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2023-2024 COVID-19 Vaccine Formula: Pfizer/BioNTech Clinical and Preclinical Supportive Data

Vaccines and Related Biological
Products Advisory Committee

June 15, 2023

Presentation Outline



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Epidemiology & Real-World Evidence

**Omicron-Adapted Vaccine Booster
Dose Humoral and Cell-Mediated
Immune Responses**

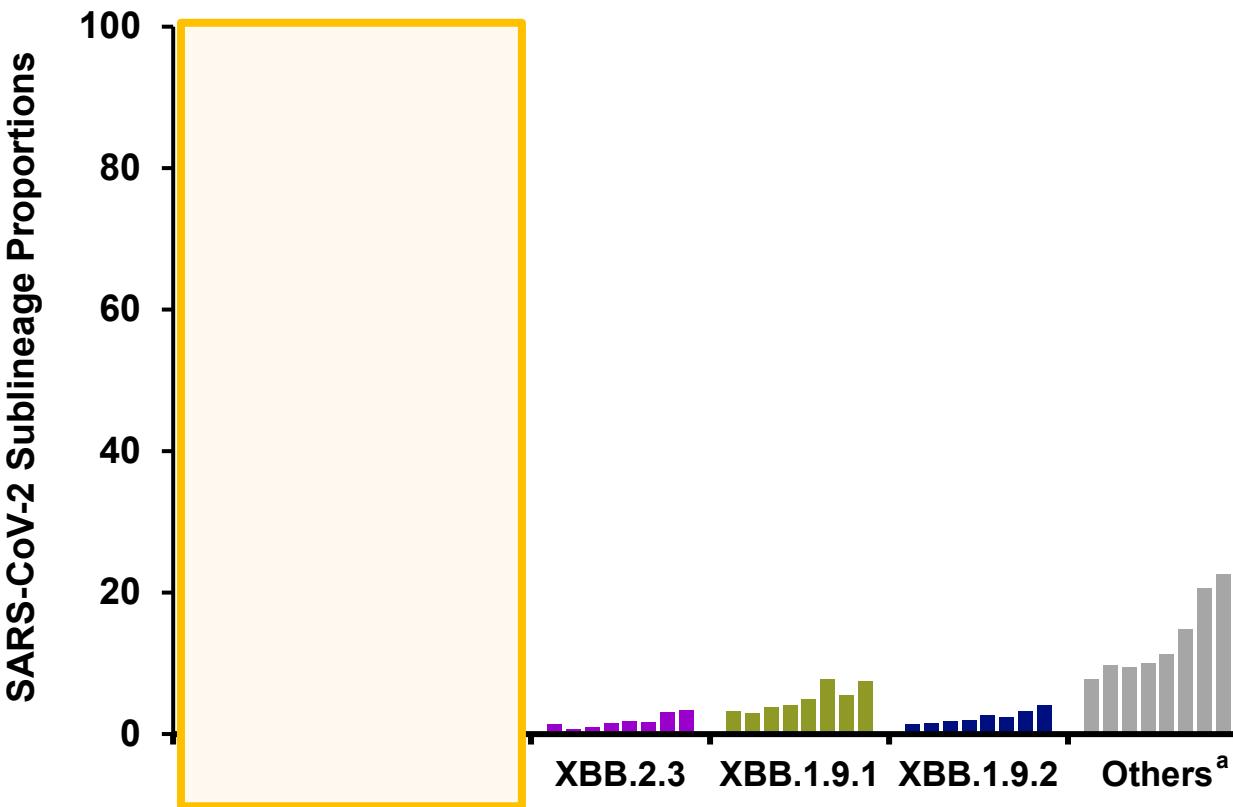
**Preclinical Evaluation Against
Contemporary Variant Vaccines**

Supply of 2023-2024 Formula



The Current COVID-19 Epidemiologic Landscape in the US is Dominated by XBB.1.5 and Related Sublineages

Weekly Proportions from 1-Apr to 20-May



Circulating XBB Sublineages are Similar

- **XBB.1.9.1 and XBB.1.9.2:** same spike amino acid sequence as XBB.1.5
- **XBB.1.16:** differs from XBB.1.5 at two spike amino acid residues
- **XBB.2.3:** differs from XBB.1.5 at three spike amino acid residues

GISAID, data accessed as of June 4, 2023

XBB.1.5, XBB.1.16, XBB.2.3, XBB.1.9.1, XBB.1.9.2 sublineage categories include descendants that have no amino acid differences in spike protein from parental sublineage.

a. Others include: XBB.1.16.1, EU.1.1.1, FL.4, FD.2, XBB.1.5.1 (sublineages that exceed a threshold of 1.8% in any week).

Waning Effectiveness of Current Bivalent Vaccines Against XBB Sublineages

Rationale for Fall Vaccine Update

- XBB sublineages dominant globally and antigenically distant from prior Omicron strains^{1,2}
- Current bivalent vaccines maintain effectiveness³⁻¹¹ but show signs of waning, including against severe COVID-19^{3,9-11}
- Immunity likely further reduced by fall
- Better-matched vaccines improve protection³

Absolute VE Against Hospitalization, CDC¹¹

Immunocompetent Adults, VISION Network, Sep 2022 – Apr 2023

| Time Since mRNA Vaccination | Adjusted VE (95% CI) |
|---------------------------------------|--------------------------|
| Monovalent only, ≥7 days* | 17 (7–26) |
| Bivalent booster, 7–59 days | 61 (44–72) |
| Bivalent booster, 60–119 days | 25 (1–43) |
| Bivalent booster, 120–179 days | 16 (-24–43) [†] |

* Median (IQR) time since last dose: 403 (306-534) days

† These estimates are imprecise and should be interpreted with caution.

