VAX-24 Phase 2 Program Results, Including Adult 65+ Data and Full Six-Month Safety Data from Both Studies

April 17, 2023

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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 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 submission of the IND application for VAX-31 and regulatory interactions and the availability of data for the VAX-24 adult, VAX-24 infant and VAX-31 studies); 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.

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Agenda

- **INTRODUCTION AND VAX-24 RESULTS OVERVIEW**
- **VAX-24 PHASE 2 STUDY RESULTS IN ADULTS AGED 65 AND OLDER (65+)**
  - Disposition and Demographics
  - Safety and Tolerability Data
  - Immunogenicity Data
- **PRESPECIFIED POOLED IMMUNOGENICITY ANALYSES OF BOTH PHASE 2 ADULT STUDIES**
- **FULL SIX-MONTH SAFETY DATA FROM BOTH ADULT STUDIES**
- **PROGRAM CONCLUSIONS, STATUS AND NEXT STEPS**

Introduction and VAX-24 Results Overview

Summary: VAX-24 Adult 65+ Study Results Confirm Prior Phase 2 Results

Positive Results Support Best-in-Class Potential for VAX-24 and Set Stage for Phase 3 Design and Advancement

SAFETY: Full six-month safety data from Phase 2 study in adults aged 65+ and prior Phase 1/2 study in adults aged 18-64 demonstrate VAX-24 safety and tolerability results similar to Prevnar 20® (PCV20) at all doses studied

IMMUNOGENICITY: 65+ study achieved target responses for all 24 serotypes at 2.2mcg dose, demonstrating potential of VAX-24 to expand coverage and improve immunogenicity over standard-of-care

- Phase 2 65+ study results (n~45/arm): VAX-24 met OPA response non-inferiority criteria for 18/20 STs common with PCV20 and met the superiority criteria for all four additional STs unique to VAX-24
- VAX-24 showed overall improvement in immune responses vs. PCV20 relative to results from Phase 2 in adults aged 50-64 and higher GMRs for 16/20 STs common with PCV20

VAX-24 WELL-POSITIONED FOR ADULT PHASE 3 PIVOTAL PROGRAM

- 2.2mcg confirmed as optimal VAX-24 dose to advance to Phase 3 pivotal study, which will include adults 50+ or 60+
- Prespecified pooled analyses of both Phase 2 adult studies for adults 50+ (n~225/group) and 60+ (n~100/group) met OPA response non-inferiority criteria for all 20 common STs and met superiority criteria for four additional STs unique to VAX-24
- End-of-Phase 2 meeting with FDA to confirm study size and population (anticipate n~750/arm)

PLATFORM: New data further support potential of our carrier-sparing PCV franchise and cell-free platform

ANTICIPATED PCV FRANCHISE MILESTONES:

- VAX-24 Adults: End-of-Phase 2 meeting with FDA 2H:23; Phase 3 pivotal immunogenicity data in 2025
- VAX-24 Infants: Phase 2 study enrolling subjects, topline data from the primary three-dose immunization series by 2025
- VAX-31 Adults: IND application submission 2H:23; topline data from Phase 1/2 study in 2024

OPA = Opsonophagocytic Activity; STs = serotypes; GMR = Geometric Mean Ratio

Global Impact of Pneumococcal Disease Remains Significant

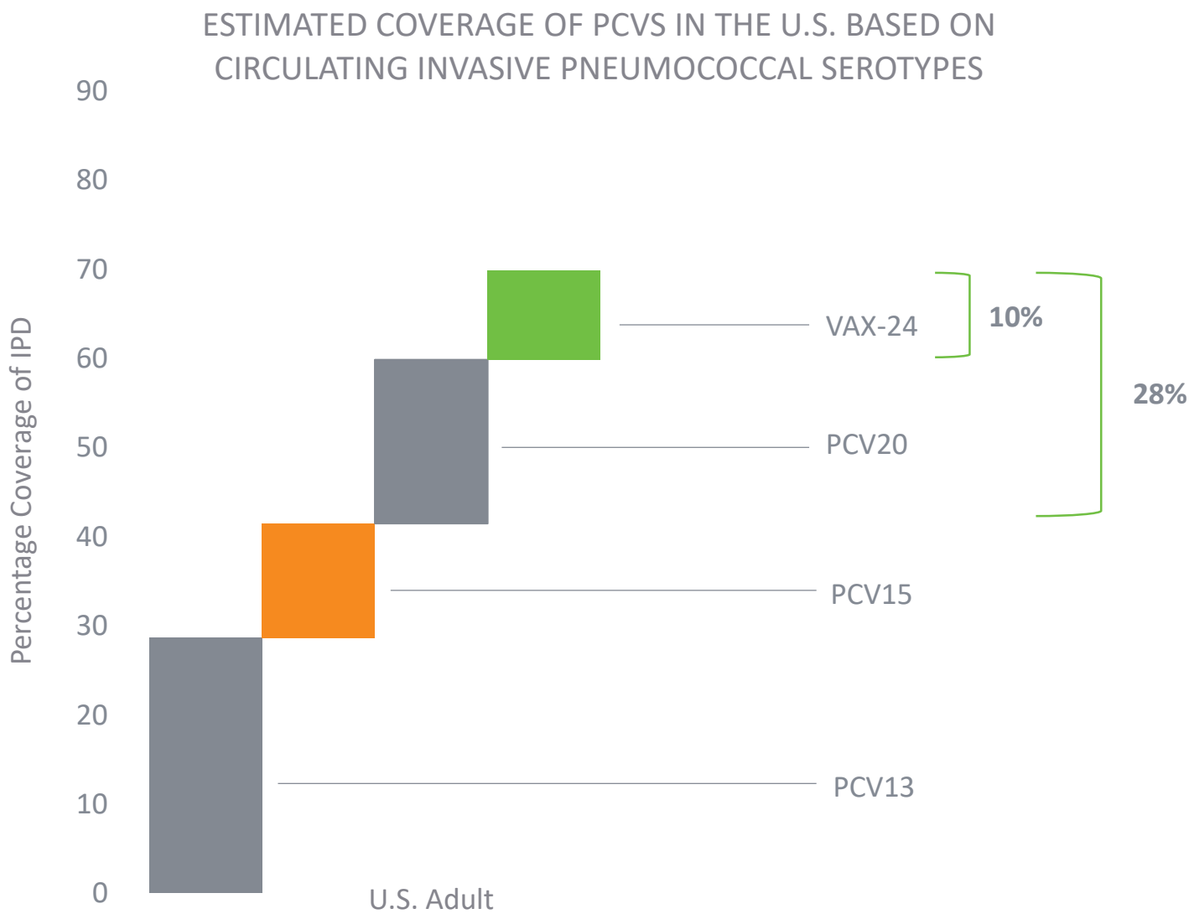
Circulating Disease Driven by Serotypes Outside of Current PCVs

- *Streptococcus pneumoniae* is the most common pathogen causing pneumococcal disease (PD).
  - In the U.S. alone, there are ~320K pneumococcal pneumonia cases per year resulting in ~150K hospitalizations.
  - Invasive pneumococcal disease (IPD) is a leading cause of invasive disease in children two years of age and under.
- Circulating strains of PD in the U.S. and globally are associated with high case-fatality rates, antibiotic resistance and/or meningitis.

