VAX-24 Phase 1/2 Proof-of-Concept Study Topline Results

October 24, 2022

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 and the ability to deliver a potentially best-in-class pneumococcal conjugate vaccine; demand for Vaxcyte's vaccine candidates; the process and timing of anticipated future development and manufacture of Vaxcyte's vaccine candidates; the achievement of future funding milestones; 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; the timing of the initiation, progress and expected results of Vaxcyte's preclinical studies, clinical trials and research and development plans (including, the availability of data for the VAX-24 Phase 2 and Phase 3 studies and related regulatory interactions; the submission of a VAX-24 infant IND application and initiation of such study; and the design of the VAX-XP clinical program, the submission of such IND and the availability of topline data); 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; sufficiency of cash and other funding to support Vaxcyte's development programs and other operating expenses; and the ongoing COVID-19 pandemic, 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 8, 2022 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.

Summary of VAX-24 Phase 1/2 Topline Data Findings

Unprecedented Results Support Best-in-Class Potential for VAX-24 and Identify Optimal Dose for Advancement

SAFETY: VAX-24 demonstrated a safety and tolerability profile similar to Prevnar 20™ (PCV20) for all doses

IMMUNOGENICITY: Met or exceeded regulatory standard for all 24 serotypes (STs) for VAX-24 conventional 2.2mcg dose without the need to push dose higher

- Optimal 2.2mcg dose being advanced to Phase 3:
  - Met the standard OPA response non-inferiority criteria for all 20 STs common with PCV20, of which 16 achieved higher immune responses
  - Met the standard superiority criteria for all 4 additional STs unique to VAX-24
- All VAX-24 doses (1.1mcg, 2.2mcg, and 2.2mcg/4.4mcg) eligible to advance

PLATFORM: VAX-24 data validate Vaxcyte's carrier-sparing PCV franchise to increase spectrum of coverage AND maintain robust immune responses to serotypes in current standard-of-care PCVs

MILESTONES: Vaxcyte to pursue Breakthrough Therapy Designation to rapidly advance VAX-24 program

- Adults: Topline data from Phase 2 study in adults 65+ expected in 1H:23, followed by end-of-Phase 2 meeting with FDA to gain agreement on Phase 3 pivotal non-inferiority study using similar design as Phase 2 POC study
- Pediatrics: Infant IND submission and Phase 2 study initiation expected in 1H:23

Global Impact of Pneumococcal Disease Remains Significant

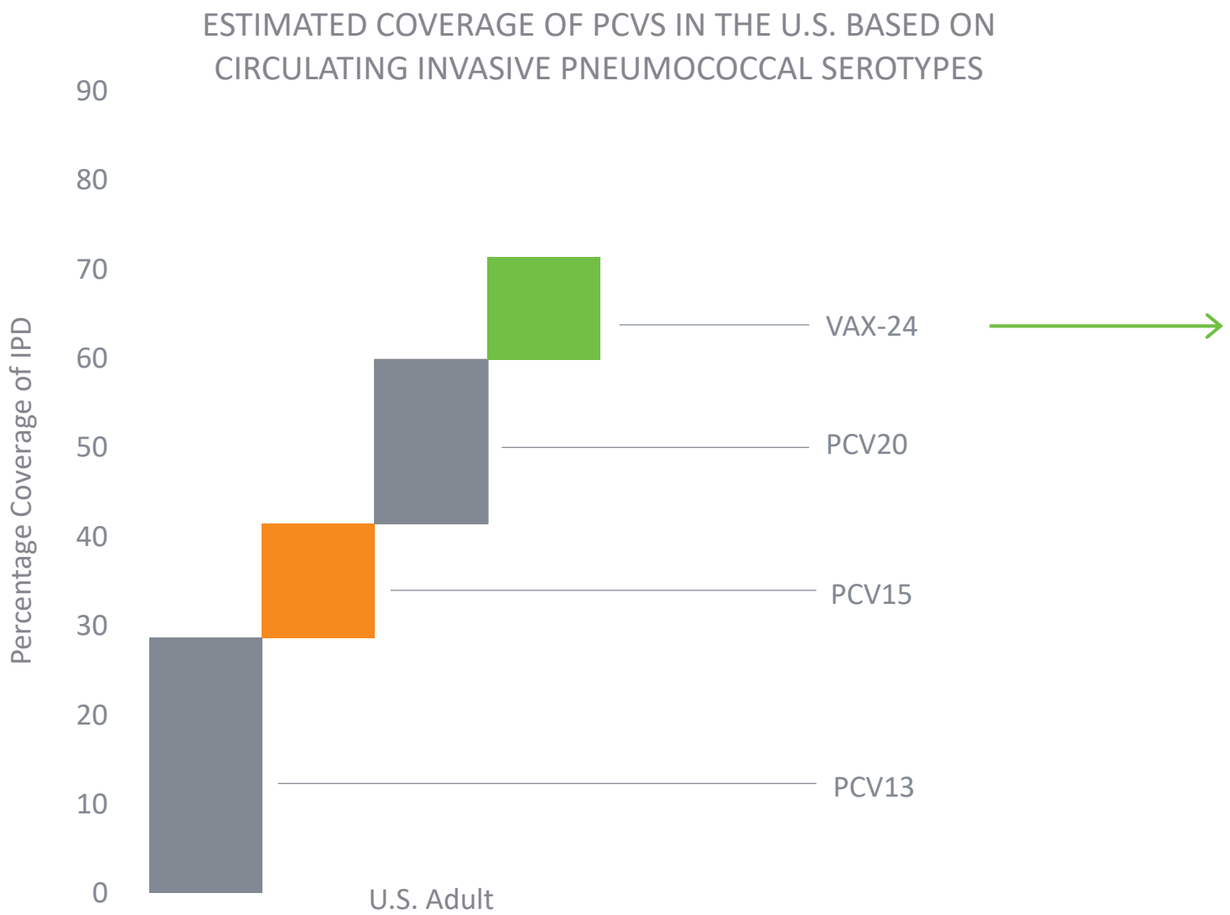
Circulating Disease Driven by Serotypes Outside of Current PCVs

- *Streptococcus pneumoniae* is the most common pathogen causing pneumococcal disease (PD).
  - In the U.S. alone, there are ~900K pneumococcal pneumonia cases per year resulting in ~150K hospitalizations.
  - Among children < age 5, PD is a leading cause of death globally.
- Circulating strains of PD in the U.S. and globally are associated with high case-fatality rates, antibiotic resistance and/or meningitis.

[1] *Gierke 2015*
[2] *https://www.cdc.gov/abcs/reports-findings/survreports/spneu18.pdf CDC 2018*
[3] *https://www.cdc.gov/pneumococcal/clinicians/clinical-features.html*

Spectrum of Coverage Drives Adoption in PCV Segment

Significant Unmet Needs Remain Despite Available Vaccines



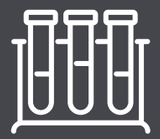
VAX-24 PROFILE

- Designed to provide broadest coverage of any PCV, including an incremental 10-15% coverage of IPD in adults
- VAX-24 provides the benefits of a conjugate vaccine while fully eclipsing the coverage of Pneumovax 23

(1) Data in the US is for 2017, inclusive of those > 5 yrs of age.
(2) Varghese et al. Clin Micro and Infect (2020) 26(4): 512.e1-512.e10.

Carrier-Sparing Approach for PCV Franchise Validated By POC Study

Site-Specific Conjugation Using Cell-Free Platform to Go Beyond Limits of Conventional Chemistry