Time Since mRNA Vaccination

| Age | Time Since mRNA Vaccination | Adjusted VE (95% CI) |
|------------|---------------------------------------|----------------------|
| Age 18–64y | Monovalent only, ≥7 days* | 24 (18–29) |
| | Bivalent booster, 7–59 days | 64 (58–68) |
| | Bivalent booster, 60–119 days | 51 (45–57) |
| | Bivalent booster, 120–179 days | 27 (15–37) |

* Median (IQR) time since last dose: 362 (245-484) days

1. World Health Organization. Weekly epidemiological update on COVID-19 - 6 April 2023. Available at: Weekly epidemiological update on COVID-19 - 6 April 2023 (who.int)

2. covSPECTRUM dashboard. Available at: <https://cov-spectrum.org/explore/World/AllSamples/Past6M>

3. Lin et al. N Engl J Med. 2023 Feb 23;388(8):764–766. doi: 10.1056/NEJMc2215471

4. Link-Gelles et al. MMWR Morb Mortal Wkly Rep 2023;72:119–124. doi: 10.15585/mmwr.mm7205e1

5. Surie et al. MMWR Morb Mortal Wkly Rep 2022;71:1625–1630. DOI: 10.15585/mmwr.mm715152e2

6. Tenforde et al. MMWR Morb Mortal Wkly Rep 2023;71:1637–1646. DOI: 10.15585/mmwr.mm7153a1

7. Fabiani et al. Euro Surveill. 2023 Feb;28(8):2300105. doi: 10.2807/1560-7917.ES.2023.28.8.2300105

8. Tartof et al. Unpublished analysis, under review.

9. Poukka et al. medRxiv 2023. doi: 10.1101/2023.03.02.23286561

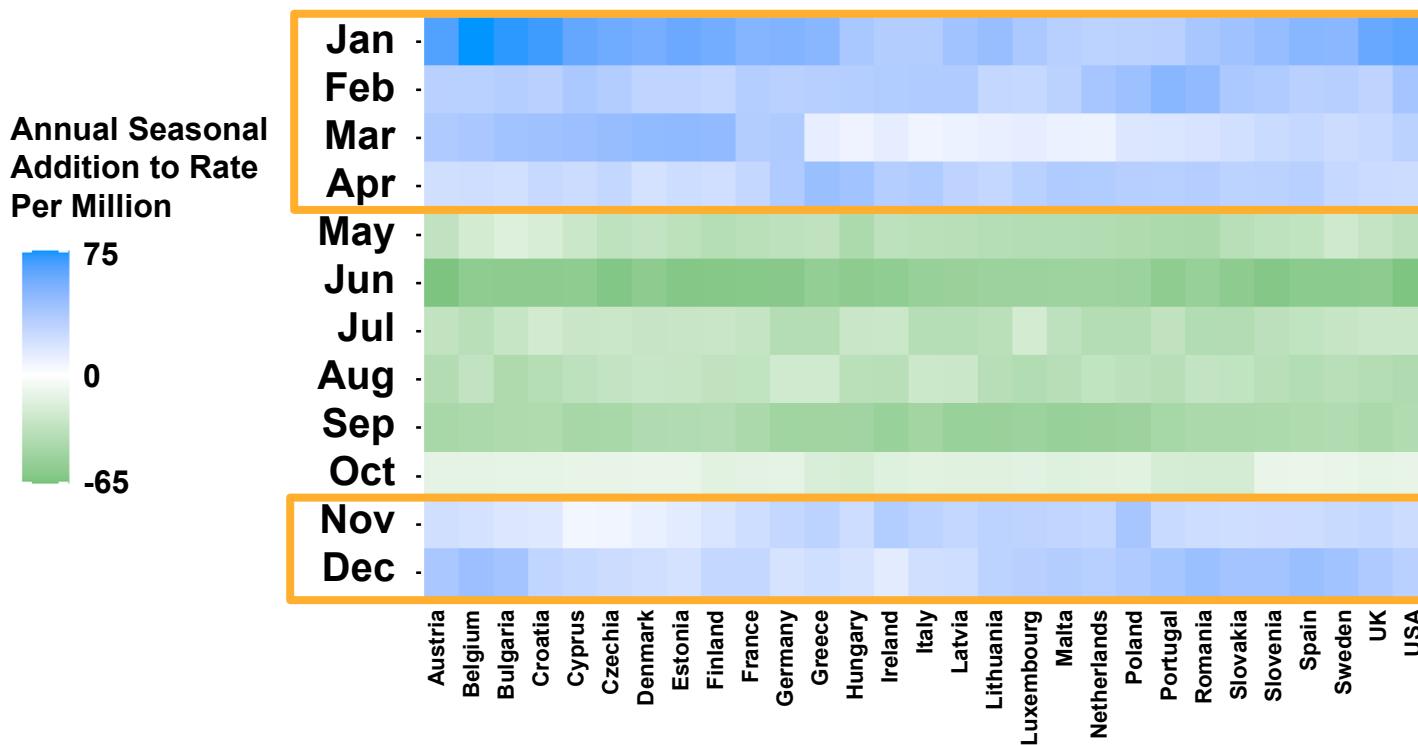
10. Link-Gelles R. CDC. Data presented at the ACIP meeting (April 19, 2023). Available at: ACIP meeting (CDC.gov)

11. Link-Gelles R. MMWR Morb Mortal Wkly Rep 2023;72:579–588. DOI: <http://dx.doi.org/10.15585/mmwr.mm7221a3>

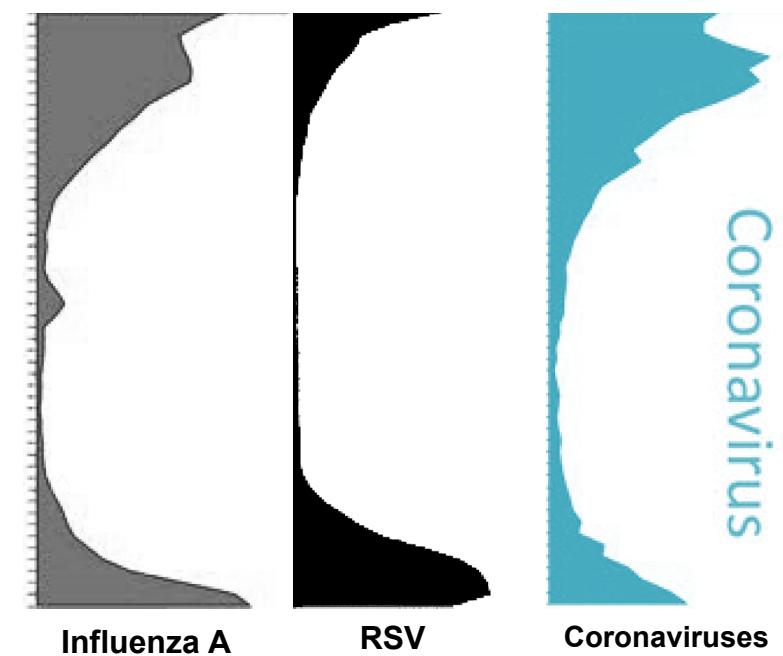
SARS-CoV-2 Activity is Expected to Increase this Autumn/Winter

