# Corporate Presentation

**May 8, 2023**

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 (PCV) and the improvement upon the standard-of-care; demand for Vaxcyte's vaccine candidates; the design, timing of the initiation, progress and expected results of Vaxcyte's preclinical studies, clinical trials and research and development plans (including, but not limited to, the timing and availability of data for the VAX-24 adult and infant studies and related regulatory interactions; the design of the VAX-24 Phase 2 clinical study in infants; the design of the VAX-31 clinical program, the timing of submission and clearance of such IND and the availability of topline data; and the announcement of guidance for VAX-A1); the use and availability of funds from CARB-X; the growth and expansion of the pneumococcal vaccine market, and the potential for Vaxcyte's PCV franchise to have sustained leadership within such market; the potential conversion by the pneumococcal vaccine market to a prime-boost schedule; the market opportunity for Vaxcyte's vaccines; Vaxcyte's expectations regarding the potential benefits, spectrum coverage, clinical or regulatory pathways, adoption speed and immunogenicity of its vaccine candidates; VAX-31's advancement as a follow-on candidate to VAX-24; the ability of Vaxcyte's strategic partnerships to deliver commercial, scalable manufacturing capabilities; 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 impacts from the 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 May 8, 2023 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.

# Highlights: Potential Best-in-Class Pneumococcal Conjugate Vaccine (PCV) Franchise

## VAX-24 Clinical Proof-of-Concept Obtained Setting Stage for Advancement to Phase 3

### POTENTIAL BEST-IN-CLASS PCV FRANCHISE: VAX-24 & VAX-31

- **Scalable platform** enabling broader-spectrum carrier-sparing PCVs
- **Lead candidate: VAX-24**
  - Potential best-in-class 24-valent PCV designed to replace SOC in adults/children
  - Successful completion of Phase 2 adult clinical program with positive results from Phase 1/2 and Phase 2 studies
  - Breakthough Therapy and Fast Track designations in adults
  - Initiated enrollment in Phase 2 infant study
- **Follow-on candidate: VAX-31**
  - Designed to provide ~95% coverage of IPD circulating in U.S. adults
  - Adult IND submission and announcement of subsequent FDA clearance anticipated 2H:23[1]

### CELL-FREE PROTEIN SYNTHESIS PLATFORM

- Leverages **site-specific** conjugation to expose on-target T- and B-cell antigens
- Enables **carrier-sparing** conjugates
- Permits production of **"tough-to-make" antigens**

### HIGHLY ATTRACTIVE PCV MARKET

- **Well-defined >$7B** market segment **poised for substantial growth**
- Honors **well-understood PCV MOA**
- Leverages established **surrogate immune endpoints** and clinical pathways
- **Spectrum of coverage is primary adoption driver**

### ROBUST DEVELOPMENT PIPELINE

- Platform unlocks large market opportunities:
  - **VAX-A1**: Novel Group A Strep conjugate vaccine
  - **VAX-PG**: Novel periodontitis therapeutic vaccine
  - **VAX-GI:** Novel Shigella vaccine

### ALIGNED CRITICAL RESOURCES

- **Strategic alignment** with Lonza (manufacturing)
- **Seasoned management team**, directors and advisors
- **Pro forma cash, cash equivalents and investments of approximately $1.5B**[(2)]

*(1) Guidance provided as of May 8, 2023.*
*(2) Reflects cash, cash equivalents and investments at March 31, 2023 of $949.9M and net proceeds from April follow-on offering of ~$545.1M.*
*SOC = Standard-of-Care.*
*IPD = Invasive Pneumococcal Disease.*

# Experienced Team with Track Record in Vaccines and Biopharma

## Management Team

**Grant Pickering, MBA**
*CEO & Co-founder*

PROVENGE® (sipuleucel-T)
ZELNATE™
Victrio
FLONASE

**Andrew Guggenhime, MBA**
*President & CFO*

Dermira
Calistoga Pharmaceuticals
Facet Biotech

**Jim Wassil, MS, MBA**
*EVP & COO*

Prevnar 13® Pneumococcal 13-valent Conjugate Vaccine (Diphtheria $CRM_{197}$ Protein)
BEXSERO Meningococcal Group B Vaccine
MENVEO Meningococcal (Groups A,C,Y and W-135) Oligosaccharide Diphtheria $CRM_{197}$ Conjugate Vaccine
RotaTeq® Solución Oral. Vacuna frente a rotavirus, virus vivos

**Mark Wiggins, MBA**
*CBO*

Pfizer
Johnson & Johnson
biogen idec
TRACON PHARMA

**Jakub Simon, MD, MS**
*CMO*

MERCK
PaxVax

**Jeff Fairman, PhD**
*VP Research & Co-founder*

ZELNATE™
Victrio

**Sally Bolmer**
*SVP Regulatory Affairs*

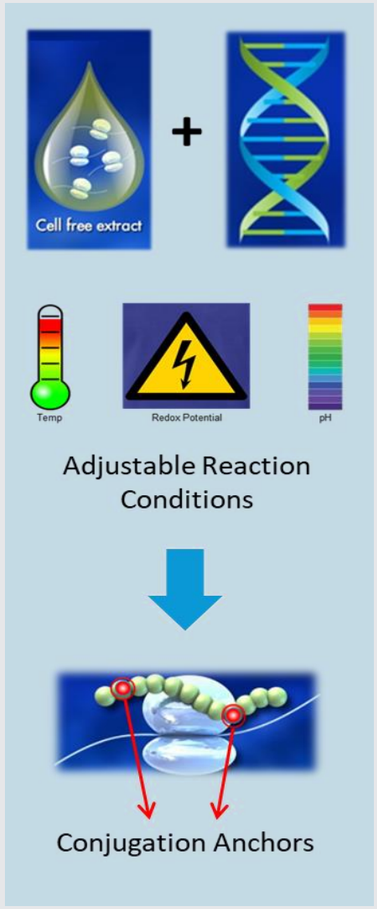
Allakos
Human Genome Sciences
centocor

**Harp Dhaliwal, MBA**
*SVP Commercial Mfg & Supply Chain*

Dermira
MEDIVATION
Biogen

# Cell-Free Protein Synthesis Platform Unlocks Multiple Vaccine Applications

## Design and Produce Proteins Beyond Reach of Conventional Methods




### CELL-FREE PROTEIN SYNTHESIS

- Transcriptional & translational (ribosomal) machinery from *E coli* stored as a frozen "extract"
- Produces singular protein of interest at high yields
- Enables site-specific conjugation via insertion of multiple nnAA conjugation anchors
- Permits protein production in non-physiological conditions

### SPEED, FLEXIBILITY, SCALABILITY

- Rapidly screen vaccine candidates
- Flexible reaction conditions
- Scaled to 1000L using standard equipment

### SUPERIOR CONJUGATE VACCINES

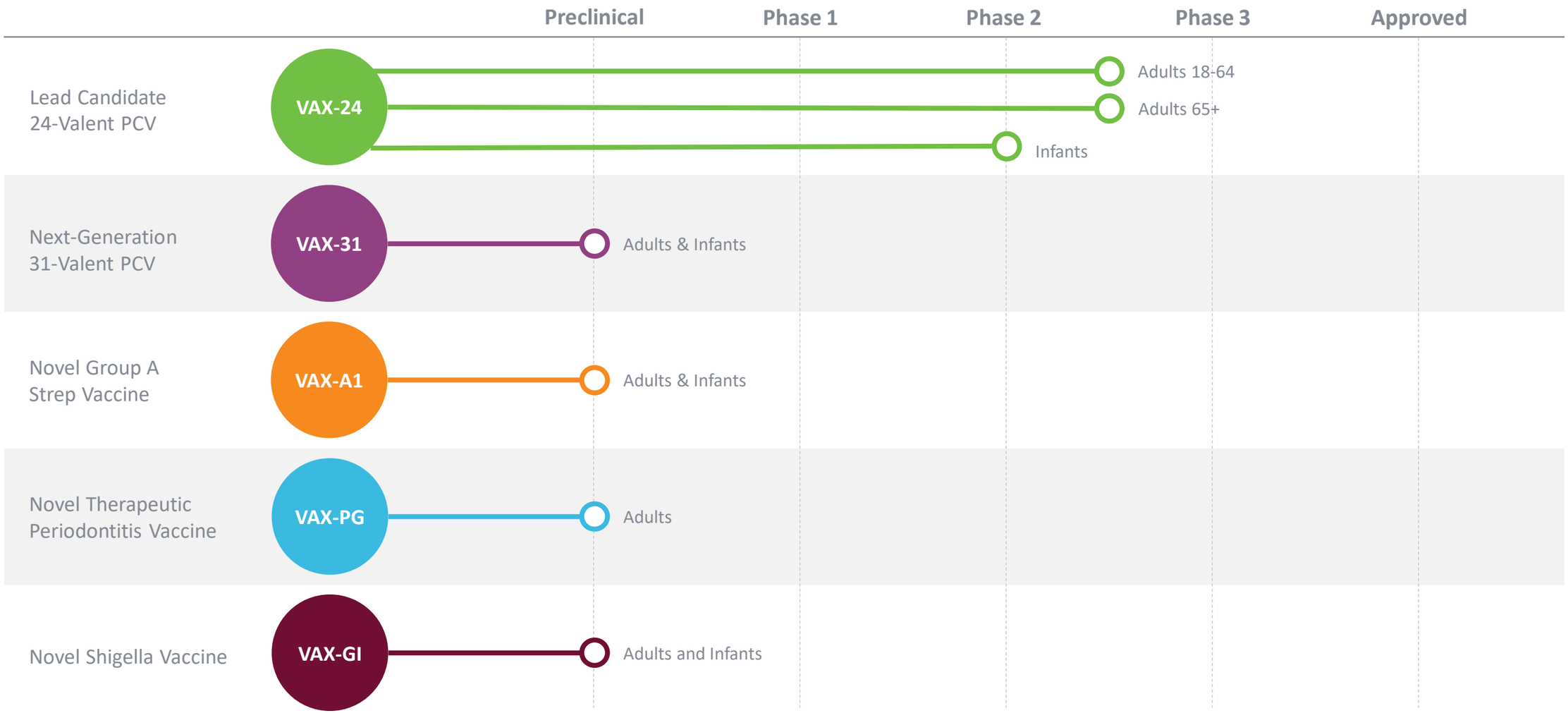
- Site-specifically attach antigens onto protein carriers designed to:
  - Enable consistent exposure of T-cell epitopes and/or B-cell epitopes on protein carrier
  - Avoid off-target effects
  - Enable use of less protein carrier without sacrificing immunogenicity
  - Enable broader-spectrum vaccines