LIMITATIONS OF CONVENTIONAL CONJUGATION CHEMISTRY

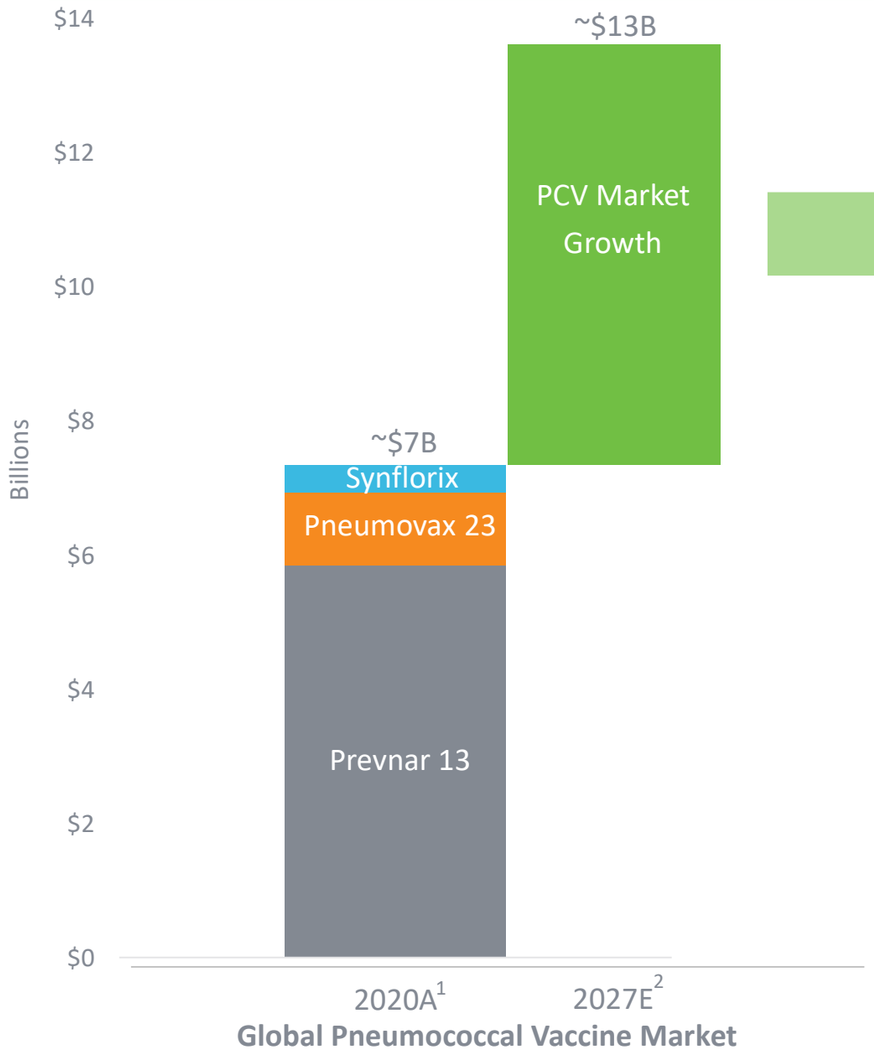
- Random conjugation masks “on-target” T-cell epitopes on the protein carrier
- Higher ratio of protein carrier to polysaccharide required
- Overabundance of protein carrier and its “off-target” effects exacerbates competition for CD4+ T-cell leading to carrier suppression

VAXCYTE’S SUPERIOR CARRIER-SPARING CONJUGATE VACCINES

- Site-specifically attach conventional antigens and protein carriers to:
  - Enable consistent exposure of T-cell epitopes (and/or B-cell epitopes) on protein carrier to drive class-defining CD4+ help
  - Avoid “off-target” effects from protein carrier that compete for the CD4+ help
  - Enable use of less protein carrier per conjugate without sacrificing immunogenicity
- Enable broader-spectrum carrier-sparing conjugate vaccines

Pneumococcal Vaccine Market Poised for Significant Growth

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



PCV Market Growth Drivers

- Strong ACIP consideration to expand U.S. universal adult vaccination to >50 years from >65 would significantly expand market
- Would necessitate prime-boost for effective long-term protection, which has been limited by continued availability of Pneumovax 23

- ACIP recently voted to support PCV20 “catch-up” for adults who previously received PCV13 and Pneumovax 23
- “At risk” adults recently added to U.S. universal PCV vaccination recommendation, which includes >25% of 50-64 year olds[3]

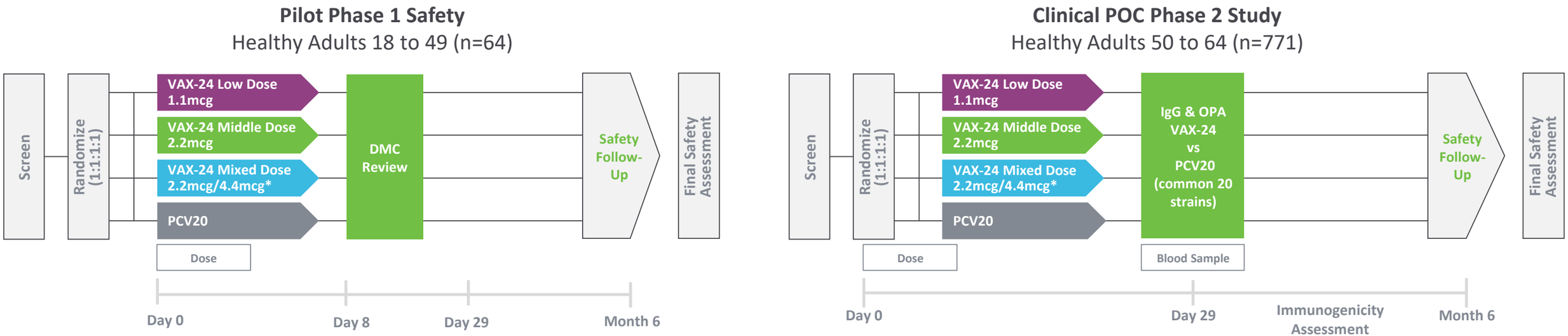
- Premium price for PCV20 and PCV15 shows value of additional serotype coverage

(1) Sources: Company websites; Prevnar 20 and Vaxneuvance have since been approved in 2021.
(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.

VAX-24 Phase 1/2 Study Design

VAX-24 Phase 1/2 Clinical Proof-of-Concept Study Design

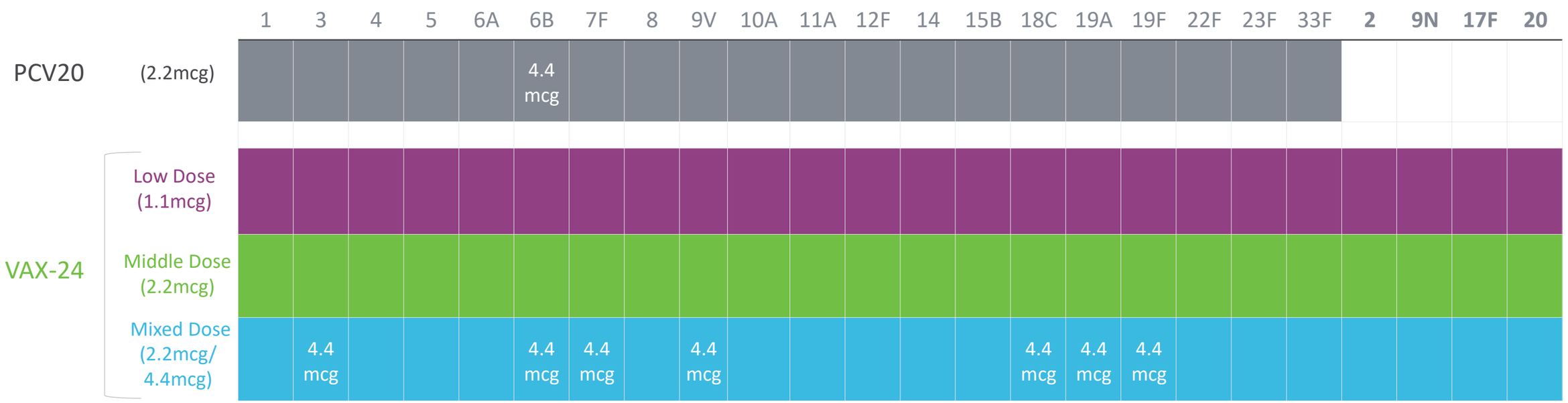
Design: Randomized, Observer-Blind, Dose-Finding, Controlled Study to Evaluate Safety, Tolerability & Immunogenicity of VAX-24 vs SOC in Adults Aged 18-64



** For the VAX-24 Mixed Dose, a 4.4mcg dose is used for serotypes 3, 6B, 7F, 9V, 18C, 19A and 19F; a 2.2 mcg dose is used for the remaining serotypes.*

.

Study Evaluated Three VAX-24 Doses



- Mixed Dose includes seven serotypes at 4.4mcg strategically chosen based on epidemiological relevance or prior evidence of dose-dependent immune responses to increase the probability of generating non-inferior immune responses for those serotypes.