Gierke 2015
https://www.cdc.gov/pneumococcal/clinicians/clinical-features.html

Spectrum of Coverage Drives Adoption in PCV Segment

Significant Unmet Needs Remain Despite Available Vaccines



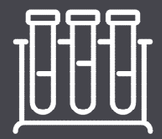
VAX-24 TARGET PRODUCT PROFILE

- Designed to provide broadest coverage of any currently approved PCV, including an incremental 10-28% coverage of IPD in U.S. adults vs. the SOC PCVs (PCV20/PCV15) today.
- Designed to provide the benefits of a conjugate vaccine while surpassing 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.
PCV13 = Prevnar 13®, PCV15 = VAXNEUVANCE™

Carrier-Sparing Approach for PCV Franchise Validated By Phase 2 Program

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



LIMITATIONS OF CONVENTIONAL CONJUGATION CHEMISTRY

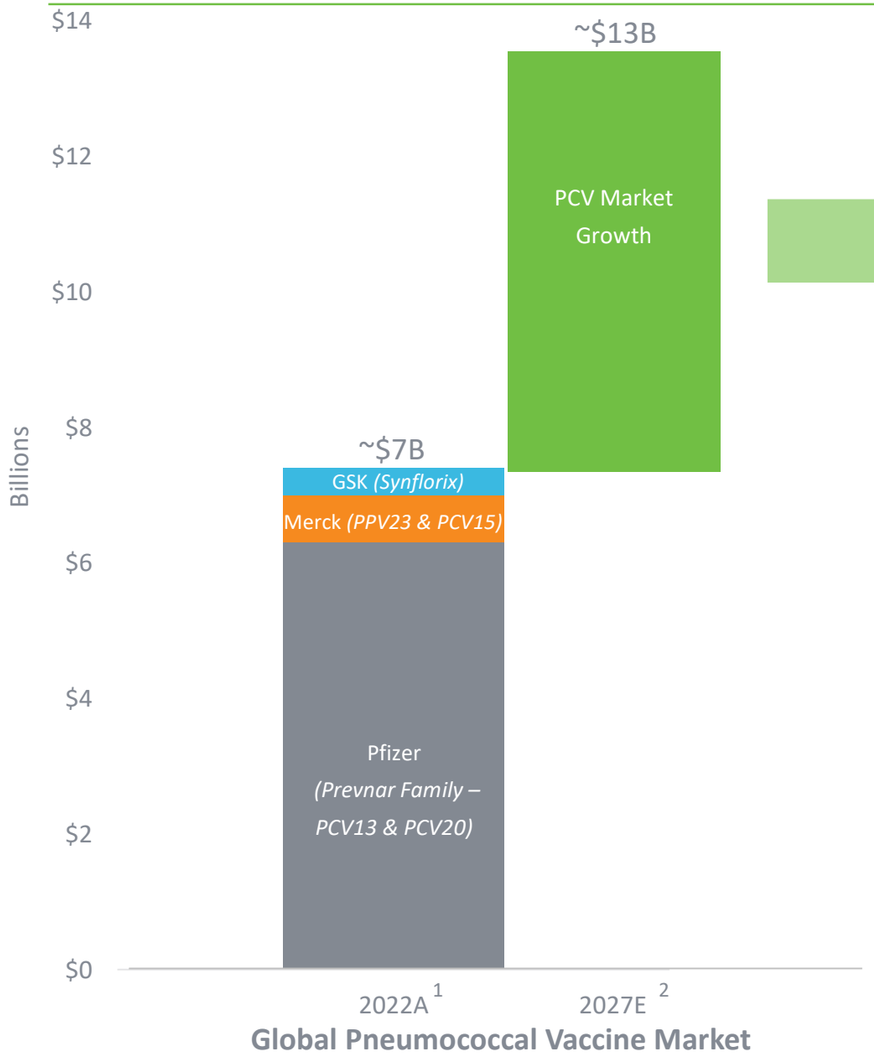
- Random conjugation masks “on-target” T-cell epitopes on the protein carrier
- Higher ratio of protein carrier to polysaccharide required
- Overabundance of protein carrier and its “off-target” effects exacerbates competition for CD4+ T-cell leading to carrier suppression

VAXCYTE’S UNIQUE CARRIER-SPARING CONJUGATE VACCINES

- Site-specifically attach conventional antigens and protein carriers designed 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

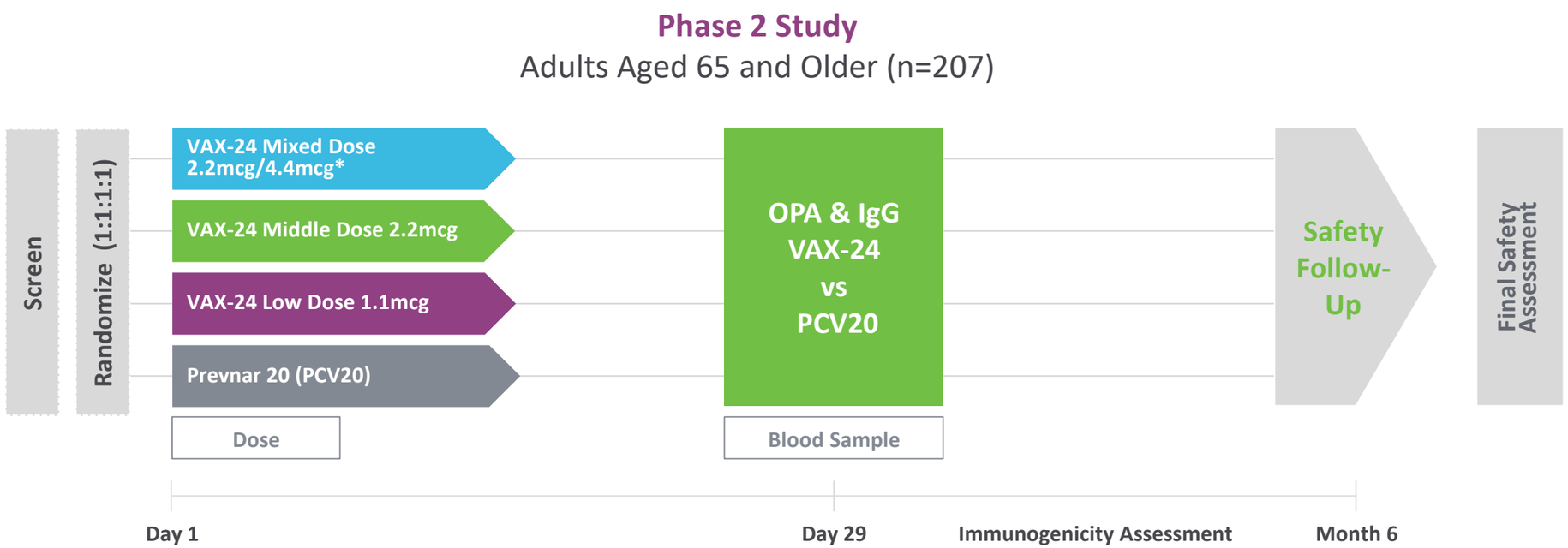
(1) Sources: Company websites; includes Merck's PCV15 sales disclosed for Q4 2022.
(2) Global Pneumococcal Vaccine Market (2022-2027), Infogence Global Research.
(3) Shea KM, Edelsberg J, Weycker D et al. (2014), Open Forum Infect Dis 1(1): ofu024.
ACIP = Advisory Committee on Immunization Practices

VAX-24 Phase 2 Study in Adults 65+

Study Design

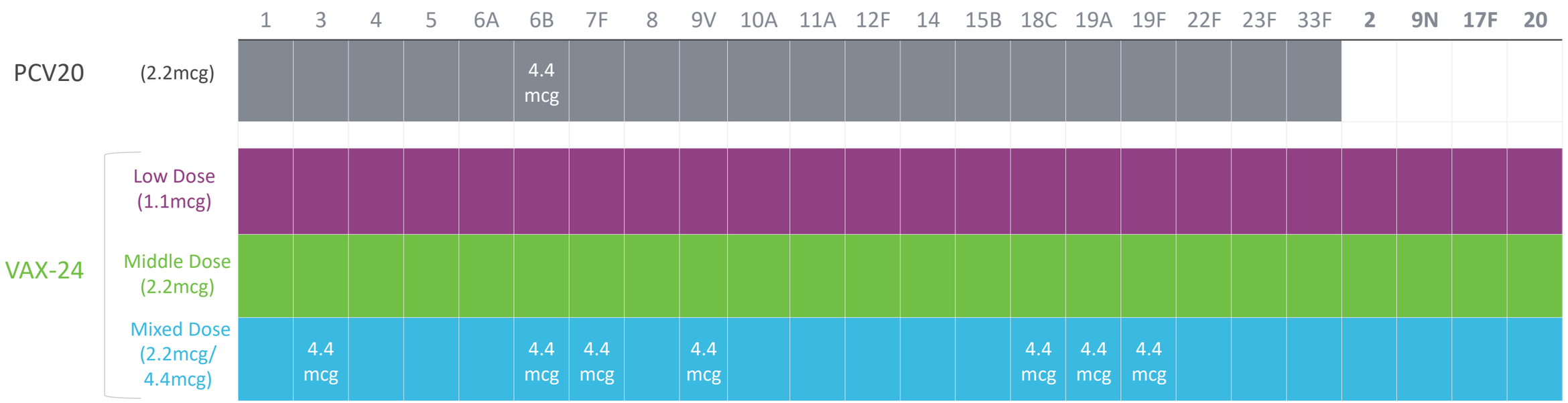
Overview of VAX-24 Phase 2 Clinical Study in Adults 65+

Design: Randomized, Observer-Blind, Dose-Finding, Controlled Clinical Study to Evaluate Safety, Tolerability & Immunogenicity of VAX-24 vs. Standard-of-Care (PCV20) in Healthy Adults Aged 65 and Older



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

Study Evaluated Three VAX-24 Doses Consistent with Prior Phase 2 Study



- 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.