### NOVEL PROTEIN VACCINES

- Able to produce "tough-to-make" protein antigens that conform to target pathogens
- Increased likelihood of protective immune response

# Pipeline of High-Fidelity Vaccines

## Broad-Spectrum Conjugate and Novel Protein Vaccines to Prevent or Treat Bacterial Infectious Diseases



# 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 Phase 3 pivotal non-inferiority study in adults in **2025**

**VAX-24 Infant**

- Announce topline safety, tolerability and immunogenicity data from primary three-dose immunization series of Phase 2 study by **2025**
- Announce topline data from booster dose approximately **nine months following** primary series data

**VAX-31 Adult**

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

*(1) Guidance provided as of May 8, 2023.*

# PCV Opportunity

# Global Impact of Pneumococcal Disease Remains Significant

## ABOUT STREPTOCOCCUS PNEUMONIAE

***Streptococcus pneumoniae* is the most common pathogen causing pneumococcal disease (PD)**

- Non-invasive PD includes otitis media, sinusitis, pneumonia
- Invasive PD (IPD) includes bacteremia, meningitis
- Pneumococci cause over 50% of bacterial meningitis cases in the U.S.

## CURRENT $7 BILLION GLOBAL VACCINE CATEGORY

**Vaccinations are recommended globally for infants and adults to prevent PD**

Standard of Care schedule in the U.S.:

- Infants: Prevnar 13® (PCV13) or Vaxneuvance™ (PCV15) x 4 doses/each
- Adults: Prevnar 20™ (PCV20) or PCV15 x 1 dose followed by Pneumovax® 23 (PPV23) x 1 dose, if PCV15

## GLOBAL INCIDENCE & IMPACT OF PD STILL SUBSTANTIAL

**Global incidence driven by emerging serotypes not covered by currently available vaccines**

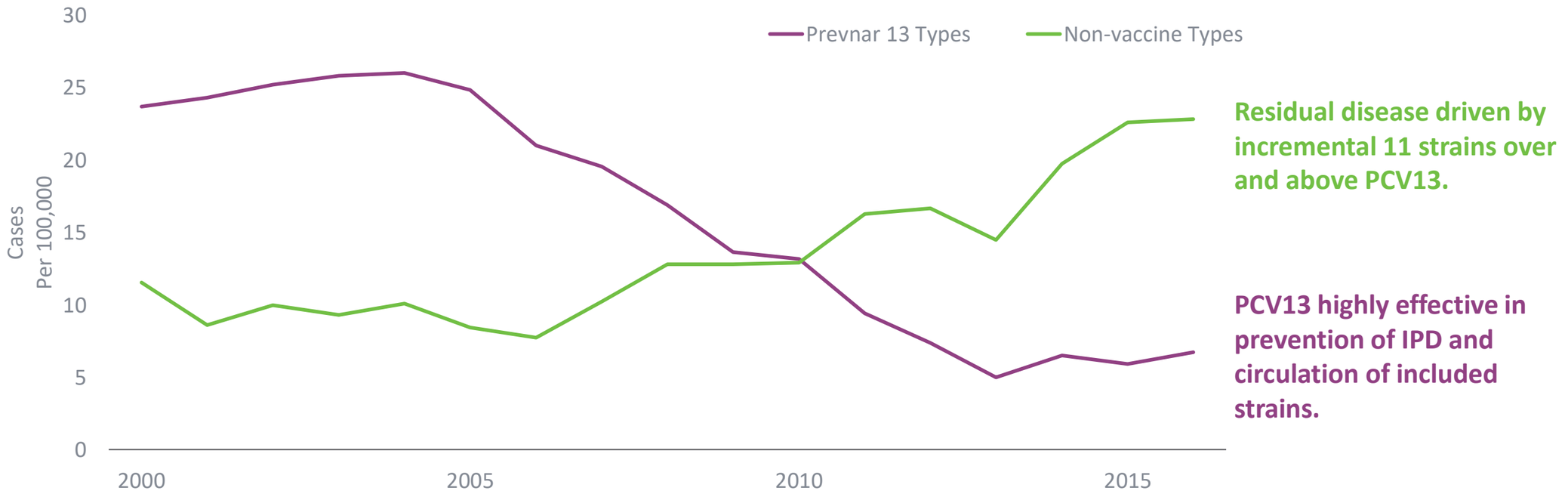
- In the U.S. alone, there are ~320K pneumococcal pneumonia cases per year resulting in ~150K hospitalizations
- IPD is a leading cause of invasive disease in children two years of age and under

*(1) https://www.cdc.gov/pneumococcal/clinicians/clinical-features.html.*
*(2) https://www.cdc.gov/vaccines/pubs/pinkbook/pneumo.html.*

# Serotype Replacement Drives Need for Broader-Spectrum Vaccines

**Non-Vaccine Serotypes Increase in Prevalence, as Circulation of Vaccine Serotypes is Eliminated, Resulting in the Need for Broader-Spectrum Vaccines**

UK IPD CASES IN ADULTS ≥ 65 [1]




**Residual disease driven by incremental 11 strains over and above PCV13.**

**PCV13 highly effective in prevention of IPD and circulation of included strains.**

*(1) Ladhani et al, Lancet Infect Dis 2018 Apr;18(4):441-45 inclusive of unpublished raw data.*

# PCVs Designed to Overcome the Limitations of Polysaccharide-Only Vaccines

## PCV Efficacy Driven by T-Cell Epitopes on Diphtheria Toxin Protein Carrier – $CRM_{197}$[1]

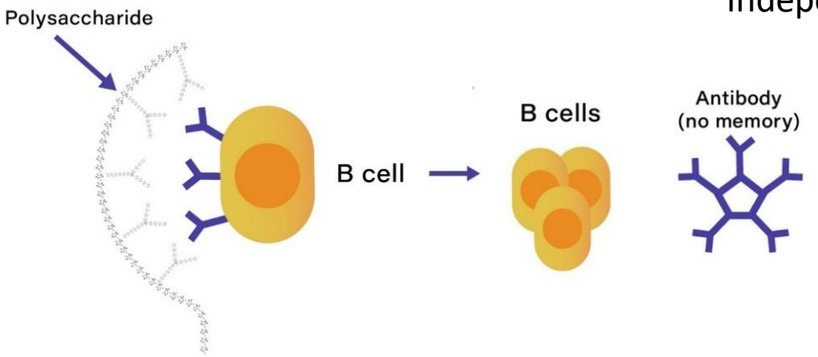
**PS-Only Vaccine**

PNEUMOVAX®23

T-Cell

Independent

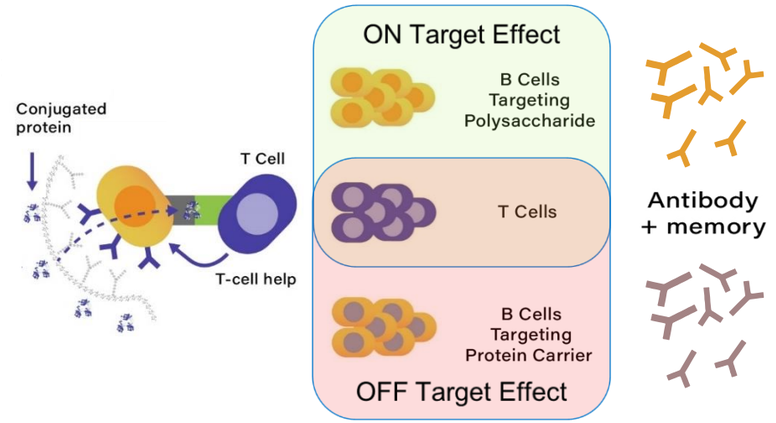
Dependent




**PCVs**

Prevnar 20® Pneumococcal 20-valent Conjugate Vaccine

Vaxneuvance™ Pneumococcal 15-valent Conjugate Vaccine




**Broad Coverage But Limited Protection in Adults - <u>Not Boostable</u>**

Pneumococcal capsular polysaccharides (PS) antigens lead to:

- Transient Ab responses (IgM) protect against sepsis, but not pneumonia
- No T-cell mediated memory responses, thus no boost
- Hyporesponsive effect inhibits ability to boost PCVs post-prime

**Narrow Coverage But Highly Effective in Adults & Infants - <u>Boostable</u>**

Conjugation of PS to protein carrier leads to:

- Enhanced Ab responses (IgG) that protect against pneumonia
- T cell-mediated memory to provide boostable, durable protection
- Characteristic interstrand crosslinked matrix-like structures

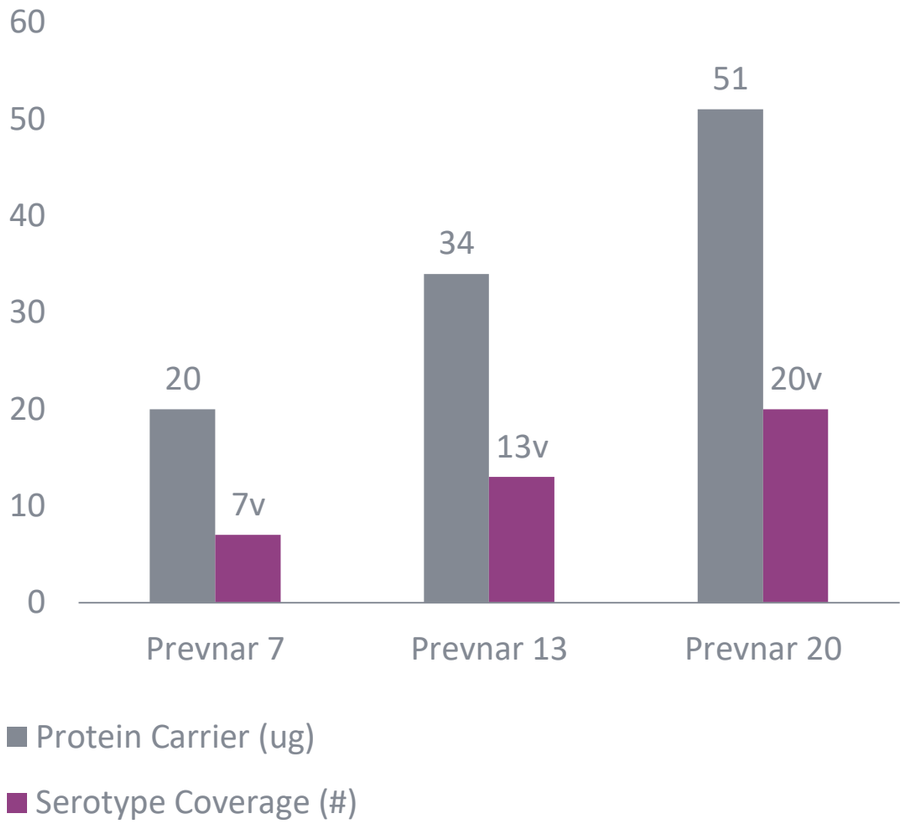
*Note: Graphics adapted from Strugnell et al, Understanding Modern Vaccines, Vol 1, Issue 1, 61-88.*
*(1) Protein carrier in Prevnar 20 is a modified form of diphtheria toxin ($CRM_{197}$).*

# Limitations of Current PCVs

## Coverage Expansion Needed to Address Circulating Disease, but Protein Carrier Backbone Problematic

### LIMITATIONS OF CONVENTIONAL CHEMISTRY

- Random conjugation
- Higher ratio of protein carrier to polysaccharide, due to reaction conditions required for conjugation
- Further exacerbates carrier suppression, due to competition for CD4+ help between disease-specific polysaccharides and non-disease specific protein carrier




*(1) Prevnar 20 BLA Clinical Review Memorandum. STN: 125731/0 June 8, 2021.*

# Limitations of Current PCVs: Adding Conjugates Results in Lower Ab Titers

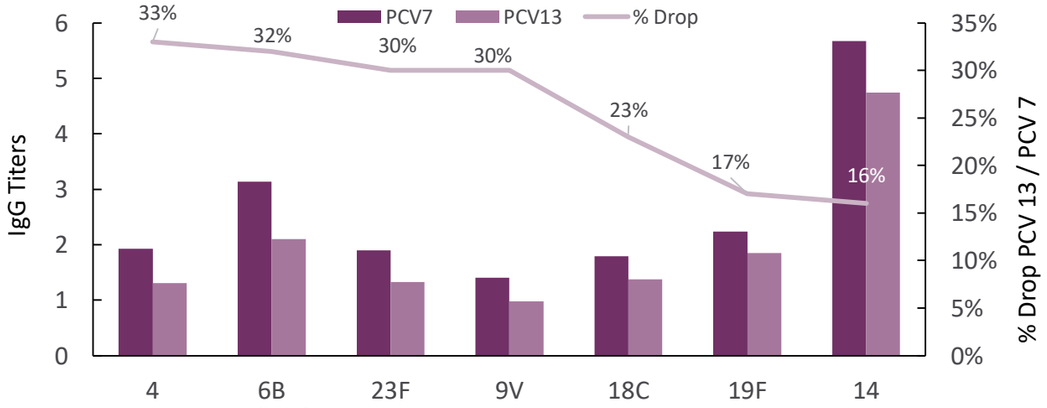
## Coverage Expansion Using Conventional Chemistry Has Led to Carrier-Induced Immune Suppression

### CARRIER SUPPRESSION

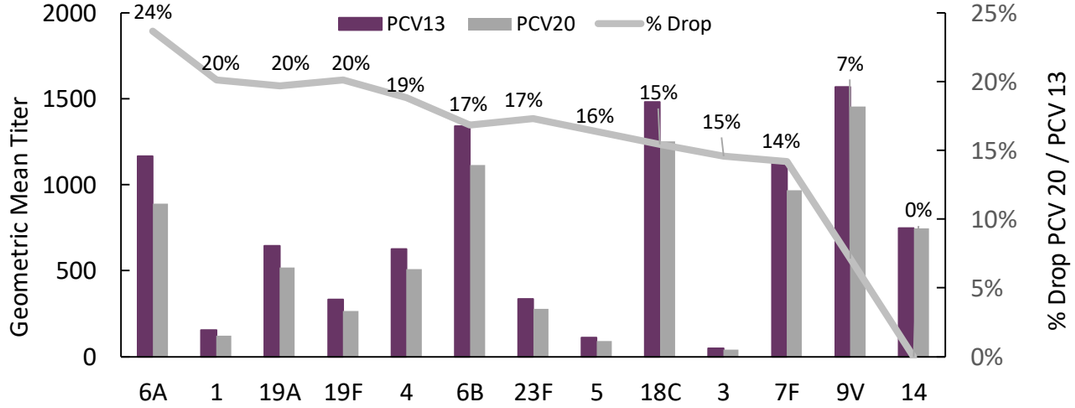
Diminished immune response to target polysaccharides due to cumulative amount of protein carrier

- Expanded spectrum of coverage requires increasing protein carrier burden
- Reduced immune responses consistently demonstrated with > spectrum PCVs in both infants and adults

INFANT IMMUNE RESPONSES (IgG):
PREVNAR 7 VS PREVNAR 13[1]




ADULT IMMUNE RESPONSES (OPA):
PREVNAR 13 VS PREVNAR 20[2]