Study Safety, Tolerability and Immunogenicity Outcome Measures

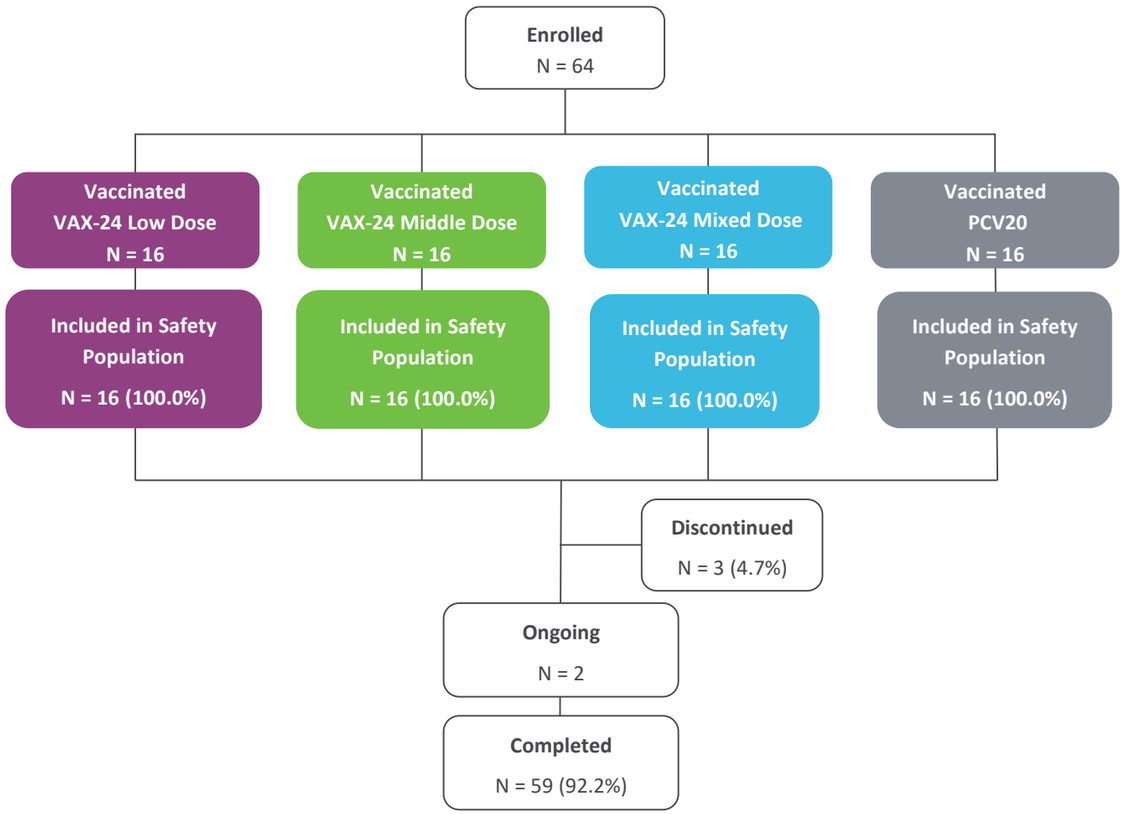
	DAY 7	DAY 29	DAY 180
SAFETY AND TOLERABILITY OUTCOME MEASURES (PHASE 1 AND 2 PORTIONS OF THE STUDY)	• Solicited local reactions • Solicited systemic events	• Unsolicited adverse events (AEs) • Serious adverse events (SAEs)	• SAEs and new onset of chronic illnesses (NOCI) medically attended adverse events
IMMUNOGENICITY OUTCOME MEASURES (PHASE 2 PORTION OF THE STUDY ONLY)		• Opsonophagocytic assay (OPA) geometric mean titer (GMTs) • IgG geometric mean concentration (GMCs) • % of subjects achieving a 4-fold rise in OPA • Geometric Mean Ratios (GMR) in serotype-specific OPA	

VAX-24 Phase 1/2 Study Disposition and Demographics

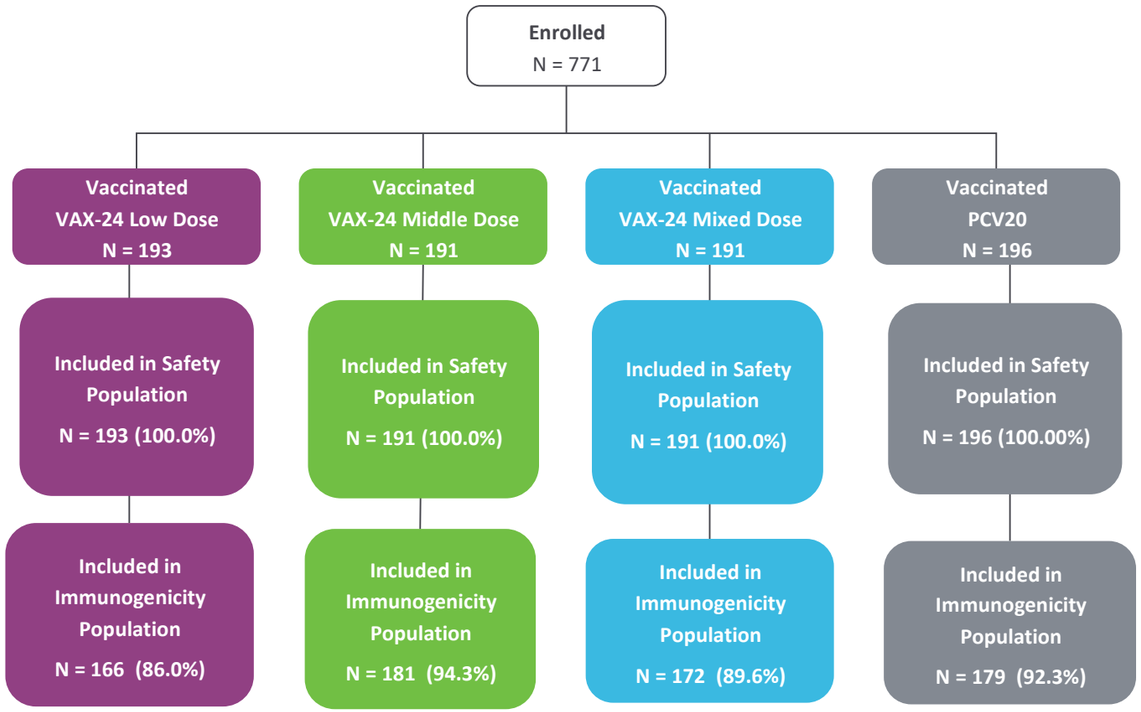
Phase 1/2 Study Disposition

Overall High Proportion of Subjects with Safety and Immunogenicity Follow-Up

Phase 1 Safety
Healthy Adults 18 to 49 (n=64)



Phase 2 POC Study
Healthy Adults 50 to 64 (n=771)



