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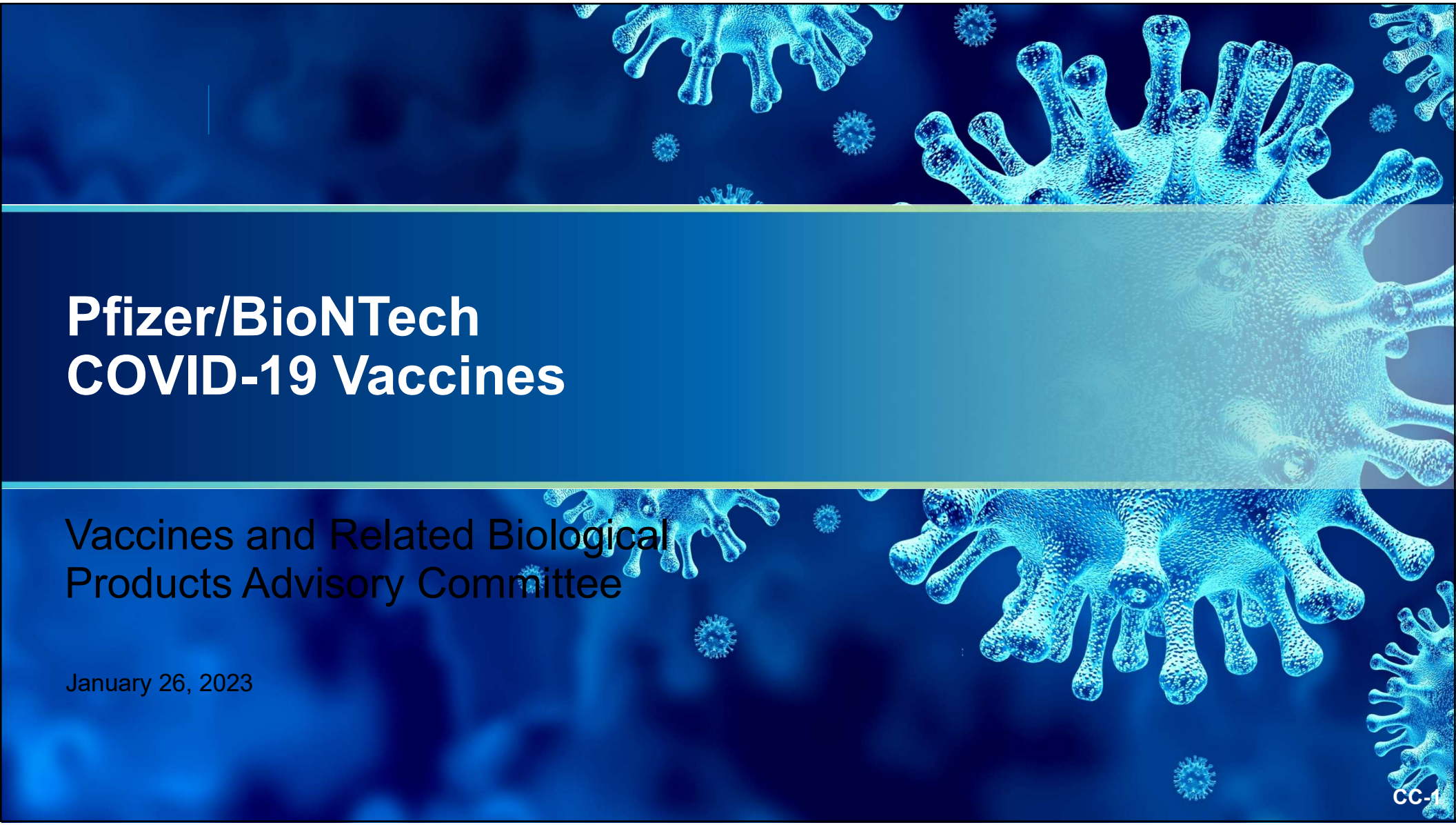


Pfizer/BioNTech COVID-19 Vaccines

Vaccines and Related Biological Products Advisory Committee

January 26, 2023

Presentation Outline

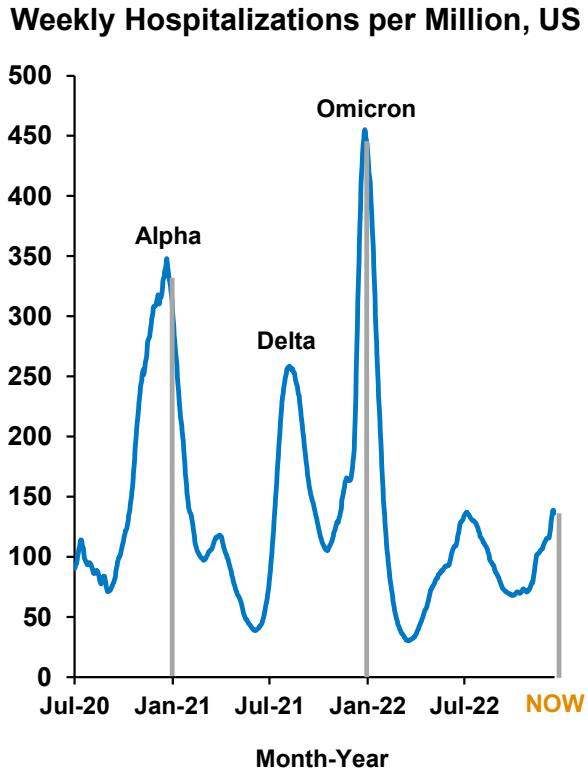
Kena A. Swanson, Ph.D.
Vice President, Viral Vaccines
Vaccine Research and Development, Pfizer Inc.