- Disease activity has peaked between November and April¹
 - Similar to patterns seen for influenza, RSV, and other coronaviruses²

Heatmap of Monthly Median COVID-19-Related Hospitalizations
Per Million Population, Northern Hemisphere, Mar 2020 – Dec 2022¹



Weekly Seasonality of Confirmed Viral Infections, England and Wales, 1989 – 2019²



1. Wiemken et al. Sci Rep. 2023 Mar 8;13(1):3886. doi: 10.1038/s41598-023-31057-1

2. Nichols et al. BMC Infect Dis. 2021 Oct 26;21(1):1101. doi: 10.1186/s12879-021-06785-2.

Omicron-Adapted Vaccine Booster Dose Humoral and Cell-mediated Immune Responses

Immunogenicity Data From Omicron BA.1 and BA.4/5-adapted Vaccine Clinical Studies Support Real World Evidence Observations



- **Omicron-adapted boosters:**
 - Result in superior variant neutralization titers (NTs) compared to the original vaccine
 - Recall spike-specific memory B cells that recognize shared epitopes; Omicron-specific B cells are also induced
 - Expand spike-specific CD4 and CD8 T cell responses

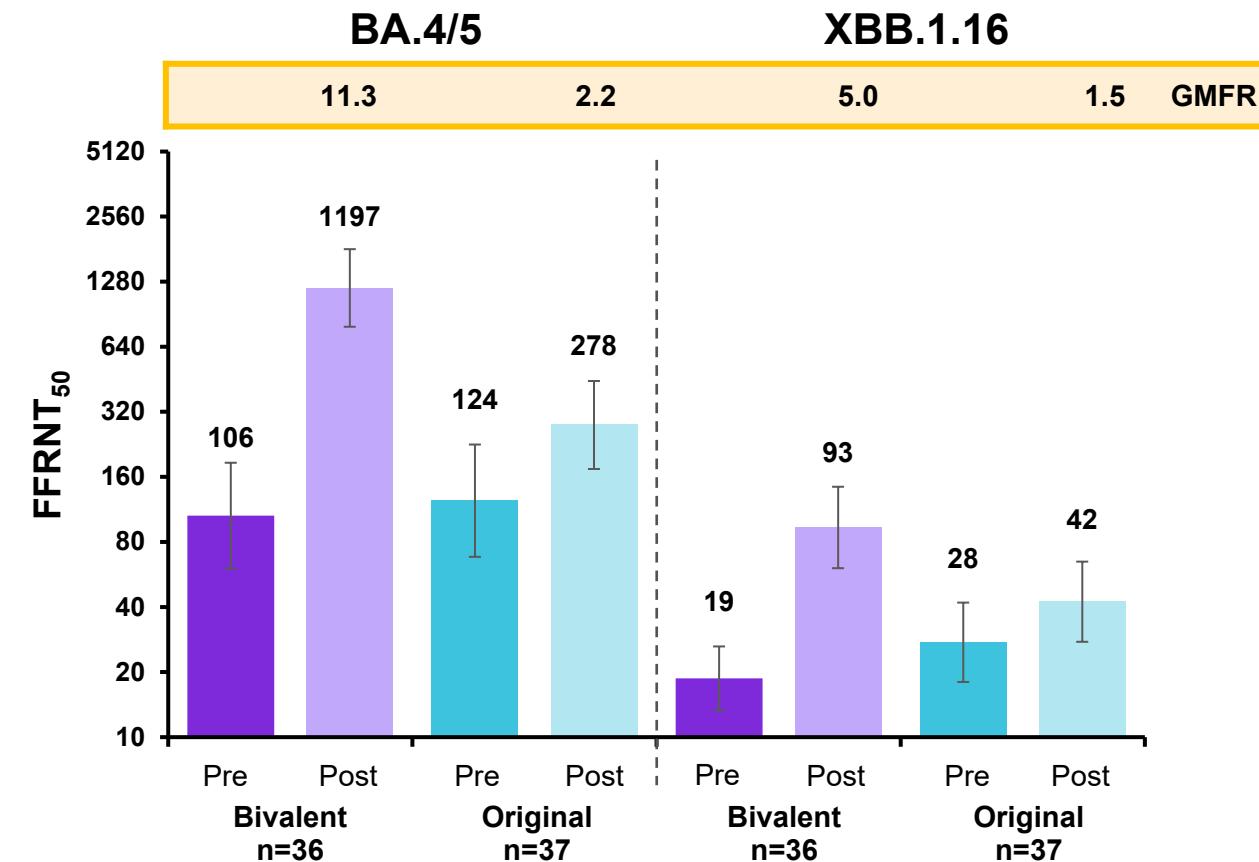
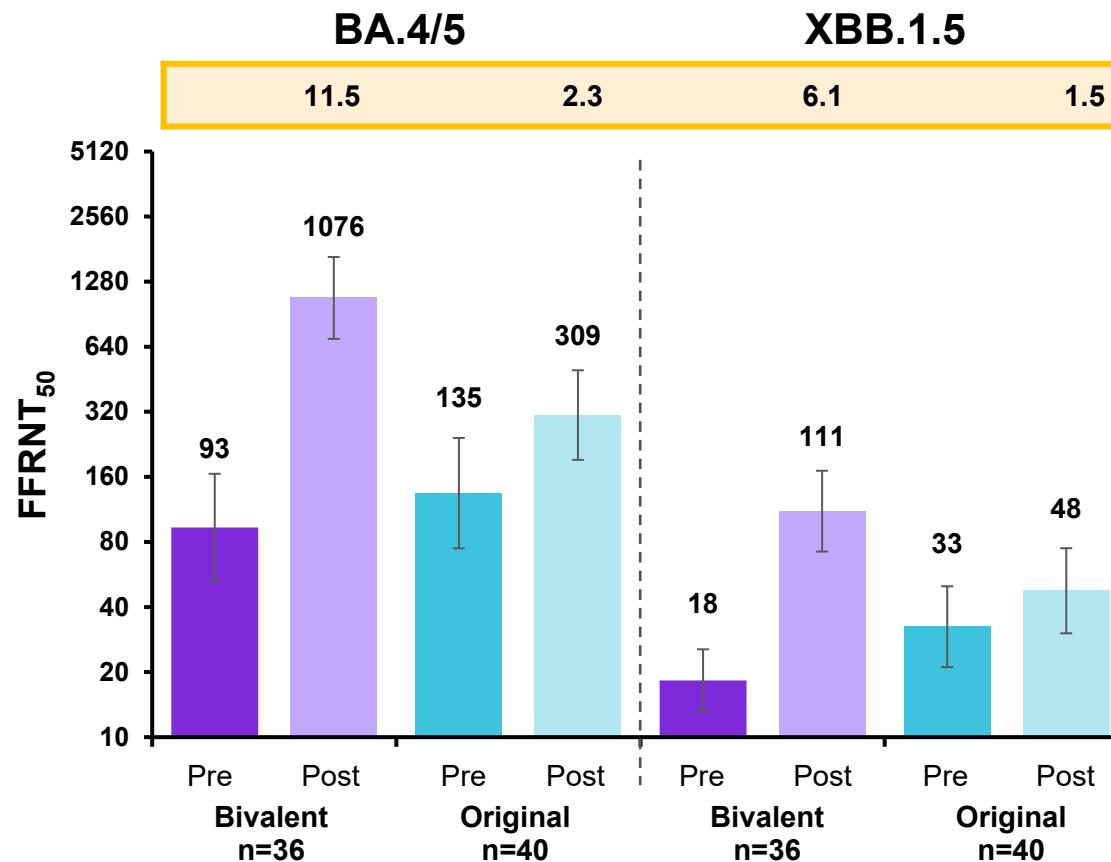
Clinical and Preclinical Experience with Variant-modified Vaccines – Supported Bivalent BA.4/5 Vaccine Authorization

