VAX-31 Phase 1/2 Study Topline Results in Adults Aged 50 and Older

September 3, 2024

VAXCYTE
protect humankind™

Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements related to the potential benefits of Vaxcyte's vaccine candidates, including breadth of coverage, the ability to deliver a potentially best-in-class pneumococcal conjugate vaccine franchise and the potential to improve upon the standard-of-care and raise the immunogenicity threshold; the process and timing of anticipated future development of Vaxcyte's vaccine candidates; the timing and availability of data for the VAX-24 infant Phase 2 study; the timing and availability of data for the VAX-31 adult Phase 3 studies and infant Phase 2 study; the potential of VAX-31 to provide unrivaled invasive pneumococcal disease coverage; the ability of Vaxcyte's cell-free platform to deliver the broadest-spectrum PCVs that provide protection against both currently circulating and historically prevalent strains; demand for Vaxcyte's vaccine candidates; the growth and expansion of the pneumococcal vaccine market; the market opportunity for Vaxcyte's vaccines; Vaxcyte's expectations regarding the spectrum coverage, regulatory pathway, adoption speed and immunogenicity of its vaccine candidates; and other statements that are not historical fact. The words "anticipate," "believe," "continue," "could," "designed," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These forward-looking statements are based on Vaxcyte's current expectations and actual results and timing of events could differ materially from those anticipated in such forward-looking statements as a result of risks and uncertainties, including, without limitation, risks related to Vaxcyte's product development programs, including development timelines, success and timing of chemistry, manufacturing and controls and related manufacturing activities; potential delays or inability to obtain and maintain required regulatory approvals for its vaccine candidates; the risks and uncertainties inherent with preclinical and clinical development processes; the success, cost and timing of all development activities and clinical trials; and the sufficiency of cash and other funding to support Vaxcyte's development programs and other operating expenses, any of which could materially and adversely affect Vaxcyte's business and operations. These and other risks are described more fully in Vaxcyte's filings with the Securities and Exchange Commission (SEC), including its Quarterly Report on Form 10-Q filed with the SEC on August 6, 2024 or in other documents Vaxcyte subsequently files with or furnishes to the SEC. Vaxcyte undertakes no duty or obligation to update any forward-looking statements contained in this release as a result of new information, future events or changes in its expectations.

VAXCYTE MISSION STATEMENT

We are on a global mission to engineer high-fidelity vaccines that protect humankind from the consequences of bacterial diseases.

Agenda

- **INTRODUCTION AND VAX-31 RESULTS OVERVIEW**
- **VAX-31 PHASE 1/2 STUDY TOPLINE RESULTS IN ADULTS AGED 50 AND OLDER**
  - Disposition and Demographics
  - Tolerability and Full Six-Month Safety Data
  - Topline Immunogenicity Data
- **PCV FRANCHISE STATUS AND NEXT STEPS**

Introduction and VAX-31 Results Overview

Summary of VAX-31 Adult 50+ Phase 1/2 Study Topline Data Findings

Unprecedented Results Support Potential Best-in-Class PCV With Broadest Serotype and Disease Coverage

SAFETY AND TOLERABILITY: At all doses studied, VAX-31 was well tolerated and demonstrated a safety profile similar to Prevnar 20® (PCV20)

IMMUNOGENICITY: At all doses studied, VAX-31 demonstrated robust OPA immune responses for all 31 serotypes (STs) -- all three doses advanceable to Phase 3

- High and Middle doses met or exceeded OPA regulatory immunogenicity criteria for all 31 STs, Low dose for 29 of 31 STs
- For the 20 STs common with PCV20: High dose, 18 had GMR greater than 1.0 and 7 achieved statistically higher immune responses; Middle dose, 13 had GMR greater than 1.0 and 5 achieved statistically higher immune responses; Low dose, 8 had GMR greater than 1.0 and 3 achieved statistically higher immune responses
- For the 11 additional STs unique to VAX-31: All 11 met the superiority criteria at all doses

PLATFORM: The VAX-31 data further validate the potential of Vaxcyte's carrier-sparing platform to deliver the broadest-spectrum PCVs that provide protection against both currently circulating and historically prevalent STs

KEY VAX-31 NEXT STEPS:

- Adults: VAX-31 selected to advance to Phase 3 with initiation of pivotal, non-inferiority study by mid-2025 and topline safety, tolerability and immunogenicity results in 2026; pursuing Breakthrough Therapy Designation
- Pediatrics: Plan to initiate VAX-31 infant Phase 2 study in 1Q:2025 following IND submission and clearance

GMR = geometric mean ratio; OPA = Opsonophagocytic activity

Global Health Impact of Pneumococcal Disease (PD) Remains Significant

Over **150,000** U.S. hospitalizations annually due to pneumococcal pneumonia

Streptococcus pneumoniae is among the World Health Organization's top antibiotic-resistant pathogens to be urgently addressed and the U.S. CDC lists drug-resistant *Streptococcus pneumoniae* as a **"serious threat"**

Streptococcus pneumoniae is the leading cause of vaccine preventable deaths globally in children under five

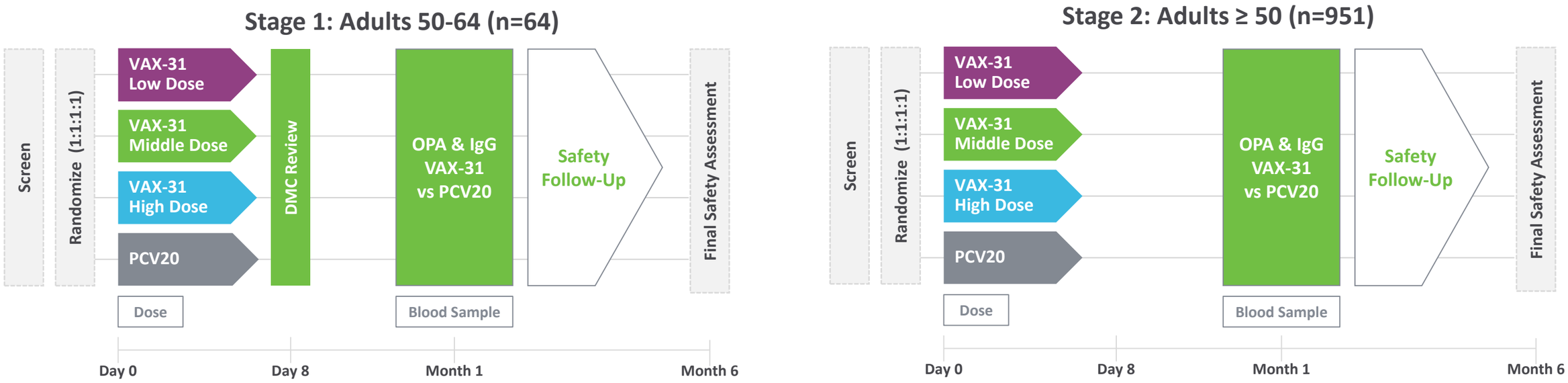
~300,000 children under five years old die annually worldwide due to *Streptococcus pneumoniae*

https://www.cdc.gov/pinkbook/hcp/table-of-contents/chapter-17-pneumococcal-disease.html#:~:text=Over%20150%2C000%20hospitalizations%20from%20pneumococcal,younger%20than%20age%205%20years.
https://iris.who.int/bitstream/handle/10665/376776/9789240093461-eng.pdf?sequence=1, https://www.cdc.gov/pneumococcal/php/drug-resistance/index.html.
GBD 2019 Diseases and Injuries Collaborators.. Lancet 2020; 396: 1204-22. Supplementary Appendix 2.
https://www.gavi.org/pneumococcal-disease-leading-vaccine-preventable-cause-death-children-under-five.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8677503/table/T2/.
https://www.cdc.gov/pneumococcal/php/surveillance/index.html#:~:text=Global%20trends,deaths%20occur%20in%20developing%20countries.