Variant-modified vaccine experience to date

Readiness to support future COVID-19 vaccine updates

Better-Matched Vaccines Restore Waning Immunity and Increase Protection Against Currently Circulating Strains

- **Increase in hospitalizations corresponding to winter respiratory season in United States[1]**
  - >4000 hospitalizations and >300 deaths per day in US[1]
- **The role of better-matched COVID-19 vaccines:**
  - **Restore waning immunity** against hospitalization observed ~3-6 months after vaccination[2-4]
  - **Better neutralizing activity** against current strains[5]
  - **Increased protection** against a range of Covid-19 outcomes including symptomatic illness, UC/ED visits, and hospitalizations[6-9]

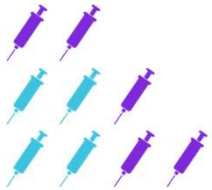
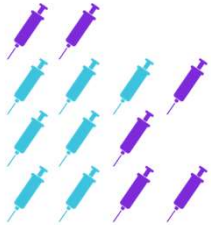


Source: OWID

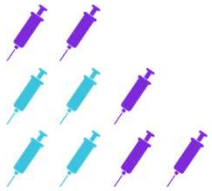
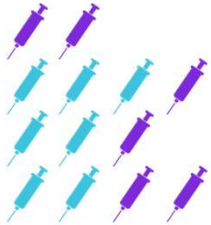
UC/ED is urgent care or emergency department visits.

1. Centers for Disease Control and Prevention. COVID Data Tracker. Atlanta, GA: US Department of Health and Human Services, CDC; 2023, January 17. https://covid.cdc.gov/covid-data-tracker; 2. Surie et al. MMWR 2022. doi: 10.15585/mmwr.mm7142a3; 3. Tartof et al. Lancet Infect Dis 2022. doi: 10.1016/S1473-3099(22)00692-2; 4. Collie et al. N Engl J Med 2022. doi: 10.1056/NEJMc2210093; 5. Davis-Gardner et al. N Engl J Med 2022. doi: 10.1056/NEJMc2214293; 6. Link-Gelles et al. MMWR 2022. doi: http://dx.doi.org/10.15585/mmwr.mm7148e1; 7. Tenforde et al. MMWR 2022. doi: 10.15585/mmwr.mm715152e1; 8. Surie et al. MMWR 2022. doi: 10.15585/mmwr.mm715152e2; 9. Arbel et al. Available at SSRN: https://dx.doi.org/10.2139/ssrn.4314067.

Preclinical Data Reliably Predicted Clinical Results for 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**		✓	✓

Preclinical Data Reliably Predicted Clinical Results for 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**		✓	✓

Clinical Study Evaluated Bivalent Omicron BA.4/5-modified Vaccine as a Booster in Vaccine-experienced Participants ≥12 years

Comparison of Responses Between Bivalent and Original Monovalent Vaccines

Original Vaccine

12-17y	**Bivalent Omicron BA.4/5 (30 µg)**	*(n=~100)*
18-55y	**Bivalent Omicron BA.4/5 (30 µg)**	*(n=~300)*
>55y	**Bivalent Omicron BA.4/5 (30 µg)**	*(n=~300)*
>55y	**Original Vaccine**	*(n=~300)*

Demographics for Bivalent Omicron BA.4/5-modified and Original Vaccine Comparator in Vaccine-Experienced Participants

	Vaccine Group			
	Bivalent BA.4/5			Original Vaccine
	12-17y N=105 n (%)	18-55y N=297 n (%)	>55y N=286 n (%)	>55y N=289 n (%)
Sex				
Male	58 (55.2)	104 (35.0)	129 (45.1)	134 (46.4)
Female	47 (44.8)	193 (65.0)	157 (54.9)	155 (53.6)
Age				
Median	15.0	41.0	65.0	66.0
Min, max	(12, 17)	(18, 55)	(56, 87)	(56, 87)
Previous SARS-CoV-2 infection status at study baseline				
Negative	26 (24.8)	84 (28.3)	110 (38.5)	246 (85.1)
Positive	79 (75.2)	213 (71.7)	176 (61.5)	41 (14.2)
Time since last dose of original vaccine prior to study vaccine (months)				
Median	8.4	11.3	11.5	6.3
Min, max	(5.6, 12.0)	(5.4, 13.0)	(5.5, 12.9)	(5.3, 13.0)

Previous SARS-CoV-2 infection status confirmed by medical history, serology and/or RT-PCR at study baseline

Omicron BA.4/5 GMR Superiority and Reference Strain GMR Non-inferiority Met for Bivalent BA.4/5 Vaccine

