Pfizer/BioNTech COVID-19 Omicron-Modified Bivalent Vaccine

Dr Kena Swanson, Ph.D.

Vice President, Viral Vaccines R&D, Pfizer

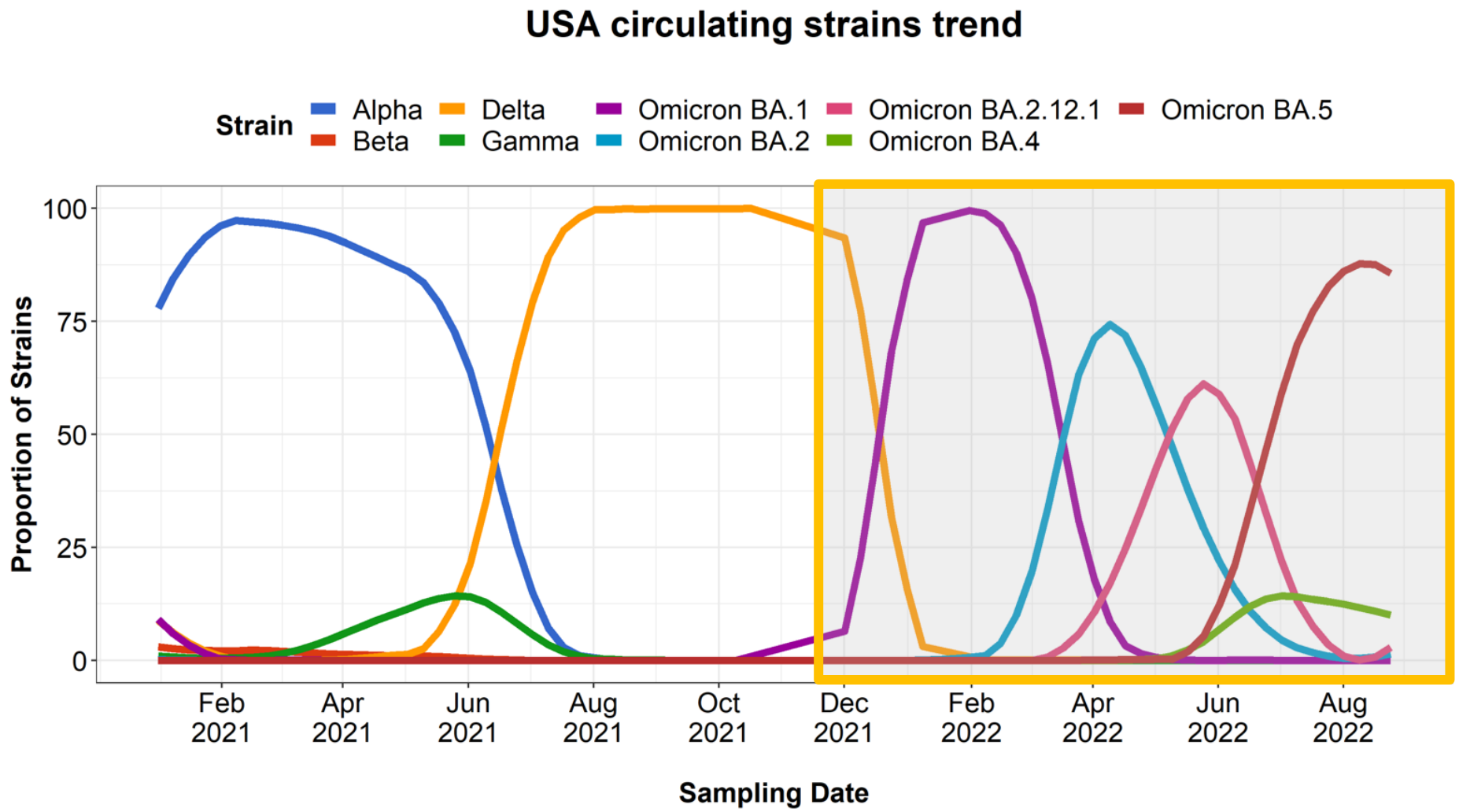
September 01, 2022

Important Disclaimer

The information in these slides and discussed during the presentation, including scientific approaches, assumptions regarding potential safety and efficacy, clinical trial and manufacturing plans and timing estimates, are subject to change based on emerging data, regulatory guidance, and manufacturing and technical developments, among other risks.

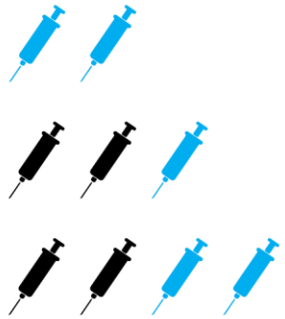
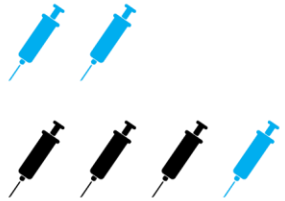
SARS-CoV-2 Epidemiology Changes Quickly