9 subjects were lost to follow-up in Phase 2

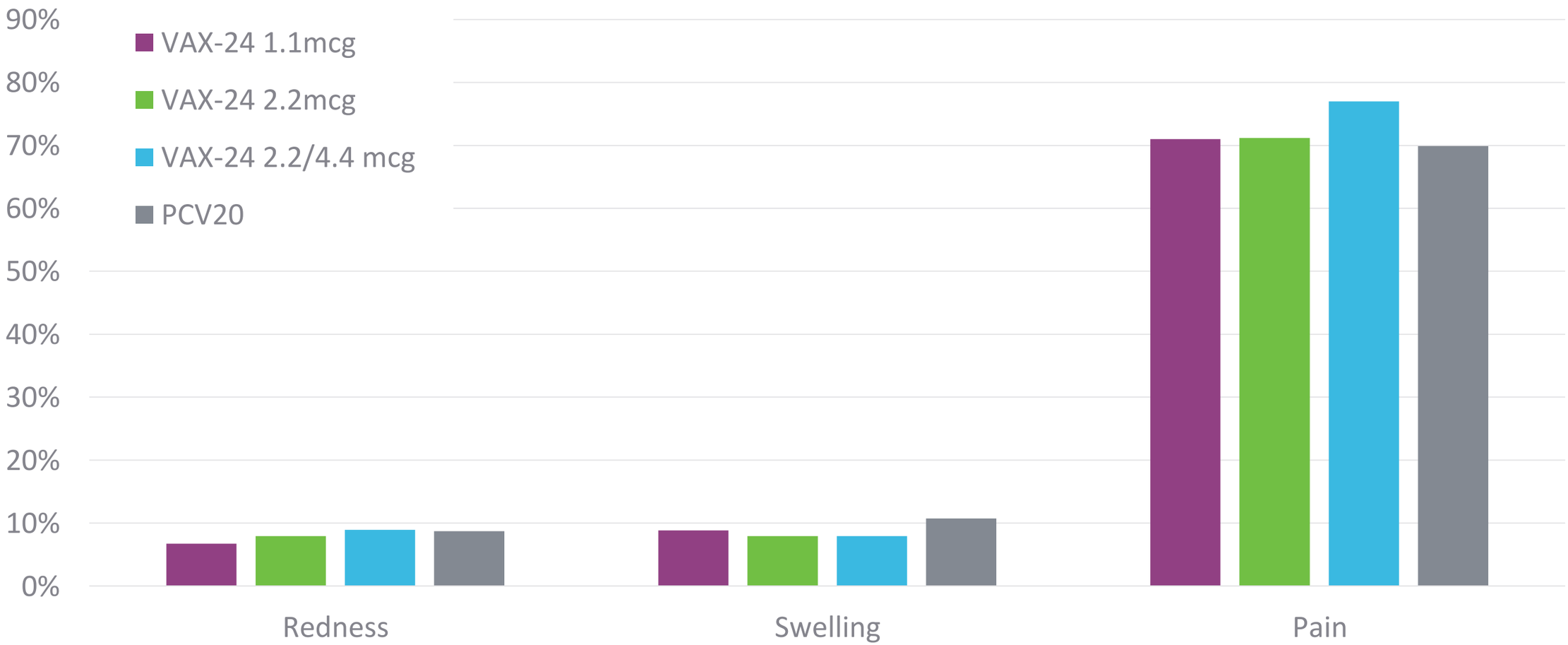
Phase 2 Demographic Population

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

	VAX-24 – Low Dose (1.1mcg)		VAX-24 – Middle Dose (2.2mcg)		VAX-24 – Mixed Dose (2.2mcg/4.4mcg)		PCV20	
	Safety	Immunogenicity	Safety	Immunogenicity	Safety	Immunogenicity	Safety	Immunogenicity
Number of Subjects	193	166	191	181	191	172	196	179
Median age, years (range)	57.0 (50-64)	57.0 (50-64)	57.0 (50-64)	57.0 (50-64)	57.0 (50-64)	57.0 (50-64)	57.0 (50-64)	57.0 (50-64)
Sex, n (%) Female	110 (57.0)	96 (57.8)	119 (62.3)	113 (62.4)	134 (70.2)	125 (72.7)	129 (65.8)	118 (65.9)
Male	83 (43.0)	70 (42.2)	72 (37.7)	68 (37.6)	57 (29.8)	47 (27.3)	67 (34.2)	61 (34.1)
Race, n (%) White	145 (75.1)	127 (76.5)	157 (82.2)	149 (82.3)	155 (81.2)	140 (81.4)	155 (79.1)	139 (77.7)
Black	40 (20.7)	32 (19.3)	31 (16.2)	29 (16.0)	29 (15.2)	27 (15.7)	30 (15.3)	29 (16.2)
Asian	1 (0.5)	1 (0.6)	0 (0.0)	0 (0.0)	2 (1.0)	2 (1.2)	3 (1.5)	3 (1.7)
Native Hawaiian	blinded	blinded	blinded	blinded	blinded	blinded	blinded	blinded
American Indian or Native Alaskan	blinded	blinded	blinded	blinded	blinded	blinded	blinded	blinded
Other	3 (1.6)	2 (1.2)	2 (1.0)	2 (1.1)	1 (0.5)	1 (0.6)	2 (1.0)	2 (1.1)
Median Height, cm (range)	168.3 (150-200)	168.4 (150-200)	167.6 (145-193)	167.6 (145-193)	167.6 (145-193)	167.6 (145-193)	167.6 (142-196)	167.6 (142-196)
Median weight, kg (range)	87.82 (49.2-159.2)	86.87 (49.8-159.2)	86.80 (51.4-155.1)	86.80 (51.4-155.1)	83.01 (47.9-205.5)	83.10 (48.9-205.5)	82.83 (45.3-189.9)	82.70 (45.3-185.5)
Median BMI, kg/m^2 (range)	29.87 (18.0-55.0)	29.39 (18.8-55.0)	30.54 (18.7-52.6)	30.44 (18.7-52.6)	29.42 (18.0-57.3)	29.48 (18.0-57.3)	29.06 (17.4-72.7)	29.11 (17.4-72.7)

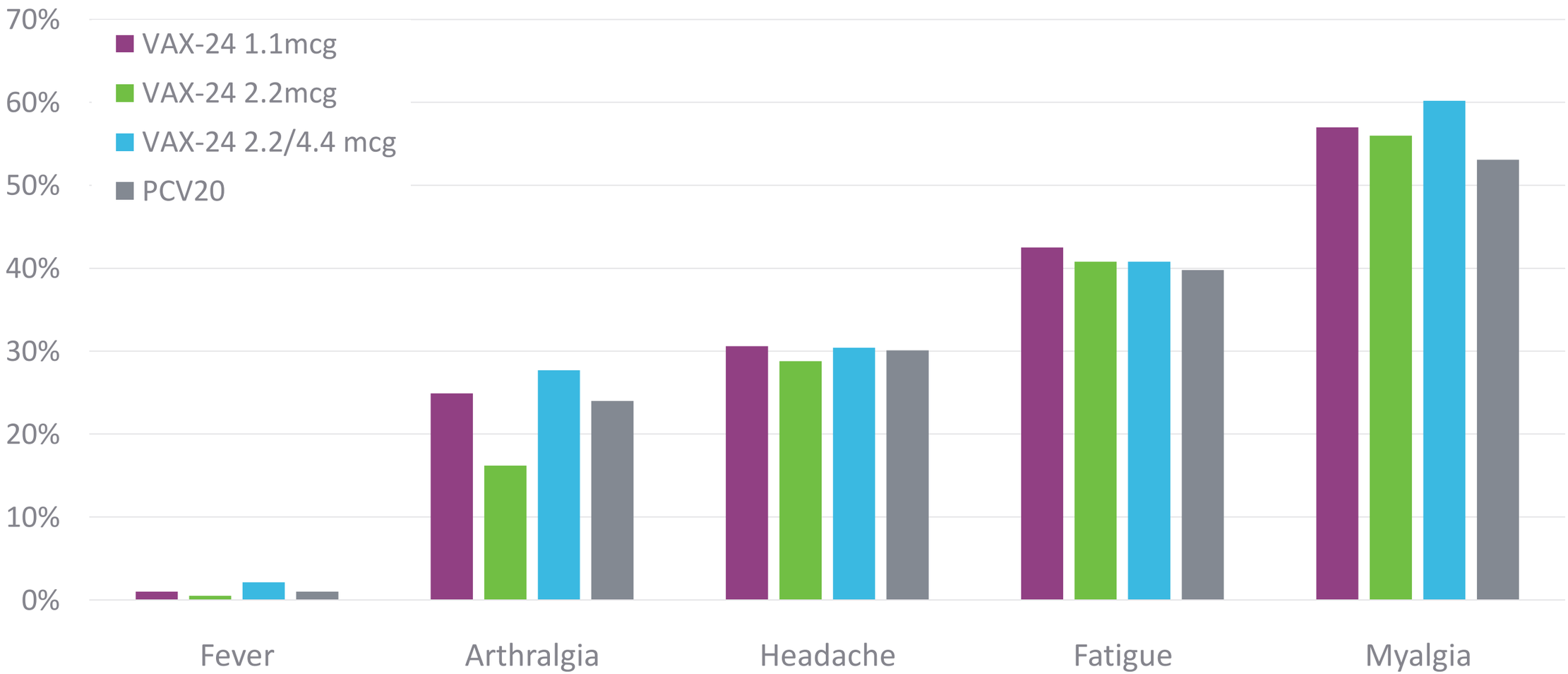
VAX-24 Phase 2 Study Topline Safety and Tolerability Results

Local Solicited AEs Similar to PCV20 and Across Cohorts Through Day 7



Represents data for the 50 – 64 year age group; as of August 31, 2022.

Systemic Solicited AEs Similar to PCV20 and Across Cohorts Through Day 7



Represents data for the 50 – 64 year age group; as of August 31, 2022.

VAX-24 Safety Profile Similar to PCV20 and Across Cohorts

	VAX-24 – Low Dose (1.1mcg)	VAX-24 – Middle Dose (2.2mcg)	VAX-24 – Mixed Dose (2.2mcg/4.4mcg)	PCV20
Number of Subjects	193	191	191	196
Subjects with TEAE, n (%)	29 (15.0)	21 (11.0)	22 (11.5)	31 (15.8)
Subjects with SAE or NOCI, n (%)	2 (1.0)	3 (1.6)	5 (2.6)	4 (2.0)
Subjects with related SAE, n (%)	0	0	0	0
Subjects with related NOCI, n (%)	0	0	0	0
Deaths, n (%)	0	0	0	0

Represents data for the 50 – 64 year age group; as of August 31, 2022.