>55y participants

Evaluable Participants With or Without Evidence of Previous Infection Through 1 Month After Vaccination

SARS CoV 2 Neutralization Assay	Bivalent BA.4/5 GMT (95% CI) n 284 286	Original Vaccine GMT (95% CI) n 282 289	GMR (95% CI)	Conclusion
Omicron BA.4/5	4158.1 (3554.8, 4863.8)	938.9 (802.3, 1098.8)	2.91 (2.45, 3.44)	Superiority Met
Reference strain	16250.1 (14499.2, 18212.4)	10415.5 (9366.7, 11581.8)	1.38 (1.22, 1.56)	Non-inferiority Met

Omicron BA.4/5 GMR Superiority Criterion: the lower bound of the 95% confidence interval for the GMR is >1

Reference strain GMR Non-inferiority Criterion: the lower bound of the 95% confidence interval for the GMR is >0.67 and the point estimate of the GMR is ≥0.8

Omicron BA.4/5 Seroresponse Also Met Non-inferiority Criterion

(Lower bound of the 95% confidence interval for the percentage difference is greater than -5)

GMRs and associated 95% CIs were calculated using a linear regression model with terms of baseline neutralizing titer and vaccine group.
Omicron BA.4/5 & Reference strain NT50 measured using validated 384-well assay

Omicron BA.4/5 GMR Non-inferiority Met for Bivalent BA.4/5 Vaccine Responses

18-55y to >55y participants

Evaluable Participants With or Without Evidence of Previous Infection Through 1 Month After Vaccination

SARS CoV 2 Neutralization Assay	Bivalent BA.4/5 GMTs (95% CI)		GMR (95% CI)	Conclusion
	18 55y n 297 296	>55y n 284 286		
Omicron BA.4/5	4455.9 (3851.7, 5154.8)	4158.1 (3554.8, 4863.8)	0.98 (0.83, 1.16)	18-55y non-inferior to >55y
Reference strain	16323.3 (14686.5, 18142.6)	16250.1 (14499.2, 18212.4)	Similar GMTs (descriptive analysis)	

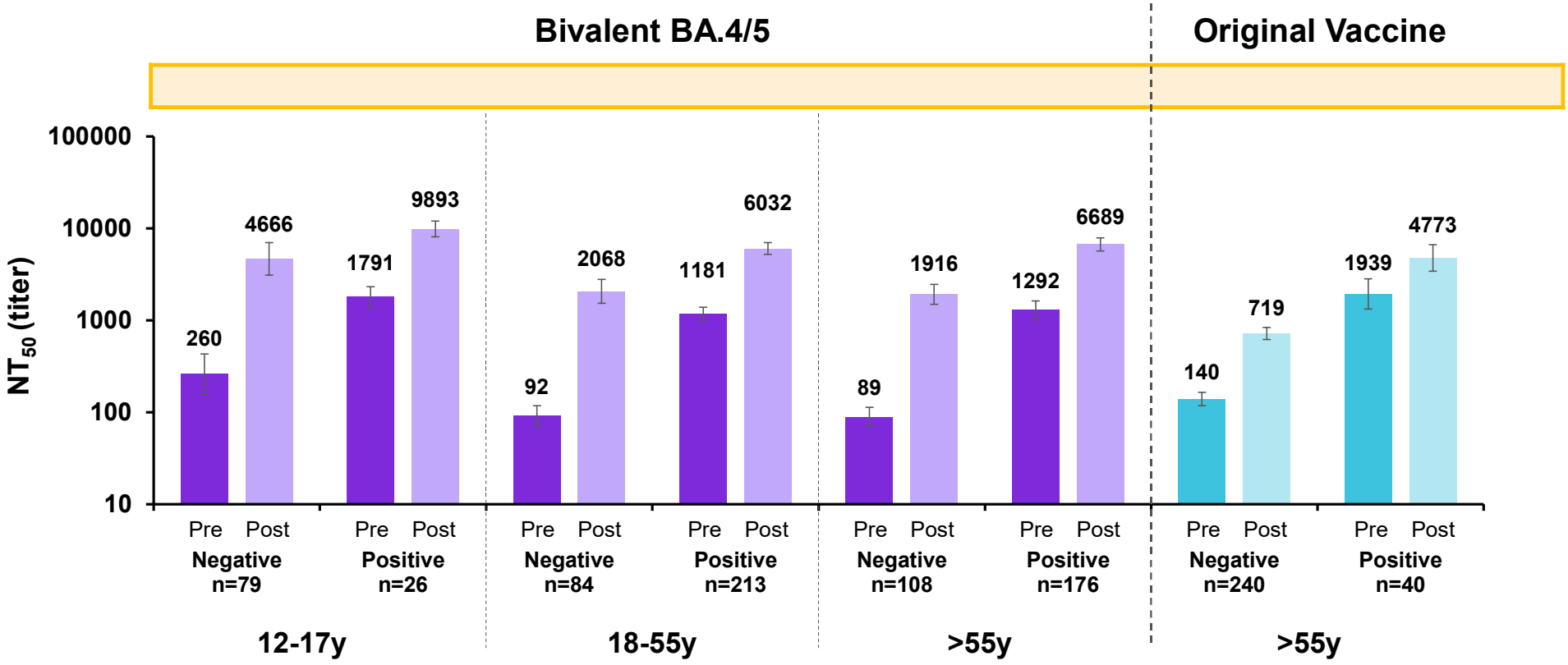
Omicron BA.4/5 GMR Non-inferiority Criterion: the lower bound of the 95% confidence interval for the GMR is >0.67