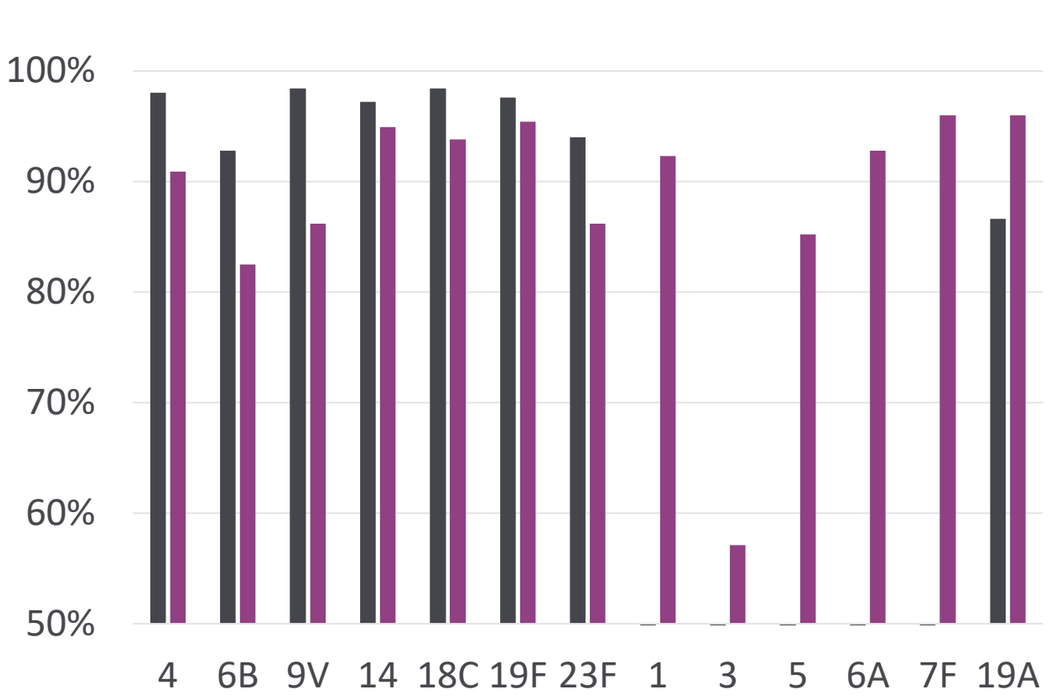



*(1) Yeh et al, Pediatrics. 126: e493 (2010).*
*(2) Prevnar 20 BLA Clinical Review Memorandum. STN: 125731/0 June 8, 2021.*
*OPA = Opsonophagocytic assay.*
*IgG - Immunoglobulin G.*

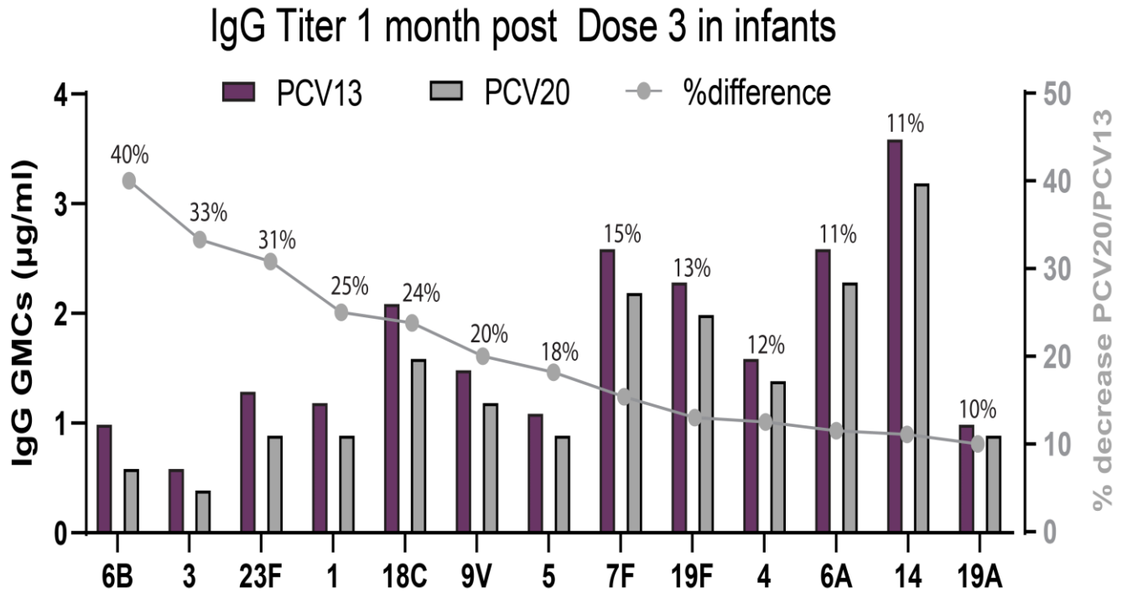
# Limitations of Current PCVs: Adding Conjugates Results in Lower Seroprotective Levels[1,2]

**CURRENT REGULATORY GUIDANCE: MUST BE WITHIN 10%[3] TO BE NON-INFERIOR POST-DOSE 3**

**PH 3 INFANT DATA % SEROPROTECTED**
**PREVNAR 7 VS PREVNAR 13[1,2]**



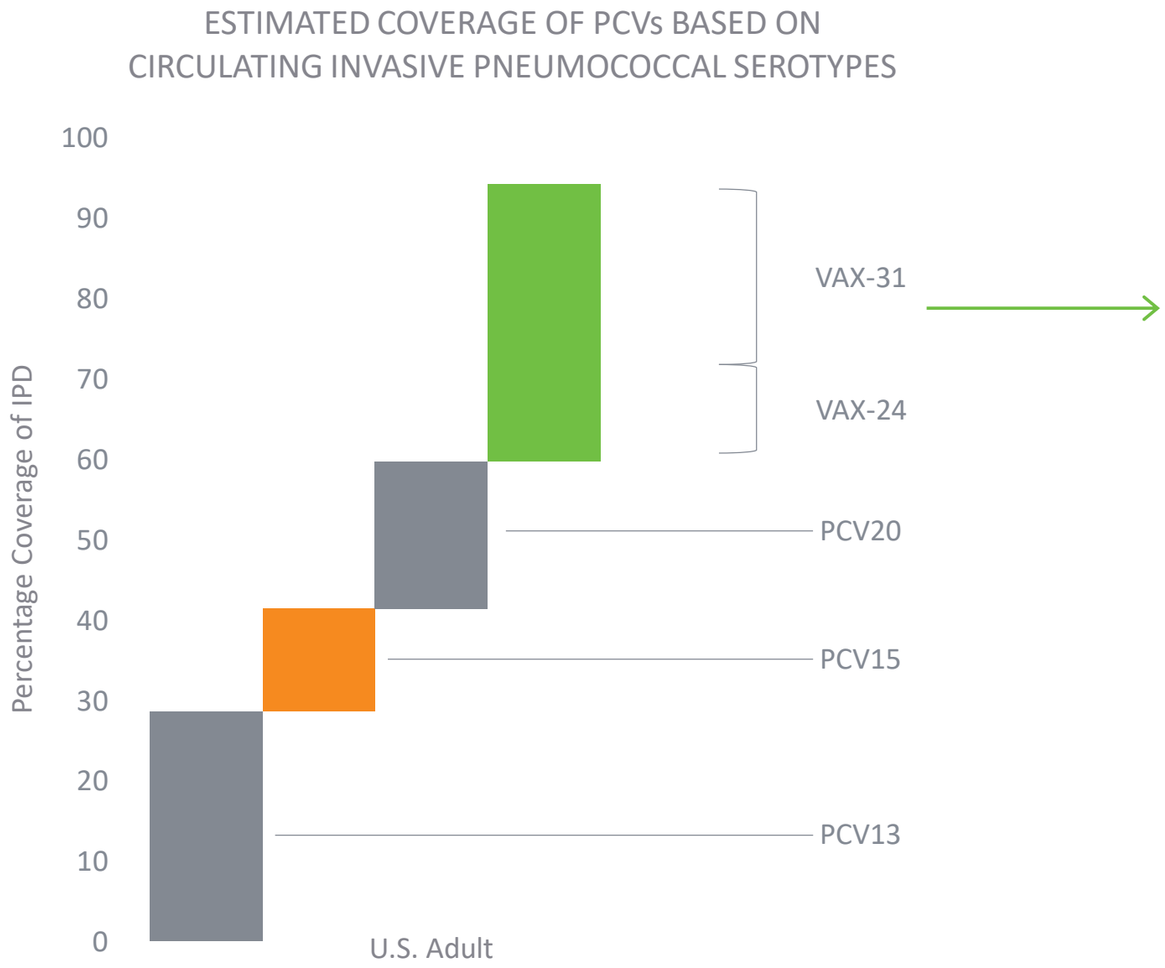

**PH 2 INFANT DATA IMMUNE TITERS**
**PREVNAR 13 VS PREVNAR 20[4]**




*(1) Prevnar 13 BLA Clinical Review Memorandum by FDA. February 17, 2010.*
*(2) Seroprotection is defined as a serotype-specific IgG antibody level of ≥0.35mcg/mL.*
*(3) Non-inferiority comparison is LL of 95% CI of the comparator to the mean % responders of the SoC.*
*(4) Clintrials.gov NCT03512288 Phase 2 study (N=460).*

