared to KP.2 Vaccine in Vaccine-Experienced Mice

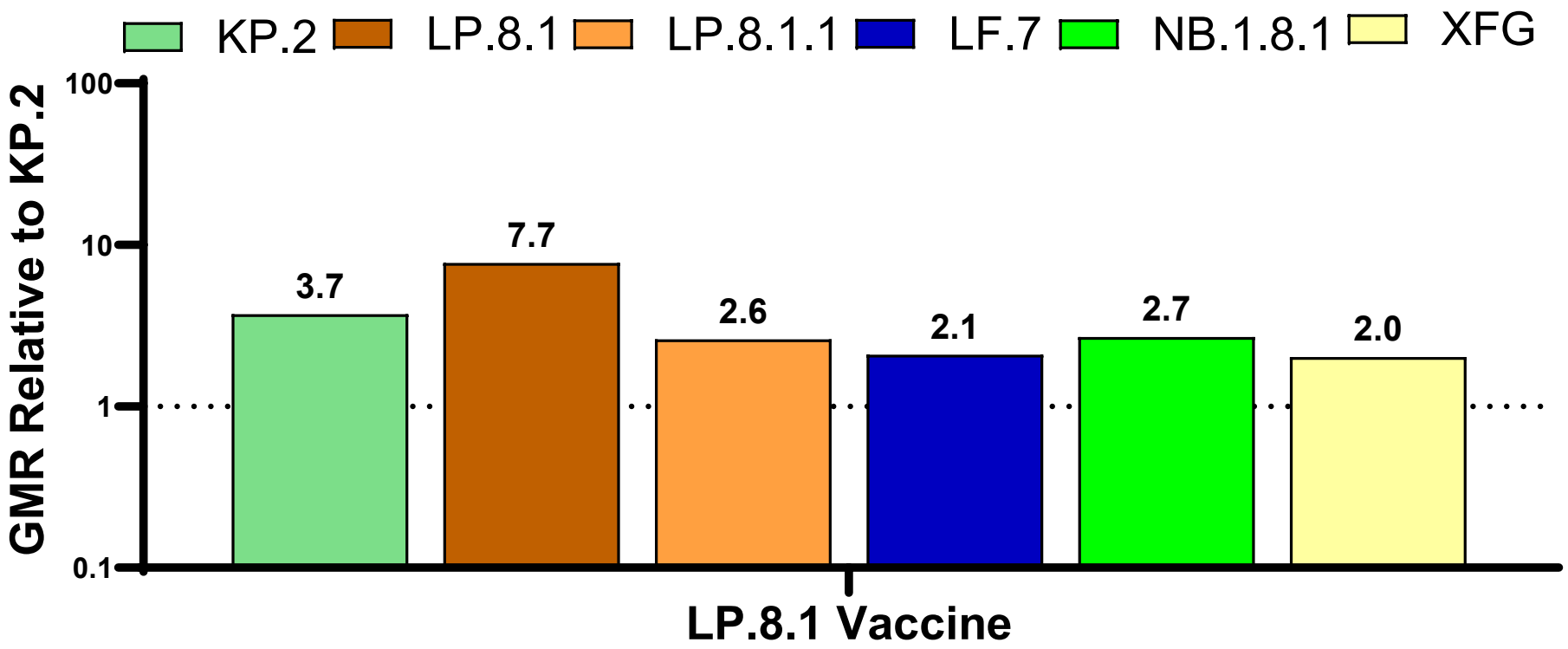




Neutralization titers measured by pseudovirus neutralization assay.
GMR = Geometric Mean Ratio of 50% neutralization titers.
N = 10 mice per vaccine group. Vaccine dose 0.5 μg.

LP.8.1 Vaccine Elicits Improved Neutralization Compared to KP.2 Vaccine in Vaccine-Naïve Mice





Neutralization titers measured by pseudovirus neutralization assay.
GMR = Geometric Mean Ratio of 50% neutralization titers.
N = 10 mice per vaccine group. Vaccine dose 0.5 μg.

Conclusions

Summary Evidence Supports Consistent Benefit of Seasonal Updates to Vaccine Formulas For Antigenically Divergent Variants

- **Processes and outcomes for variant-adapted vaccine updates have been reliable in their clinical benefit**
- **KP.2 vaccine demonstrates cross-reactive clinical response to LP.8.1, continued effectiveness and favorable benefit-risk profile consistent with original vaccine**
- **LP.8.1 vaccine confers improved immune response, in preclinical models, against currently dominant and emerging variants**
- **Pfizer/BioNTech prepared to supply 2025/2026 vaccine formula per FDA guidance, upon approval**

2025-2026 COVID-19 Vaccine Formula: Pfizer/BioNTech Supportive Data

Vaccines and Related Biological Products Advisory Committee

May 22, 2025

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