VAX-24 Phase 2 Study Topline Immunogenicity Results

Standard Regulatory Criteria for Evaluating PCV Immunogenicity Results

CRITERIA FOR 20 SEROTYPES COMMON TO VAX-24 AND PCV20:

Non-inferiority Standard:

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

Superiority Standard:

- Lower bound of 2-sided 95% CI of the OPA GMT ratio is greater than 1.2
- Lower bound of the 2-sided 95% CI of the difference in proportions of participants with a ≥4-fold increase from Day 1 to Day 29 is greater than 0

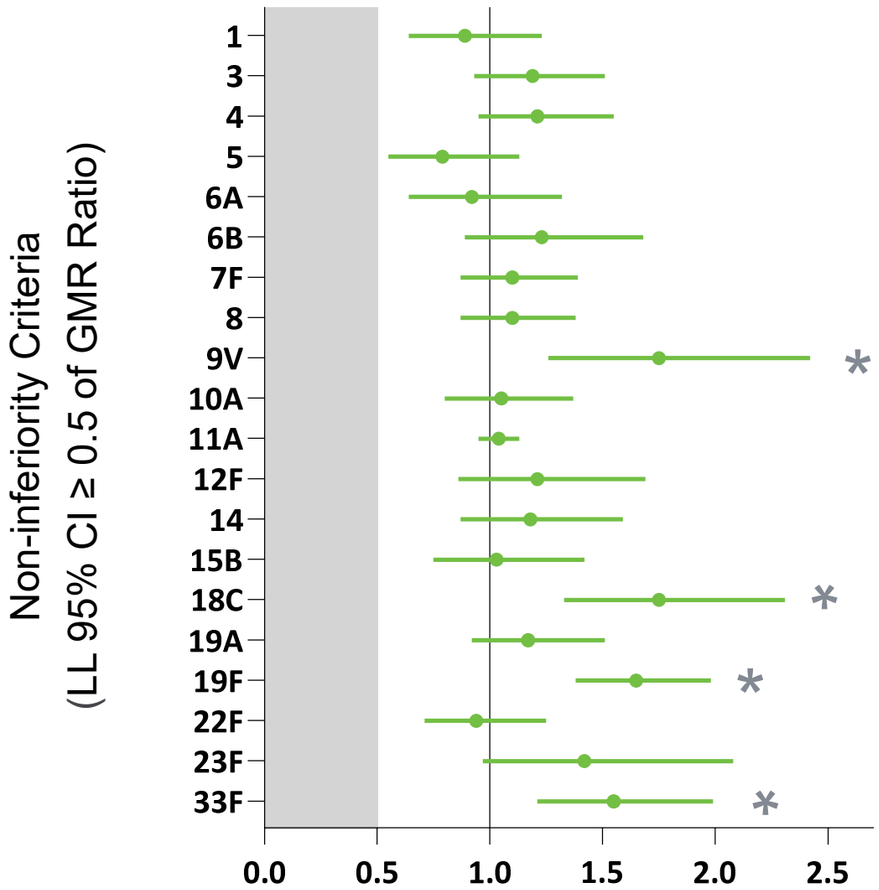
CRITERIA FOR 4 INCREMENTAL SEROTYPES IN VAX-24:

Superiority Standard:

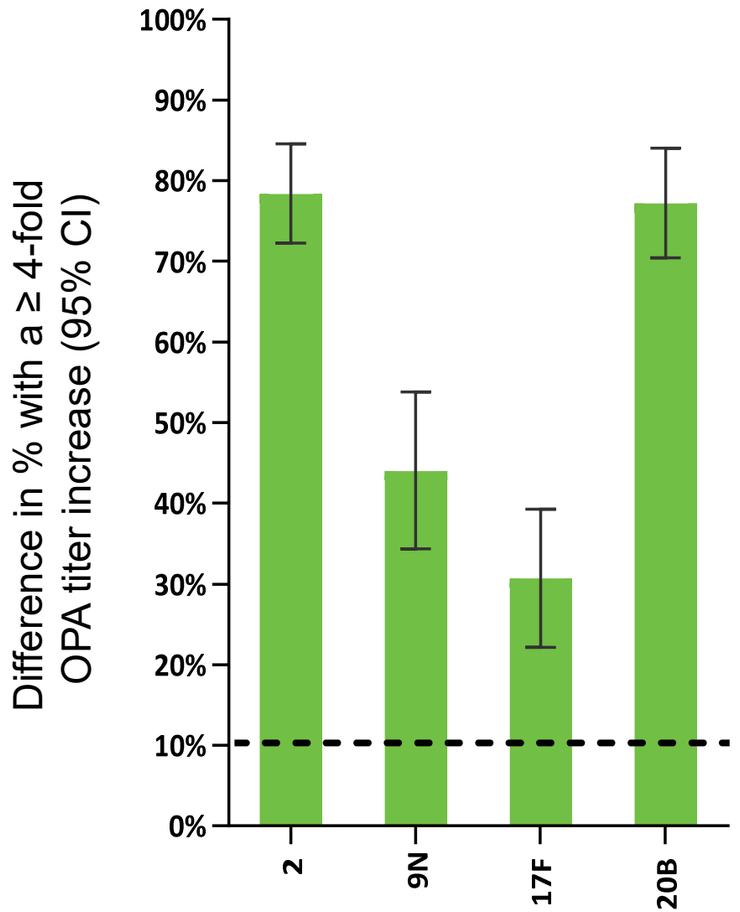
- Lower bound of the 2-sided 95% CI of the difference in the proportions of participants with a ≥4-fold increase from Day 1 to Day 29 is greater than 10%
- Lower bound of the 2-sided 95% CI of the OPA GMT ratio is greater than 2.0

VAX-24 2.2mcg Dose Met Regulatory Criteria for All 24 Serotypes in Adults 50-64 Years of Age

Met non-inferiority standard for all 20 common serotypes for the OPA GMR of VAX-24 : PCV20



Met superiority standard for all 4 incremental serotypes in VAX-24 based on difference in 4-fold rise[1]



VAXCYTE

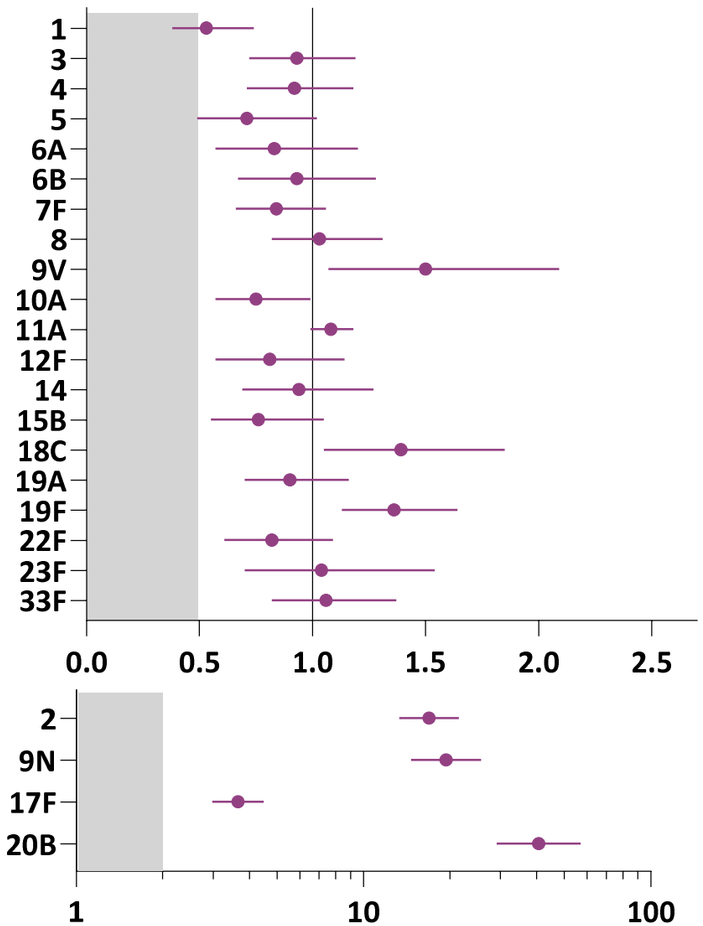
[1] *Previous version showed % of subjects with a ≥ 4-fold increase in absolute OPA titer (not comparative difference vs PCV20).*