| Modified Vaccine | Age Group | Vaccine Regimen | Clinical Data | Preclinical Data |
|-------------------------|---|-----------------|-----------------------|------------------|
| Beta monovalent | 18 to 55 years | | ✓ ✓ ✓ ✓ | ✓ ✓ ✓ |
| Omicron BA.1 monovalent | 18 to 55 years | | ✓ ✓ ✓ ✓ ✓ | ✓ ✓ ✓ ✓ |
| Omicron BA.1 bivalent | 18 to 55 years >55 years | | ✓ | ✓ |
| Omicron BA.4/5 bivalent | 6 months to 11 years 12 to 55 years >55 years | | ✓ | ✓ |



Bivalent BA.4/5 Boosts Neutralization Activity Against XBB.1.5 and XBB.1.16

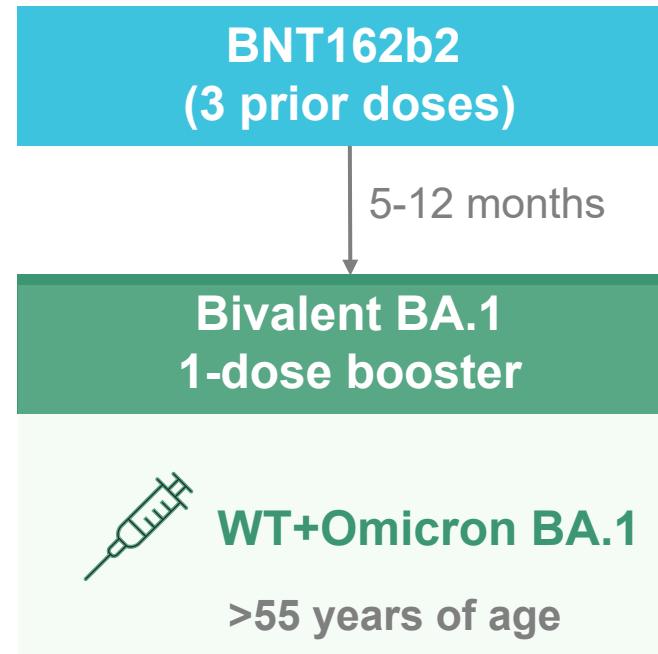
Participants >55 years With or Without Prior SARS-CoV-2 Infection at Baseline



Pre = Pre-dose 4; Post = 1-month post dose 4; FFRNT₅₀ = 50% fluorescent focus reduction neutralization titers; GMFR = geometric mean fold rises; GMT = geometric means of neutralization titers
The whiskers indicate 95% CI.