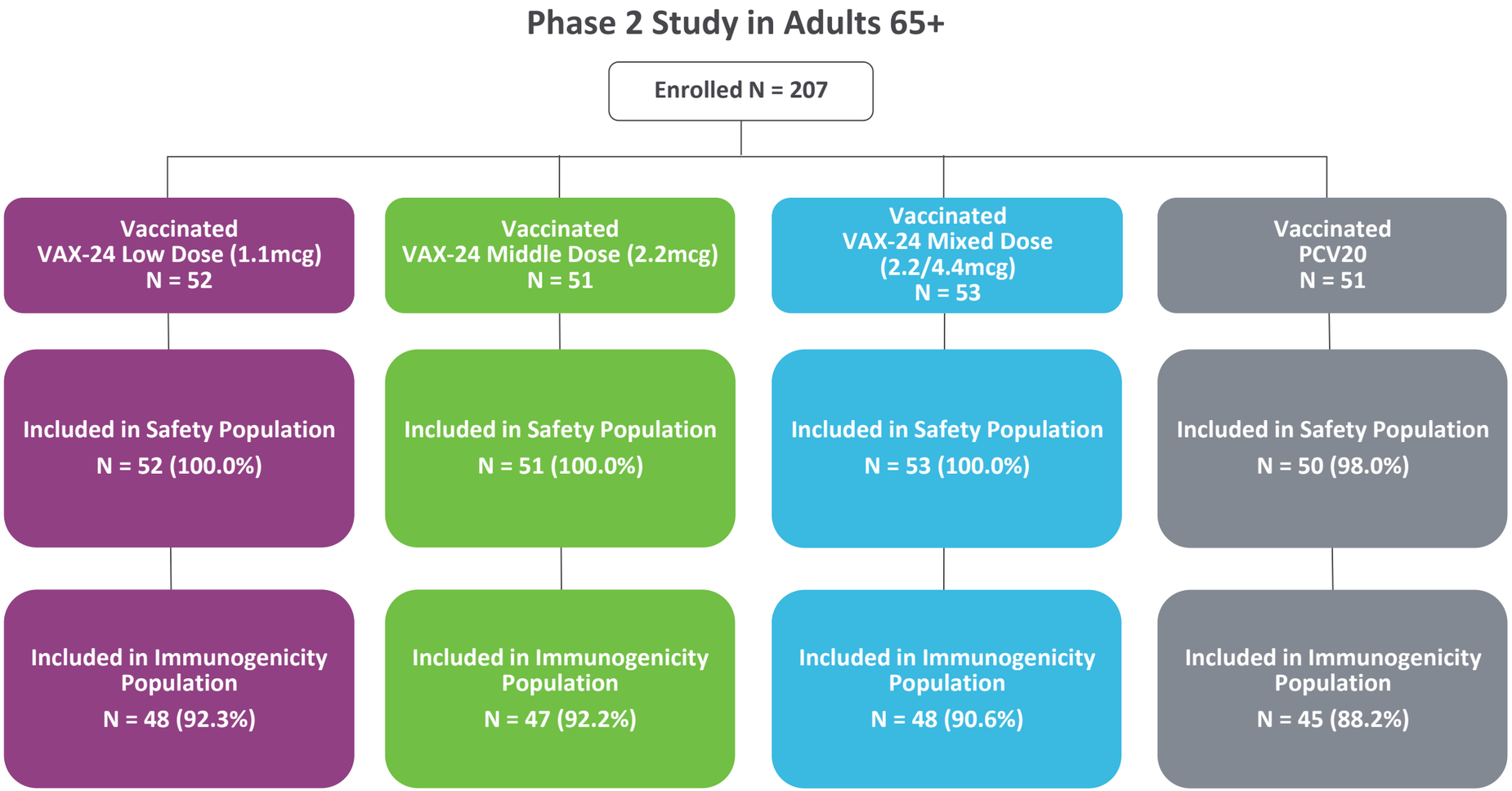
Study Safety, Tolerability and Immunogenicity Key Outcome Measures

	DAY 7	DAY 29	DAY 180
SAFETY AND TOLERABILITY OUTCOME MEASURES	• Solicited local reactions • Solicited systemic events	• Unsolicited adverse events (AE) • Serious adverse events (SAE)	• SAE, new onset of chronic illnesses (NOCI) and medically attended adverse events (MAAE)
IMMUNOGENICITY OUTCOME MEASURES		• Opsonophagocytic assay (OPA) geometric mean titer (GMT) • IgG geometric mean concentration (GMC) • % of subjects achieving a 4-fold rise in OPA • Geometric Mean Ratios (GMR) in serotype-specific OPA	