Omicron BA.4/5 Seroresponse Also Met Non-inferiority Criterion

(Lower bound of the 95% confidence interval for the percentage difference is greater than -10)

GMR and associated 95% CI were calculated using a linear regression model with terms of baseline neutralizing titer and vaccine group.
Omicron BA.4/5 & Reference strain NT50 measured using validated 384-well assay

Bivalent Omicron BA.4/5 Elicits Improved Omicron BA.4/5 Neutralizing Response Compared to Original Vaccine Across Age Groups



Pre = Pre-dose 4; Post = 1-month post dose 4.

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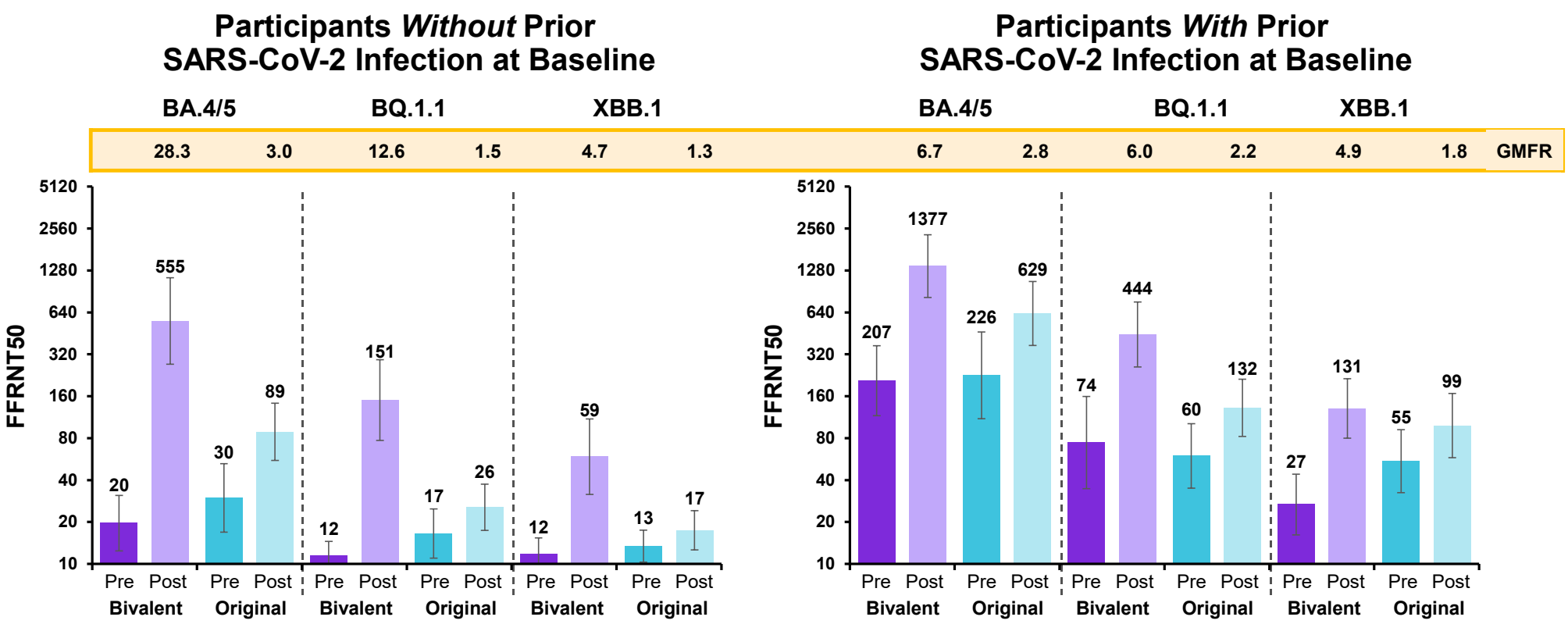
Higher Omicron Sublineage Neutralizing Responses with Bivalent BA.4/5 Vaccine Regardless of Prior SARS-CoV-2 Infection