# Spectrum of Coverage Drives Adoption in PCV Segment

## Significant Unmet Needs Remain Despite Available Vaccines



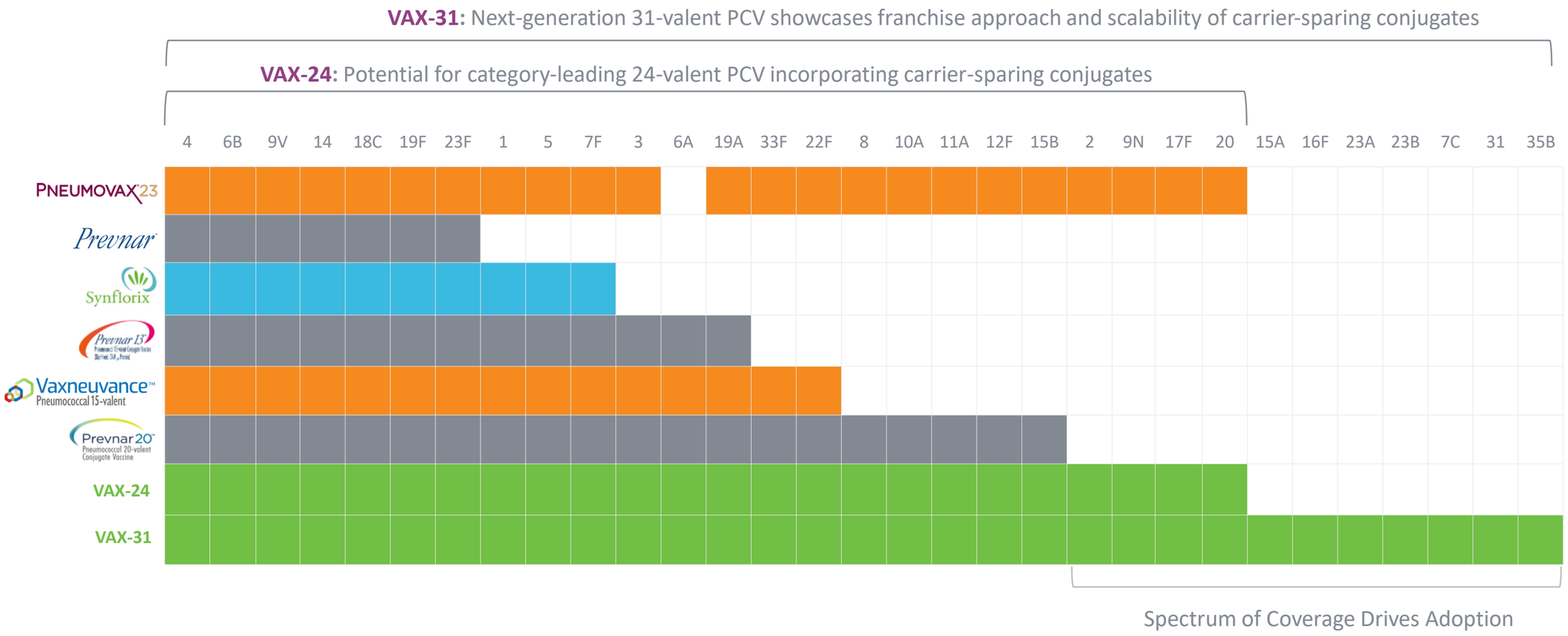

### VAX-24 & VAX-31 TARGET PRODUCT PROFILE

Vaxcyte's carrier-sparing PCV franchise designed to provide broadest coverage of any PCVs:

- VAX-24 has the potential to provide an incremental 10-28% coverage of IPD in U.S. adults vs. the SOC PCVs today, which would surpass the coverage of Pneumovax 23
- VAX-31 is designed to provide coverage for ~95% of the IPD currently circulating in the U.S. adult population

*(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.*
*SOC = standard of care.*

# Vaxcyte Carrier-Sparing 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.*

# Pneumococcal Vaccine Market is Highly Attractive

## VAX-24 has the Potential to Become the Most Broad-Spectrum PCV

### PNEUMOCOCCAL VACCINE MARKET DYNAMICS

#### SPECTRUM OF COVERAGE DRIVES ADOPTION

- Potential for rapid adoption, with ACIP recommendation driving uptake
- Examples: PCV13 vs Prevnar 7 (PCV7) and Shingrix® vs Zostavax®

#### ATTRACTIVE MARGINS

- Pneumococcal vaccines are premium priced in the U.S., delivering highly attractive margins
- Broader-spectrum PCVs maintain premium price

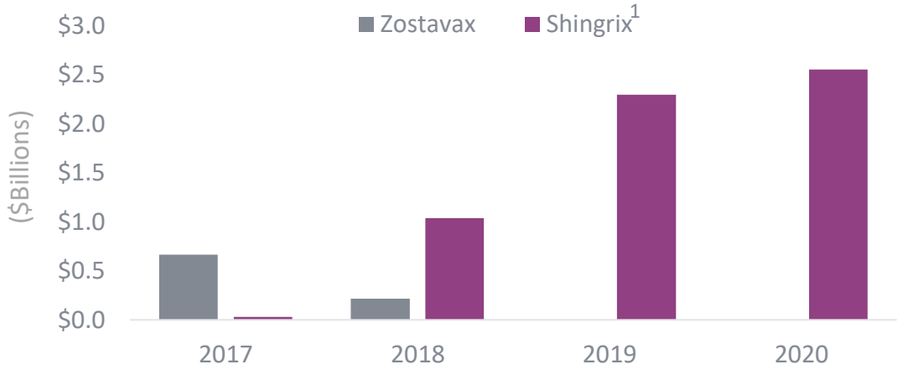
#### PCVs ARE BEST-IN-CLASS

- Well-understood T-cell dependent MOA tied to co-presentation of disease-specific polysaccharide antigens with T-cell epitopes on protein carrier to drive durable and boostable immune responses
- Well-defined clinical development path: Non-inferiority to SOC using validated surrogate immune endpoints adequate for full approval for follow-on PCVs

#### DURABLE REVENUE STREAM

- Prevnar Family (PCV7/PCV13/PCV20) & PPV23 have generated >$100B in revenues; PCV13 and PCV20 had combined annual sales of ~$6B in 2022

SHINGRIX
HERPES ZOSTER VACCINE (NON-LIVE RECOMBINANT, AS01B ADJUVANTED)

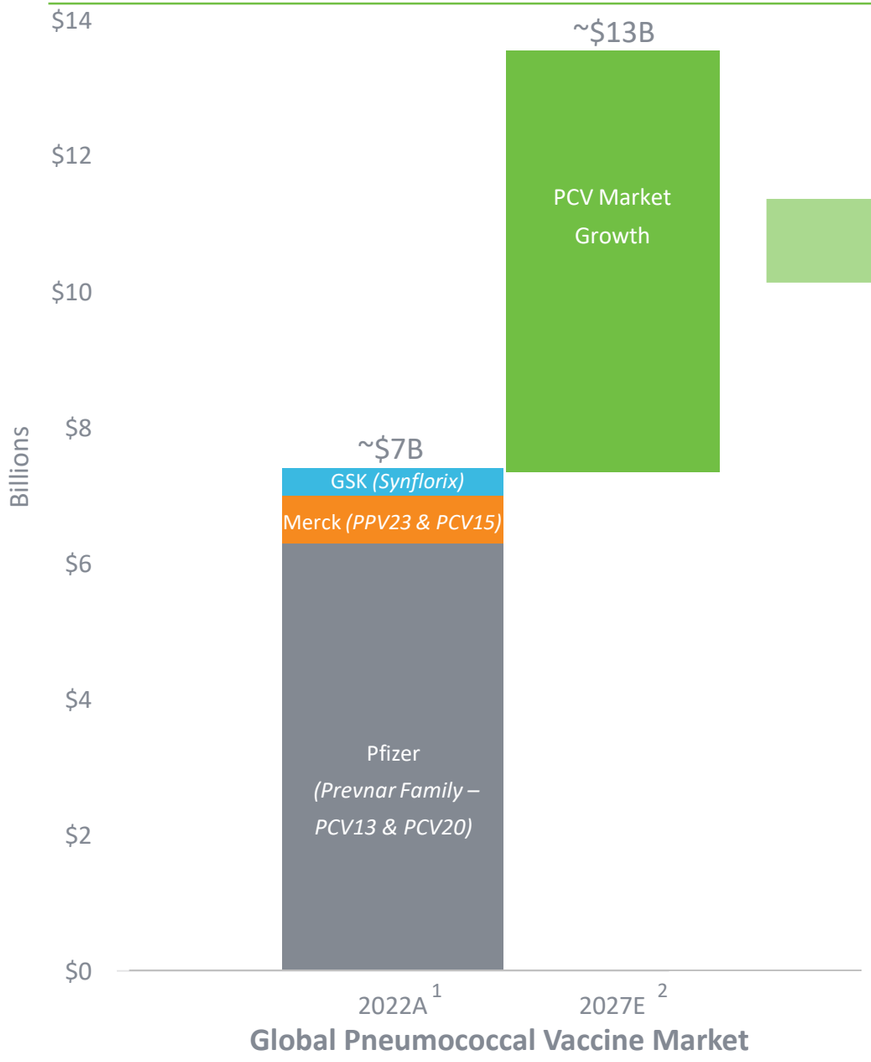



- FDA approved in 4Q:2017 to prevent shingles in adults
- ACIP granted “preferred recommendation”
- Replaced the incumbent (Zostavax from Merck)

*MOA = mechanism of action; SOC = standard of care; ACIP = US CDC Advisory Committee on Immunization Practices.*
*(1) Revenues reported in GSK (Shingrix) and Merck (Zostavax) financial filings.*