Disposition and Demographics

Study Disposition

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



7 Subjects (3.4%) Discontinued

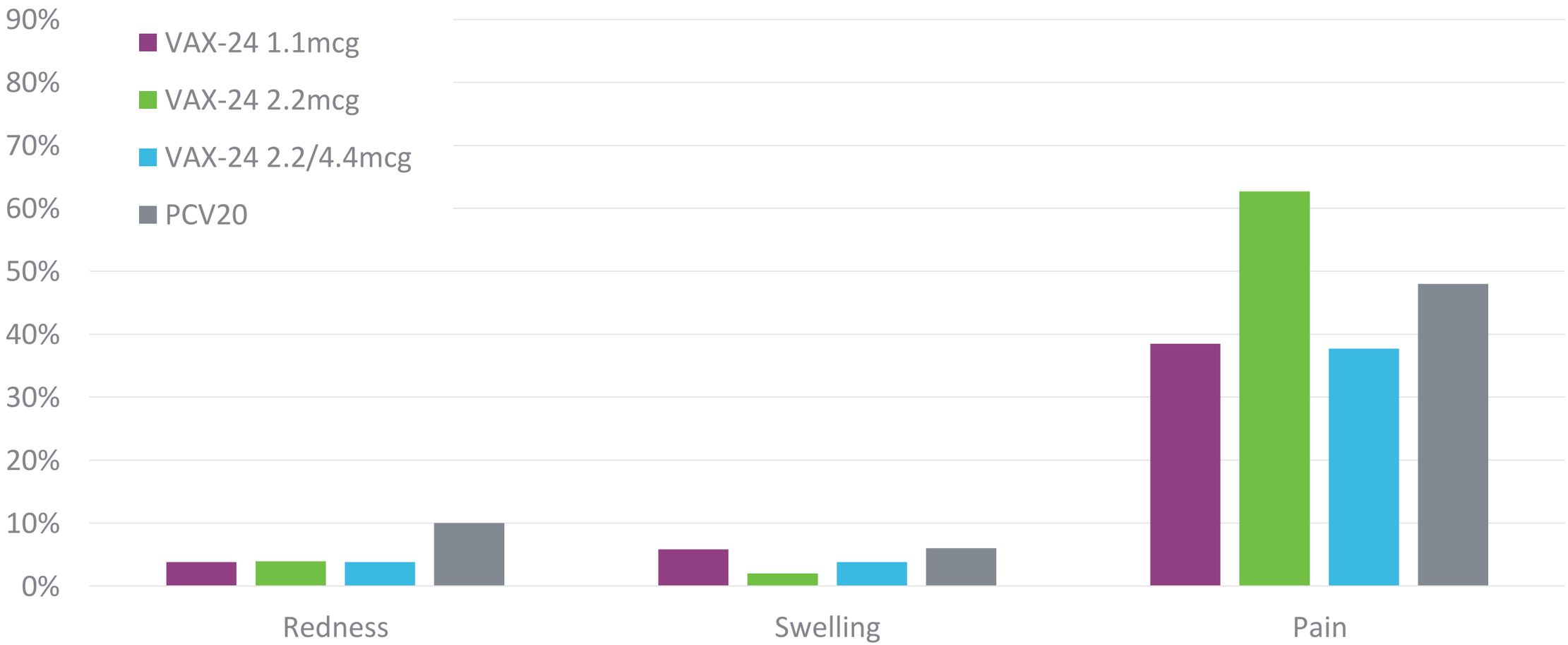
Demographic Population

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

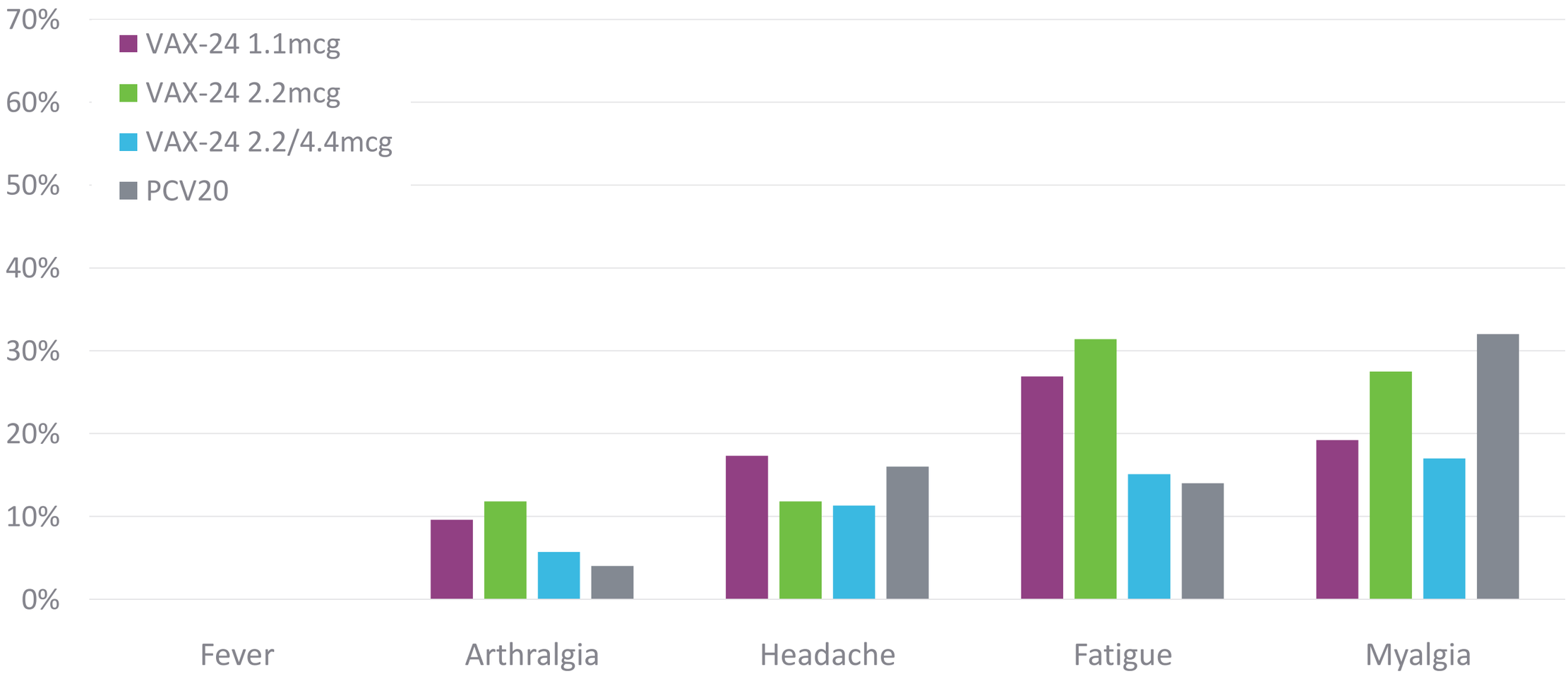
	VAX-24 Low Dose (1.1mcg)		VAX-24 Middle Dose (2.2mcg)		VAX-24 Mixed Dose (2.2mcg/4.4mcg)		PCV20	
	Safety	Immunogenicity	Safety	Immunogenicity	Safety	Immunogenicity	Safety	Immunogenicity
Number of Subjects	52	48	51	47	53	48	50	45
Median Age, Years (range)	67.5 (65-80)	67.5 (65-80)	66.0 (65-79)	66.0 (65-79)	67.0 (65-88)	67.0 (65-88)	67.0 (65-80)	67.0 (65-80)
Sex, n (%) Female	38 (73.1)	35 (72.9)	34 (66.7)	32 (68.1)	37 (69.8)	33 (68.8)	30 (60.0)	27 (60.0)
Male	14 (26.9)	13 (27.1)	17 (33.3)	15 (31.9)	16 (30.2)	15 (31.3)	20 (40.0)	18 (40.0)
Race, n (%) White	44 (84.6)	40 (83.3)	40 (78.4)	37 (78.7)	38 (71.7)	33 (68.8)	35 (70.0)	31 (68.9)
Black	7 (13.5)	7 (14.6)	10 (19.6)	9 (19.1)	14 (26.4)	14 (29.2)	14 (28.0)	13 (28.9)
Asian	0 (0)	0 (0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Native Hawaiian	0 (0)	0 (0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
American Indian or Native Alaskan	1 (1.9)	1 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0)	0 (0)	1 (2.0)	1 (2.1)	1 (1.9)	1 (2.1)	0 (0.0)	0 (0.0)
Multiracial	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.0)	1 (2.2)
Median Height, cm (range)	165.5 (146-183)	165.5 (146-183)	166.6 (151-194)	166.6 (151-194)	167.6 (145-188)	167.6 (145-188)	166.5 (150-185)	166.6 (150-185)
Median Weight, kg (range)	75.05 (50.6-161.9)	74.91 (50.6-161.9)	80.01 (48.5-150.0)	80.70 (48.5-150.0)	86.32 (53.5-130.2)	85.35 (53.5-130.2)	81.33 (47.7-147.4)	81.65 (47.7-147.4)
Median BMI, kg/m^2 (range)	27.42 (20.4-50.7)	27.36 (20.4-50.7)	28.92 (19.9-49.2)	29.04 (19.9-49.1)	29.64 (20.1-44.9)	28.99 (20.1-44.9)	29.38 (17.6-52.5)	29.77 (17.6-52.5)

Safety and Tolerability Data

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



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



Immunogenicity Data

Precedent Regulatory Criteria for Phase 2/3 PCV Immunogenicity Studies

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

Non-inferiority:

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

Superiority:

- Lower bound of 2-sided 95% CI of the OPA GMR 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 FOUR INCREMENTAL SEROTYPES IN VAX-24:

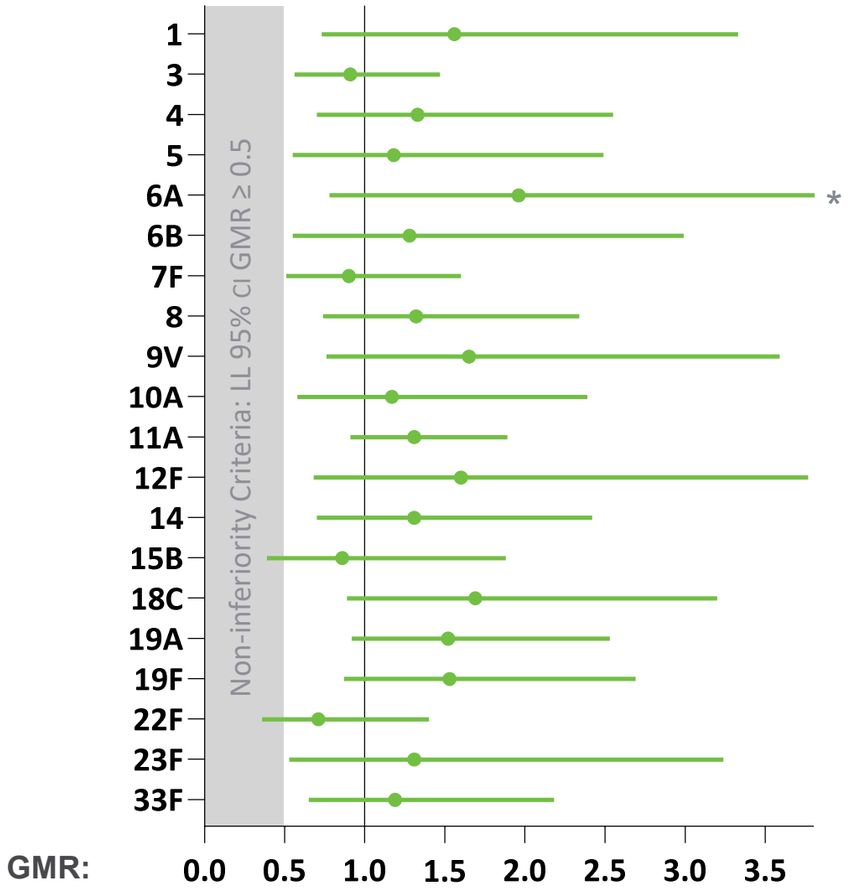
Superiority:

- 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 Day 29 is greater than 10%
- Lower bound of the 2-sided 95% CI of the OPA GMR is greater than 2.0

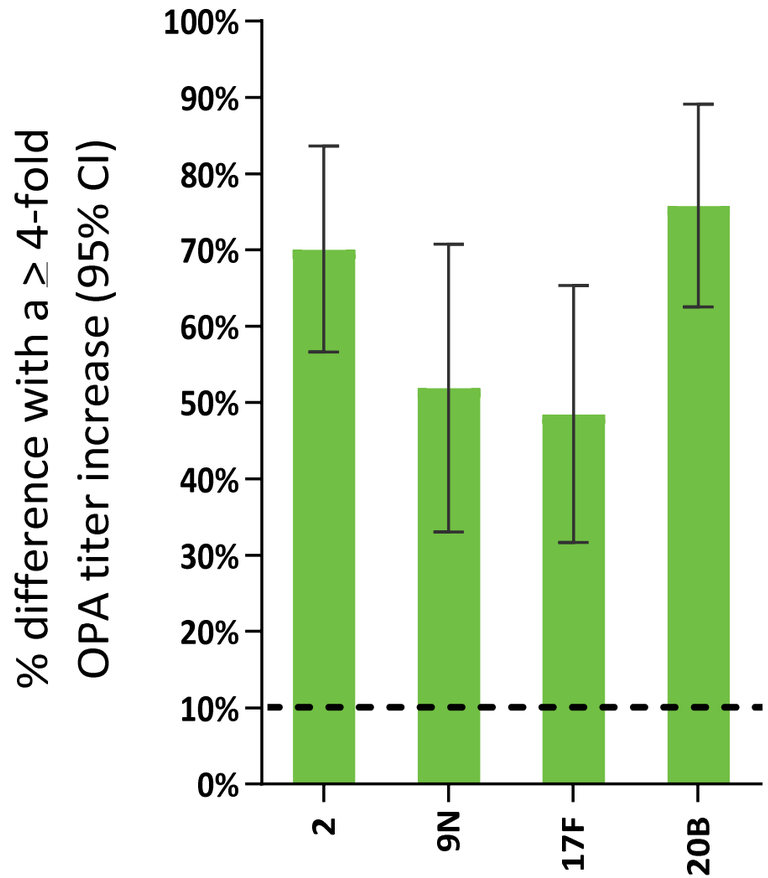
CI = confidence interval

VAX-24 2.2mcg Dose Showed Robust Immune Responses for All 24 Serotypes

Met non-inferiority criteria for 18 of 20 common STs for the OPA GMR of VAX-24 : PCV20 (n~45)



Met superiority criteria for all four incremental STs in VAX-24 based on 4-fold rise vs. PCV20 (n~45)

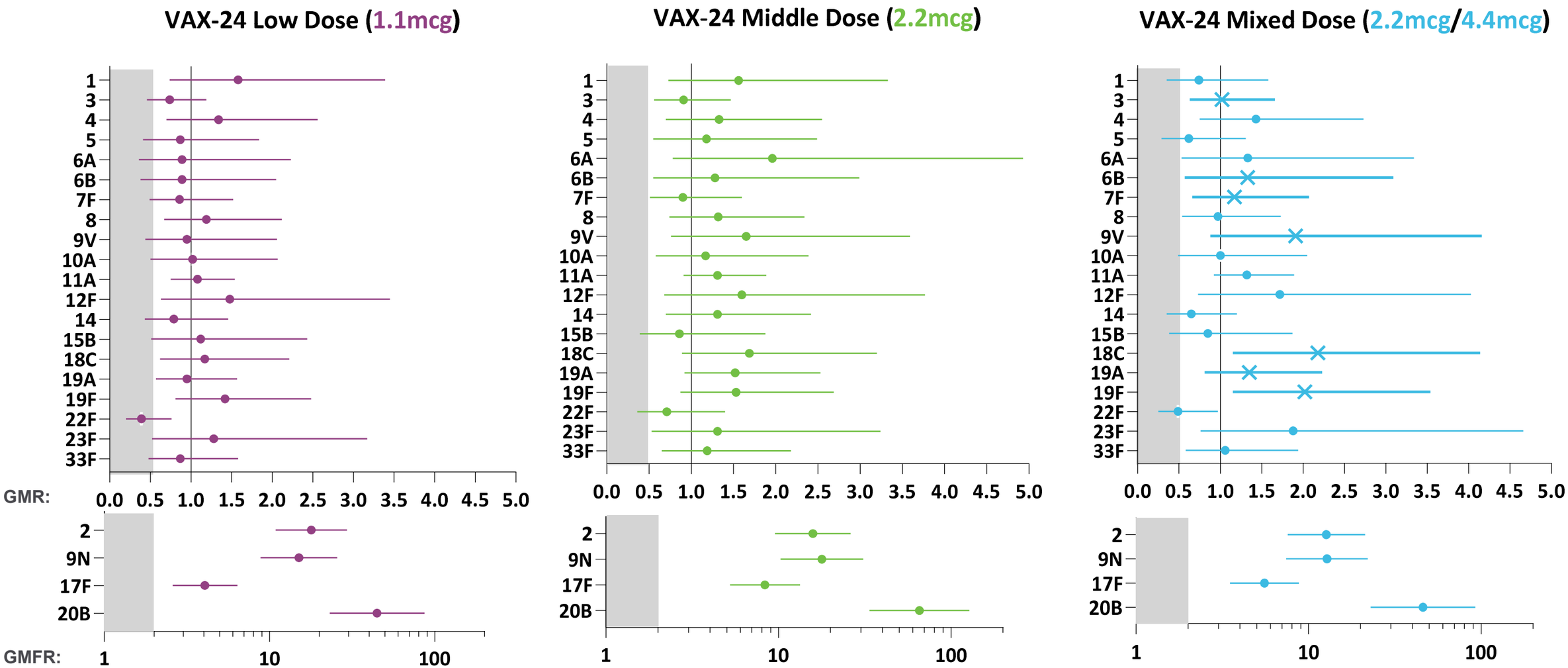


Threshold for Superiority (LL95%CI > 10%)

* *Upper Limit = 4.93; sample size of 45 calculated as median between immunogenicity evaluable VAX-24 n=47 and PCV20 n=45 rounded to nearest 5.*

