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

Vaccines and Related Biological
Products Advisory Committee

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Presentation Outline

Kayvon Modjarrad, M.D., Ph.D.
Executive Director,
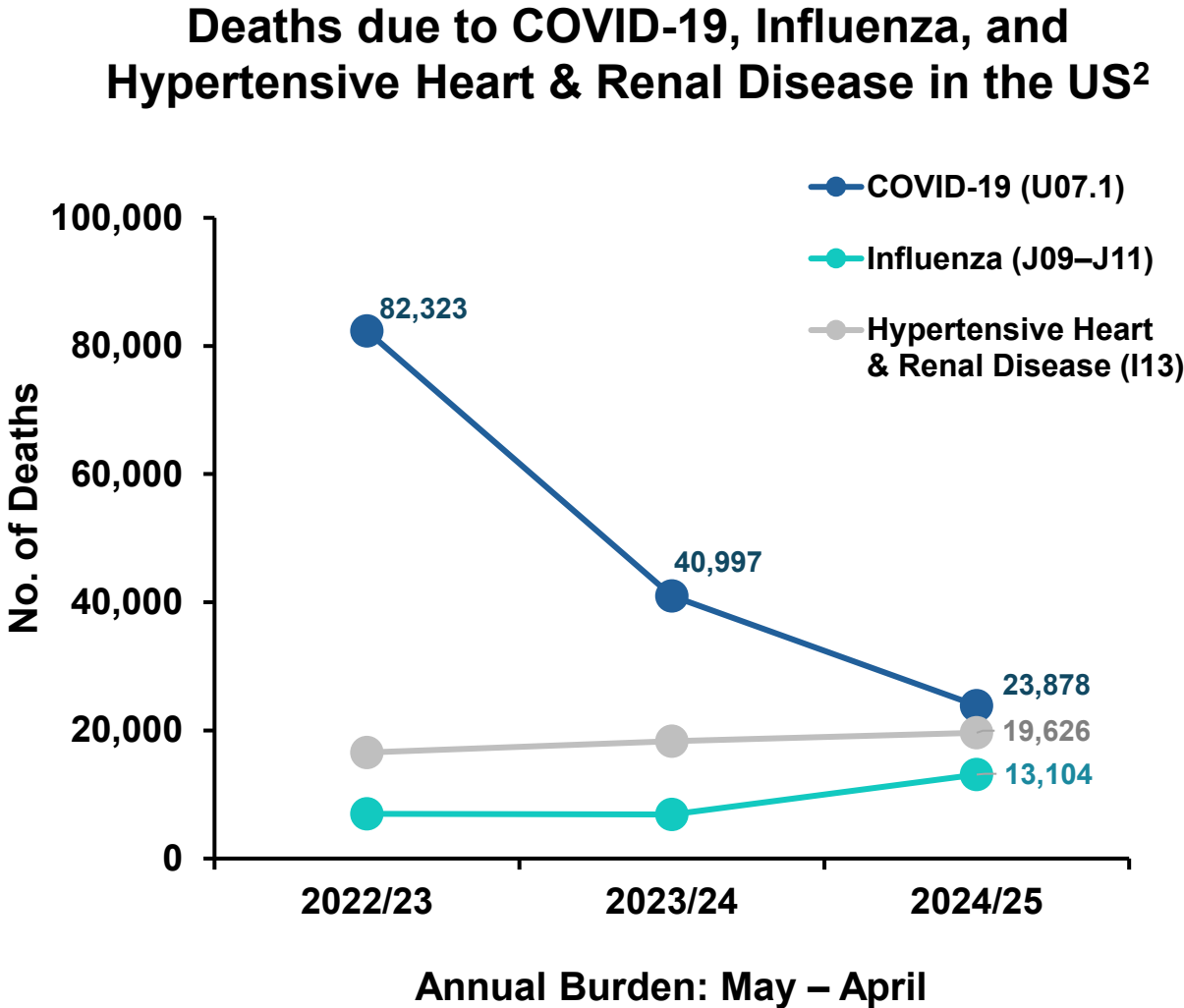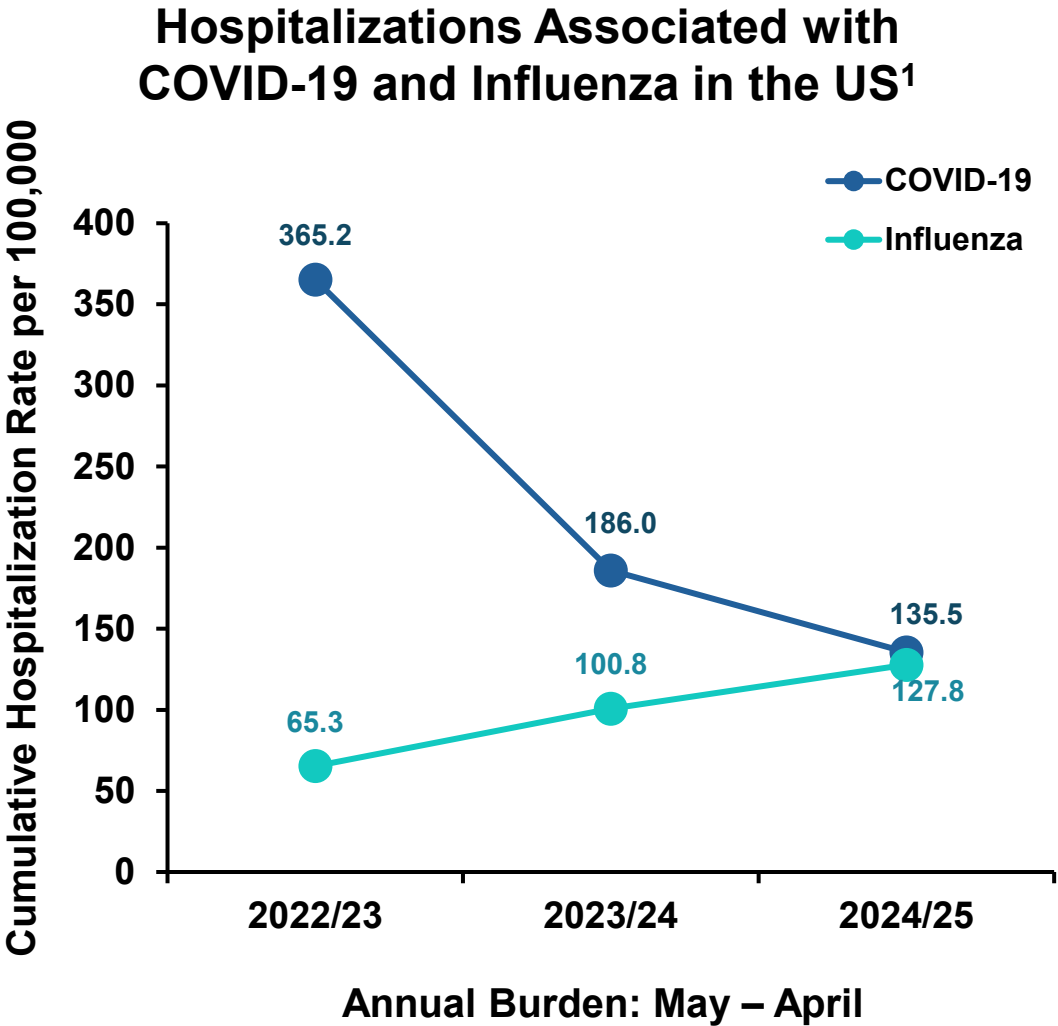Vaccine Research & Development
Pfizer Inc.