# 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

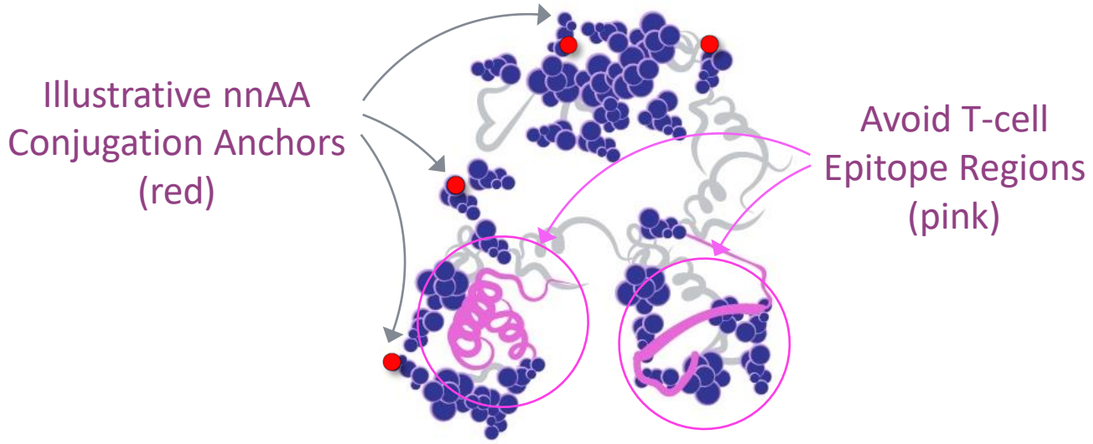
*(1) Sources: Company websites; includes Merck's PCV15 sales disclosed for Q4 2022.*
*(2) Global Pneumococcal Vaccine Market (2022-2027), Infogence Global Research.*
*(3) Shea KM, Edelsberg J, Weycker D et al. (2014), Open Forum Infect Dis 1(1): ofu024.*

# Differentiated PCV Franchise Led by VAX-24

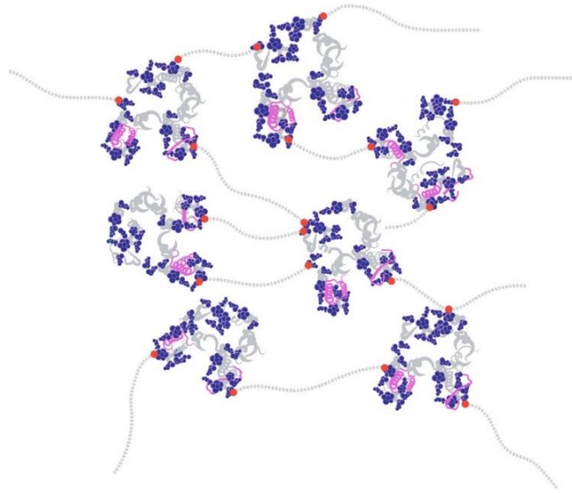
# Vaxcyte's PCV Franchise Employs Carrier-Sparing Conjugates

## Cell-Free Platform Enables Precise Conjugation to Enhance Potency of Standard Protein Carrier

PRECISE, SITE-SPECIFIC CONJUGATION SITES ON PROPRIETARY eCRM® PROTEIN CARRIER




FINAL VAX-24 CONJUGATES IN CUSTOMARY MATRIX FORM



**eCRM: Enhanced Potency Potential**

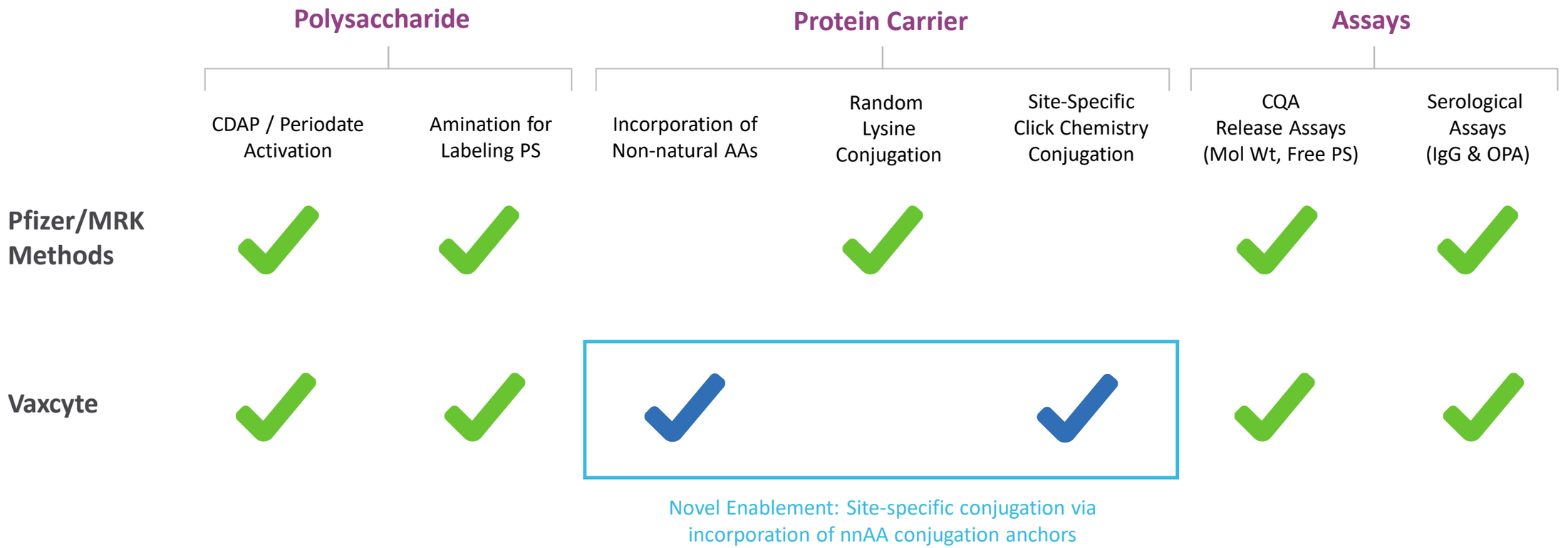
- Avoids masking sites on $CRM_{197}$ carrier responsible for T-cell help
- Optimized sites for conjugation using copper-free click chemistry
- More consistent antigenic presentation

**Carrier-Sparing Conjugates**

- Less protein carrier / conjugate may allow addition of more serotypes while minimizing carrier suppression and maintaining immunogenicity
- VAX-24 and VAX-31 conjugates form standard PCV interstrand crosslinked matrices
  - Perceived as foreign by the host
  - Allows use of standard critical quality attributes and serological assays

# Vaxcyte PCV Franchise Design Leverages Many Standard PCV Conventions

## Utilizes Proven Components, Chemistries and Assays to Reduce Risk and Uncertainty




- Where appropriate, we expect to capitalize on the efficiencies of well-established clinical, manufacturing & regulatory precedents by leveraging conventional methods for the development of VAX-24 and VAX-31
- Vaxcyte has leveraged the same animal models utilized in the development of both approved PCVs (Prevnar and Synflorix)

# VAX-24 Adult Phase 2 Program

# VAX-24 Phase 1/2 Study in Adults Aged 18-64

# Phase 1/2 Adult Proof-of-Concept Study Topline Data Key Take-Aways

## 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 in adults aged 18-64 (Phase 1 portion adults aged 18-49, Phase 2 portion adults aged 50-64)**

**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 in adults 50-64 years of age**

- 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

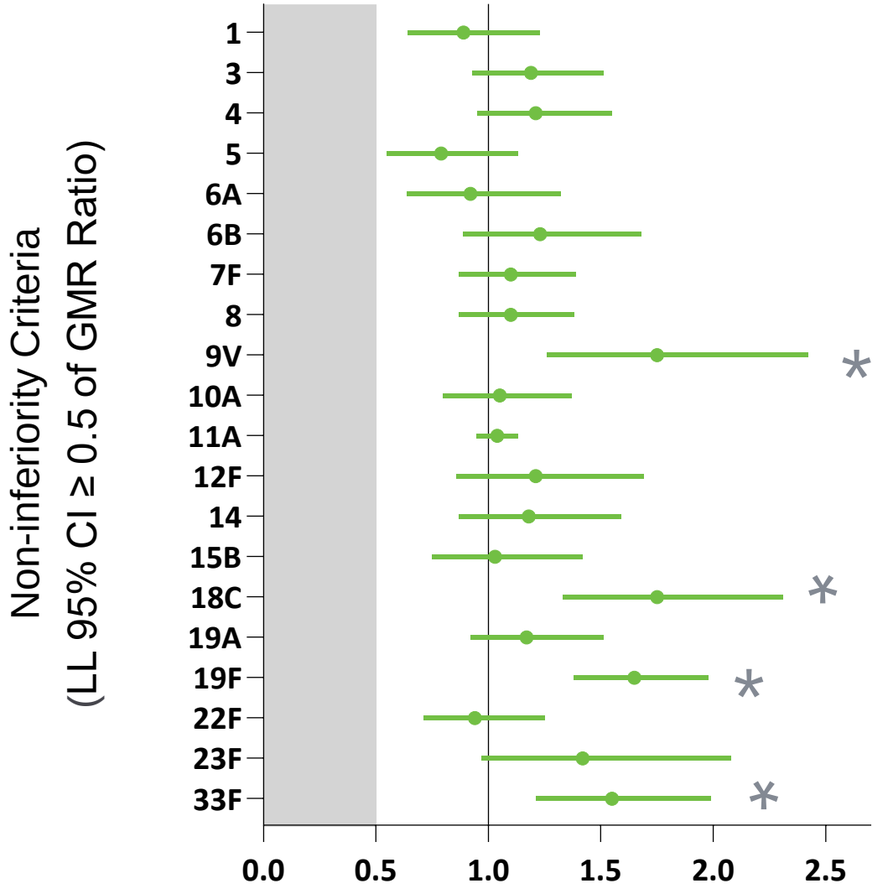
**PLATFORM: VAX-24 data validate Vaxcyte's carrier-sparing PCV franchise to increase spectrum of coverage AND maintain robust immune responses to serotypes in current standard-of-care PCVs**