* *Reached statistical significance for superiority.*

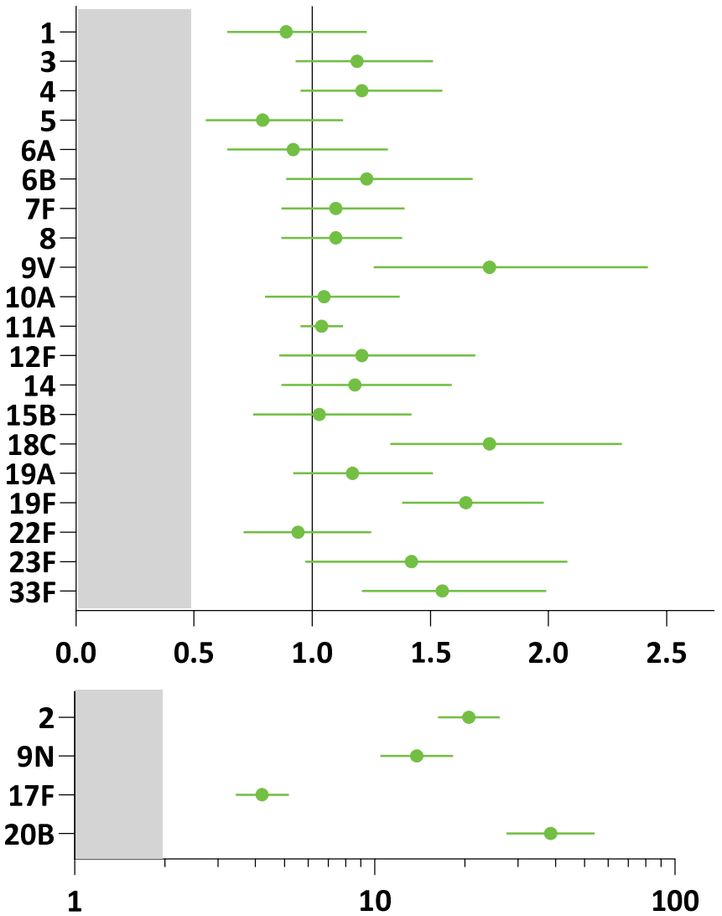
All 3 Doses Induced Immune Responses Sufficient to Move to Phase 3

2.2mcg Dose Demonstrated Higher OPA GMRs for 16 of the 20 Shared Serotypes and Will be Advanced

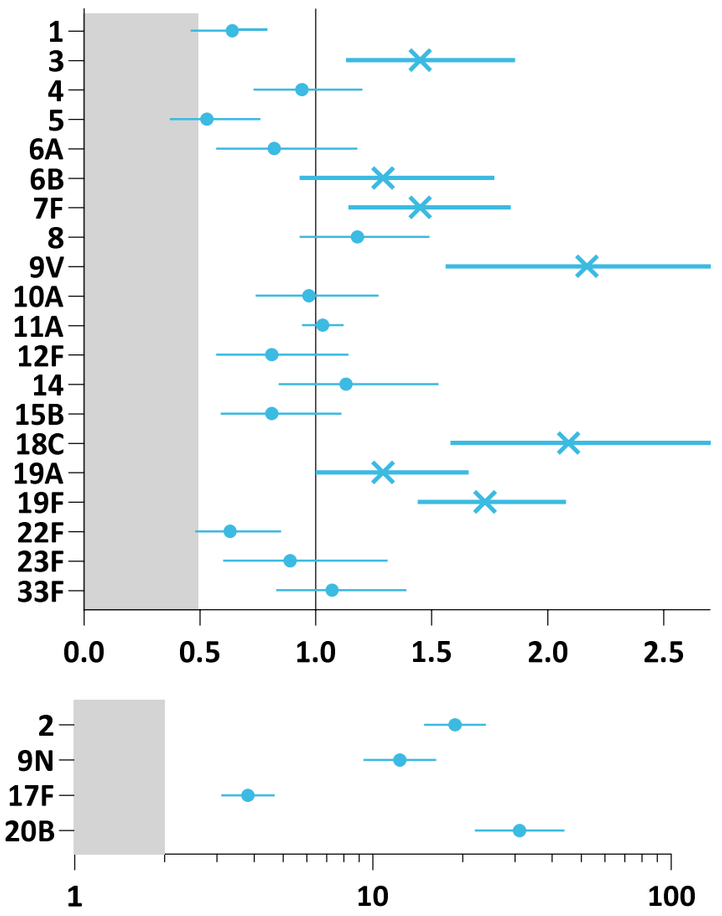
VAX-24 Low Dose (1.1mcg)



VAX-24 Middle Dose (2.2mcg)

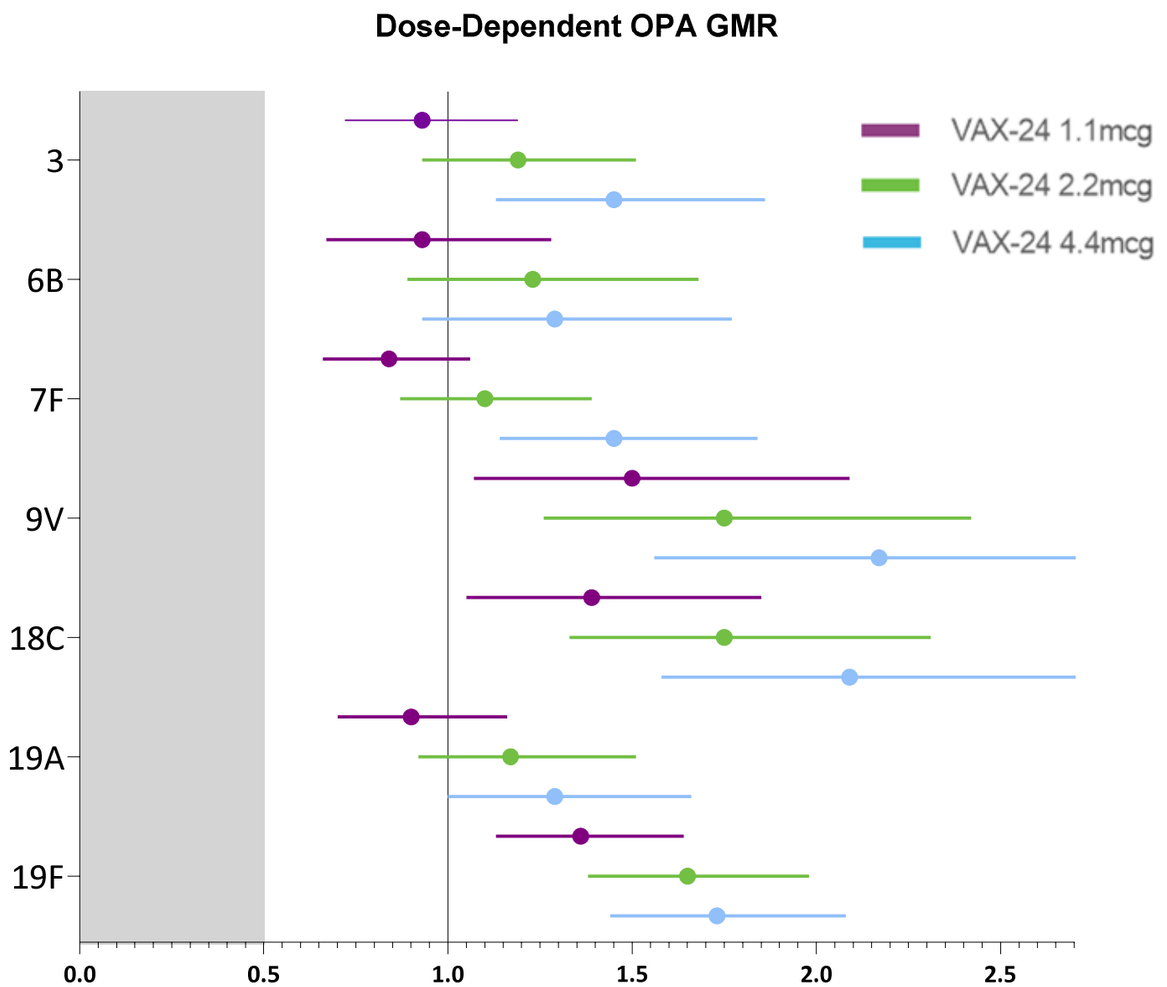


VAX-24 Mixed Dose (2.2mcg/4.4mcg)