>55y participants



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

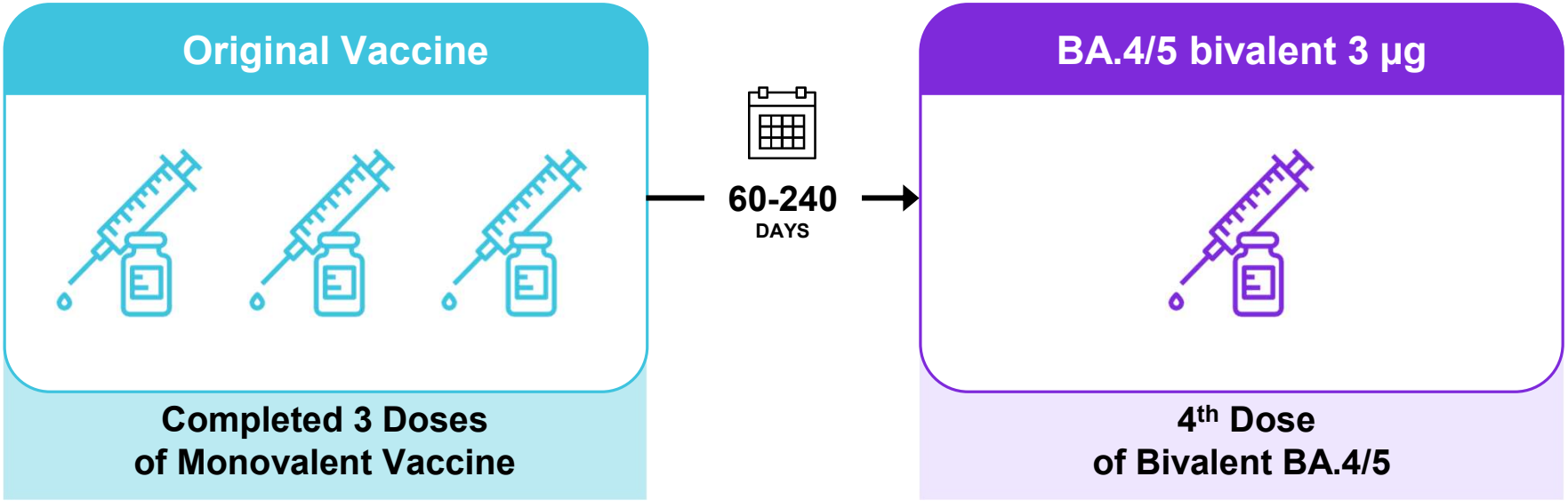
Bivalent BA.4/BA.5 Vaccine Post-Authorization Studies

Modified Vaccine	Age Group	Vaccine Regimen	Clinical Data
Omicron BA.4/BA.5 bivalent	**6 months to 11 years** **12 to 55 years** **>55 years**		✓
Omicron BA.4/BA.5 bivalent Booster	**5 to 11 years**		✓
Omicron BA.4/BA.5 bivalent Primary series	**6 months to 5 years**		**Ongoing**
Omicron BA.4/BA.5 bivalent Booster	**6 months to 5 years**		✓

Clinical Study to Evaluate Bivalent Omicron BA.4/5-modified Vaccine in Vaccine-Experienced Participants

6M to <5y participants

Immunogenicity and Safety of 4th Dose of Bivalent BA.4/5 (3 µg) (n = ~300)



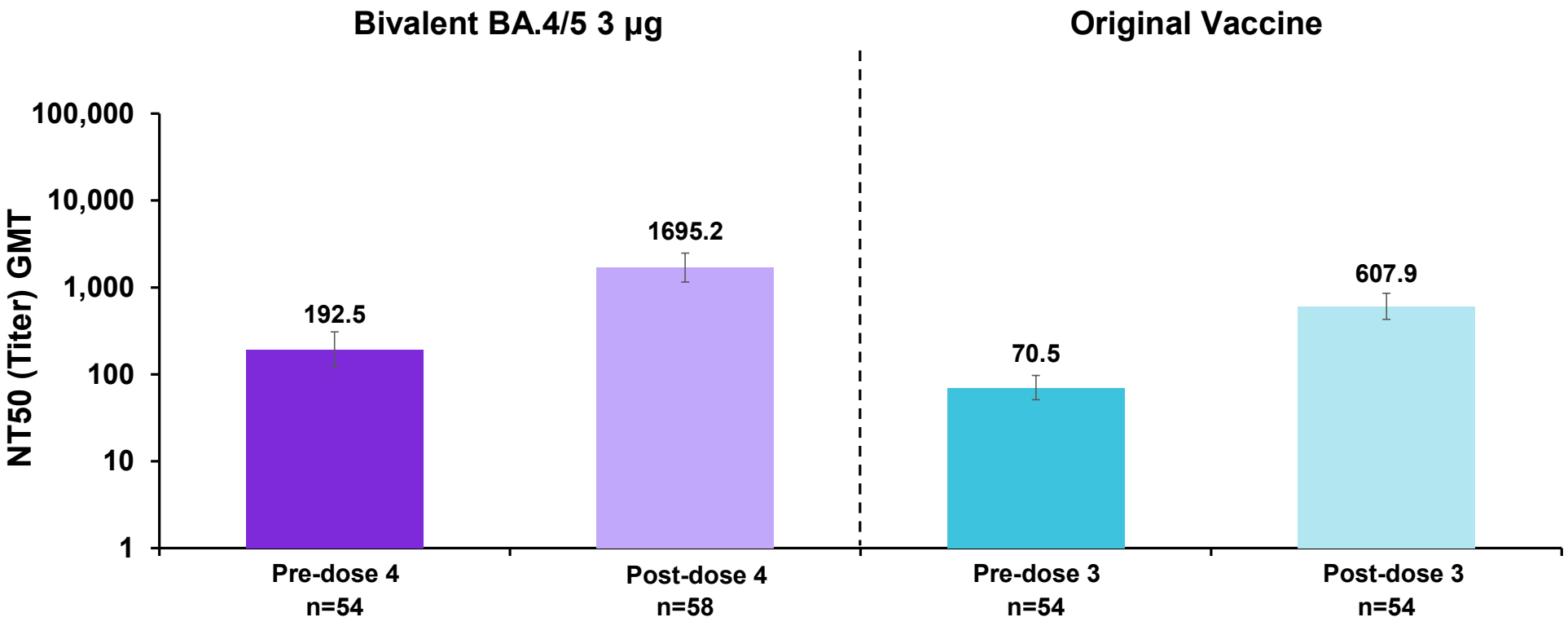
Safety and immunogenicity was assessed in a subset of 60 participants.
Median interval from Dose 3 to 4th Dose Booster was ~6.5 months.