VAX-31 Phase 1/2 Study Topline Results in Adults Aged 50 and Older

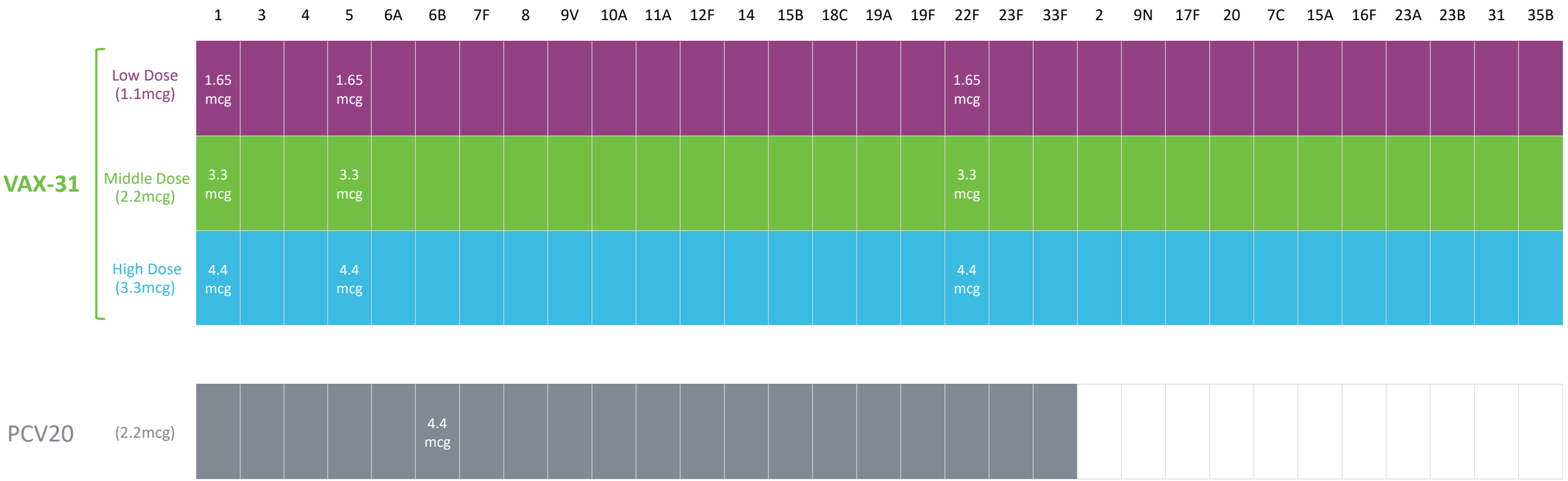
VAX-31 Phase 1/2 Clinical Study Design (N=1,015)

Randomized, Observer-Blind, Dose-Finding, Controlled Study to Evaluate Safety, Tolerability and Immunogenicity of VAX-31 vs Standard-of-Care (PCV20) in 1,015 Healthy Adults ≥ 50 Years



DMC: Data Monitoring Committee, IgG: Immunoglobulin G

Study Evaluated Three VAX-31 Doses



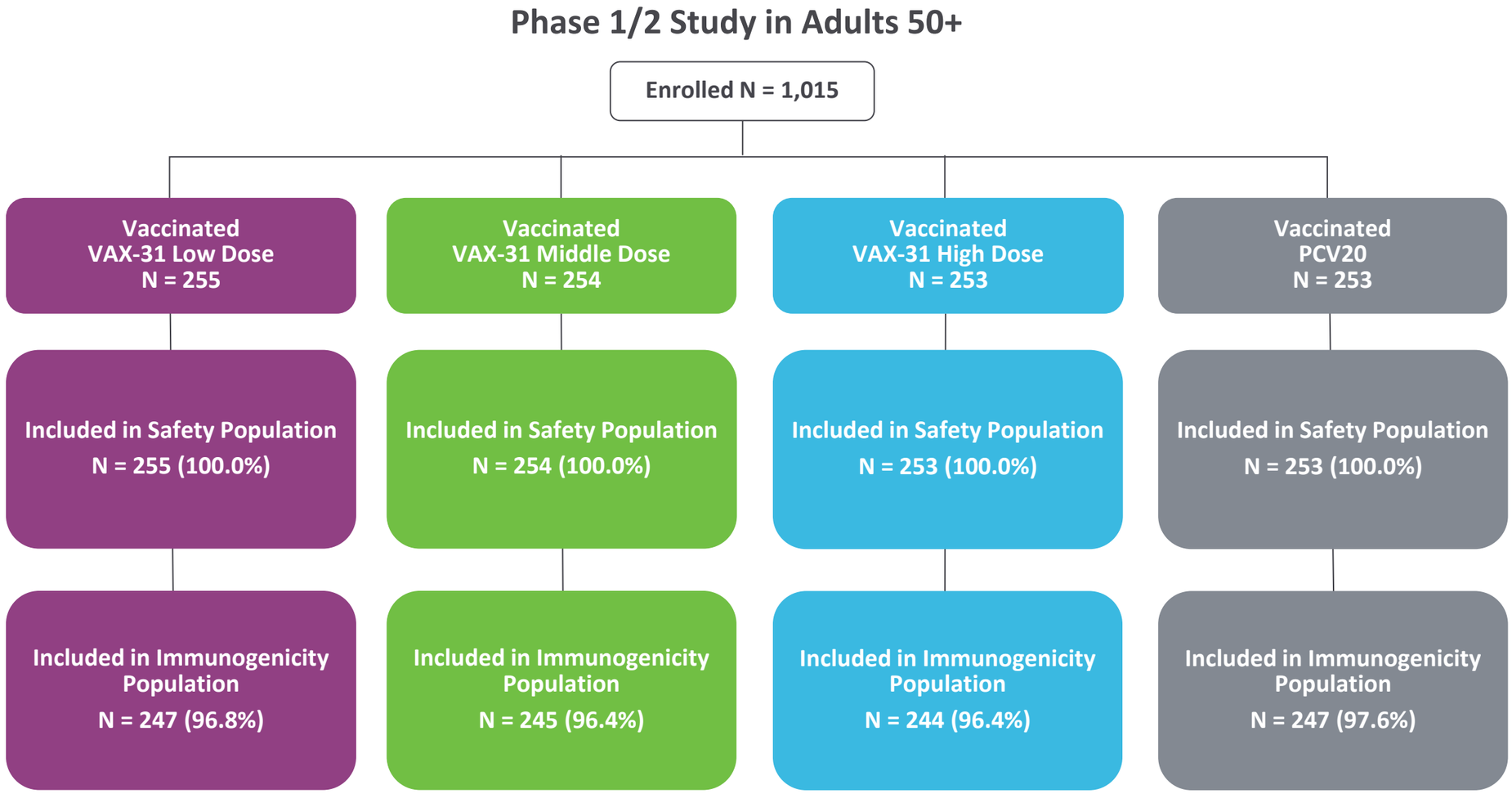
Study Safety, Tolerability and Immunogenicity Key Outcome Measures

	DAY 8	MONTH 1	MONTH 6
SAFETY AND TOLERABILITY OUTCOME MEASURES	• Solicited local reactions • Solicited systemic events	• Unsolicited adverse events (AE) • Laboratory parameters	• Serious adverse events (SAE), new onset of chronic illnesses (NOCI) and medically attended adverse events (MAAE)
IMMUNOGENICITY OUTCOME MEASURES		• Opsonophagocytic activity (OPA) geometric mean titer (GMT) • OPA geometric mean ratio (GMR) • Percent of subjects achieving a 4-fold rise in OPA • Immunoglobulin G (IgG) geometric mean concentration (GMC)	

Disposition and Demographics

Study Disposition

High Proportion of Subjects with Safety and Immunogenicity Follow-Up



24 subjects (2.4%) discontinued and did not complete the full Month 6 safety follow-up (lost to follow-up (13), withdrawal by subject (11)).