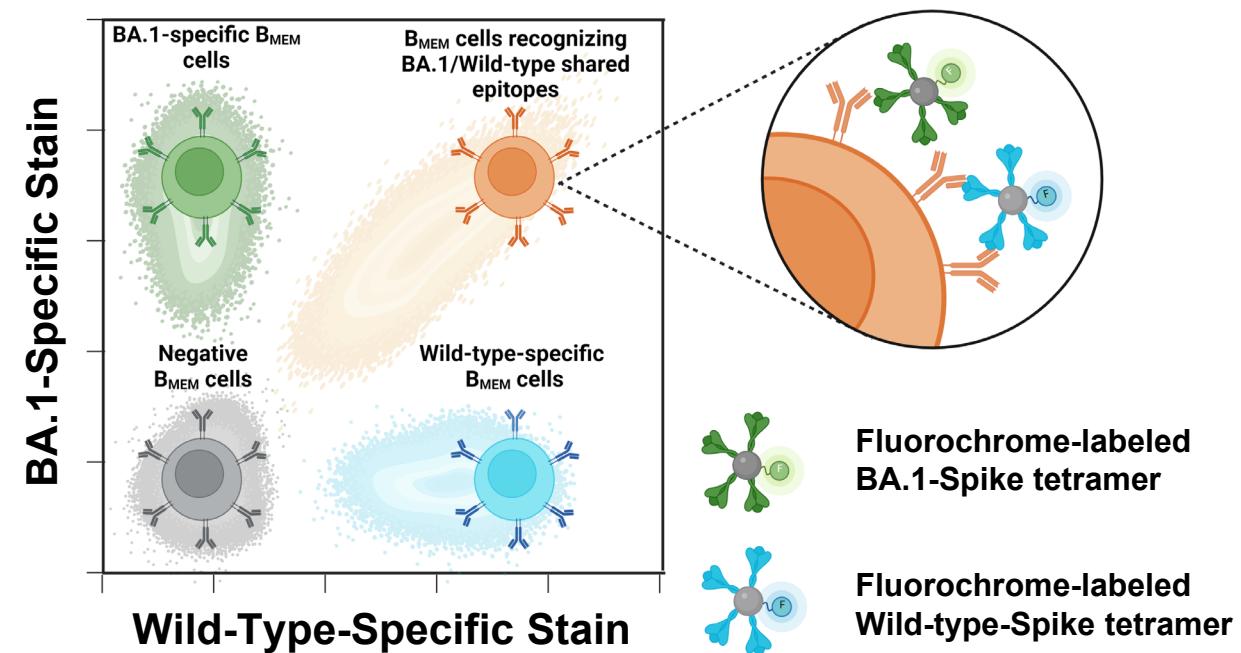
Omicron XBB.1.16 and concurrent Omicron BA.4/5 analyses shown on the right of this slide run after Omicron XBB.1.5 and concurrent Omicron BA.4/5 analyses on the left.

Spike-Specific Memory B cell (B_{mem}) Assessment After Bivalent Omicron BA.1 Booster Vaccination



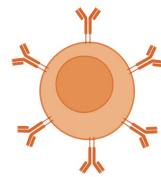
Assessment of Spike-specific Memory B cells

Wild-type strain and Omicron BA.1 Spike protein are used to measure memory B cells recognizing wild-type or Omicron BA.1 exclusive and wild-type/Omicron BA.1 shared epitopes

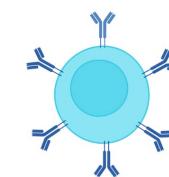
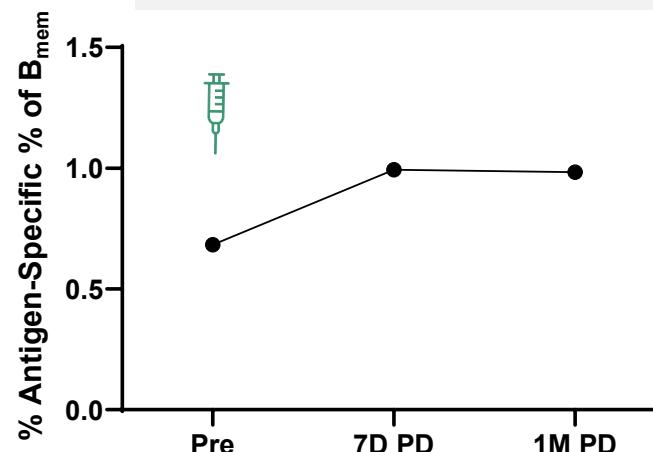


Bivalent Omicron BA.1 Booster Increases the Frequencies of Memory B Cells Recognizing Shared and BA.1-Specific Epitopes

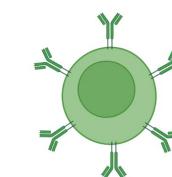
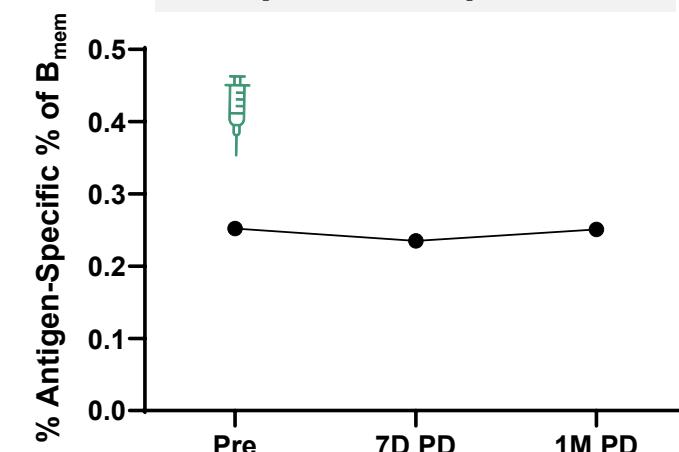
Omicron BA.1 Booster in BNT162b2-experienced Individuals >55 years of Age