**PCV FRANCHISE: VAX-31, a 31-valent PCV candidate, advancing as follow-on to VAX-24**

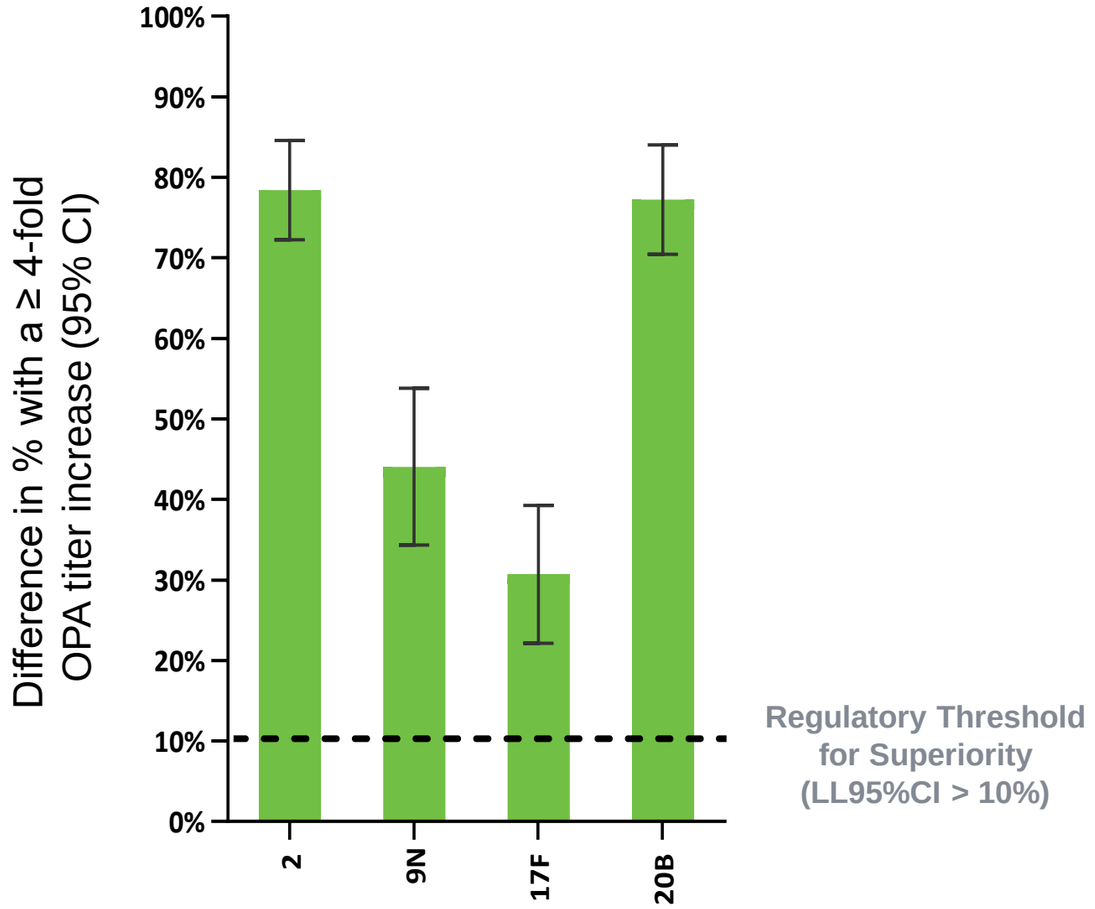
- Learnings from Phase 1/2 study to inform optimal design for VAX-31 clinical program given ability to add STs without sacrificing overall immune responses

# 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.*

# VAX-24 Phase 2 Study in Adults Aged 65 and Older (65+)

# 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**

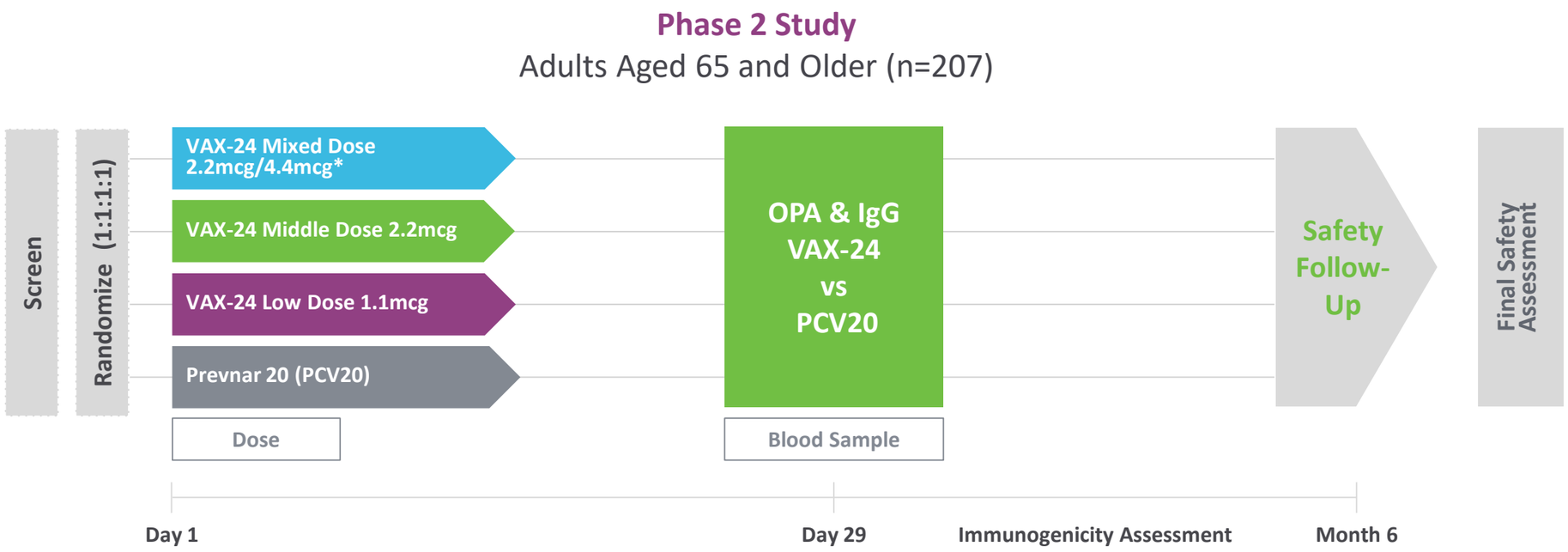
**ANTICIPATED PCV FRANCHISE MILESTONES[1]:**

- 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, followed by topline data from the booster dose approximately nine months later
- VAX-31 Adults: Submission of the IND application and announcement of subsequent FDA clearance 2H:23; topline data from Phase 1/2 study in 2024

*(1) Guidance provided as of May 8, 2023. OPA = Opsonophagocytic Activity; STs = serotypes; GMR = Geometric Mean Ratio*

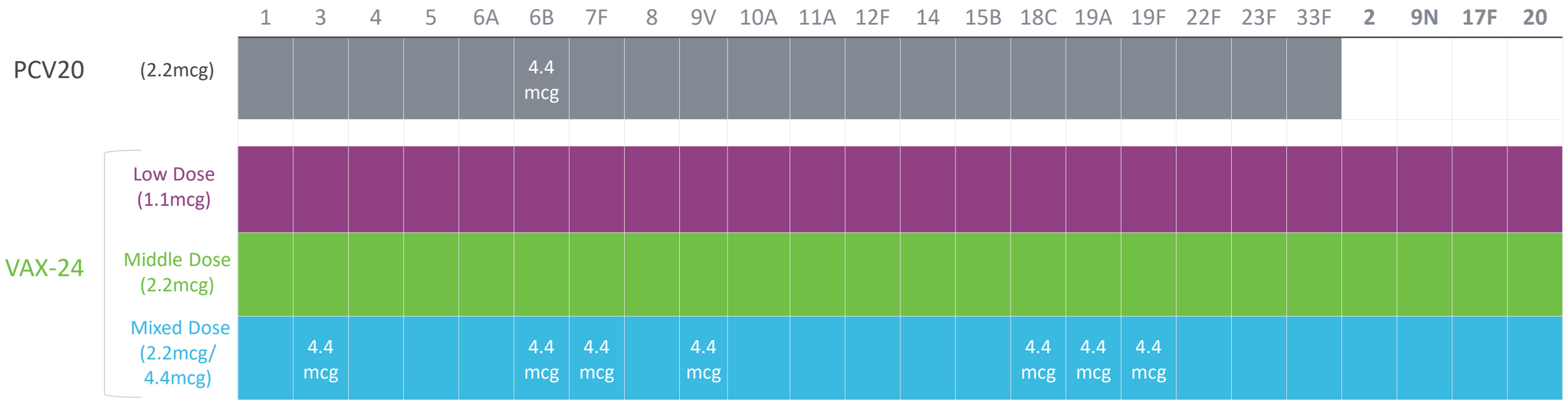
# Overview of VAX-24 Phase 2 Clinical Study in Adults 65+