**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]

Cumulative Hospitalization Rate per 100,000

- COVID-19
- Influenza

COVID-19: 365.2 (2022/23), 186.0 (2023/24), 135.5 (2024/25)
Influenza: 65.3 (2022/23), 100.8 (2023/24), 127.8 (2024/25)

Annual Burden: May – April

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

No. of Deaths

- COVID-19 (U07.1)
- Influenza (J09–J11)
- Hypertensive Heart & Renal Disease (I13)

COVID-19: 82,323 (2022/23), 40,997 (2023/24), 23,878 (2024/25)
Hypertensive Heart & Renal Disease: 19,626 (2024/25)
Influenza: 13,104 (2024/25)

Annual Burden: May – April

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	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.
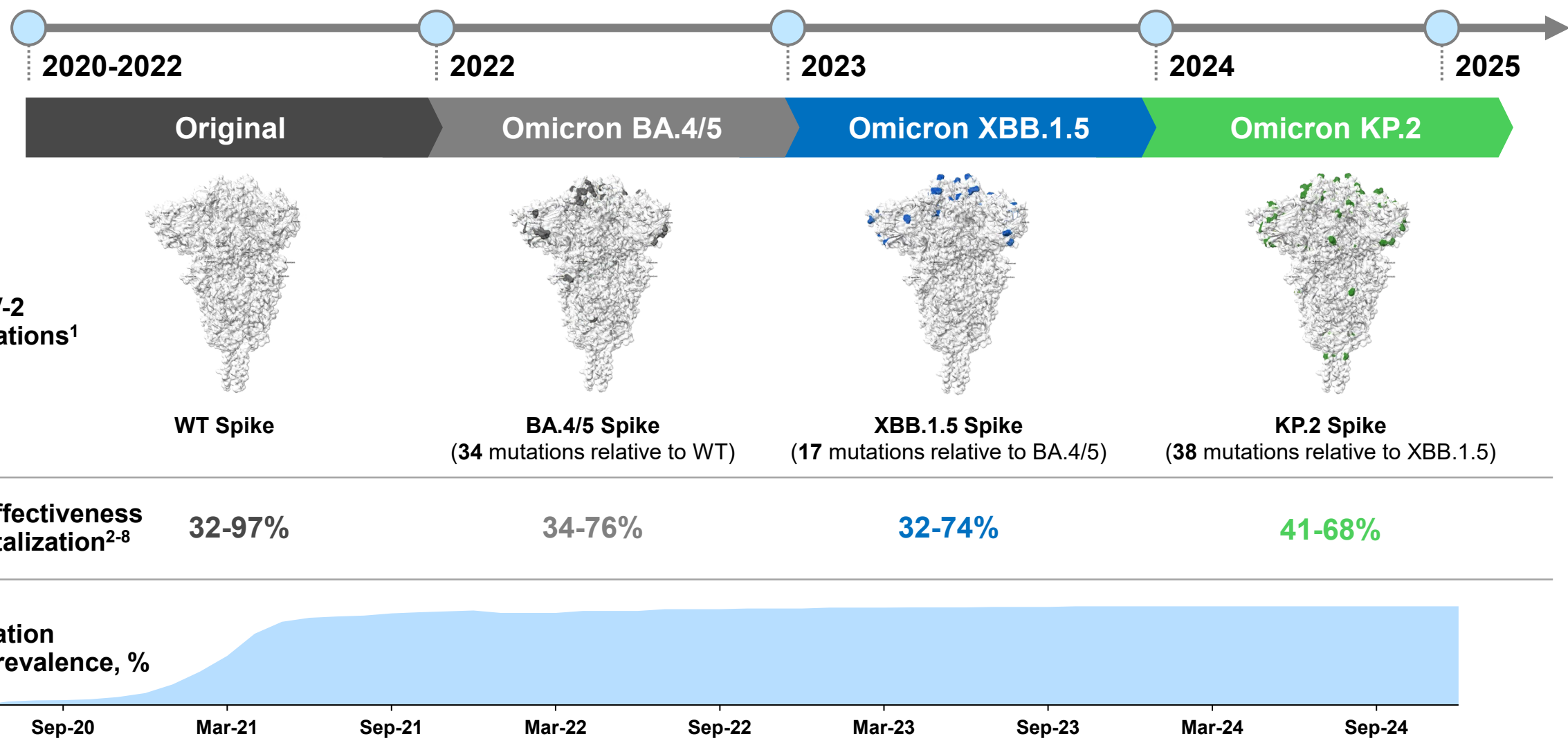ICU = Intensive Care Unit