Note: Subset includes the first 24 and 36 participants enrolled in ≥6 months to <2 years age group and ≥2 years to <5 years age group, respectively
Additional evaluations in 6M to <5 years:
1. 3rd and 4th doses Bivalent BA.4/5 (3 µg) vaccine (n = ~200)
2. 4th dose of Bivalent BA.4/5 for safety (n=~ 3600)

Bivalent Omicron BA.4/5 Booster Elicits Improved Omicron BA.4/5 Neutralizing Response Compared to 3-Dose Original Vaccine Primary Series

6M to <5y participants

Evaluable Participants With and Without Evidence of Infection



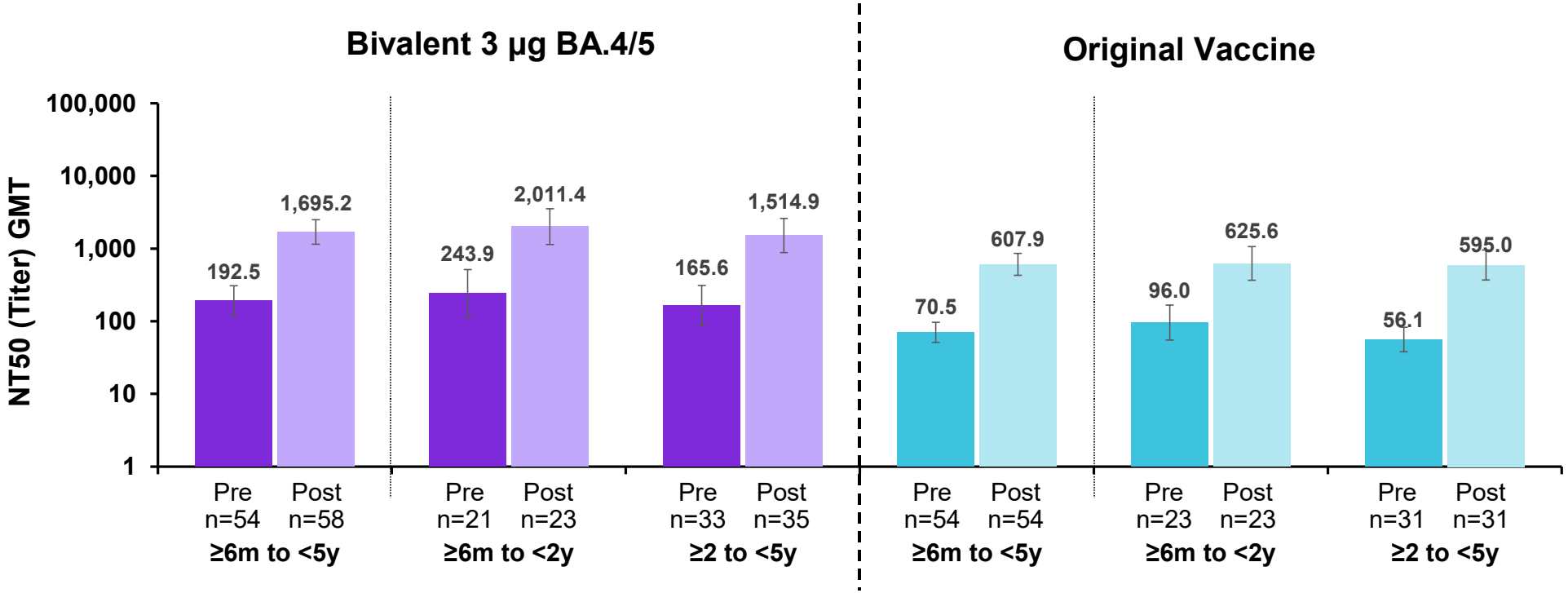
Comparisons were matched by age, baseline status and interval

Note: Subset includes the first 24 and 36 participants enrolled in ≥6 months to <2 years age group and ≥2 years to <5 years age group respectively

GMT=Geometric mean titer; NT50=50% neutralizing titer

Bivalent Omicron BA.4/5 Elicits Improved Omicron BA.4/5 Neutralizing Response Compared to Original Vaccine