Omicron BA.5 Now Predominant VOC



GISAID data as of August 30, 2022

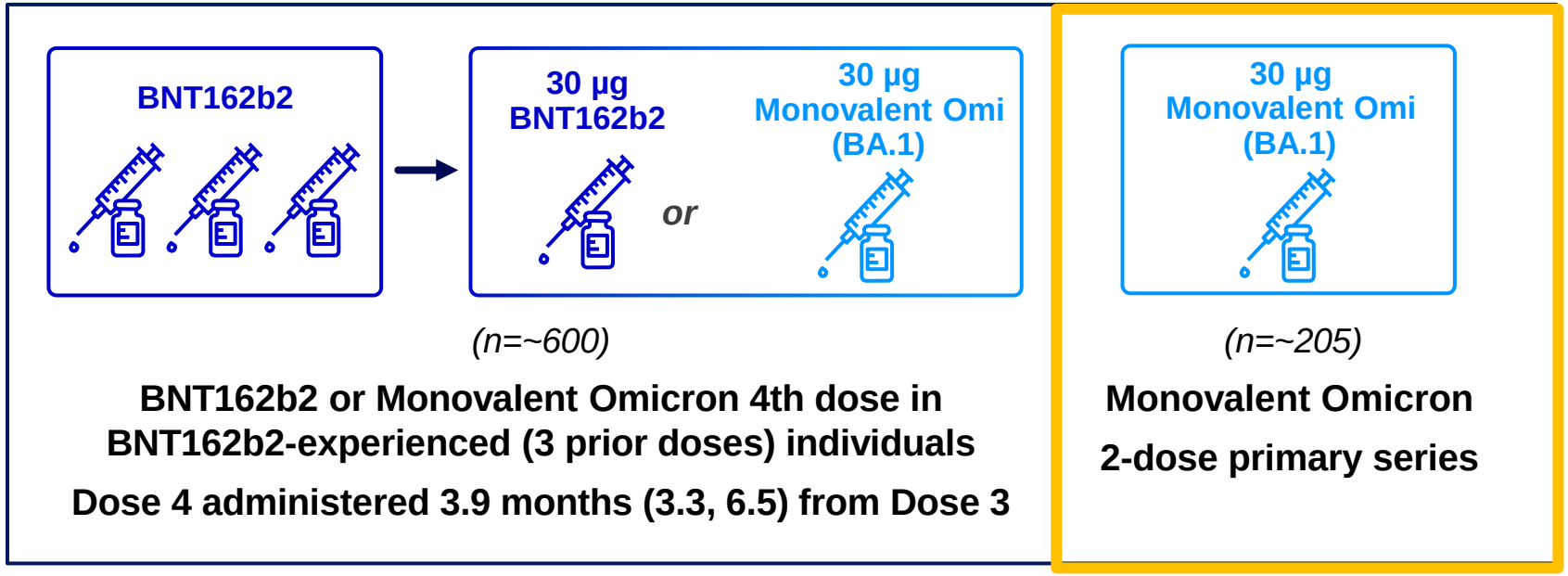
Preclinical Data Have Reliably Predicted Clinical Results for Variant-modified Vaccines

Modified Vaccine	Age Group	Vaccine Regimen	Clinical Data	Preclinical Data
Beta B.1.351 *monovalent*	18-55y		✓	✓
Omicron BA.1 *monovalent*	18-55y		✓	✓
Omicron BA.1 *bivalent*	>55y		✓	✓
Omicron BA.4/5 *bivalent*	12-55y >55y		*Study Ongoing*	✓

Clinical Study For Monovalent Omicron BA.1-modified Vaccine Candidate Booster and Primary Series

18-55y Participants

C4591031 Substudy D evaluates safety and immunogenicity in ~1,420 participants



EUA Guidance

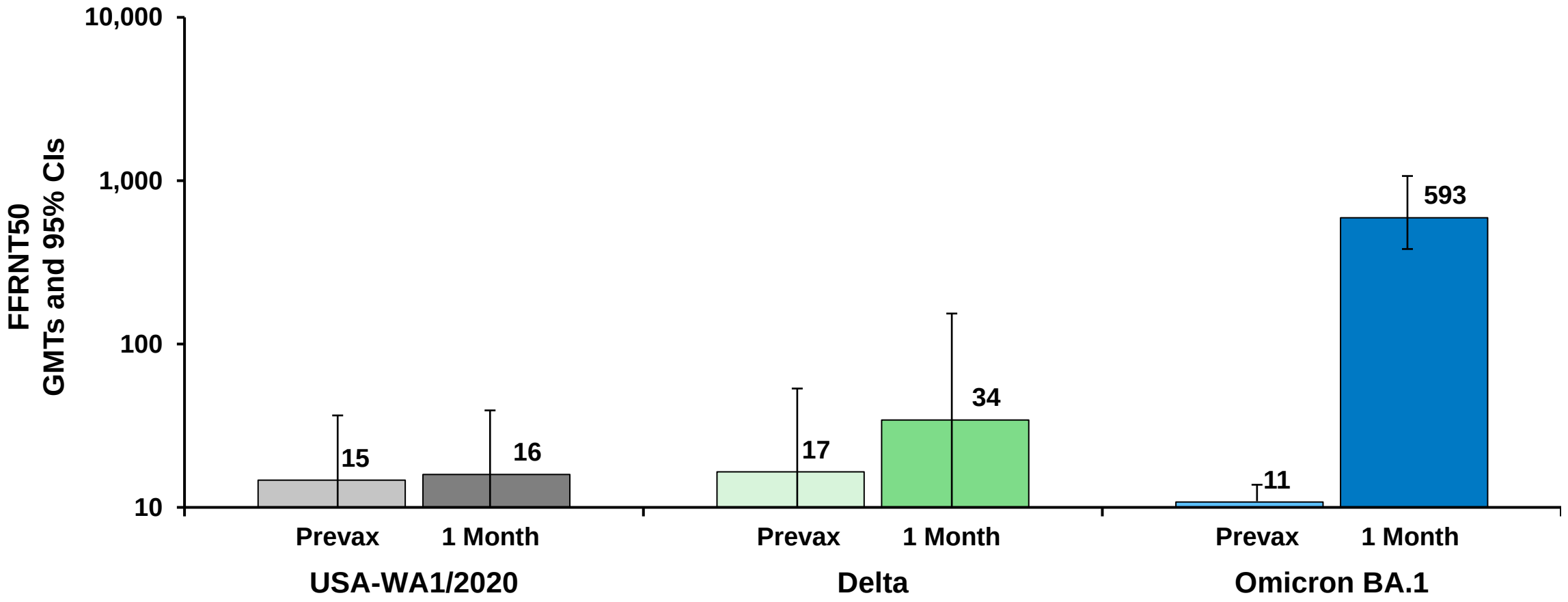
- **Omicron neutralization:**
  - **GMR Simple Superiority:** the lower bound of the 95% confidence interval for the GMR is >1
  - **Seroresponse Noninferiority:** the lower bound of the 95% confidence interval for the percentage difference is greater than -5
- **Reference strain neutralization:**
  - **Descriptive analyses:** comparison of geometric mean neutralizing titers for reference strain (USA-WA1/2020)