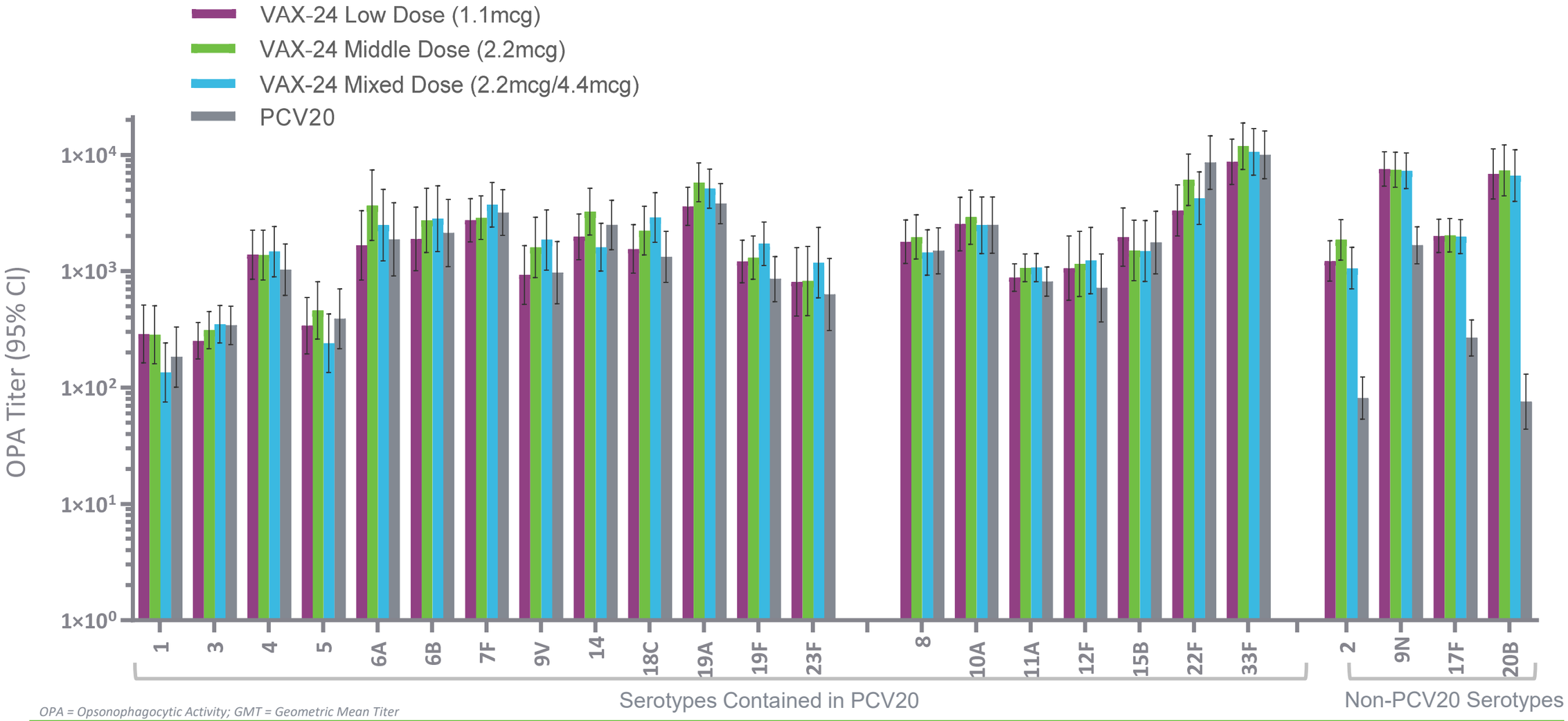
65+ Study Results Confirm 2.2mcg is Optimal Dose to Advance to Phase 3

Consistent with Prior Phase 2 Study, 2.2mcg Dose Demonstrated Higher OPA GMR for 16/20 Shared STs



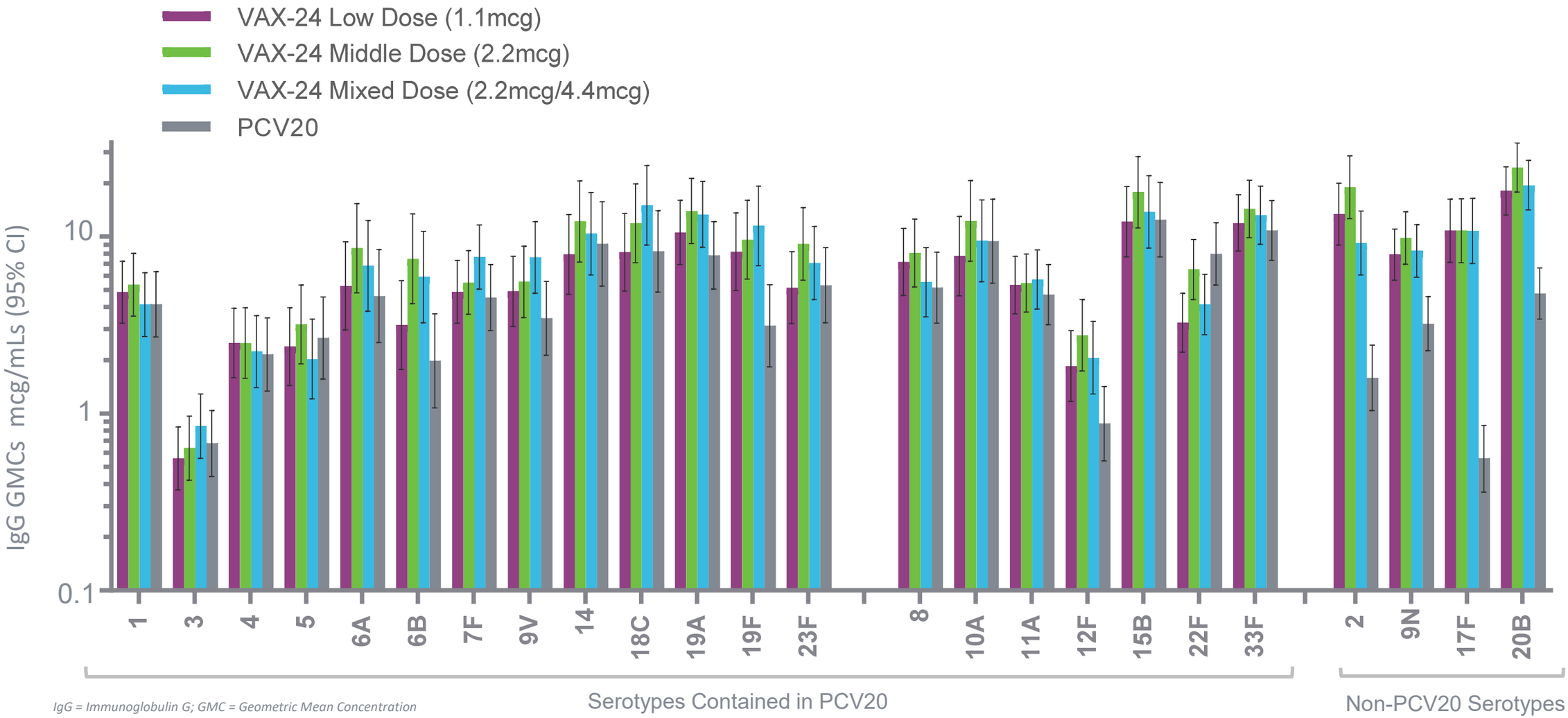
X = 7 VAX-24 serotypes at the 4.4mcg dose; GMR = Geometric Mean Ratio; GMFR = Geometric Mean Fold Ratio