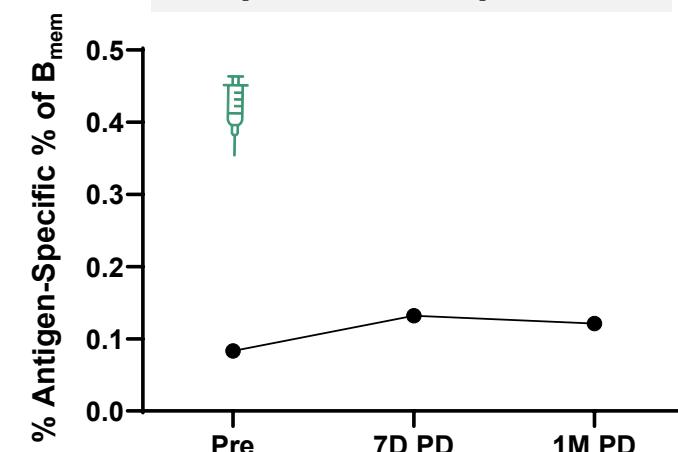
Spike Shared



Spike WT-Specific

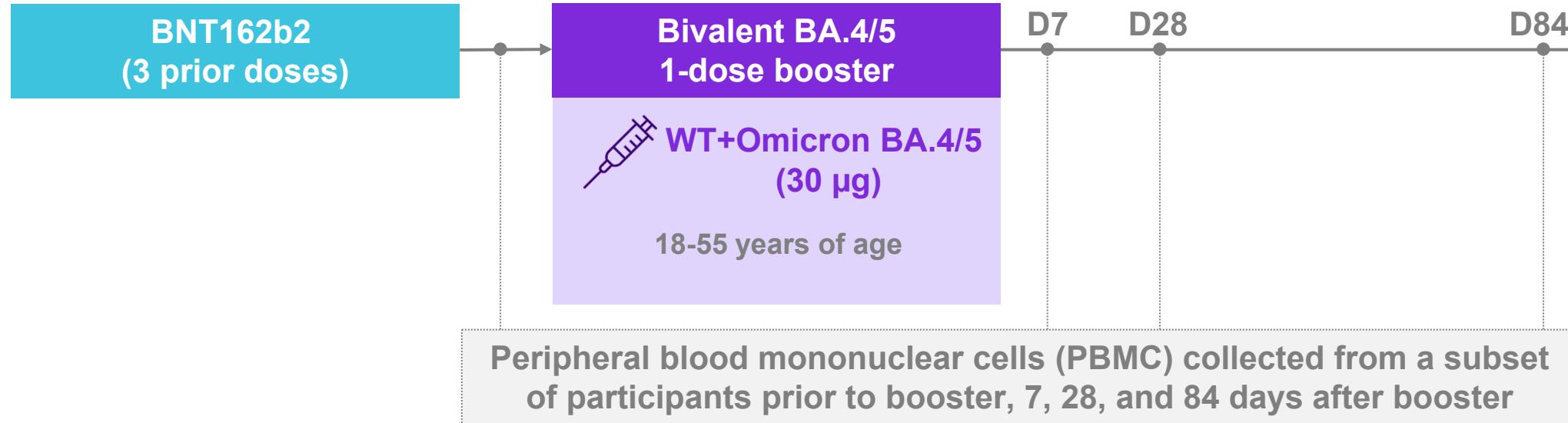


Spike BA.1-Specific



Similar trends were observed with a monovalent Omicron BA.1 booster

Clinical Study Evaluated CD4 and CD8 T