Evaluable Participants With and Without Evidence of Infection



Note: Subset includes the first 24 and 36 participants enrolled in ≥6 months to <2 years age group and ≥2 years to <5 years age group respectively
Bivalent BA.4/5: Pre = Pre-dose 4; Post = 1-month post dose 4; BNT162b2 Pre = Pre-dose 3; Post = 1-month post dose 3
GMT=Geometric mean titer; NT50=50% neutralizing titer

Bivalent Variant-Modified Vaccines Demonstrate Improved Effectiveness and Comparable Safety Profile Compared to Original Vaccine

Safety

- Safety profile for bivalent vaccines (BA.1 and BA.4/5) consistent with original vaccine
- The benefit-risk profile for the original and the bivalent vaccine in authorized populations continues to be favorable

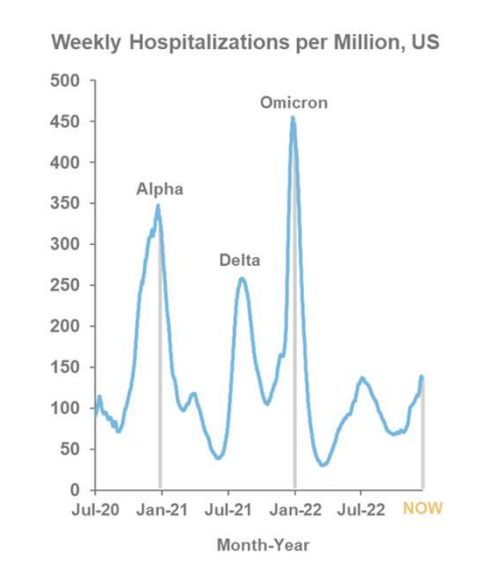
Effectiveness

- Bivalent BA.4/5 enhances protective immunity against circulating Omicron sublineages
- Benefits both SARS-CoV-2 naïve and those with prior infection

Factors Impacting Future Vaccine Updates

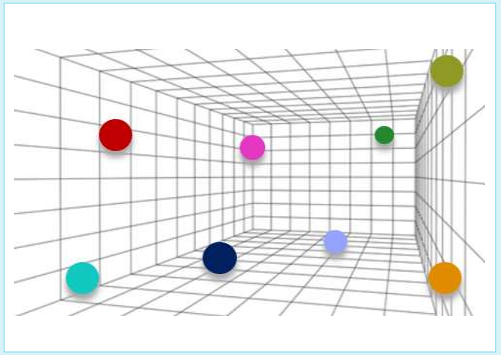
Effectiveness & Disease Severity

1. Real world effectiveness
2. Clinical phenotype



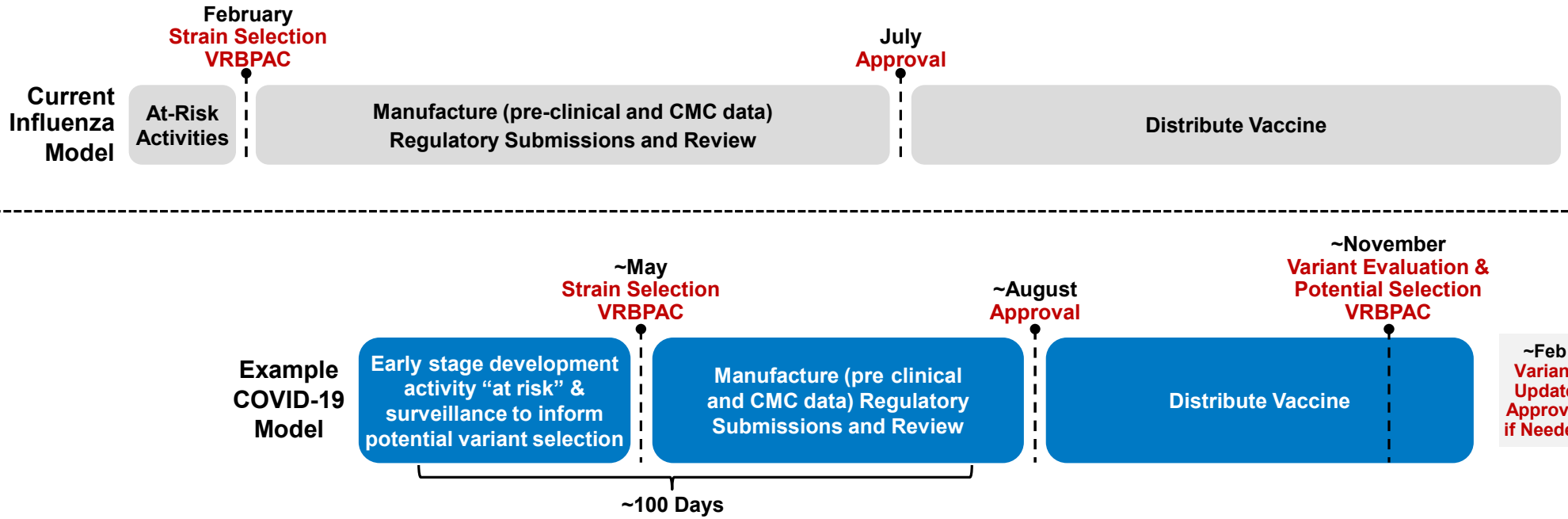
Evidence Collection

1. Immunology
   - Antigenic distance
   - Immune escape
   - Immune imprinting
2. Epidemiology
   - Populations
   - Localization
   - Transmissibility
3. Valency