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



OPA = Opsonophagocytic Activity; GMT = Geometric Mean Titer

All 24 Serotypes in VAX-24 Demonstrated Robust IgG GMC Responses



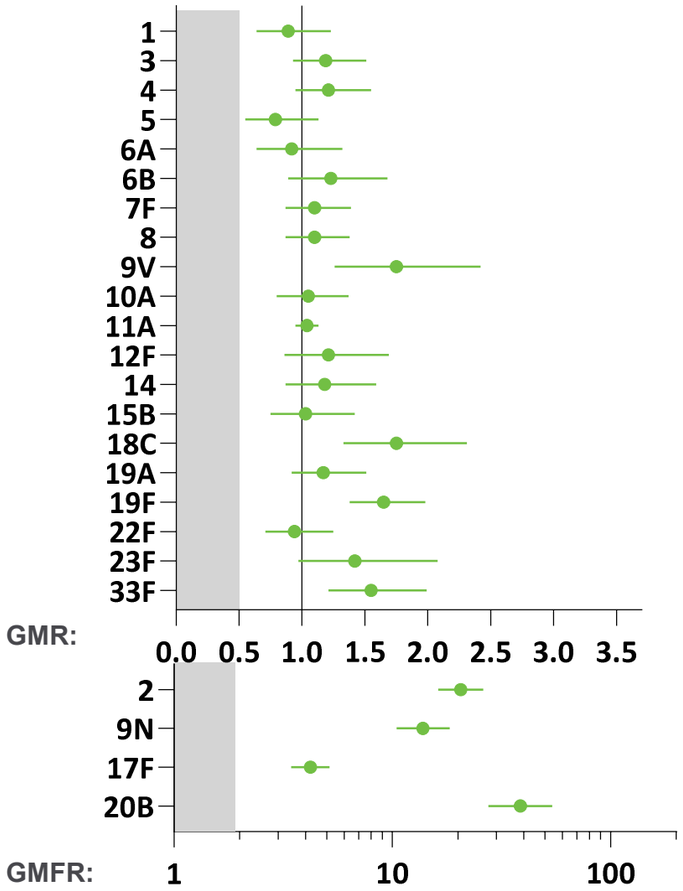
IgG = Immunoglobulin G; GMC = Geometric Mean Concentration

Prespecified Pooled Immunogenicity Analyses of Both VAX-24 Phase 2 Adult Studies

Phase 2 Program Confirms 2.2mcg as Optimal Dose in Adult Population

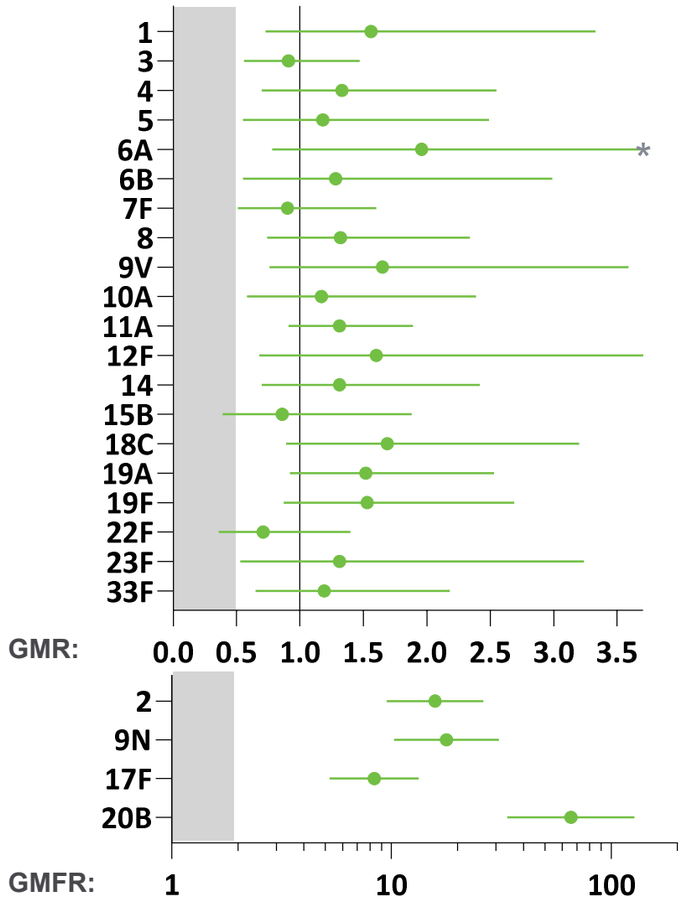
65+ Study Data Show Further Improvement in Overall Immune Response vs. PCV20

VAX-24 Phase 2 Study in Adults Aged 50-64
2.2mcg (n~180)



ST	GMR	95%CI	
1	0.89	1.23	0.64
3	1.19	1.51	0.93
4	1.21	1.55	0.95
5	0.79	1.13	0.55
6A	0.92	1.32	0.64
6B	1.23	1.68	0.89
7F	1.1	1.39	0.87
8	1.1	1.38	0.87
9V	1.75	2.42	1.26
10A	1.05	1.37	0.8
11A	1.04	1.13	0.95
12F	1.21	1.69	0.86
14	1.18	1.59	0.87
15B	1.03	1.42	0.75
18C	1.75	2.31	1.33
19A	1.17	1.51	0.92
19F	1.65	1.98	1.38
22F	0.94	1.25	0.71
23F	1.42	2.08	0.97
33F	1.55	1.99	1.21

VAX-24 Phase 2 Study in Adults Aged 65+
2.2mcg (n~45)



ST	GMR	95%CI	
1	1.56	3.33	0.73
3	0.91	1.47	0.56
4	1.33	2.55	0.70
5	1.18	2.49	0.55
6A	1.96	4.93	0.78
6B	1.28	2.99	0.55
7F	0.90	1.60	0.51
8	1.32	2.34	0.74
9V	1.65	3.59	0.76
10A	1.17	2.39	0.58
11A	1.31	1.89	0.91
12F	1.6	3.77	0.68
14	1.31	2.42	0.70
15B	0.86	1.88	0.39
18C	1.69	3.20	0.89
19A	1.52	2.53	0.92
19F	1.53	2.69	0.87
22F	0.71	1.40	0.36
23F	1.31	3.24	0.53
33F	1.19	2.18	0.65

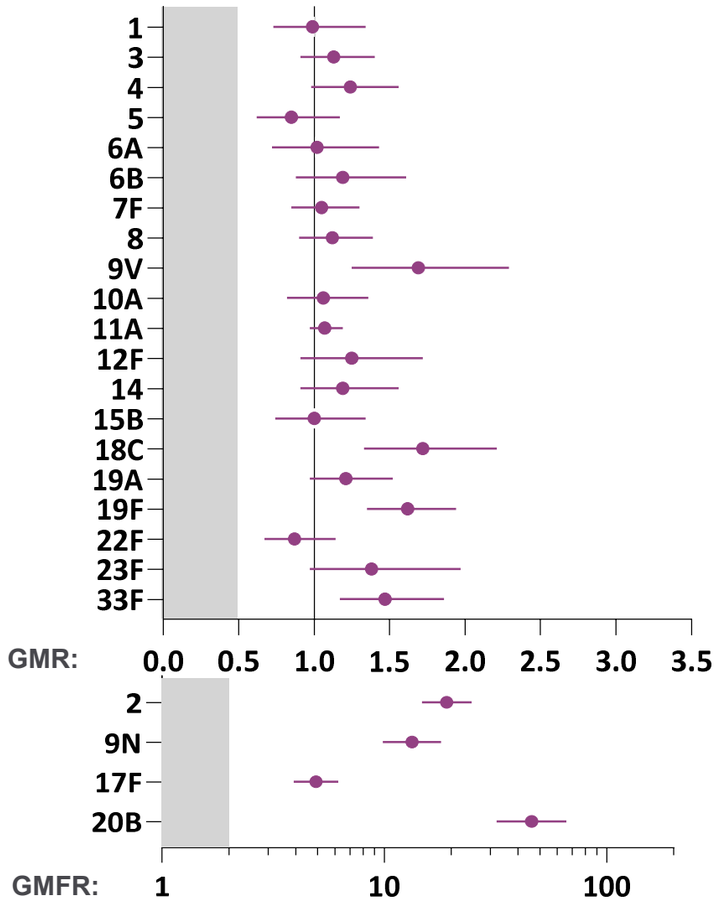
VAXCYTE

* *Upper Limit = 4.93; sample size of 180 calculated as median between immunogenicity evaluable VAX-24 n=179 and PCV20 n=181 rounded to nearest 10.*