Population Demographics

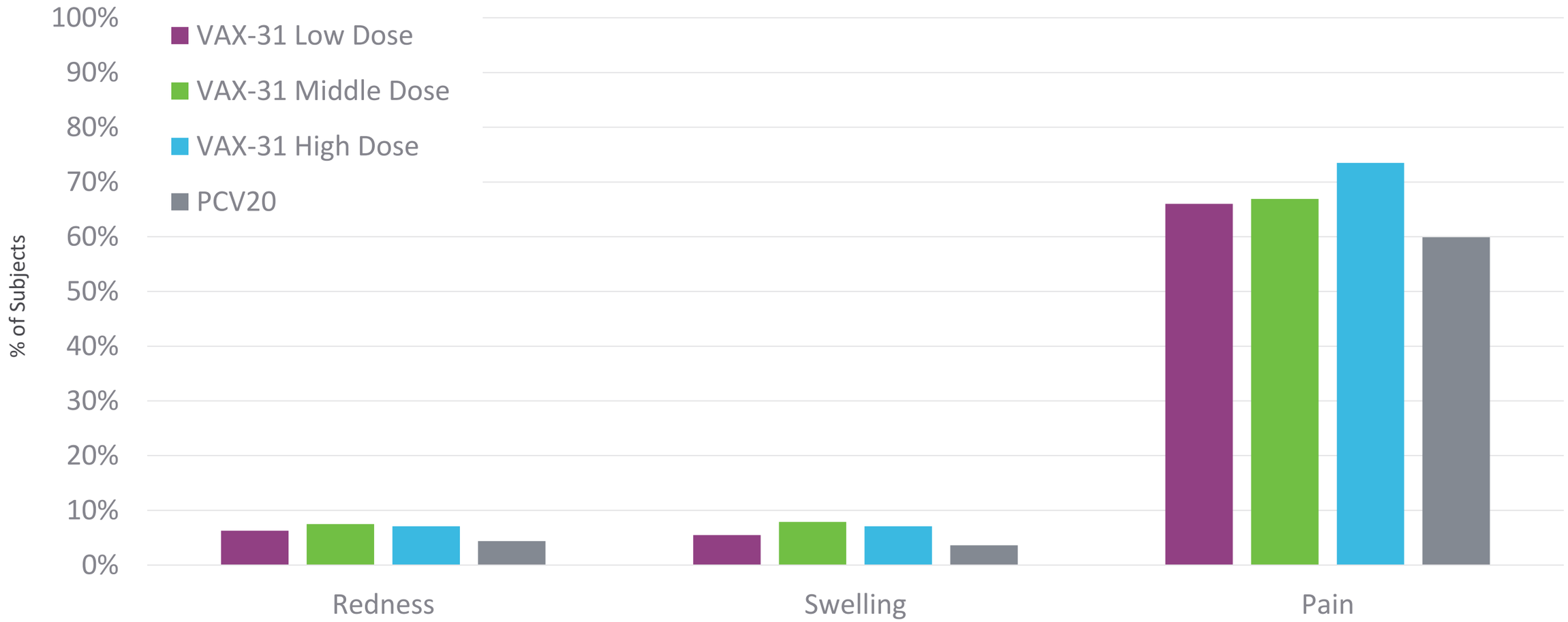
Generally Balanced Across Cohorts and Similar for the Safety and Immunogenicity Populations

	VAX-31 Low Dose		VAX-31 Middle Dose		VAX-31 High Dose		PCV20	
	Safety	Immunogenicity	Safety	Immunogenicity	Safety	Immunogenicity	Safety	Immunogenicity
Number of Subjects	255	247	254	245	253	244	253	247
Median Age, Years (range)	58.0 (50-84)	58.0 (50-84)	58.0 (50-86)	58.0 (50-86)	59.0 (50-79)	59.0 (50-79)	60.0 (50-82)	60.0 (50-82)
Sex, n (%) Female	151 (59.2)	147 (59.5)	160 (63.0)	154 (62.9)	150 (59.3)	145 (59.4)	148 (58.5)	146 (59.1)
Male	104 (40.8)	100 (40.5)	94 (37.0)	91 (37.1)	103 (40.7)	99 (40.6)	105 (41.5)	101 (40.9)
Race, n (%) White	189 (74.1)	183 (74.1)	190 (74.8)	184 (75.1)	196 (77.5)	190 (77.9)	185 (73.1)	180 (72.9)
Black	59 (23.1)	57 (23.1)	56 (22.0)	55 (22.4)	51 (20.2)	49 (20.1)	60 (23.7)	59 (23.9)
Asian	3 (1.2)	3 (1.2)	5 (2.0)	3 (1.2)	4 (1.6)	3 (1.2)	3 (1.2)	3 (1.2)
Native Hawaiian	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
American Indian or Native Alaskan	2 (0.8)	2 (0.8)	3 (1.2)	3 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	2 (0.8)	2 (0.8)	0 (0.0)	0 (0.0)	2 (0.8)	2 (0.8)	3 (1.2)	3 (1.2)
Multiracial	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Median Height, cm (range)	167.6 (146-196)	167.6 (146-196)	169.1 (142-188)	169.1 (142-188)	168.0 (145-196)	168.0 (145-196)	167.6 (147-190)	167.6 (147-190)
Median Weight, kg (range)	82.56 (44.5-176.6)	82.2 (44.5-176.6)	85.80 (43.7-167.0)	85.9 (43.7-167.0)	84.00 (49.9-152.8)	84.01 (49.9-152.8)	83.64 (43.9-170.6)	83.9 (43.9-170.6)
Median BMI, kg/m² (range)	28.90 (16.9-53.5)	28.86 (16.9-53.5)	30.42 (18.2-58.3)	30.37 (18.2-58.3)	28.82 (18.2-53.6)	28.85 (18.2-53.6)	29.11 (16.6-57.6)	29.23 (16.6-57.6)