GMR, geometric mean ratio

In Naïve Individuals, Monovalent Omicron BA.1 Vaccine Candidate Elicits a Predominantly Omicron-specific Response

30 µg Dose, Evaluable Immunogenicity Population – Sentinel Group

Participants WITHOUT Evidence of Infection up to 1 Month After Dose 2

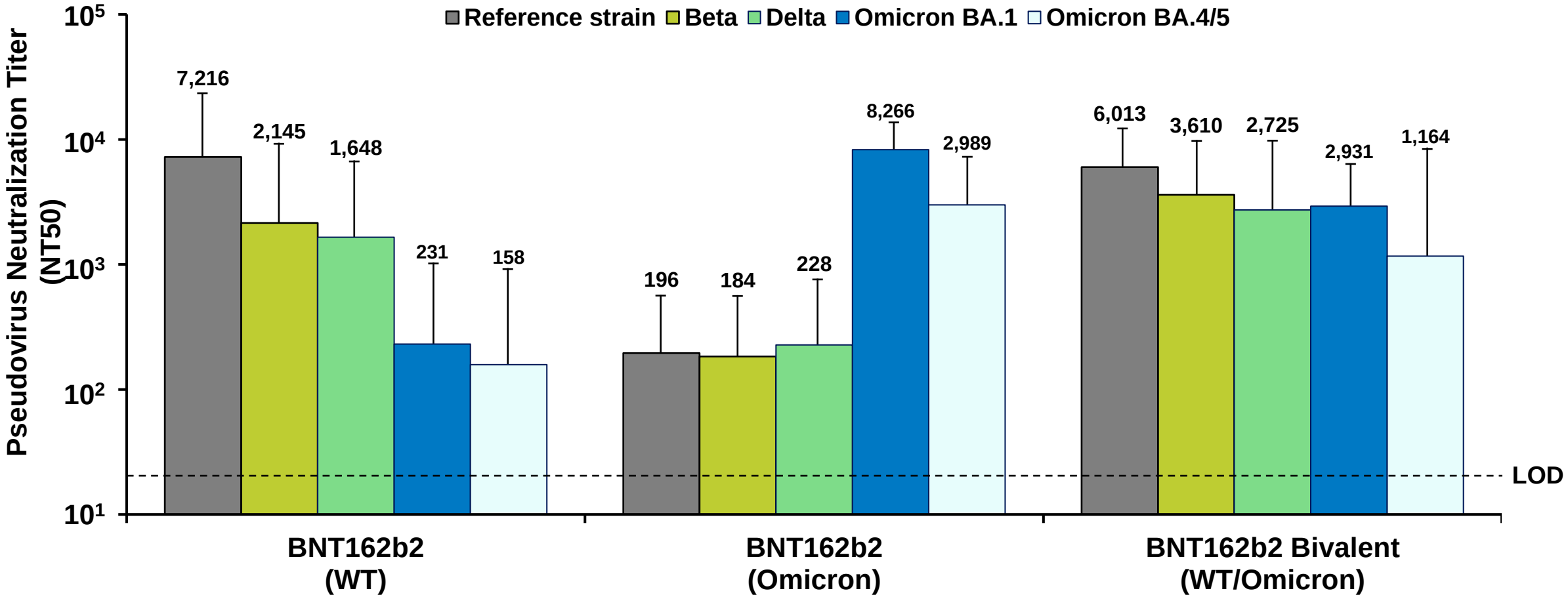


FFRNT, fluorescent focus reduction neutralization test
N=9 for all groups without evidence of infection up to 1 month after dose 2 shown out of total N=30 sentinel cohort