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

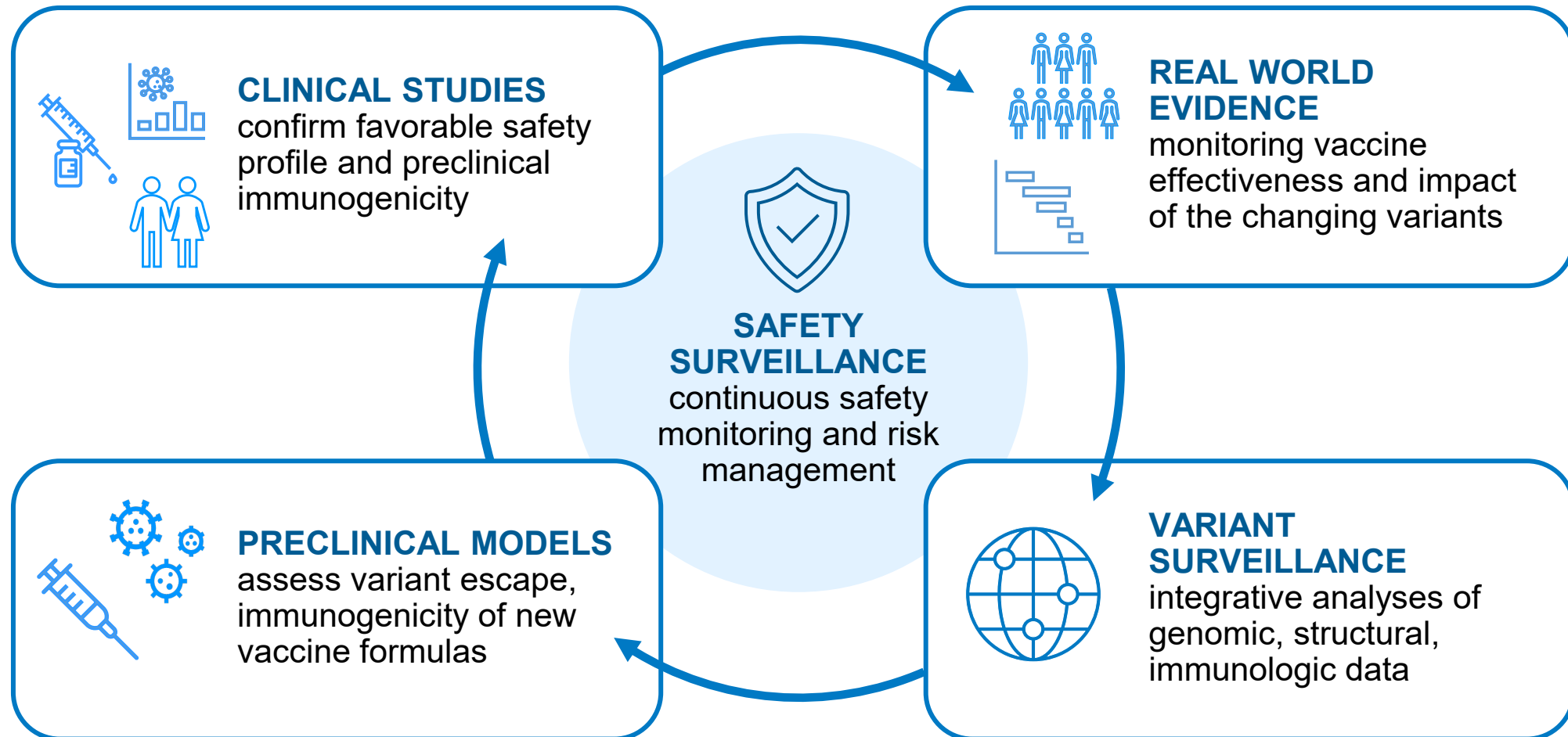# COVID-19 Variant-Adapted Vaccine Approvals Keeping Pace with Virus Evolution

Timeline: 2020-2022 · 2022 · 2023 · 2024 · 2025

| Original | Omicron BA.4/5 | Omicron XBB.1.5 | Omicron KP.2 |

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% |

Population Seroprevalence, %

Y-axis: 0, 20, 40, 60, 80, 100
X-axis: Mar-20, Sep-20, Mar-21, Sep-21, Mar-22, Sep-22, Mar-23, Sep-23, Mar-24, Sep-24

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
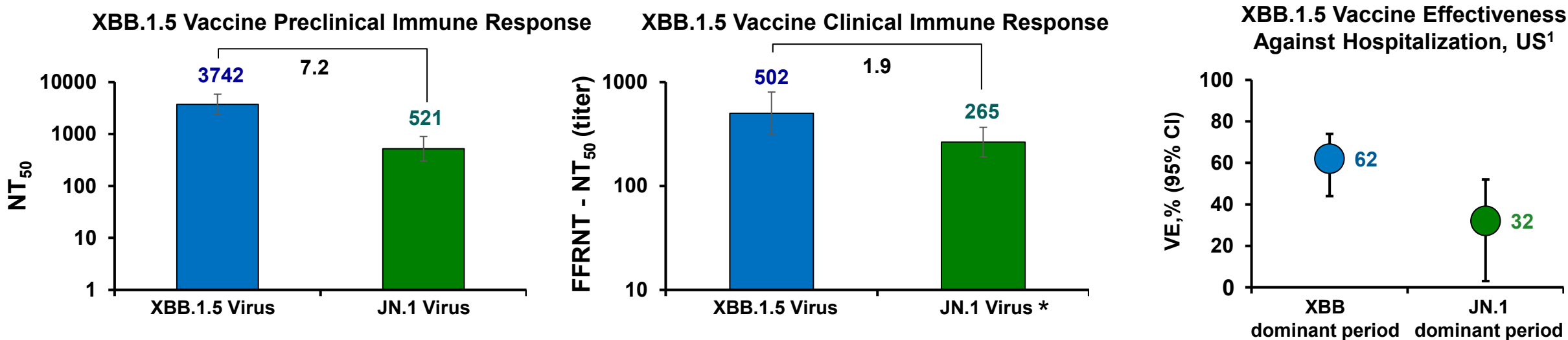
Evidence Supporting Vaccine Variant Updates