Tolerability and Full Six-Month Safety Data

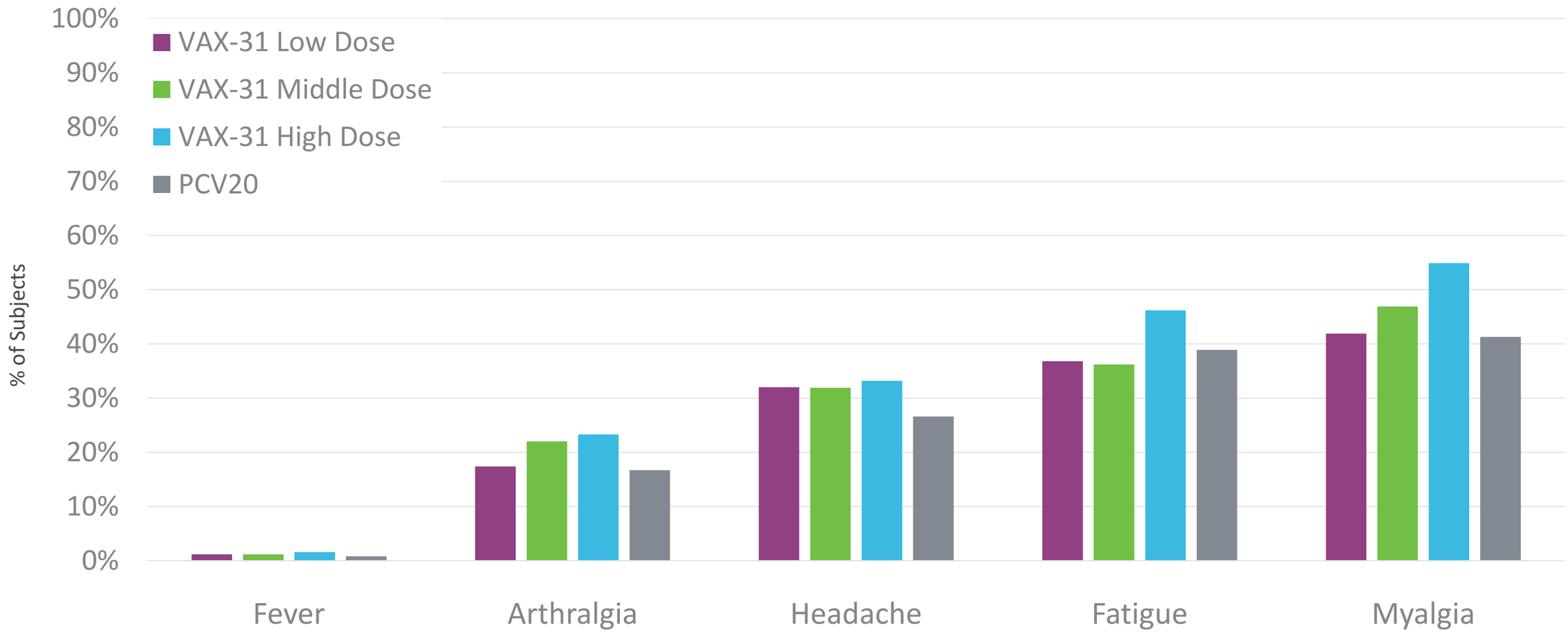
All VAX-31 Doses Well Tolerated and Consistent with PCV20 Across Cohorts

Local Solicited AEs Through 7 Days



All VAX-31 Doses Well Tolerated and Consistent with PCV20 Across Cohorts

Systemic Solicited AEs Through 7 Days



VAX-31 Full Six-Month Safety Data Similar to PCV20 and Across Cohorts

	VAX-31 Low Dose	VAX-31 Middle Dose	VAX-31 High Dose	PCV20
NUMBER OF SUBJECTS WITH:	255	254	253	253
Unsolicited TEAE, n (%)	42 (16.5)	43 (16.9)	47 (18.6)	42 (16.6)
Related Unsolicited TEAE, n (%)	7 (2.7)	11 (4.3)	17 (6.7)	12 (4.7)
MAAE, n (%)	45 (17.6)	42 (16.5)	35 (13.8)	31 (12.3)
Related MAAE, n (%)	1 (0.4)	4 (1.6)	0	0
NOCI, n (%)	2 (0.8)	6 (2.4)	5 (2.0)	5 (2.0)
Related NOCI, n (%)	1 (0.4)	0	0	0
SAE, n (%)	2 (0.8)	3 (1.2)	5 (2.0)	3 (1.2)
Related SAE, n (%)	0	0	0	0
Death, n (%)	0	0	0	0
Related Death, n (%)	0	0	0	0

TEAE = Treatment emergent adverse events; MAAE = Medically attended adverse events; NOCI = New onset of chronic illnesses; SAE = Serious adverse events. Excludes Solicited AEs.

Topline Immunogenicity Data

Precedent Immunogenicity Regulatory Criteria for Phase 2/3 PCV Studies

CRITERIA FOR 20 SEROTYPES COMMON TO VAX-31 AND PCV20:

Non-inferiority:

- Lower bound of the 2-sided 95% CI of the OPA GMR is greater than 0.5

CRITERIA FOR 11 INCREMENTAL SEROTYPES IN VAX-31:

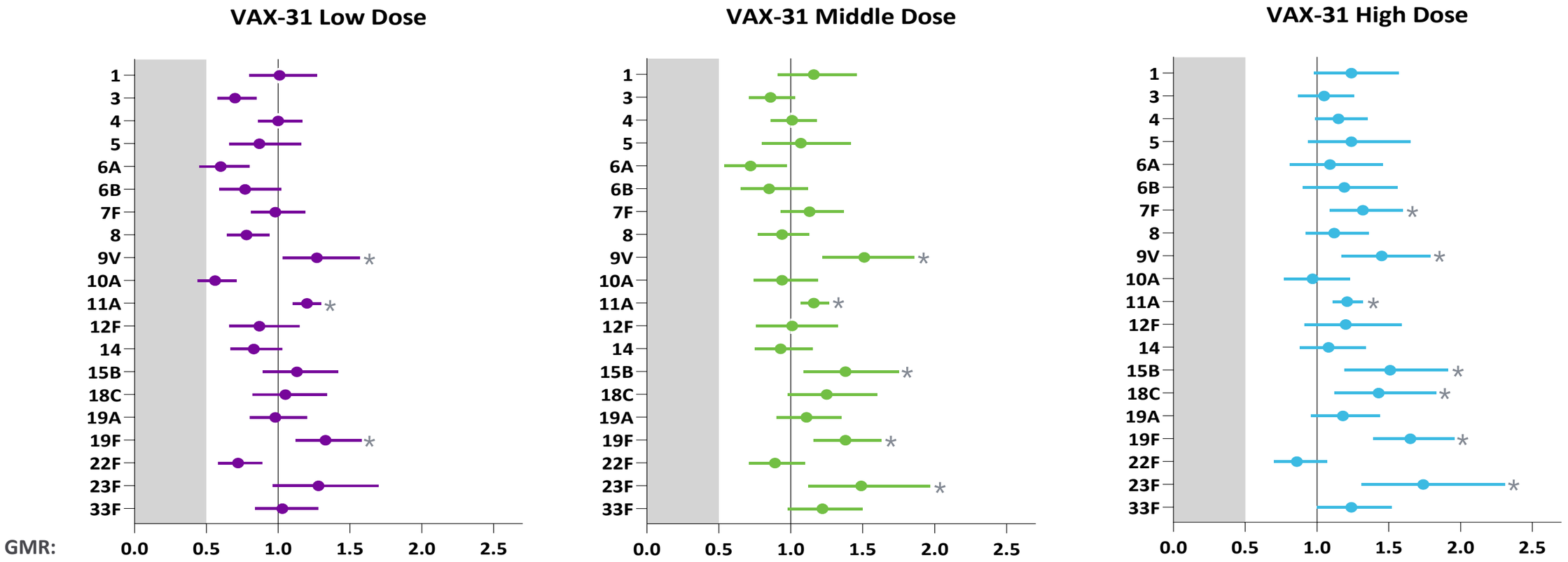
Superiority:

- Lower bound of the 2-sided 95% CI of the difference in the proportions of participants with a ≥4-fold increase from Day 1 to Month 1 is greater than 10%
- Lower bound of the 2-sided 95% CI of the OPA GMR is greater than 2.0

CI = confidence interval

VAX-31 Induced Robust Immune Responses for All 20 Common STs

Middle and High Doses Met OPA Response Non-Inferiority Criteria for All 20 Common STs Compared to PCV20



Low dose: 8 of 20 STs had a GMR greater than 1.0 and 3 STs achieved statistically higher immune responses

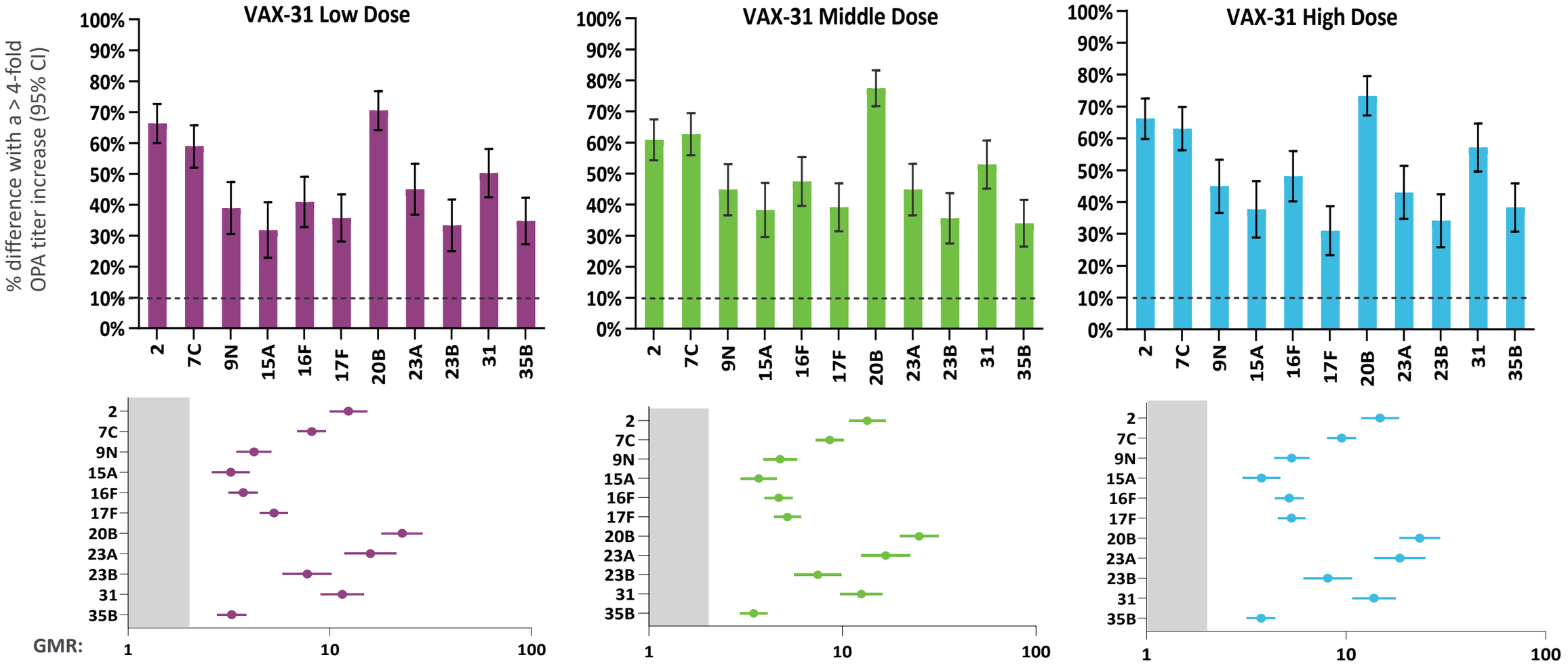
Middle dose: 13 of 20 STs had a GMR greater than 1.0 and 5 STs achieved statistically higher immune responses

High dose: 18 of 20 STs had a GMR greater than 1.0 and 7 STs achieved statistically higher immune responses

* *Reached statistical significance for superiority.*

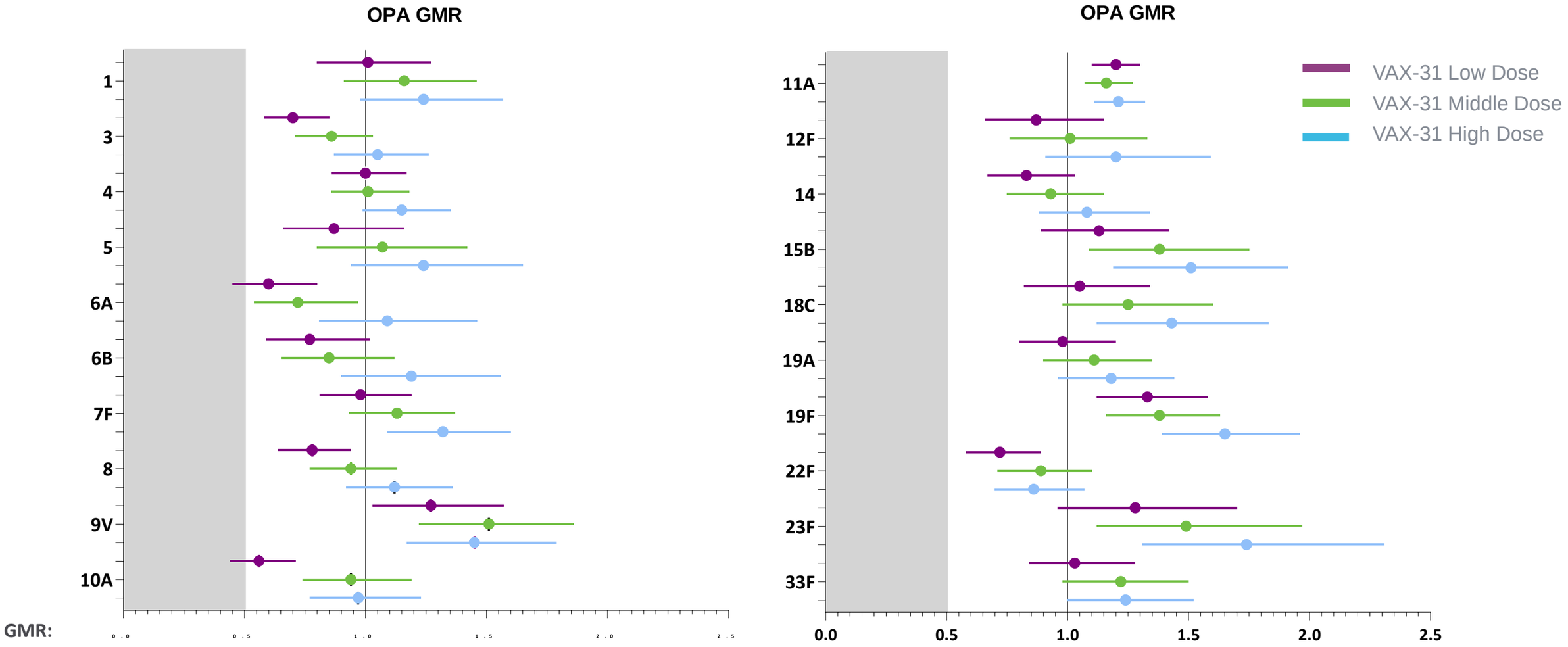
VAX-31 Induced Robust Immune Responses for All 11 Incremental STs