Preclinical Data Demonstrate Superior Neutralization Breadth with Bivalent WT/Omicron BA.1 Vaccine 2-Dose Primary Series Compared to Prototype and Omicron BA.1 Monovalent Vaccine Candidate

1M Post-Dose 2 in Naive Mice

Fold decrease from BA.1: 1.5 2.8 2.5

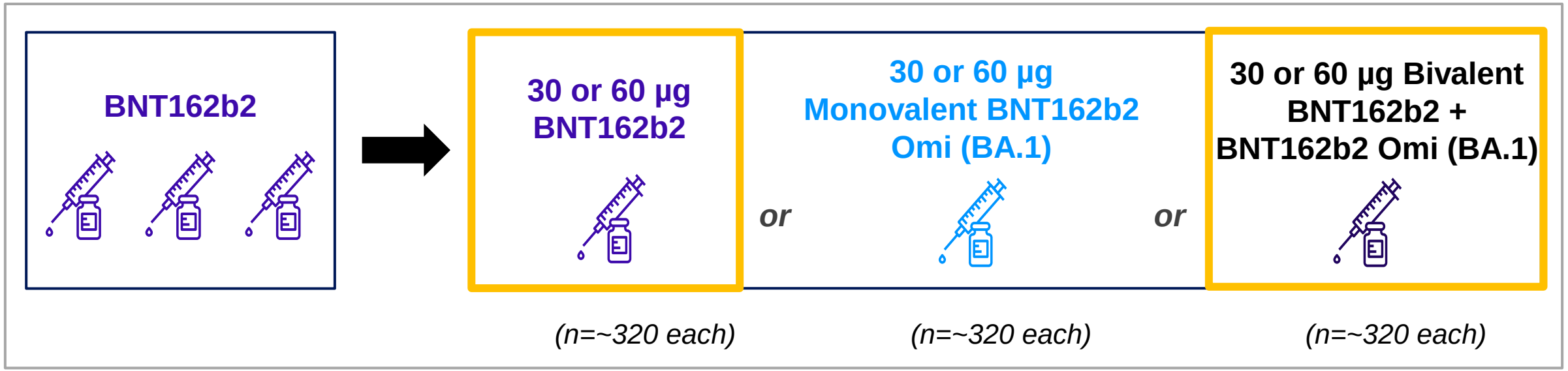


Vaccines administered at 0.5 mcg dose level at Days 0 and 21 to naïve mice
LOD, Limit of Detection; Reference strain, Wuhan-Hu-1

Clinical Study to Evaluate Monovalent and Bivalent Omicron BA.1-modified Vaccine Candidates in Vaccine-experienced Participants

>55y Participants

C4591031 Substudy E Evaluates Safety & Immunogenicity in ~1920 participants >55 Years



Dose 4 administered a median of 6.3 months (4.7, 12.9) from Dose 3

Monovalent BNT162b2 Omi (BA.1) 60 µg (N~330), bivalent BNT162b2 + BNT162b2 Omi (BA.1) 30 µg (N~180) and 60 µg (N~480) also being evaluated in participants 18-55 years of age

Omicron BA.1 GMR Consistent with Superiority Criteria for Bivalent Omicron BA.1-modified Vaccine Candidate

>55y Participants

Participants WITHOUT Evidence of Infection up to 1 Month After the Study Vaccination

Assay	Vaccine Groups	n	GMT (95% CI) 1M Post-Dose	Vaccine Group / BNT162b2 30 µg	
				GMR (95% CI)	Met Superiority (Y/N)*
SARS-CoV-2 neutralization assay – Omicron BA.1 – NT50 (titer)	BNT162b2 30 µg	163	455.8 (365.9, 567.6)		
	Bivalent OMI BA.1 30 µg	178	711.0 (588.3, 859.2)	1.56 (1.17, 2.08)	Y

GMR Simple/Super superiority criteria: the lower bound of 95% confidence interval for GMR is >1.0/1.5 respectively

Omicron BA.1 NT50 measured using validated 384-well assay

Omicron BA.1 Seroresponse Rate Exceeds Non-inferiority Criterion for Bivalent Omicron BA.1-modified Vaccine Candidate

>55y Participants

Participants WITHOUT Evidence of Infection up to 1 Month After the Study Vaccination

Assay	Vaccine Groups	N	n (%)	(95% CI) 1M Post-Dose	Seroresponse Difference in % Vaccine Group – BNT162b2 30 µg % (95% CI)	Met Non-inferiority (Y/N)*
SARS-CoV-2 neutralization assay – Omicron BA.1 – NT50 (titer)	BNT162b2 30 µg	149	85 (57.0)	(48.7, 65.1)		
	Bivalent OMI BA.1 30 µg	169	121 (71.6)	(64.2, 78.3)	14.6 (4.0, 24.9)	Y