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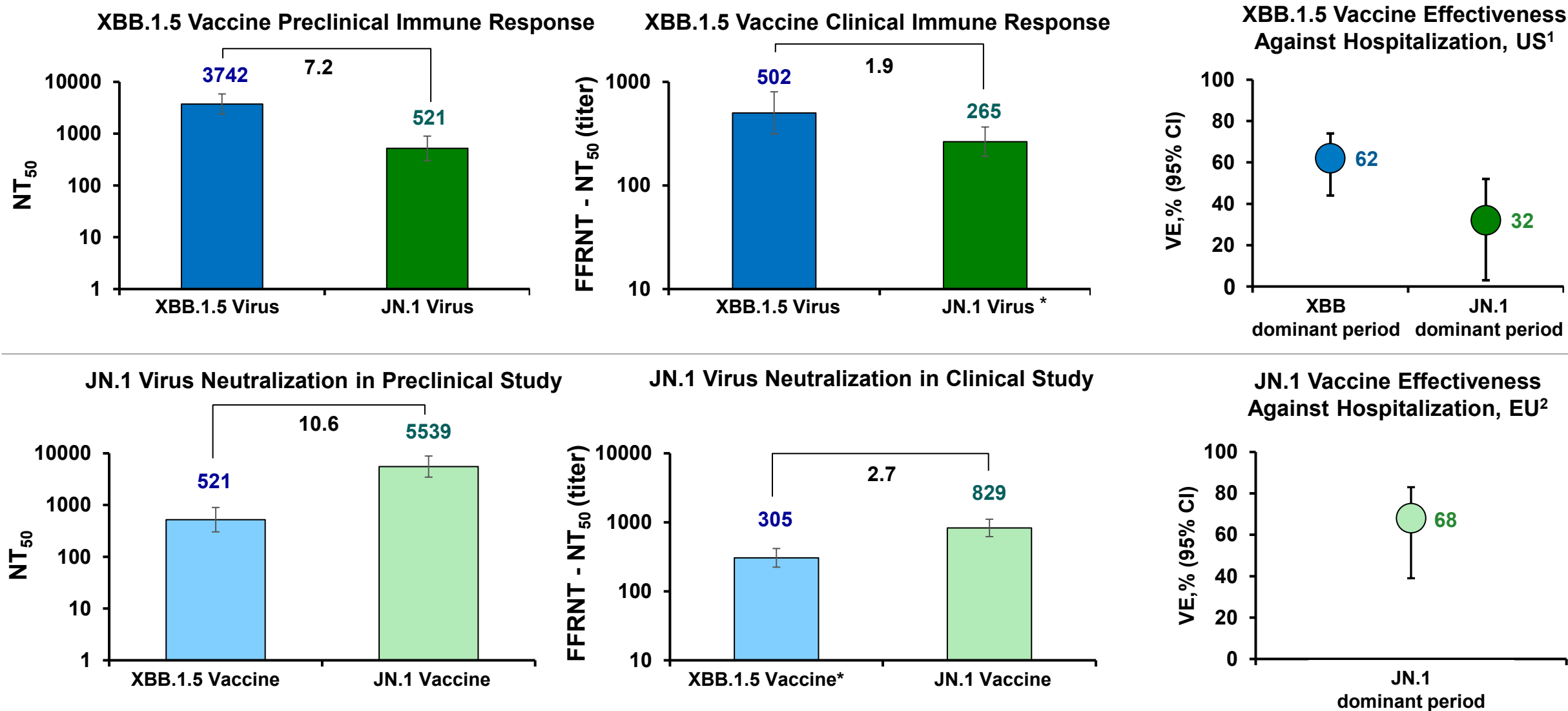

CLINICAL STUDIES confirm favorable safety profile and preclinical immunogenicity

REAL WORLD EVIDENCE monitoring vaccine effectiveness and impact of the changing variants

SAFETY SURVEILLANCE continuous safety monitoring and risk management

PRECLINICAL MODELS assess variant escape, immunogenicity of new vaccine formulas

VARIANT SURVEILLANCE integrative analyses of genomic, structural, immunologic data

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

XBB.1.5 Vaccine Preclinical Immune Response

7.2

3742

521

NT_{50}

XBB.1.5 Virus   JN.1 Virus

XBB.1.5 Vaccine Clinical Immune Response

1.9

502

265

$FFRNT - NT_{50}$ (titer)

XBB.1.5 Virus   JN.1 Virus *

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

VE,% (95% CI)