Cell Responses Elicited by Bivalent Omicron BA.4/5-Adapted Booster



Spike peptide pools included those:

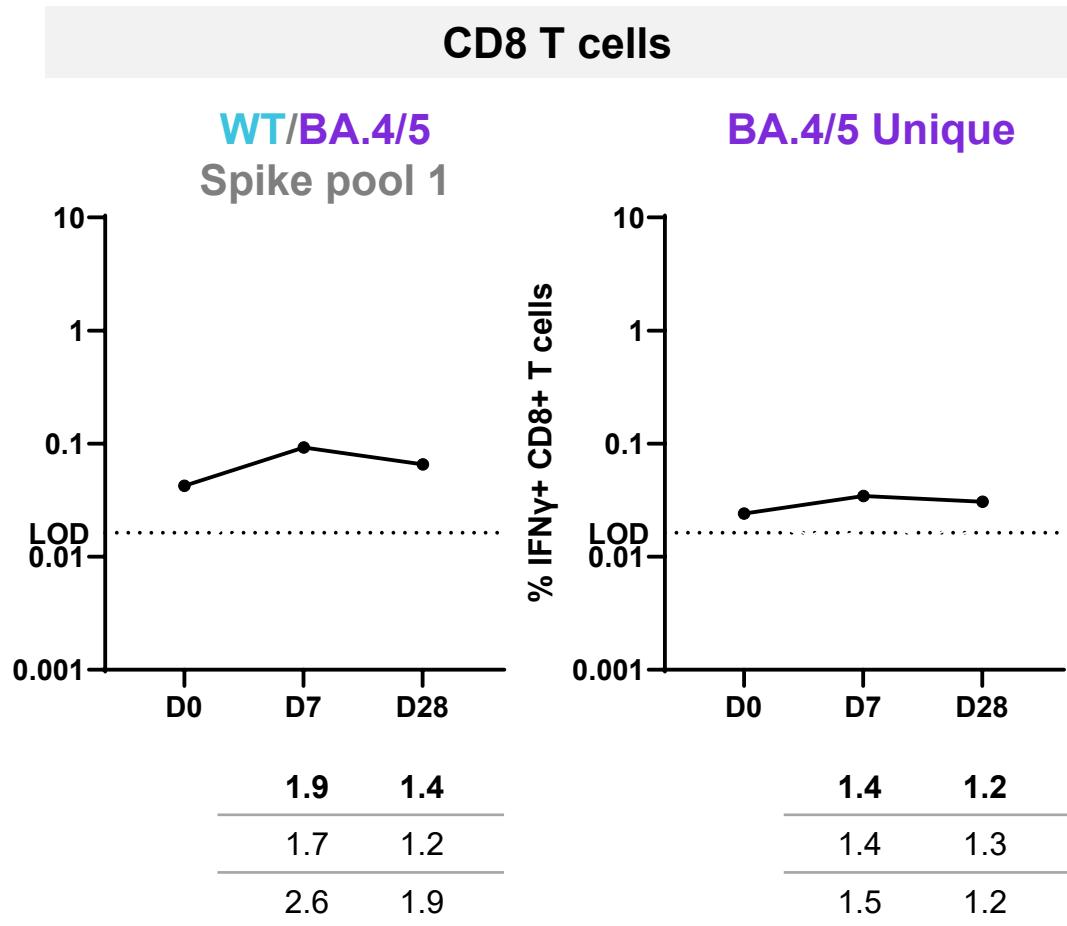
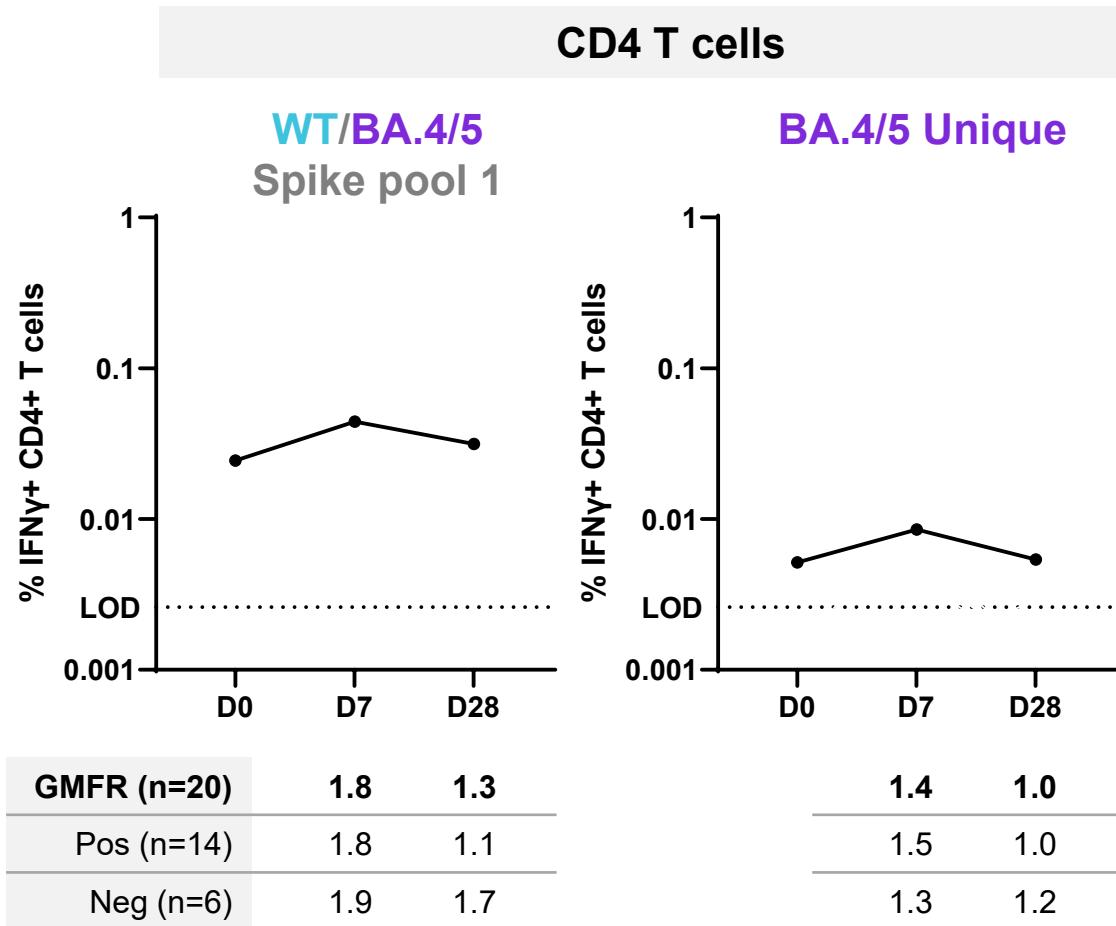
- Covering both **WT** and **BA.4/5**
- Unique to **BA.4/5**