Readiness to Support Future COVID-19 Vaccine Updates

- **Adapt the flu model and pathway to enable:**
  - Later Strain Selection
  - Shortened Review - (~30-day approval post final submission)

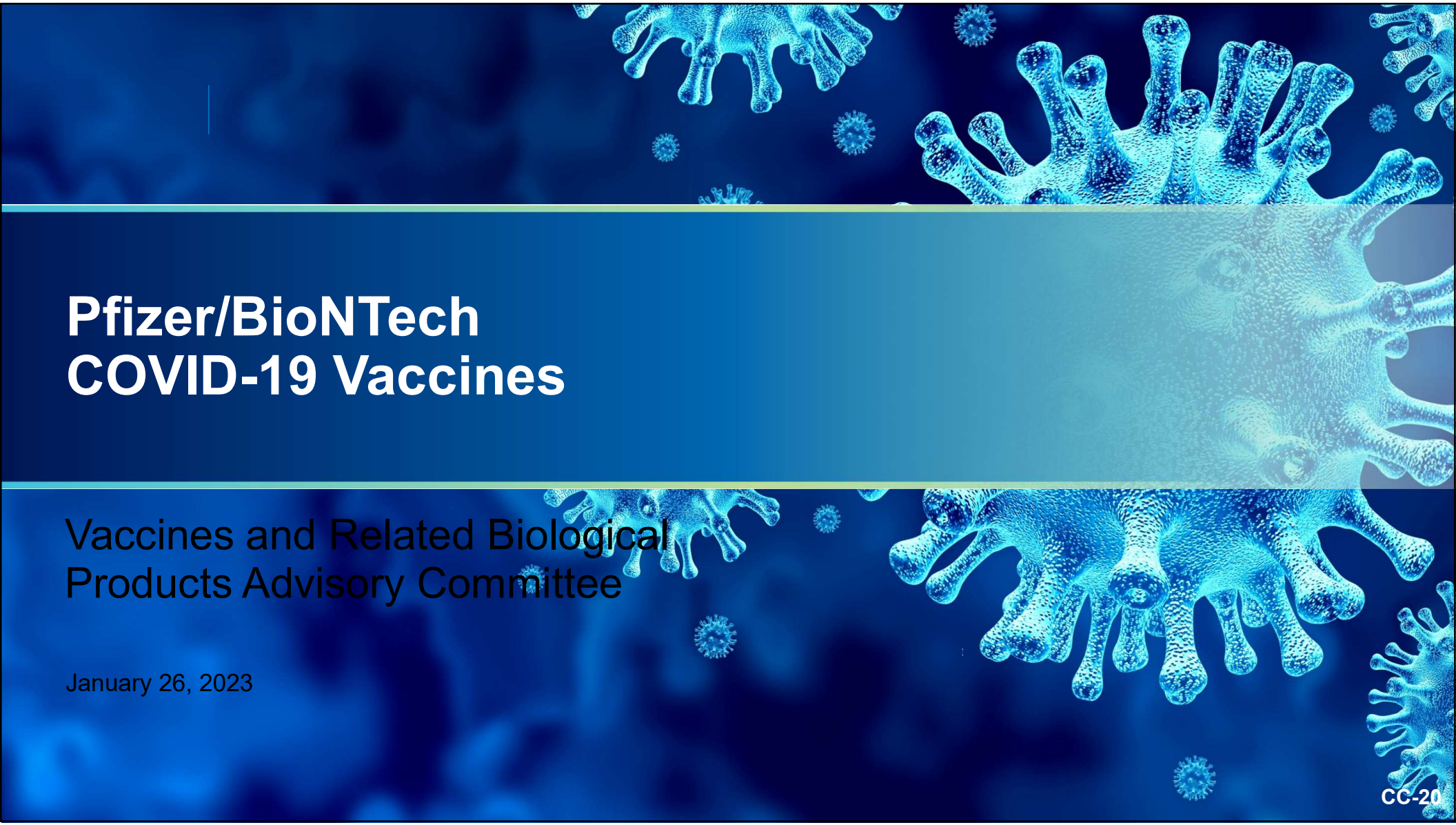


Pfizer/BioNTech can support for off-cycle strain selection if needed

Note: Southern Hemisphere Influenza strain selection happens September/October timeframe.

Conclusions

- **Extensive clinical experience for variant-modified vaccines demonstrating safety across age groups**
- **Demonstrated effectiveness of bivalent vaccine against COVID-19 due to Omicron sublineages – better-matched vaccines offer improved protection**
- **An established model for vaccine strain selection and approval is critical to enable access to optimally matched vaccines**
  - Updates driven by variant epidemiology and vaccine effectiveness
  - Adapt new model based on existing flu model



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