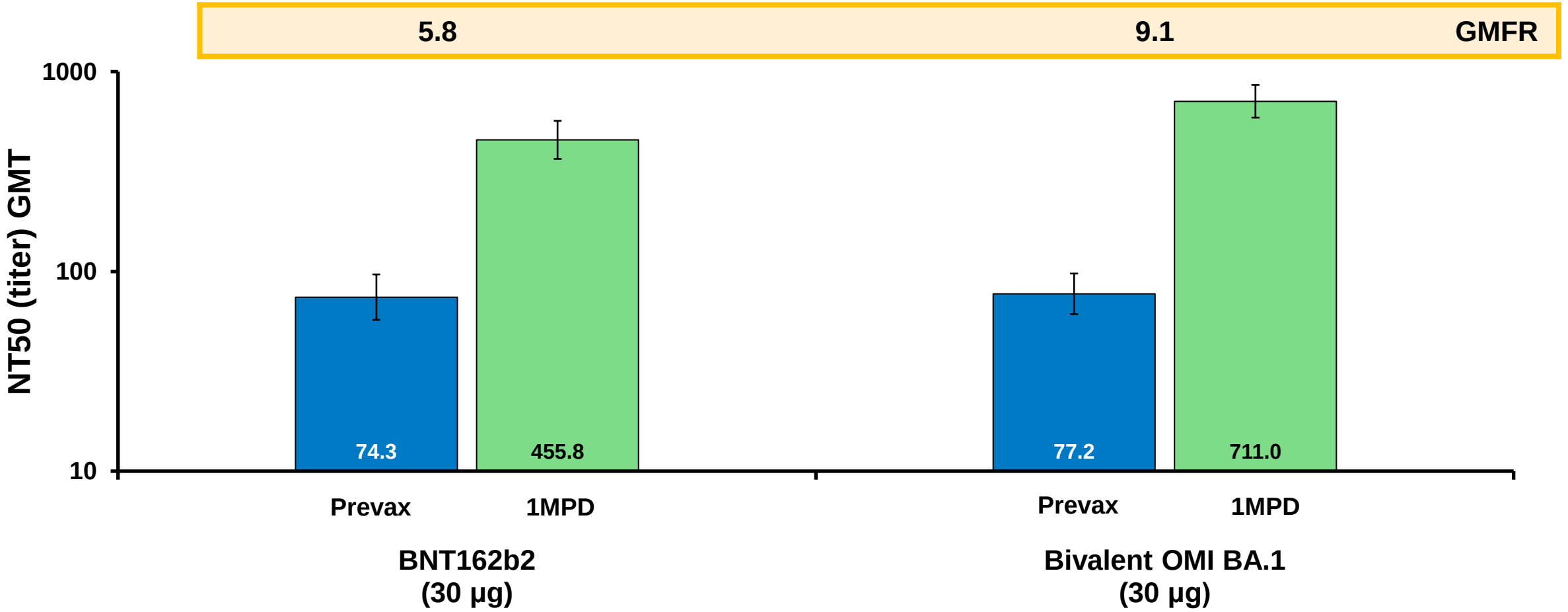
Non-inferiority criterion: the lower bound of 95% confidence interval for interval for the percentage difference is >-5

Omicron BA.1 NT50 measured using validated 384-well assay

Omicron BA.1 Neutralization Activity Substantially Increased with Bivalent Omicron BA.1-modified Vaccine Candidate as 4th Dose Booster

>55y Participants

>55 Year Olds Without Evidence of Prior Infection
Median Time from Dose 3 to Study Vaccination: 6.3 Months (4.7, 12.9)



Omicron BA.1 NT50 measured using validated 384-well assay

Non-inferiority of Reference Strain GMR Demonstrated for Bivalent Omicron BA.1 Vaccine Candidate

>55y Participants, Expanded Cohort (Evaluable Immunogenicity Population)

Participants WITHOUT Evidence of Infection up to 1 Month After the Study Vaccination

Assay	Vaccine Groups	n	GMT (95% CI) 1M Post-Dose	Vaccine Group / BNT162b2 30 µg	
				GMR (95% CI)	Met Non-inferiority (Y/N)
SARS-CoV-2 neutralization assay – reference strain – NT50 (titer)	BNT162b2 30 µg	182	5998.1 (5223.6, 6887.4)		
	Bivalent OMI BA.1 30 µg	186	5933.2 (5188.2, 6785.2)	0.99 (0.82, 1.20)	Y

Non-inferiority criterion: the lower bound of 95% confidence interval for GMR >0.67 (1.5-fold criterion)

Reference strain (USA-WA1/2020) NT50 measured using validated 384-well assay

Reactogenicity Profile of Bivalent Omicron BA.1 Variant Vaccine Candidate Overall Similar to Prototype BNT162b2 Vaccine