62

32

XBB dominant period   JN.1 dominant period

* These data are generated from different subsets of participants in the same study (C4591054 SSA), and samples tested at different times
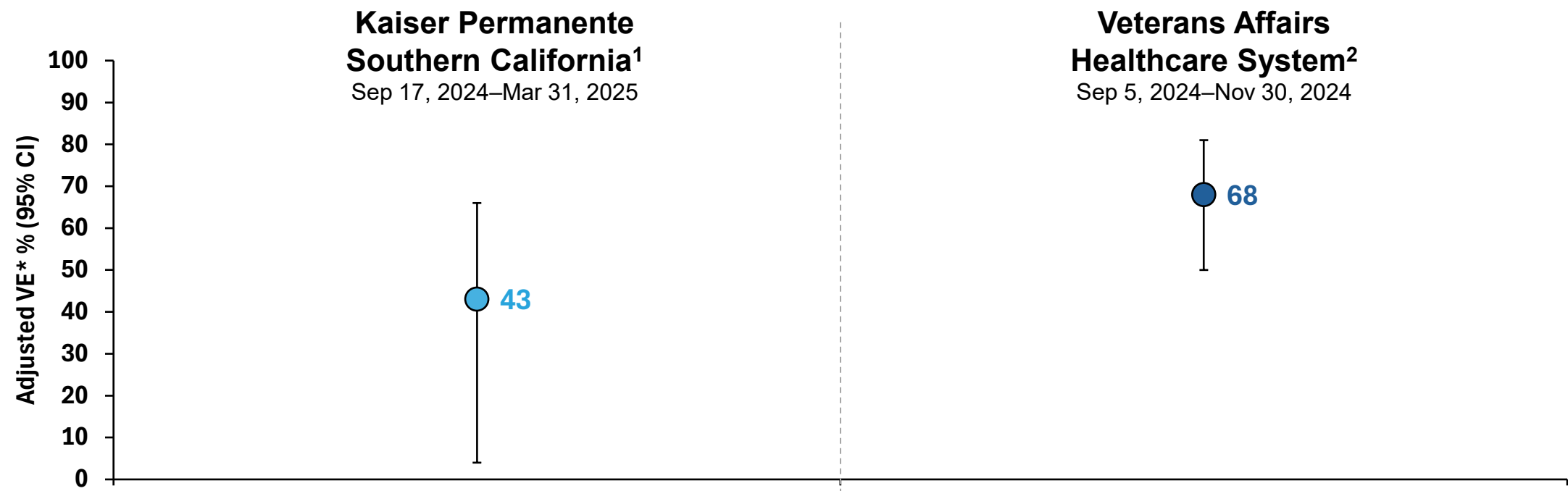
Virus Evolution to New Variant Results in Immune Escape; Updating Vaccine Provides Benefit

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

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Real World Effectiveness and Variant Epidemiology

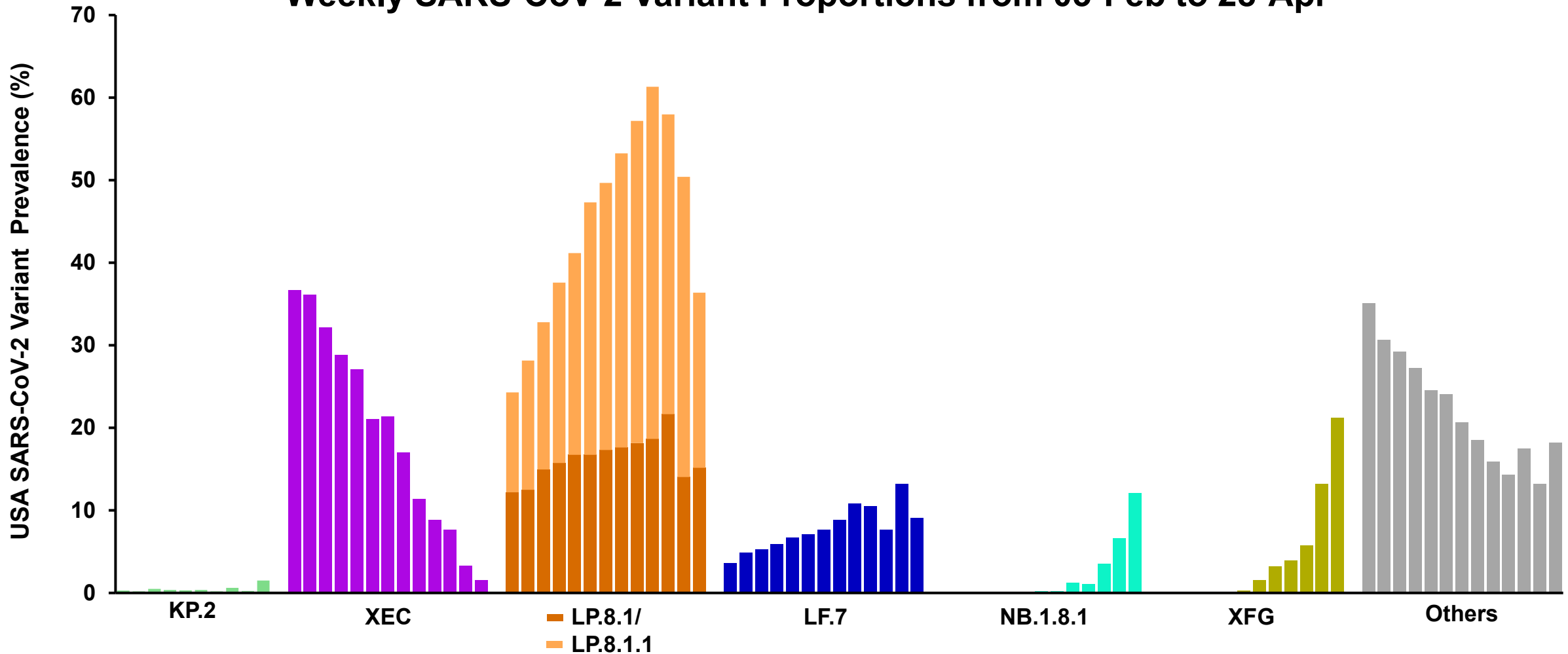# KP.2-Adapted Vaccine Provides Effectiveness Against Hospital Admission

Kaiser Permanente Southern California[1]
Sep 17, 2024–Mar 31, 2025

Veterans Affairs Healthcare System[2]
Sep 5, 2024–Nov 30, 2024

Adjusted VE * % (95% CI)

- Kaiser Permanente Southern California: **43**
- Veterans Affairs Healthcare System: **68**