All Three Doses Met Superiority Criteria for All Incremental STs Compared to PCV20



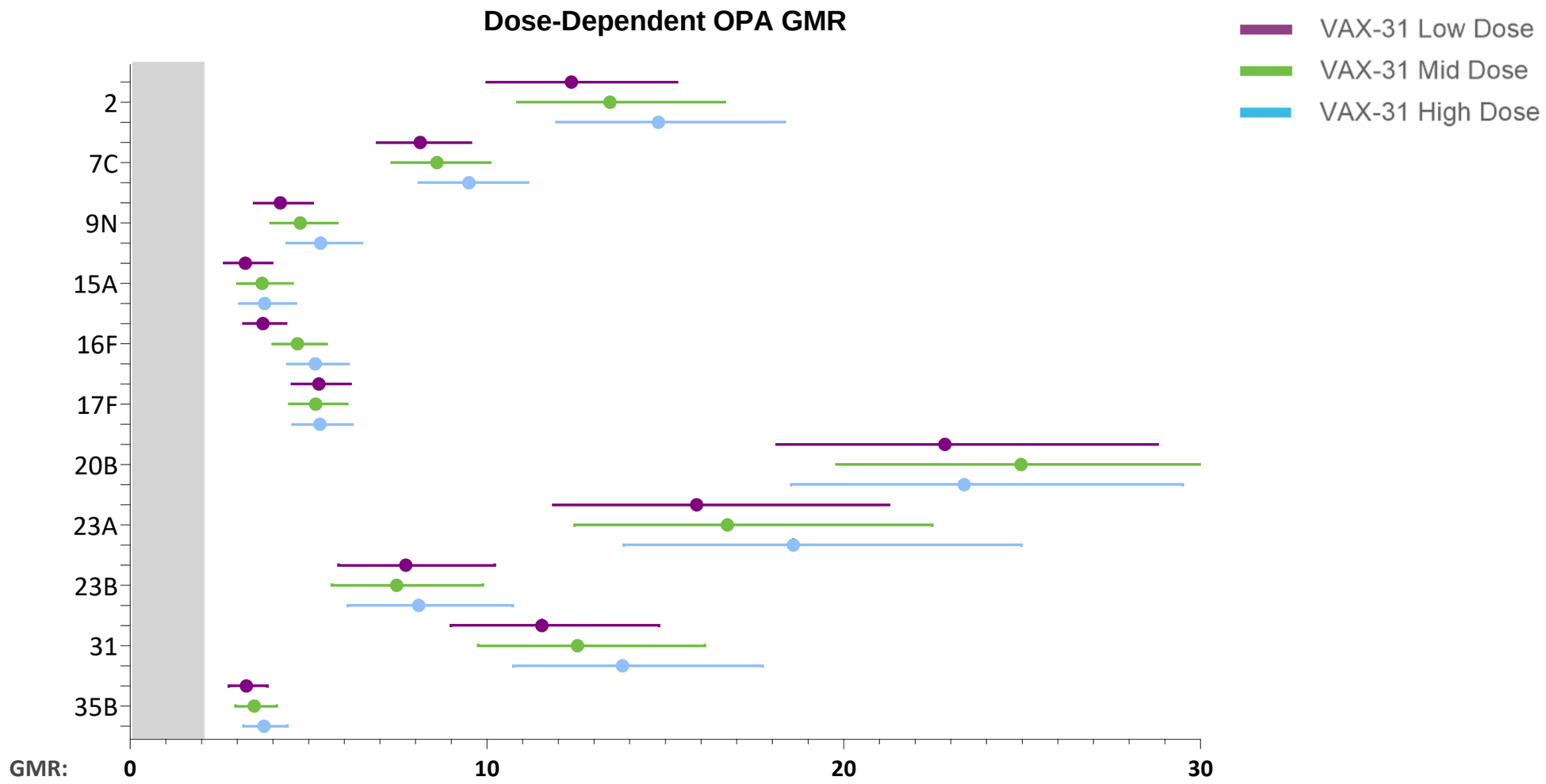
Consistent Dose-Dependent Response for Common STs

Topline Data Affirm Potential Predictability and Scalability of Site-Specific, Carrier-Sparing Approach



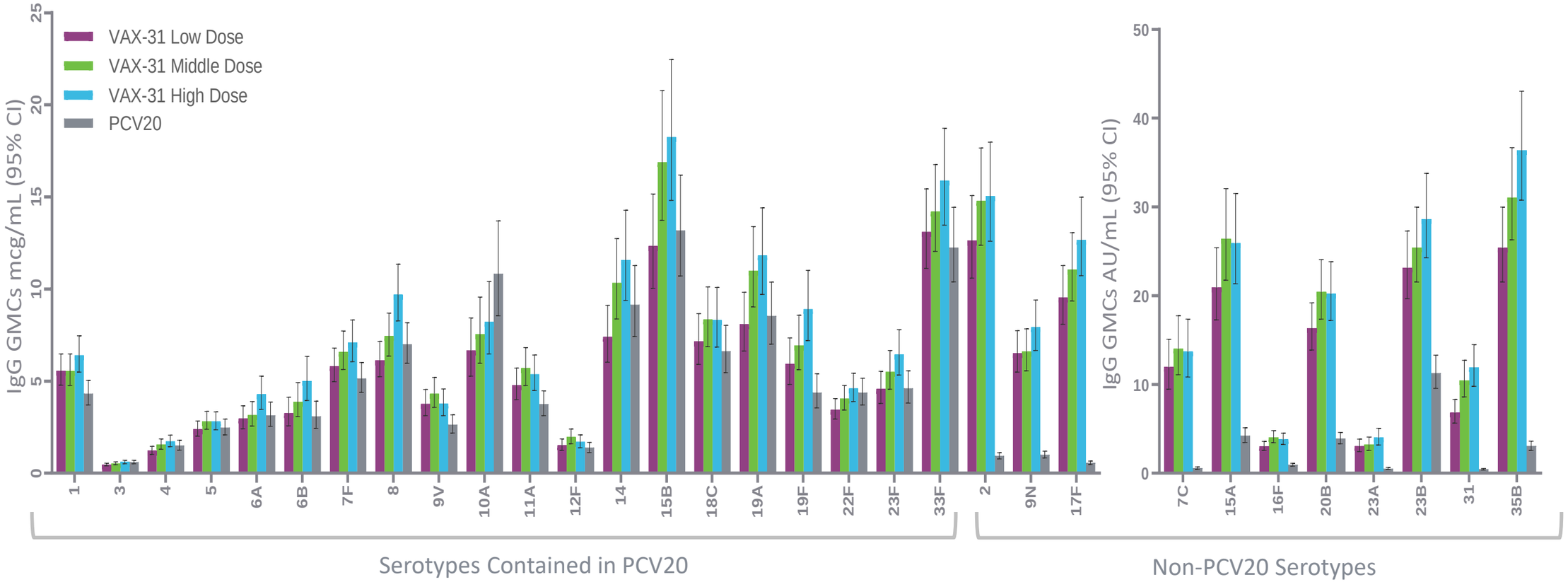
Consistent Dose-Dependent Response for Incremental STs

Topline Data Affirm Potential Predictability and Scalability of Site-Specific, Carrier-Sparing Approach



All 31 Serotypes in VAX-31 Demonstrated Robust IgG GMC Responses

IgG Data Consistent with OPA Results



IgG = Immunoglobulin G; GMC = Geometric Mean Concentration

PCV Franchise Status and Next Steps

Potential to Set New Standard-of-Care with Broadest Coverage and Raise Immunogenicity Threshold