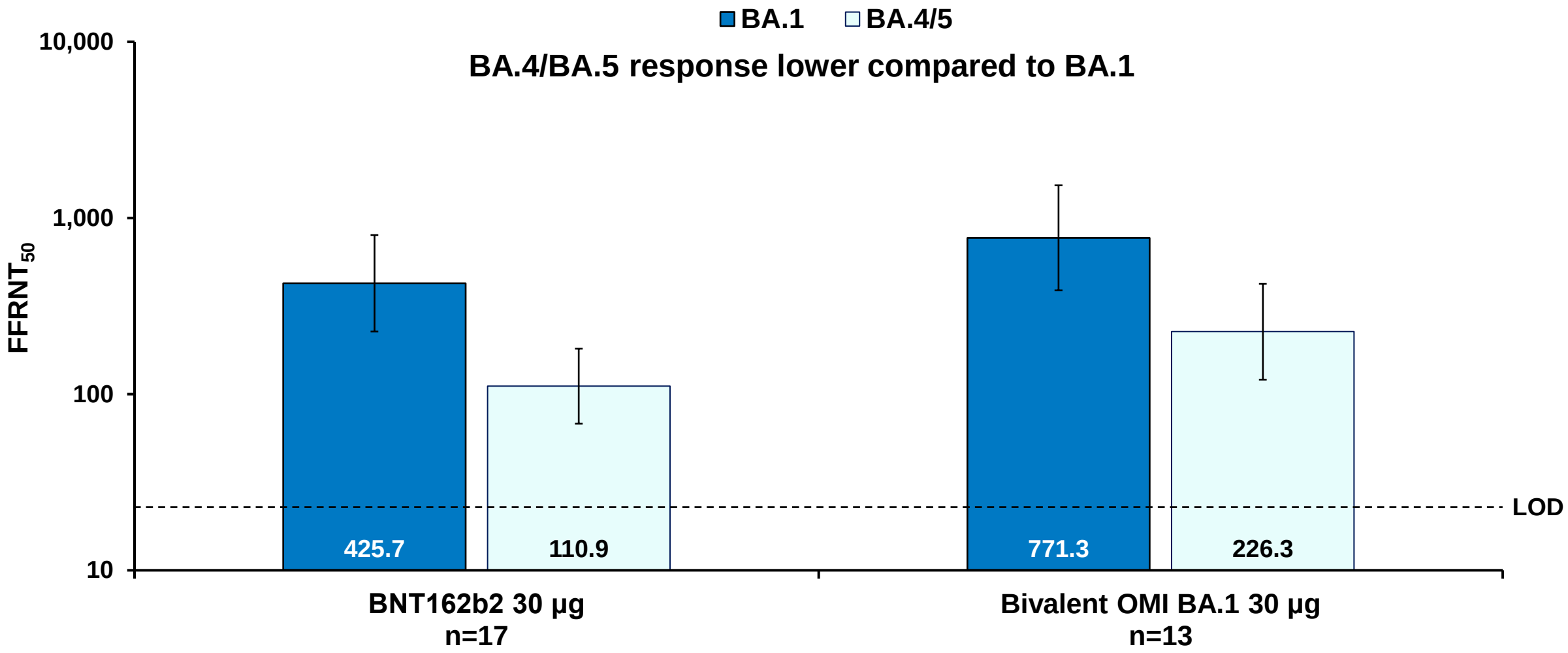
	C4591031 Substudy E[a] (>55y)	
	BNT162b2 30 µg Dose 4 (N=298)	Bivalent OMI BA.1 30 µg Dose 4 (N=301)
Local reaction at injection site		
Pain	60.1%	58.1%
Swelling	6.0%	6.6%
Redness	6.4%	7.0%
Systemic events		
Fatigue	45.3%	49.2%
Headache	26.5%	33.6%
Muscle pain	19.8%	22.3%
Chills	16.4%	13.0%
Joint pain	9.1%	11.3%
Fever (≥38.0°C)	3.7%	5.0%
Vomiting	1.3%	1.7%
Diarrhea	4.4%	9.0%

a. BNT162b2-experienced participants (>55 years of age) who received BNT162b2 30 µg or BNT162b2 + BNT162b2 OMI BA.1 30 µg as a booster dose (Dose 4) approximately 5 to 12 months after their last dose (Dose 3).

Bivalent Omicron BA.1-modified Variant Vaccine Candidate as 4th Dose Elicits Improved Omicron BA.1 Neutralization Response; BA.4/BA.5 Neutralized to Lesser Extent

>55y Participants Sentinel Cohort, 30 and 60 µg Dose

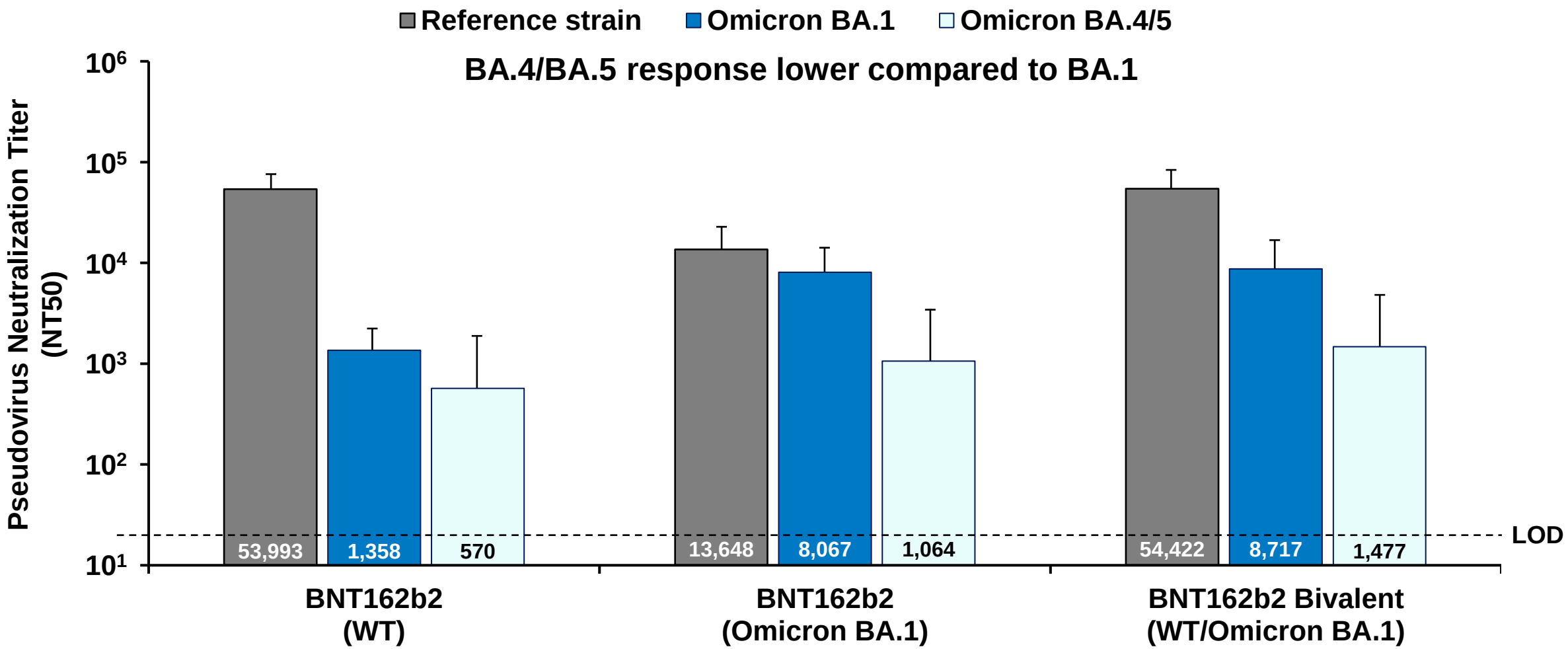
Participants WITHOUT Evidence of Infection up to 1 Month After First Study Vaccination