	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

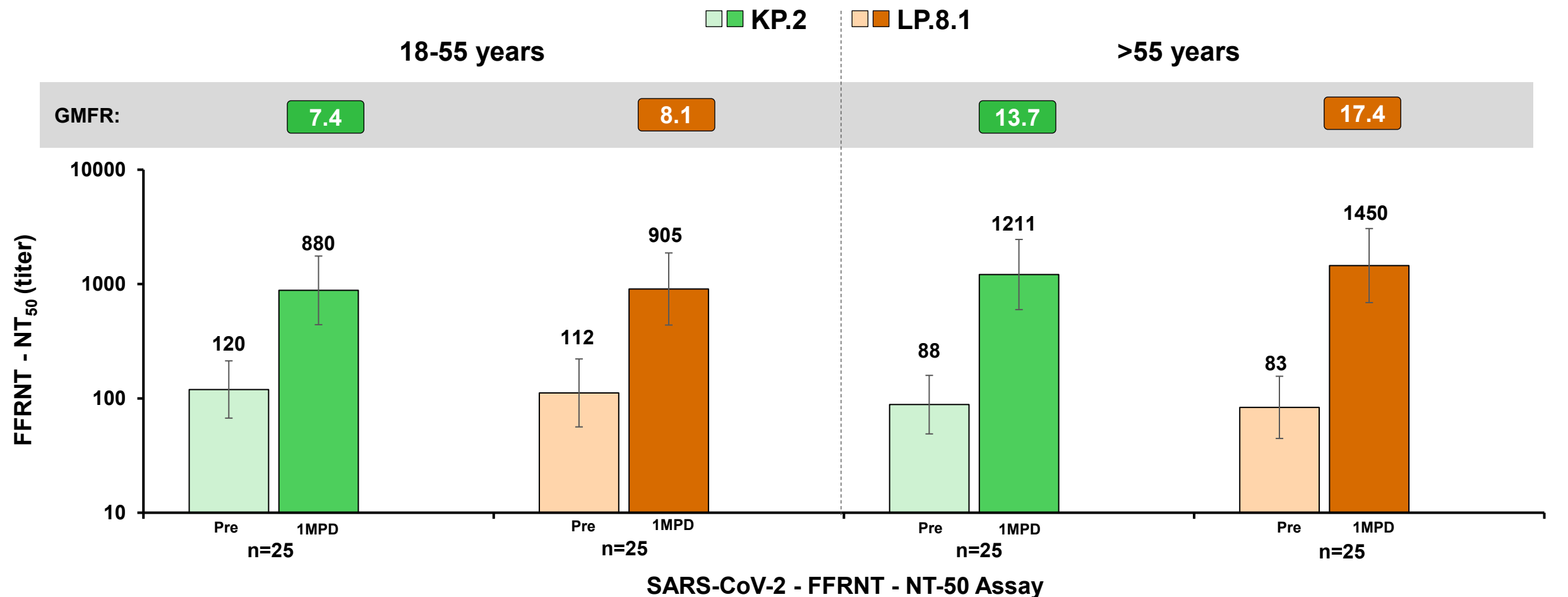**Weekly SARS-CoV-2 Variant Proportions from 03-Feb to 28-Apr**

Y-axis: USA SARS-CoV-2 Variant Prevalence (%)

Categories: KP.2, XEC, LP.8.1/ LP.8.1.1, LF.7, NB.1.8.1, XFG, Others

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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

KP.2   LP.8.1

18-55 years   **>55 years**

| GMFR: | 7.4 | 8.1 | 13.7 | 17.4 |

Y-axis: $FFRNT - NT_{50}$ (titer), ranging 10 to 10000

18-55 years:
- KP.2: Pre = 120, 1MPD = 880, n=25
- LP.8.1: Pre = 112, 1MPD = 905, n=25

>55 years:
- KP.2: Pre = 88, 1MPD = 1211, n=25
- LP.8.1: Pre = 83, 1MPD = 1450, n=25

X-axis: SARS-CoV-2 - FFRNT - NT-50 Assay

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

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Preclinical Evaluation of an Omicron LP.8.1-Adapted Vaccine

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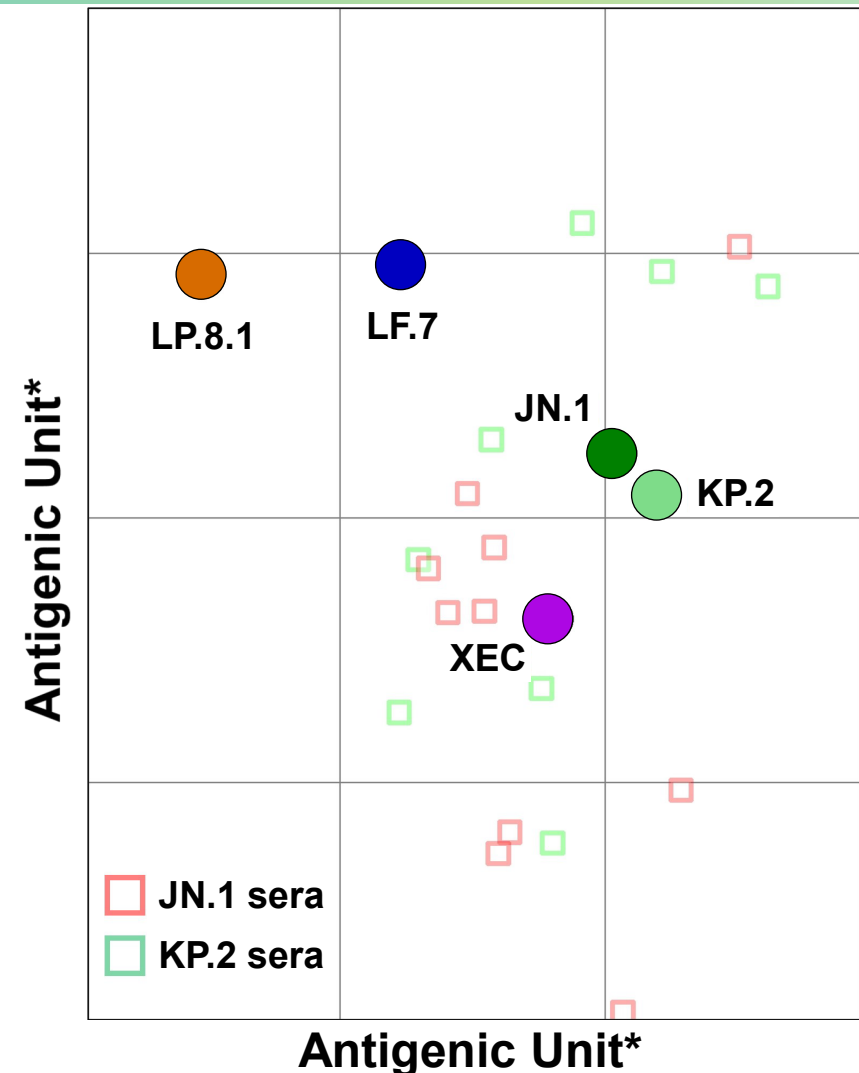
*Each box represents 1 antigenic unit = 2-fold difference in neutralization titer.
Antigenic map generated in Racmacs package in R using 2000 optimizations, with the minimum column basis parameter set to "none."
Generated from pseudovirus neutralization titers elicited by JN.1- and KP.2-adapted vaccines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