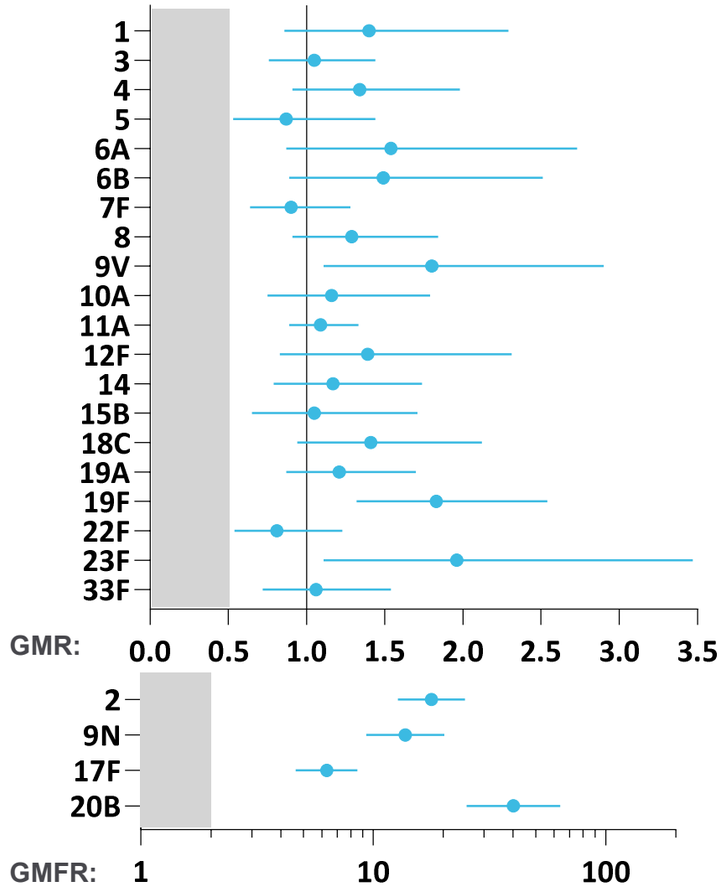
Prespecified Pooled Analyses Support Advancement of VAX-24 to Phase 3

Met Standard OPA Response Non-Inferiority Criteria for All 20 Common STs

Prespecified Pooled Data From VAX-24 2.2mcg Phase 2 Studies in Adults Aged 50+ (n~225)



Prespecified Pooled Data From VAX-24 2.2mcg Phase 2 Studies in Adults Aged 60+ (n~100)



Sample size of ~225 calculated as median between immunogenicity evaluable VAX-24 n=228 and PCV20 n=224 rounded to nearest 5 for 50+ and ~100 calculated as median between immunogenicity evaluable VAX-24 n=101 and PCV20 n=104 rounded to nearest 5 for 60+.

Full Six-Month Safety and Tolerability Data from Both VAX-24 Adult Studies

Six-Month Safety Data from VAX-24 Phase 2 Study in Adults Aged 65+

Safety Results 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 with	52	51	53	50
Unsolicited TEAE, n (%)	6 (11.5)	4 (7.8)	4 (7.5)	8 (16.0)
Related Unsolicited TEAE, n (%)	1 (1.9)	4 (7.8)	2 (3.7)	5 (10.0)
MAAE, n (%)	5 (9.6)	3 (5.9)	3 (5.7)	6 (12.0)
Related MAAE, n (%)	0	0	1 (1.9)	0
NOCI, n (%)	1 (1.9)	1 (2.0)	1 (1.9)	0
Related NOCI, n (%)	0	0	0	0
SAE, n (%)	1 (1.9)	1 (2.0)	1 (1.9)	0
Related SAE, n (%)	0	0	0	0
Death, n (%)	0	1 (2.0)[1]	0	0
Related Death, n (%)	0	0	0	0

(1) 66-year-old white, obese male (BMI:47.4) with hypertension. No solicited AEs were reported after vaccination. Participant suffered sudden cardiac death six months post-vaccination determined by Principal Investigator to be not related to study product due to participant's history of hypertensive cardiovascular disease.

TEAE = Treatment emergent adverse events

Excludes Solicited AEs

Six-Month Safety Data from VAX-24 Phase 1/2 Study in Adults Aged 18-64

Safety Results 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 with	209	207	207	212
Unsolicited TEAE, n (%)	32 (15.3)	24 (11.6)	26 (12.6)	34 (16.0)
Related Unsolicited TEAE, n (%)	4 (1.9)	9 (4.3)	5 (2.4)	8 (3.8)
MAAE, n (%)	27 (12.9)	26 (12.6)	24 (11.6)	31 (14.6)
Related MAAE, n (%)	0	0	0	0
NOCI, n (%)	3 (1.4)	3 (1.4)	6 (2.9)	5 (2.4)
Related NOCI, n (%)	0	0	0	0
SAE, n (%)	2 (1.0)	3 (1.4)	1 (0.5)	4 (1.9)
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
Excludes Solicited AEs

Combined Six-Month Safety Data from Both Adult VAX-24 Studies

Safety Results 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 with	261	258	260	262
Unsolicited TEAE, n (%)	38 (14.6)	28 (10.9)	30 (11.5)	42 (16.0)
Related Unsolicited TEAE, n (%)	5 (1.9)	13 (5.0)	7 (2.7)	13 (5.0)
MAAE, n (%)	32 (12.2)	29 (11.2)	27 (10.4)	37 (14.1)
Related MAAE, n (%)	0	0	1 (0.4)	0
NOCI, n (%)	4 (1.5)	4 (1.6)	7 (2.7)	5 (1.9)
Related NOCI, n (%)	0	0	0	0
SAE, n (%)	3 (1.1)	4 (1.6)	2 (0.77)	4 (1.5)
Related SAE, n (%)	0	0	0	0
Death, n (%)	0	1 (0.39)[1]	0	0
Related Death, n (%)	0	0	0	0

(1) 66-year-old white, obese male (BMI:47.4) with hypertension. No solicited AEs were reported after vaccination. Participant suffered sudden cardiac death six months post-vaccination determined by Principal Investigator to be not related to study product due to participant's history of hypertensive cardiovascular disease.

TEAE = Treatment emergent adverse events

Excludes Solicited AEs

Phase 2 Program Conclusions, Status & Next Steps

Positive Phase 2 Program Results Support Best-in-Class Potential for VAX-24 and Set Stage for Phase 3 Program

SUCCESSFUL VAX-24 PHASE 2 PROGRAM MET ALL KEY OBJECTIVES

- Full six-month VAX-24 data (n=779) showed safety and tolerability results similar to PCV20
- Improved immunogenicity vs. PCV20 with no evidence of dose-dependent safety and tolerability issues
- Confirmed 2.2mcg as optimal dose to advance to Phase 3 pivotal study
  - Achieved target immune responses for all 24 serotypes in both Phase 2 studies
  - Met non-inferiority criteria for all 24 STs in prespecified pooled analyses, with sample sizes expected to increase in Phase 3 program (n~750/arm)

WELL-POSITIONED FOR PHASE 3 PIVOTAL PROGRAM

- Well-established regulatory pathway, with multiple precedents of approval based on surrogate immune endpoints
- Historically, consistent study design and endpoints across Phase 2 and pivotal Phase 3 programs
- Precedent Phase 3 programs and VAX-24 Phase 2 data support flexibility of choice in ultimate adult age range for pivotal study
- With positive Phase 2 data, Vaxcyte is excited to advance VAX-24 into Phase 3

Anticipated PCV Franchise Milestones for 2023-2025[1]

Vaxcyte is Advancing Clinical Development of VAX-24 and VAX-31 with Several Key Upcoming Milestones

VAX-24 Adult

- Conduct FDA End-of-Phase 2 meeting to finalize adult Phase 3 program in **2H:23**
- Announce topline safety, tolerability and immunogenicity data from the Phase 3 pivotal non-inferiority study in adults in **2025**

VAX-24 Infant

- Announce topline safety, tolerability and immunogenicity data from the primary three-dose immunization series of the Phase 2 study by **2025**

VAX-31 Adult

- Submit adult IND application to FDA in **2H:23**
- Announce topline safety, tolerability and immunogenicity data from adult Phase 1/2 study in **2024**

(1) Guidance provided as of April 17, 2023.

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
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