FFRNT, fluorescent foci reduction neutralization test; LOD, Limit of Detection

Similar to Clinical Data, Omicron BA.1 Monovalent and Bivalent Booster in Mice Increases Omicron Neutralization Response; Continued Trend for Reduced BA.4/BA.5 Neutralization Compared to BA.1

1M Post 3rd Dose Booster Following 2 Doses of BNT162b2

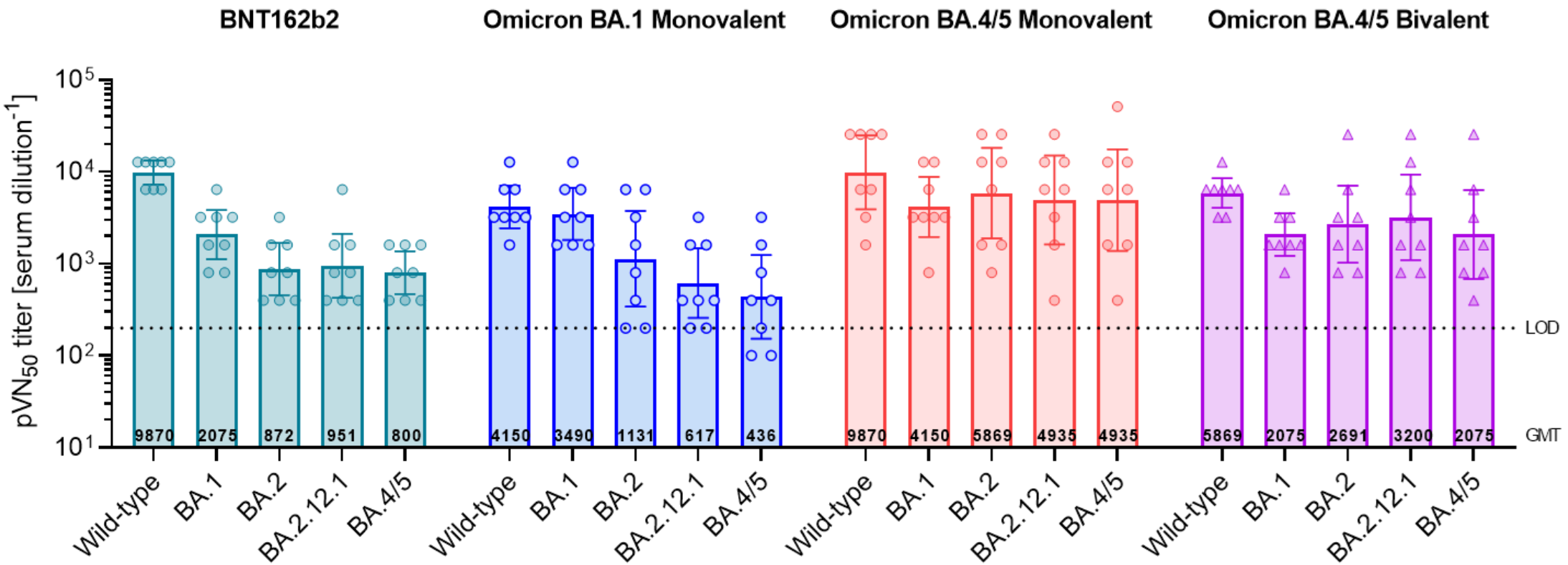


Mice preimmunized with 2 doses of BNT162b2; boosters given 1 month post Dose 2
Vaccines administered at 0.5 mcg dose level. LOD, Limit of Detection; Reference strain, Wuhan-Hu-1

Omicron BA.4/BA.5 Monovalent and Bivalent Boosters in Mice Substantially Increase Omicron Neutralization Responses to all Omicron Variants Including BA.4/5