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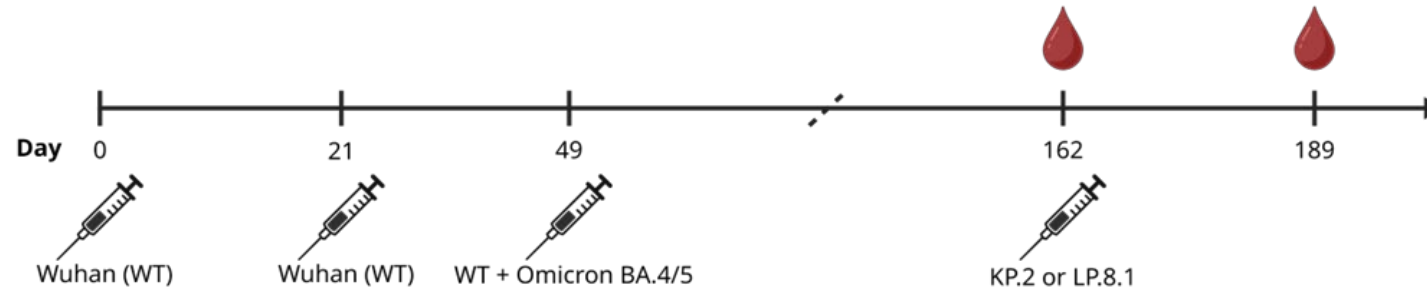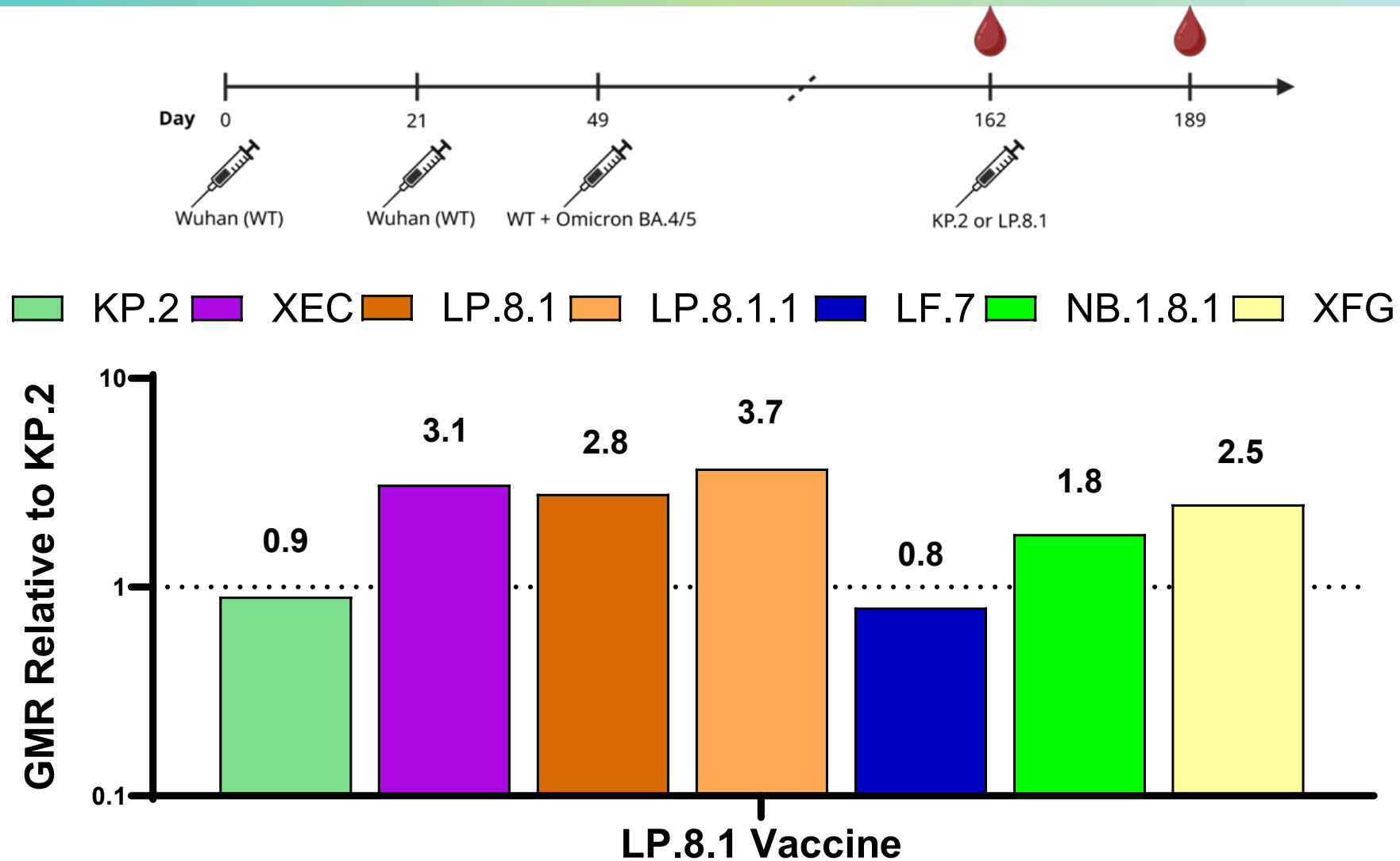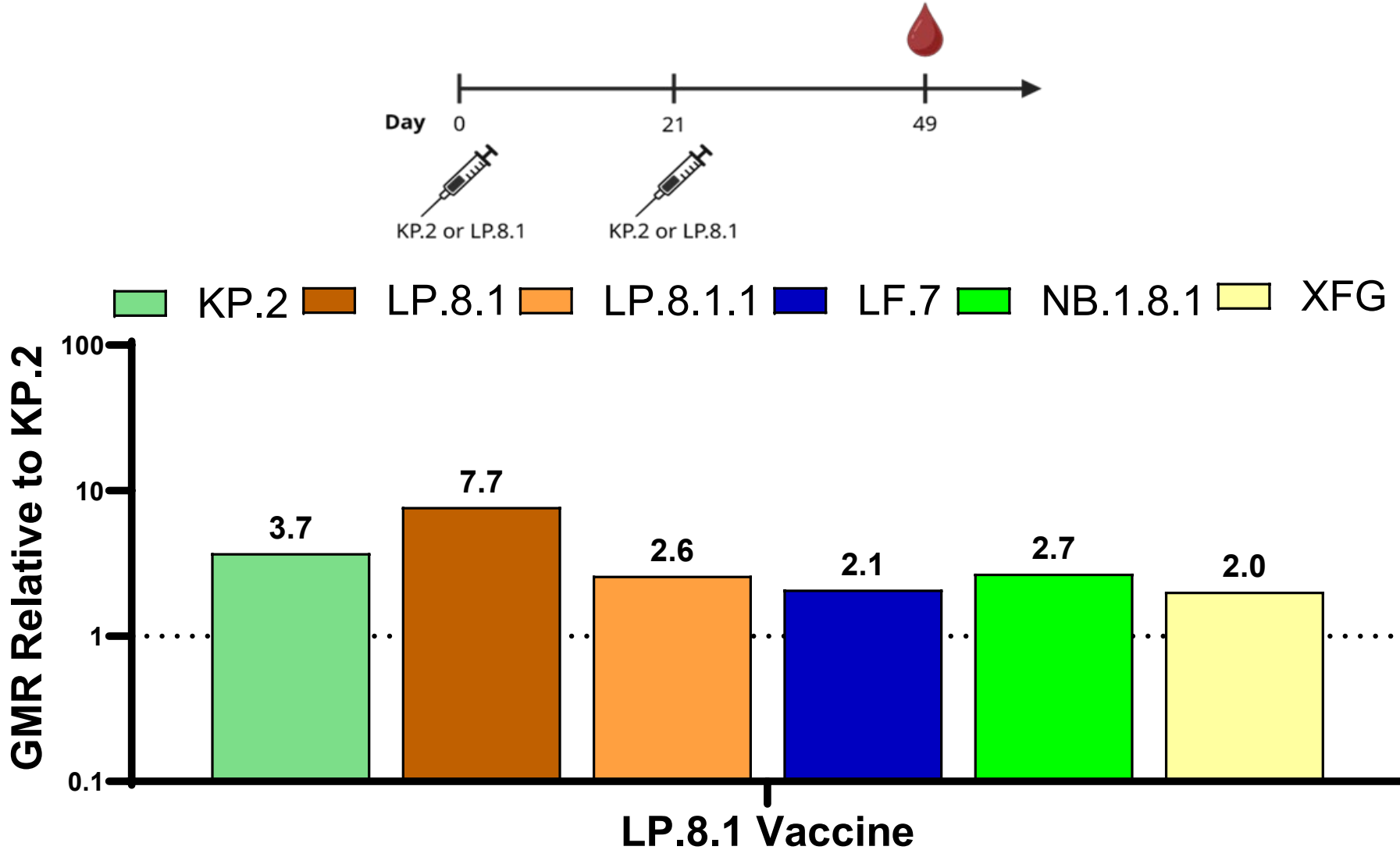