SAFETY AND TOLERABILITY:
- At all doses studied, VAX-31 was well tolerated and demonstrated a safety profile similar to PCV20

IMMUNOGENICITY:
- At all doses studied, VAX-31 demonstrated robust OPA immune responses for all 31 STs
- High and middle doses met or exceeded regulatory immunogenicity criteria for all 31 STs

PLATFORM:
- The data further validate potential of Vaxcyte's site-specific, carrier-sparing platform to deliver the broadest-spectrum PCVs that provide protection against both currently circulating and historically prevalent STs

PCV FRANCHISE STRATEGY:
- **Adult:** VAX-31 selected to advance to Phase 3; dose to be chosen prior to study initiation
- **Pediatric:** Advance both VAX-24 and VAX-31
- **Next-generation readiness**

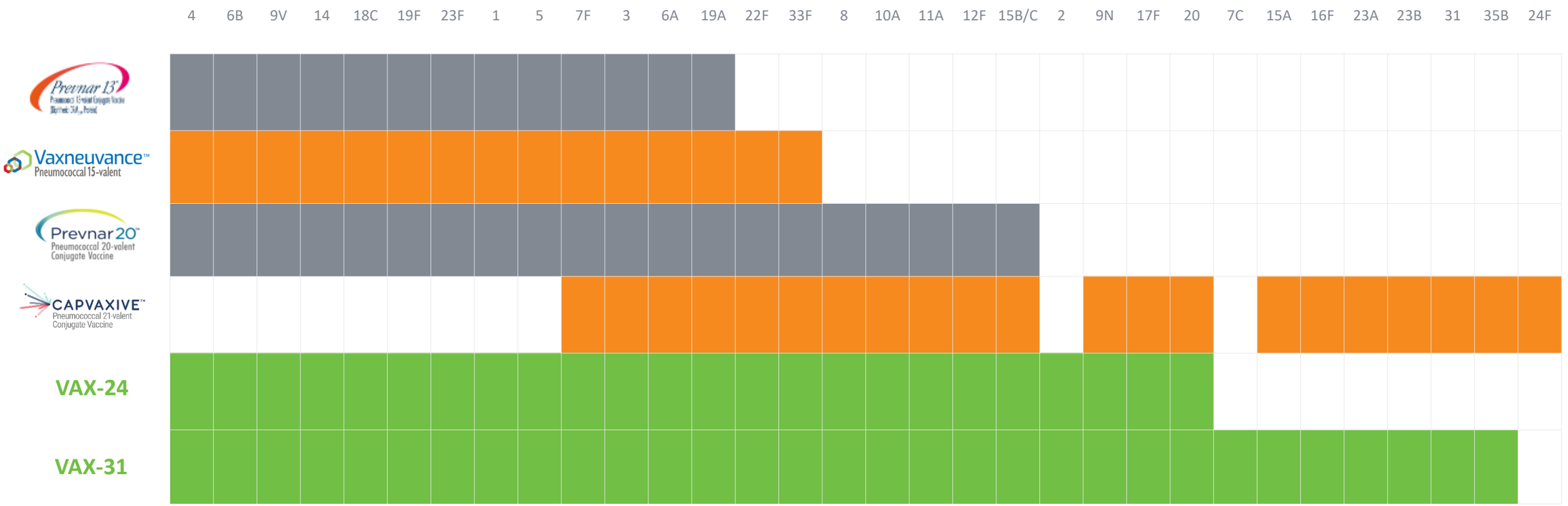
Clinical Development Next Steps and Anticipated Milestones[1]

Potential Best-in-Class PCV Franchise for Adult and Infant Segments

Population	Investigational PCV	Key Anticipated Milestones
 **Adults**	**VAX-31** **31-valent PCV candidate**	• Following FDA End-of-Phase 2 meeting, initiate Phase 3 pivotal, non-inferiority study by mid-2025 and announce topline safety, tolerability and immunogenicity data in 2026. • Initiate remaining Phase 3 studies in 2025 and 2026.
 **Infants**	**VAX-24** **24-valent PCV candidate**	• Announce topline safety, tolerability and immunogenicity data from primary three-dose immunization series of Phase 2 study, which is fully enrolled with 802 healthy infants, by end of 1Q:2025, followed by topline data from booster dose by end of 2025.
	VAX-31 **31-valent PCV candidate**	• Initiate Phase 2 study in 1Q:2025 following IND submission and clearance. • Announce topline safety, tolerability and immunogenicity data from VAX-31 infant Phase 2 study primary three-dose immunization series in mid-2026, followed by topline data from booster dose approximately nine months later.

[1]Guidance as of September 3, 2024.

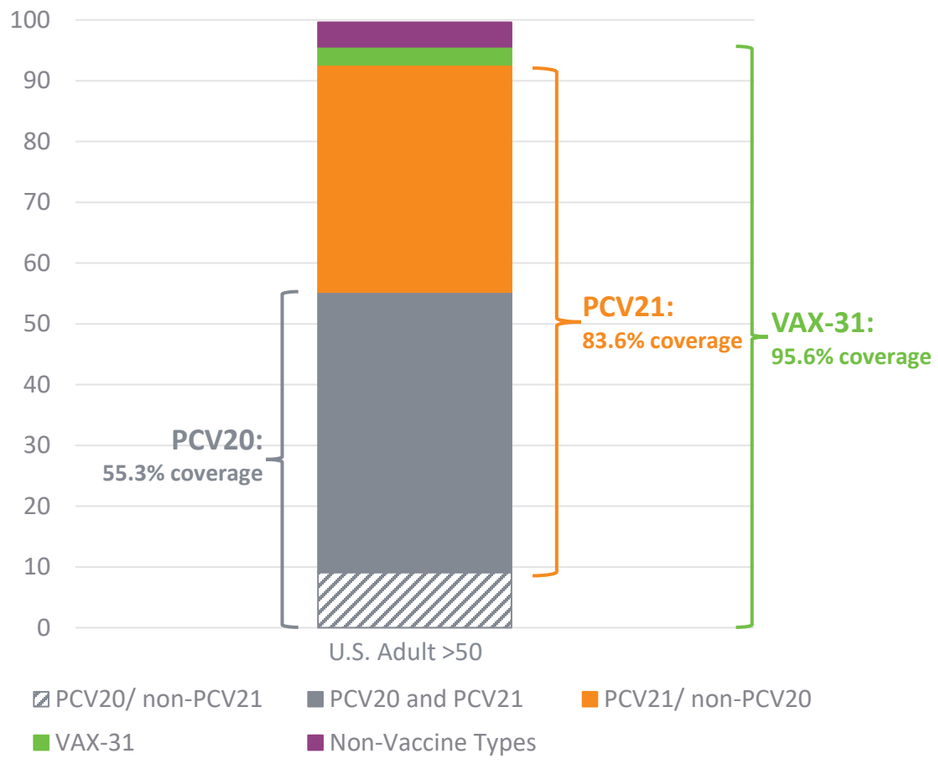
VAX-31 Poised to Establish New Standard for Spectrum of Coverage



Source: Prescribing information for Prevnar, Prevnar 13, Prevnar20, Vaxneuvance, Prevnar 20 and Capvaxive. Company filings for Vaxcyte.
Capvaxive is approved for use in adults only.