WT / BA.4/5

Bivalent WT+BA.4/5 Vaccine Boosts CD4 and CD8 T cell Responses

Omicron BA.4/5 Booster in BNT162b2-experienced Individuals 18-55 Years of Age

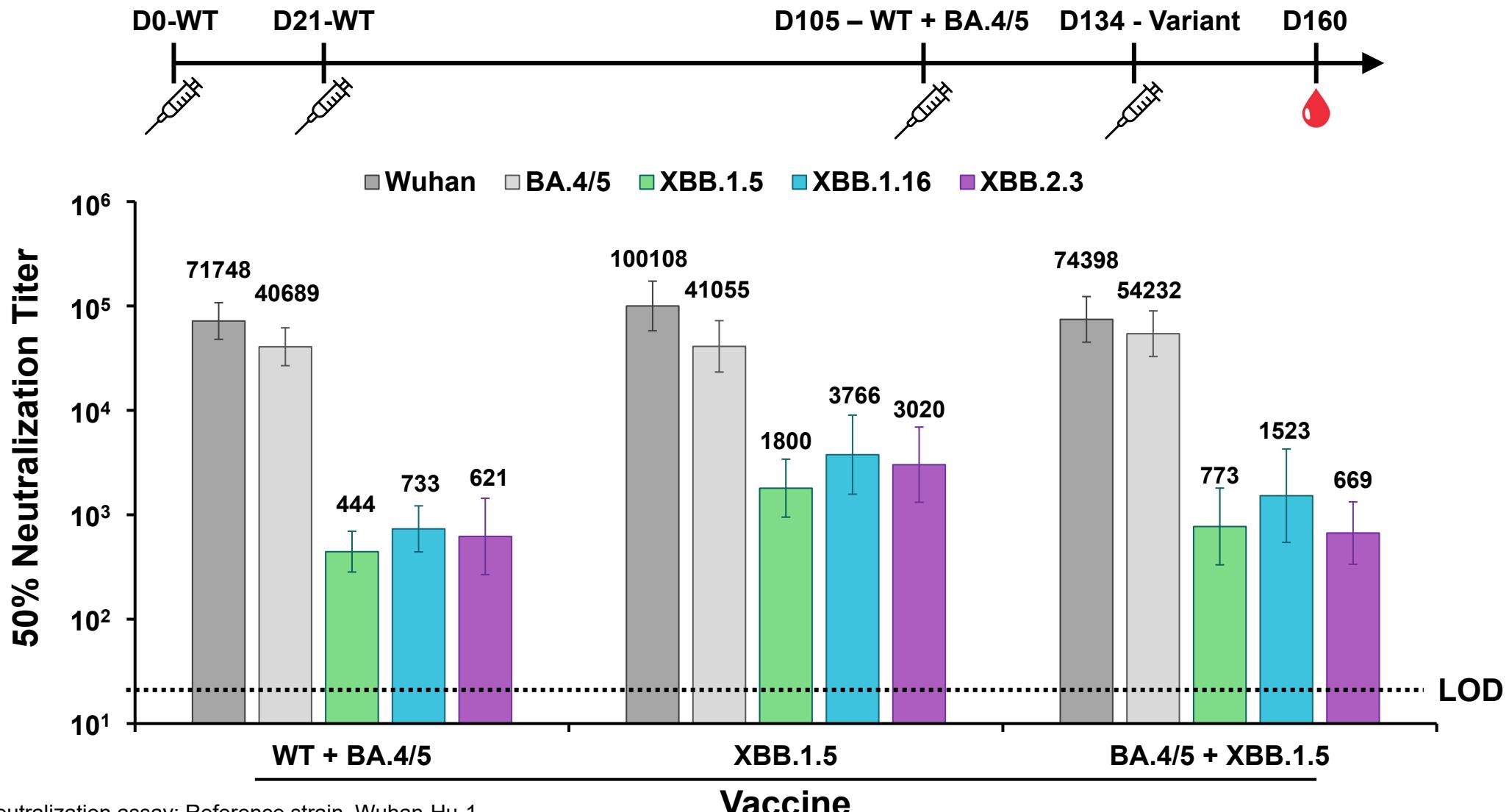


WT/BA.4/5 Spike pool 1: Pool of peptides representing aa 1-643 of WT and BA.4/5

BA.4/5 Unique: Pool of peptides representing mutations unique to BA.4/5

Preclinical Evaluation of Contemporary Variant Vaccines

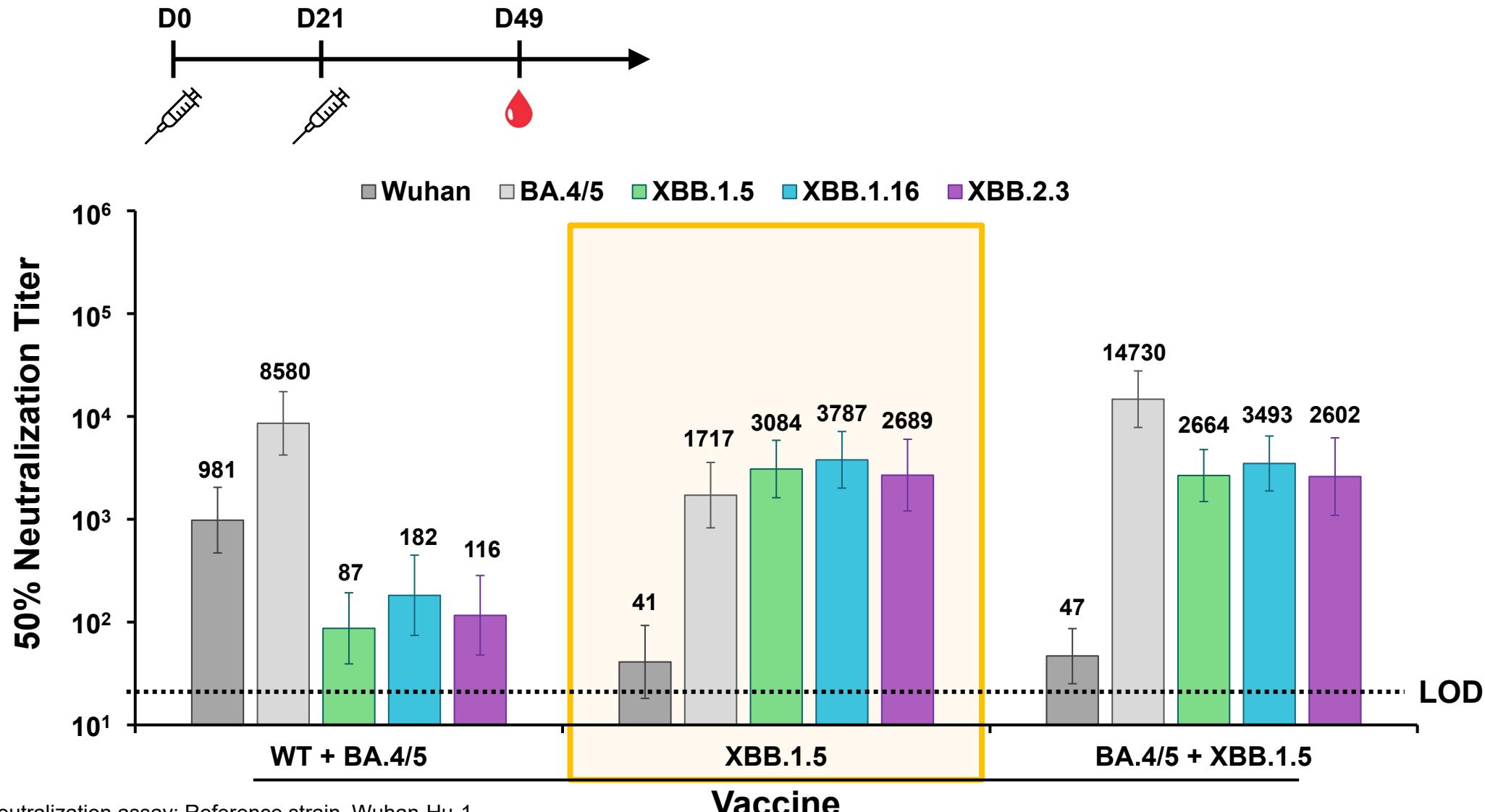
Monovalent XBB.1.5 Booster Elicits Highest XBB Sublineage Neutralization Response



Pseudovirus neutralization assay; Reference strain, Wuhan-Hu-1

LOD = Limit of detection; the lowest serum dilution of 1:20. N = 10 mice per vaccine group

Monovalent XBB.1.5 Vaccine, as a Primary Series, Elicits Highest XBB Sublineage Neutralization Response



Pseudovirus neutralization assay; Reference strain, Wuhan-Hu-1

LOD = Limit of detection; the lowest serum dilution of 1:20. N = 10 mice per vaccine group

CC-16

Supply Readiness

Readiness to Supply Updated COVID-19 Vaccine

- **Dose distribution can begin as follows, subject to regulatory approval**
 - XBB.1.5 monovalent: end July
 - XBB.1.16 monovalent: August
 - Any other formulation: October
- **Note: ~60% of flu doses are distributed by end of September**
 - Above timelines for both XBB monovalent formulations enable parallel distribution of flu and COVID-19 vaccines
- **Primary presentation will be single dose units – enabling greater access and efficiency**

Should the need arise Pfizer/BioNTech can support an off-cycle strain selection at a later date

Conclusions

Preclinical and Clinical Data Support a Monovalent XBB-adapted Vaccine for the 2023-2024 Formula

- **XBB.1.5 and XBB.1.16 are most predominant in the US**
- **Improved humoral and cell-mediated immunity with Omicron-adapted vaccines**
- **Preclinical data show XBB-adapted vaccines offer improved responses against circulating strains**
 - Higher responses with monovalent than bivalent vaccines

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