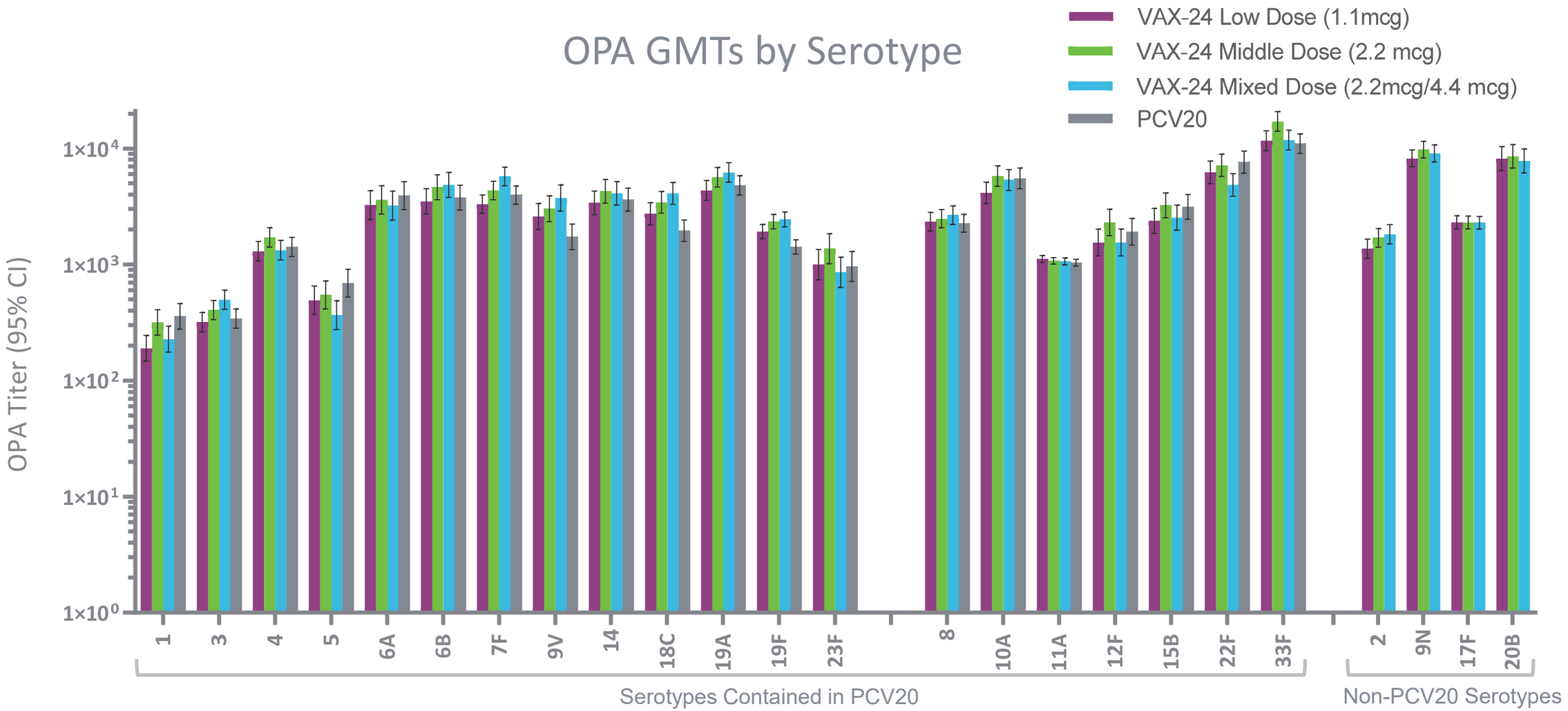
X = 7 VAX-24 serotypes at the 4.4mcg dose; GMR = Geometric Mean Ratio; LL= Lower Limit; CI = Confidence Interval

Strong Evidence of a Dose-Dependent Response for the 7 VAX-24 Serotypes Tested at 1.1mcg, 2.2mcg and 4.4mcg

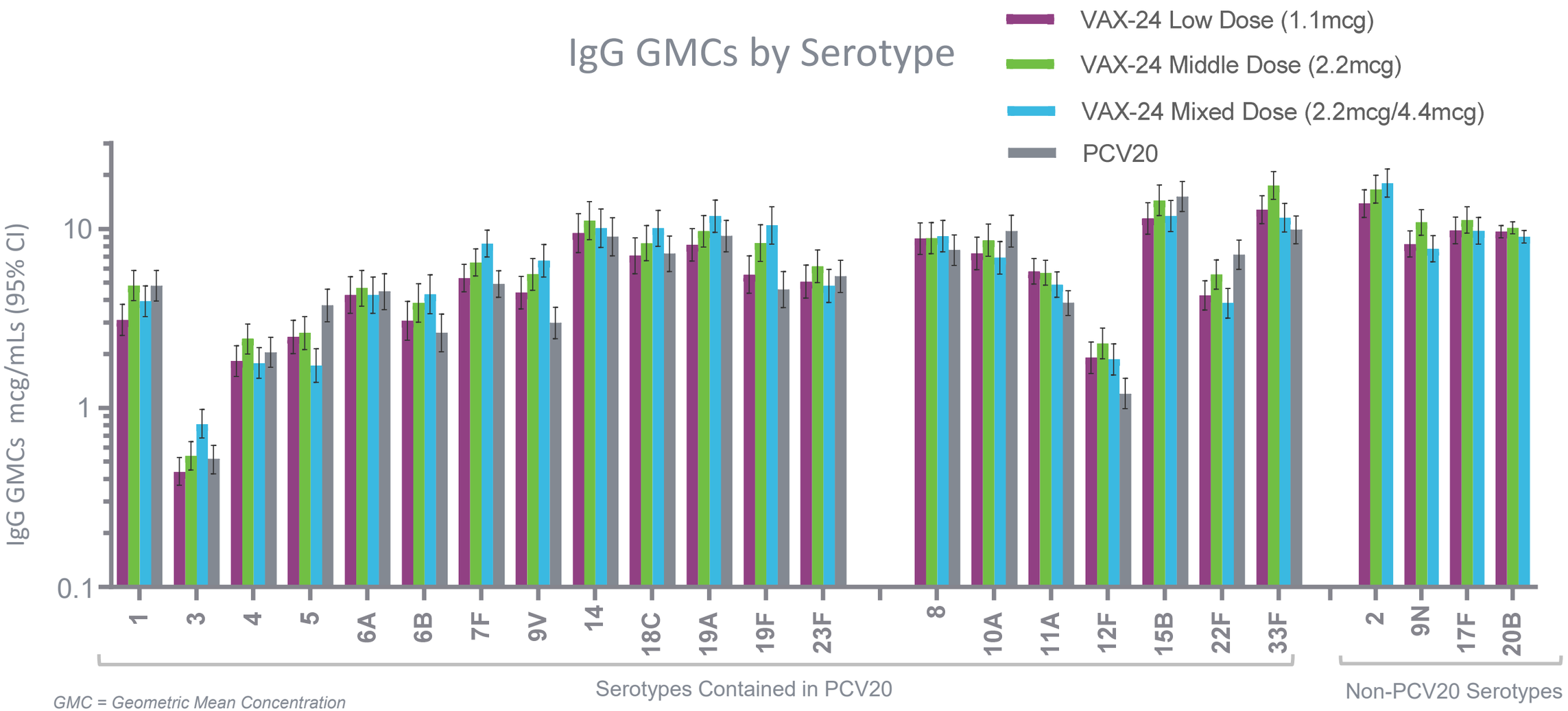


4.4mcg dose deemed not necessary as 2.2mcg dose demonstrated higher OPA GMRs for all 7 serotypes tested versus PCV20.

All 24 Serotypes in VAX-24 Demonstrated Robust OPA Immune Responses



All 24 Serotypes in VAX-24 Demonstrated Robust IgG Responses



GMC = Geometric Mean Concentration

Study Conclusions & Program Status

Study Conclusions

Supports Best-in-Class Potential for VAX-24 and Carrier-Sparing PCV Franchise

- VAX-24 demonstrated a safety and tolerability profile similar to PCV20 at all doses among 50-64 year olds
- Met or exceeded regulatory standard for all 24 serotypes (STs) for VAX-24 conventional 2.2mcg dose without the need to push dose higher
- Optimal 2.2mcg dose being advanced to Phase 3:
  - Met the standard OPA response non-inferiority criteria for all 20 STs common with PCV20, of which 16 achieved higher immune responses
  - Met the standard superiority criteria for all 4 additional STs unique to VAX-24
- Learnings inform optimal design for VAX-XP clinical program given ability to add STs without sacrificing overall immune responses

Vaxcyte PCV Franchise Leverages Established Regulatory Pathway

Well-Trodden Clinical Plan Aligned with Current FDA, EMA and WHO Guidance and Precedent PCVs

CURRENT FDA, EMA & WHO GUIDANCE AND PRECEDENT

- Well-defined established surrogate immune endpoints
- No anticipated requirement for field efficacy trials

- Licensure via non-inferior immune responses vs. SOC (1)
- Consistent with Merck (PCV15) & Pfizer (PCV20) BLAs(2)(3)

- Consistency across Ph 2 POC and Ph 3 pivotal studies for immune response in adult and infant programs (4)(5)(6)