VAX-31 Positioned to Potentially Provide Unrivaled IPD Coverage

ESTIMATED COVERAGE OF PCVs BASED ON CIRCULATING IPD SEROTYPES[1]



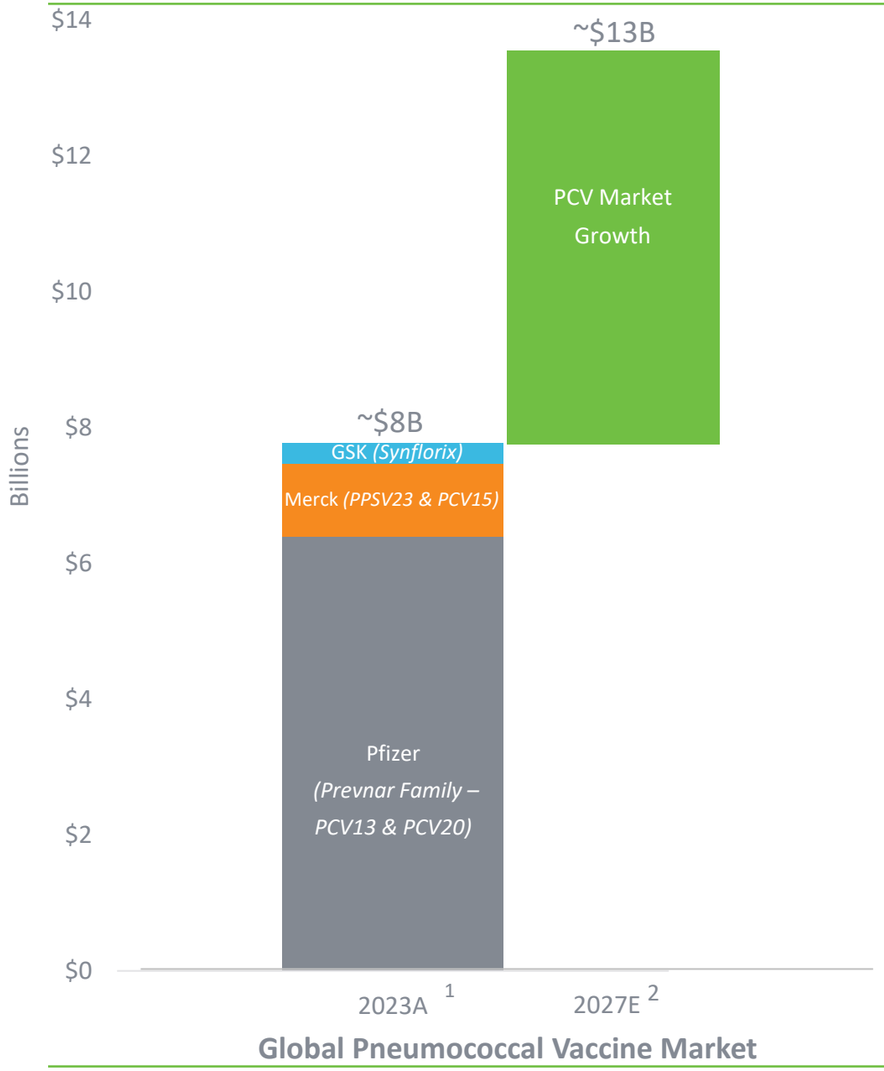
VAX-31

- The broadest-spectrum PCV to enter U.S. clinics; designed to increase coverage to more than 95% of IPD circulating in U.S. adults
- Includes STs designed to provide protection against both currently circulating and historically prevalent STs, with potential to surpass standard-of-care adult PCVs with 12-40% incremental coverage

(1) % US coverage is the percentage of IPD caused in individuals >50yrs of age in the United States in the 2022 based on ABC surveillance data. Reference: https://data.cdc.gov/Public-Health-Surveillance/1998-2022-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p/about_data.

Pneumococcal Vaccine Market Poised for Significant Growth

Expected to Reach ~$13B by 2027 Driven Primarily by Growth in Adult Market



Global Pneumococcal Vaccine Market

PCV MARKET – KEY GROWTH DRIVERS

Strong ACIP consideration to expand U.S. universal adult vaccination to ≥50 years from ≥65, which would significantly expand market and necessitate prime-boost for effective long-term protection

Serotype epidemiology and availability of broader-valency PCVs may lead to additional adult recommendations outside the U.S.

"At risk" adults added to U.S. universal PCV vaccination recommendation, which includes >25% of 50-64 year olds[3]

(1) Sources: Company websites.
(2) Global Pneumococcal Vaccine Market (2022-2027), Infogence Global Research.
(3) Shea KM, Edelsberg J, Weycker D et al. (2014), Open Forum Infect Dis 1(1): ofu024.

VAXCYTE MISSION STATEMENT

We are on a global mission to engineer high-fidelity vaccines that protect humankind from the consequences of bacterial diseases.

Q&A with Management

Grant Pickering
Chief Executive Officer, Director and Founder

Jim Wassil
Executive Vice President and Chief Operating Officer

Andrew Guggenhime
President and Chief Financial Officer


VAXCYTE
protect humankind™

Appendix

VAX-31: OPA GMRs with 95% CI for 20 STs Common with PCV20

ST	GMR	95% CI	
1	1.01	1.27	0.80
3	0.70	0.85	0.58
4	1.00	1.17	0.86
5	0.87	1.16	0.66
6A	0.60	0.80	0.45
6B	0.77	1.02	0.59
7F	0.98	1.19	0.81
8	0.78	0.94	0.64
9V	1.27	1.57	1.03
10A	0.56	0.71	0.44
11A	1.20	1.30	1.10
12F	0.87	1.15	0.66
14	0.83	1.03	0.67
15B	1.13	1.42	0.89
18C	1.05	1.34	0.82
19A	0.98	1.20	0.80
19F	1.33	1.58	1.12
22F	0.72	0.89	0.58
23F	1.28	1.70	0.96
33F	1.03	1.28	0.84

ST	GMR	95% CI	
1	1.16	1.46	0.91
3	0.86	1.03	0.71
4	1.01	1.18	0.86
5	1.07	1.42	0.80
6A	0.72	0.97	0.54
6B	0.85	1.12	0.65
7F	1.13	1.37	0.93
8	0.94	1.13	0.77
9V	1.51	1.86	1.22
10A	0.94	1.19	0.74
11A	1.16	1.27	1.07
12F	1.01	1.33	0.76
14	0.93	1.15	0.75
15B	1.38	1.75	1.09
18C	1.25	1.60	0.98
19A	1.11	1.35	0.90
19F	1.38	1.63	1.16
22F	0.89	1.10	0.71
23F	1.49	1.97	1.12
33F	1.22	1.50	0.98

ST	GMR	95% CI	
1	1.24	1.57	0.98
3	1.05	1.26	0.87
4	1.15	1.35	0.99
5	1.24	1.65	0.94
6A	1.09	1.46	0.81
6B	1.19	1.56	0.90
7F	1.32	1.60	1.09
8	1.12	1.36	0.92
9V	1.45	1.79	1.17
10A	0.97	1.23	0.77
11A	1.21	1.32	1.11
12F	1.20	1.59	0.91
14	1.08	1.34	0.88
15B	1.51	1.91	1.19
18C	1.43	1.83	1.12
19A	1.18	1.44	0.96
19F	1.65	1.96	1.39
22F	0.86	1.07	0.70
23F	1.74	2.31	1.31
33F	1.24	1.52	1.00

All 31 Serotypes in VAX-31 Demonstrated Robust OPA GMT Immune Responses