Compared to BNT162b2 Neutralizing BA.4/5 titers increase by ~6.2 fold [mono BA.4/5] or ~2.6 fold (bivalent BA.4/5)

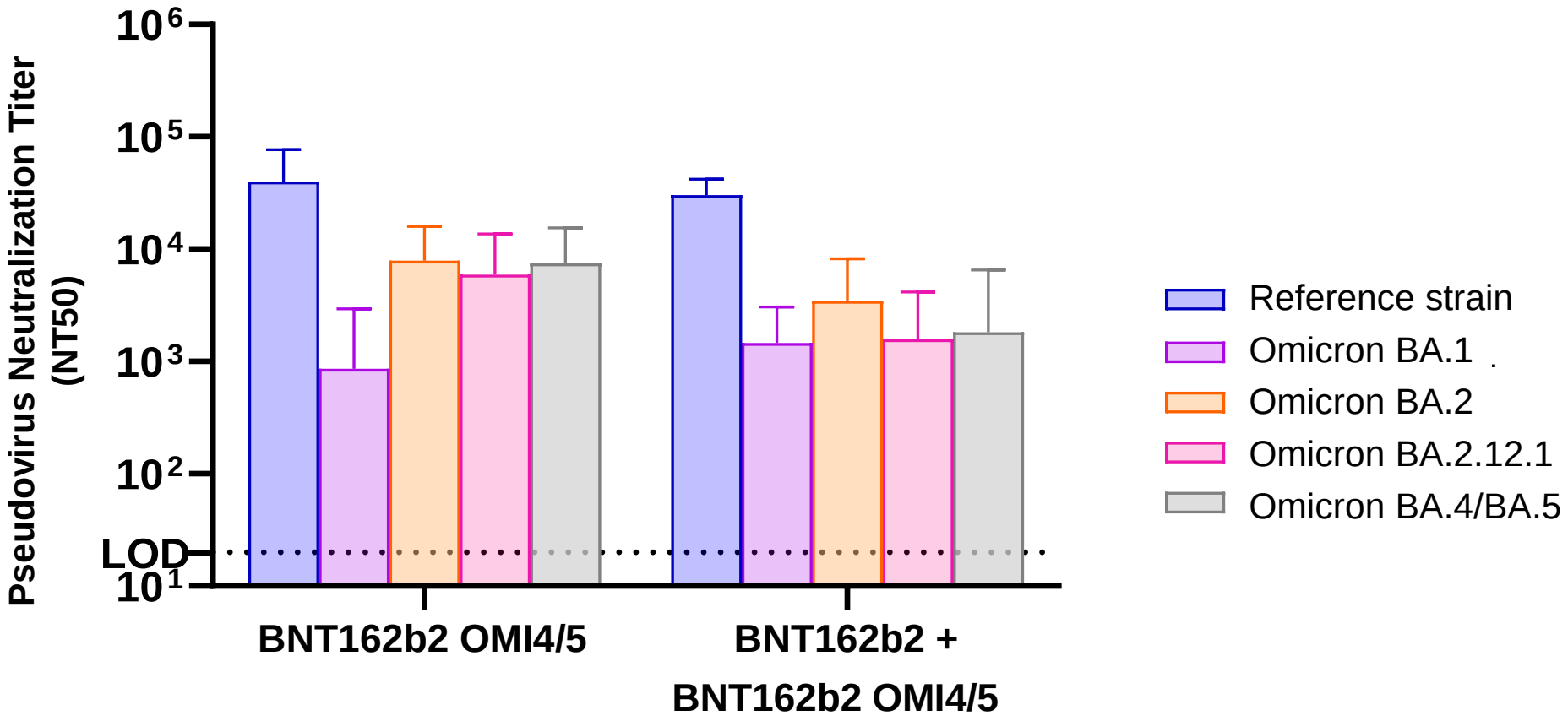
Day 7 PD3



Mice preimmunized with 2 doses of BNT162b2; boosters given at day 104 post Dose 2
Vaccines administered at 1 mcg dose level; Wild type, Wuhan-Hu-1; LOD, Limit of Detection

Confirmatory Study: Omicron BA.4/BA.5 Monovalent and Bivalent Boosters in Mice Substantially Increase Omicron Neutralization Responses to all Omicron Variants Including BA.4/5

7d Post 3rd Dose Booster Following 2 Doses of BNT162b2



Mice preimmunized with 2 doses of BNT162b2; boosters given 1 month post Dose 2
Vaccines administered at 0.5 mcg dose level; LOD, Limit of Detection; Reference strain, Wuhan-Hu-1

Omicron BA.4/BA.5-modified Variant Vaccine Summary

- **Reactogenicity profile of variant vaccines (Beta, Omicron BA.1) overall similar to prototype BNT162b2 vaccine**
- **Neutralizing responses for Omicron-containing vaccines are consistent with regulatory criteria:**
  - Simple superiority for Omicron BA.1 GMR and non-inferiority for seroresponse (monovalent and bivalent vaccines)
  - Non-inferiority for reference strain GMR
- **Preclinical immunogenicity data reliably predict observations in humans**
- **Omicron BA.4/5-modified variant vaccine booster elicits improved neutralizing response across Omicron sublineages**

THANK YOU!