(1) For adults: Lower limit of the 95% CI for the OPA GMR ≥0.5 for each serotype comparison. For infants: Lower limit of the 95% CI for the IgG GMC ratio post dose 4 is ≥0.5 and LL of the 95% CI for % of subjects achieving an IgG concentration ≥ 0.35 µg/mL 1 month after dose 3 is < -10%.
(2) Clinicaltrials.gov: Pfizer clinical studies for 20vPnC NCT03512288, NCT03550313, NCT03313050, NCT03313037, NCT03760146, NCT03835975, and NCT03828617.
(3) Clinicaltrials.gov: Merck clinical studies for V114 (PCV15) NCT02987972, NCT03620162, NCT03692871, NCT03731182, NCT03480763, NCT03615482, NCT03547167, NCT03480802, and NCT03565900.
(4) WHO. Recommendations to assure the quality, safety and efficacy of pneumococcal conjugate vaccines, in WHO Expert Committee on Biological Standardization, 60th report. Geneva, Switzerland: WHO; 2013:91-521.
(5) Prevenar 13 FDA Summary Basis for Regulatory Action. BLA/STN: 125324, 2010. ttps://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM206140.pdf. Accessed January 10, 2020.
(6) Guidelines on clinical evaluation of vaccines. EMEA/CHMP/VWP/164653/05, April 2018. https://www.ema.europa.eu/en/documents/scientific-guideline/draft-guideline-clinical-evaluation-vaccines-revision-1_en.pdf, Accessed Feb 11, 2020.

VAX-24 Program Anticipated Key Milestones

ADULT PROGRAM

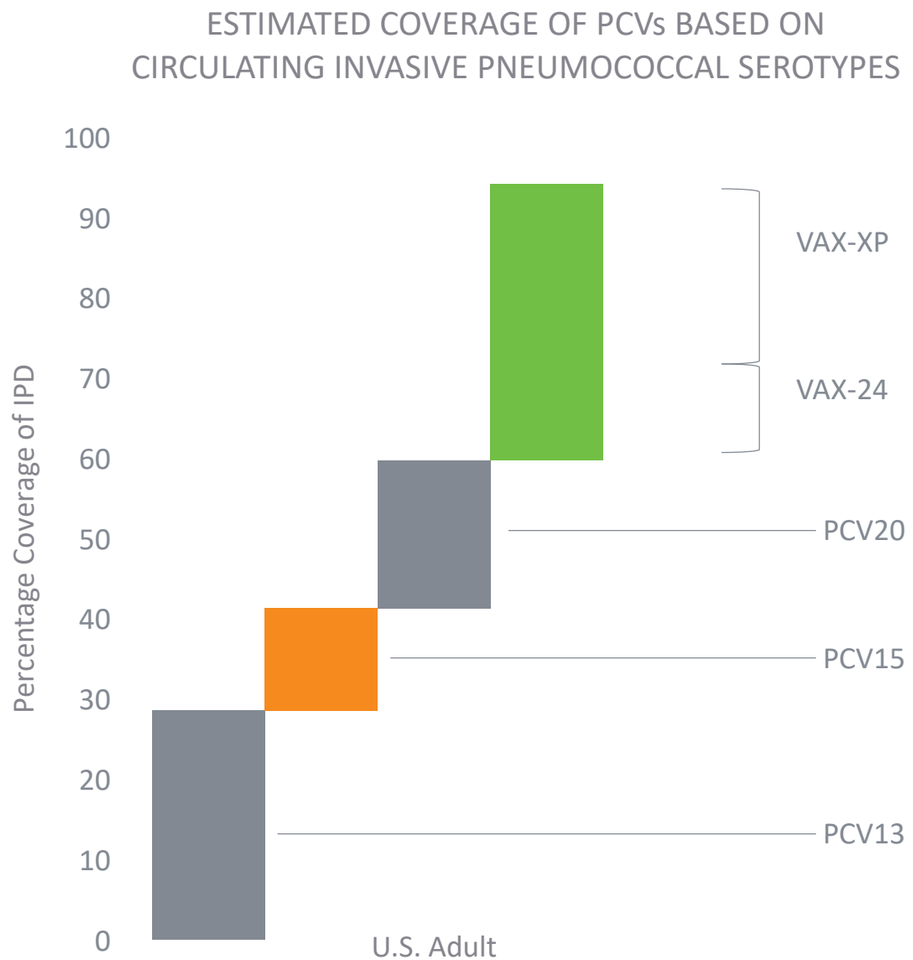
- Topline safety, tolerability and immunogenicity data from Phase 2 study in adults 65 and older anticipated in 1H:23
- Final results with 6-month safety data for both Phase 2 adult studies anticipated in 1H:23
- Regulatory interactions to inform Phase 3 program anticipated in 2H:23
- Topline data from Phase 3 non-inferiority study in adults expected in 2025

PEDIATRIC PROGRAM

- Infant IND submission and Phase 2 study initiation anticipated in 1H:23
- Topline data from infant primary 3-dose immunization series expected by 2025

Platform and Pipeline Update

Vaxcyte Carrier-Sparing PCV Franchise Positioned to Deliver Broadest Coverage

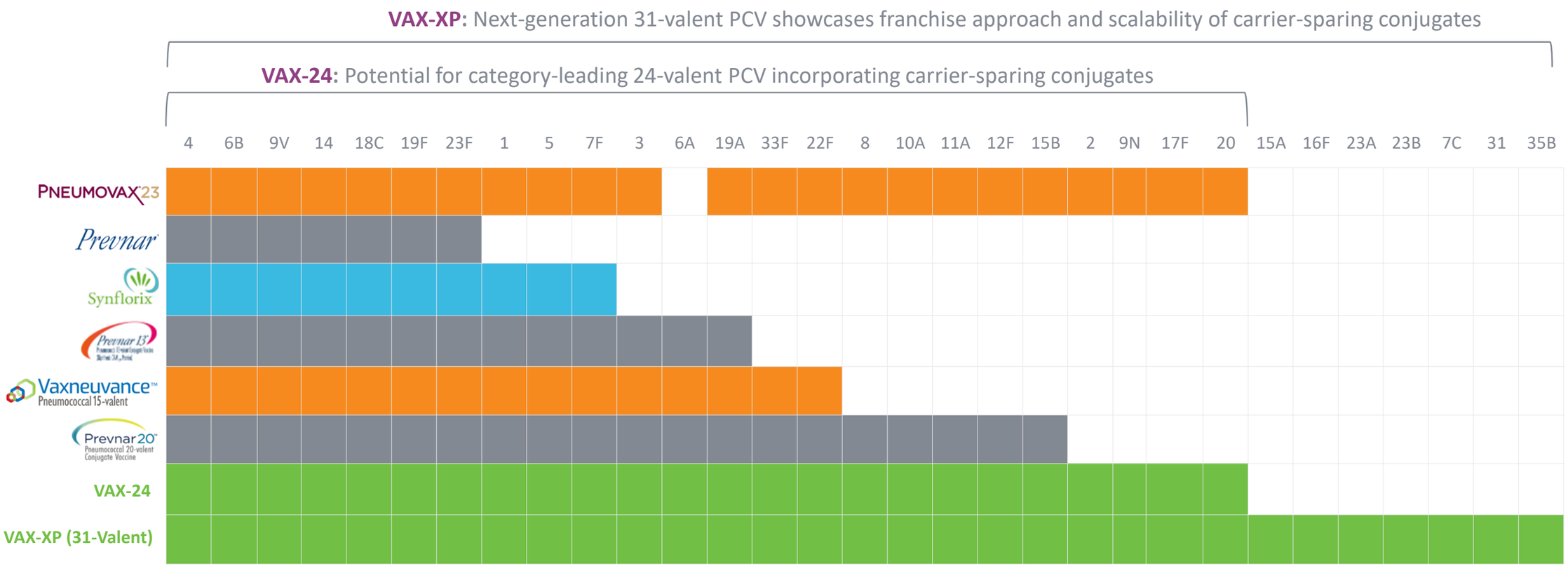


VAX-XP PROFILE AND ANTICIPATED MILESTONES

- Designed to provide coverage for ~95% of the pneumococcal disease currently circulating in the U.S. adult population
- Anticipate adult IND application submission to FDA in 2H:23
- Topline data in adults expected in 2024

(1) Data in the US is for 2017, inclusive of those > 5 yrs of age.
(2) Varghese et al. Clin Micro and Infect (2020) 26(4): 512.e1-512.e10.

Vaxcyte PCV Franchise has Potential for Sustained Leadership in Growing >$7B Pneumococcal Vaccine Market



Source: Prescribing information for Prevnar, Prevnar 13, Prevnar20, Synflorix, Vaxneuvance, and Prevnar 20. Company filings for Vaxcyte

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™