Neutralization titers measured by pseudovirus neutralization assay.
N = 10 mice per vaccine group. Vaccine dose 0.5 μg.
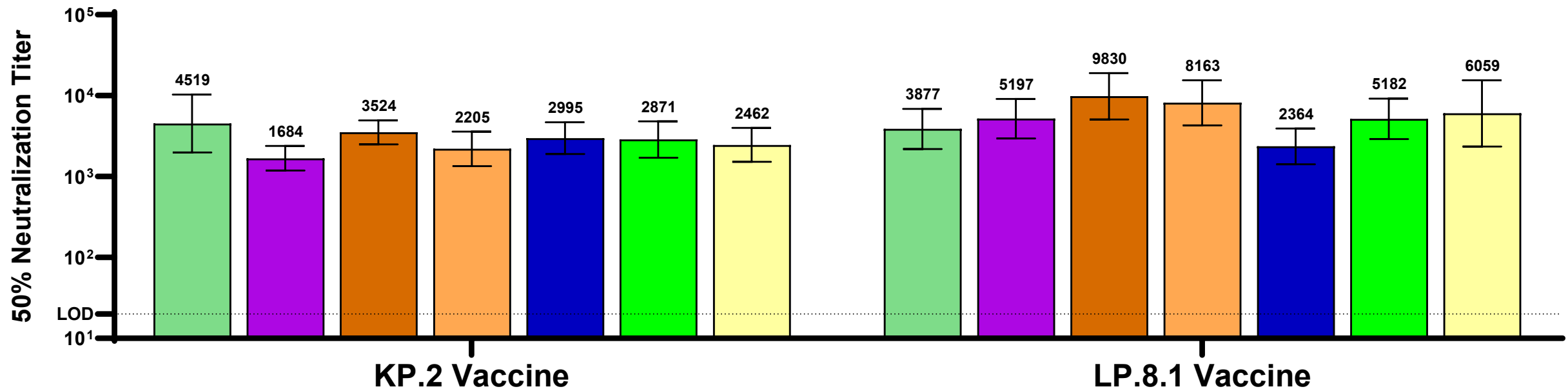
LP.8.1 Vaccine Elicits Improved Neutralization Compared to KP.2 Vaccine in Vaccine-Experienced Mice

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

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