**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 theremaining serotypes.*

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



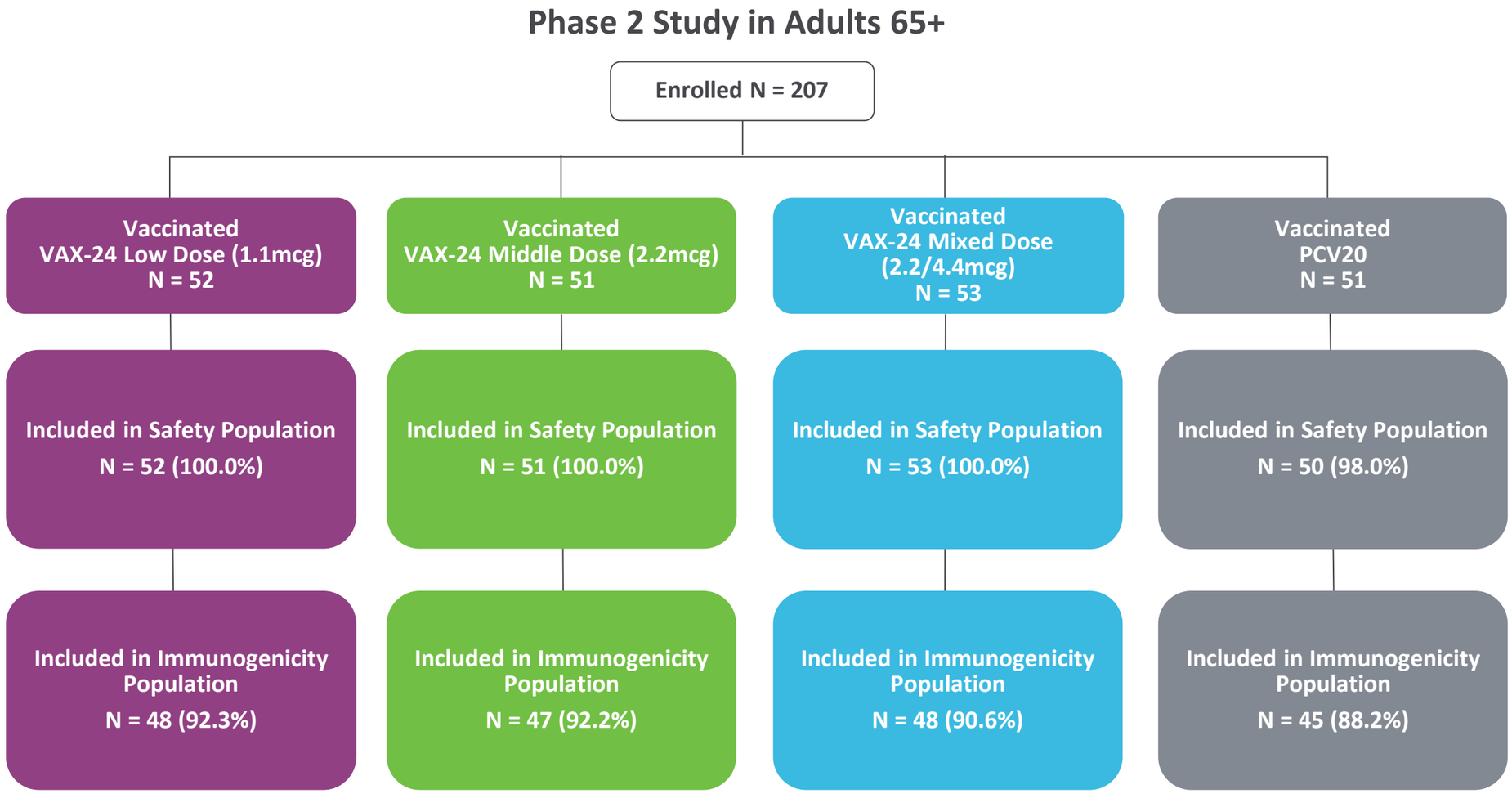

- Mixed Dose includes seven serotypes at 4.4mcg strategically chosen based on epidemiological relevance or prior evidence of dose-dependent immune responses to increase the probability of generating non-inferior immune responses for those serotypes.

# Study Safety, Tolerability and Immunogenicity Key Outcome Measures

| | DAY 7 | DAY 29 | DAY 180 |
|---|---|---|---|
| **SAFETY AND TOLERABILITY OUTCOME MEASURES** | • Solicited local reactions<br>• Solicited systemic events | • Unsolicited adverse events (AE)<br>• 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)<br>• IgG geometric mean concentration (GMC)<br>• % of subjects achieving a 4-fold rise in OPA<br>• Geometric Mean Ratios (GMR) in serotype-specific OPA | |

# Study Disposition

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



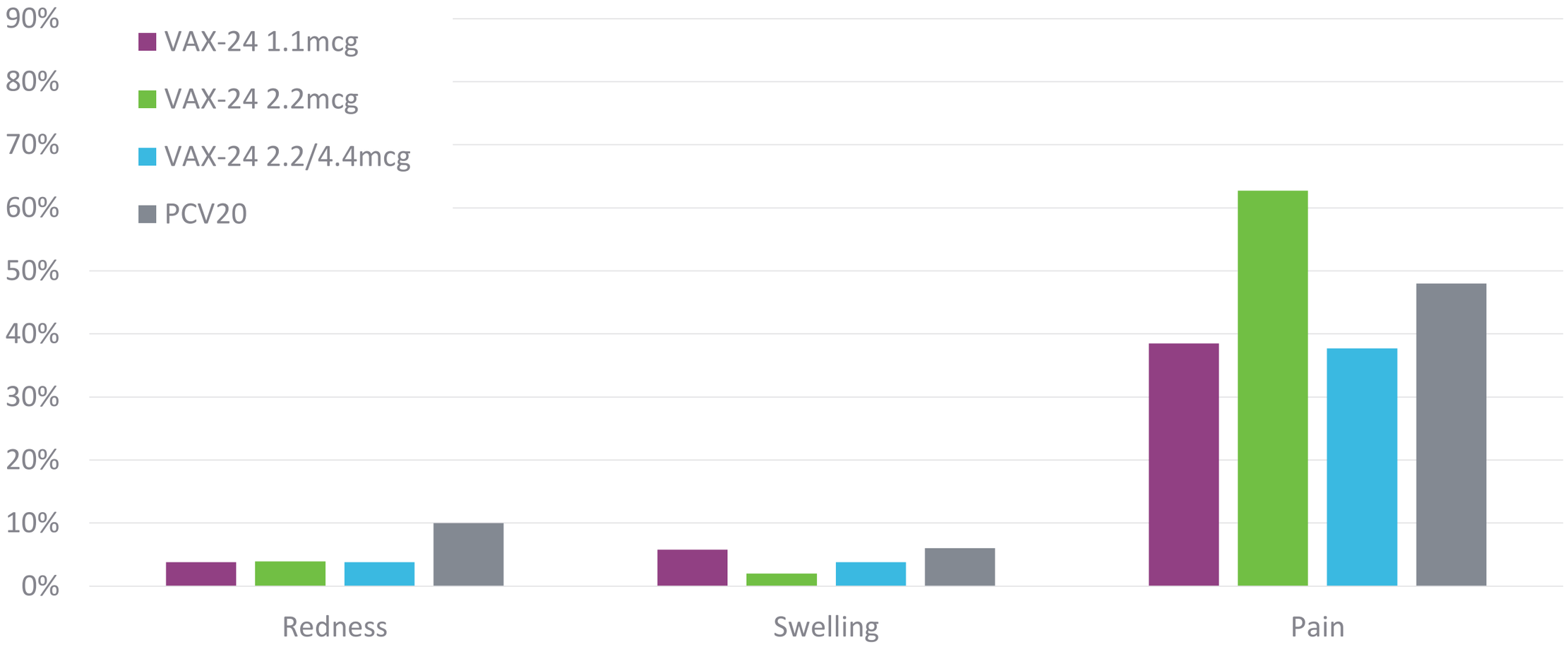

*7 Subjects (3.4%) Discontinued*

# Demographic Population

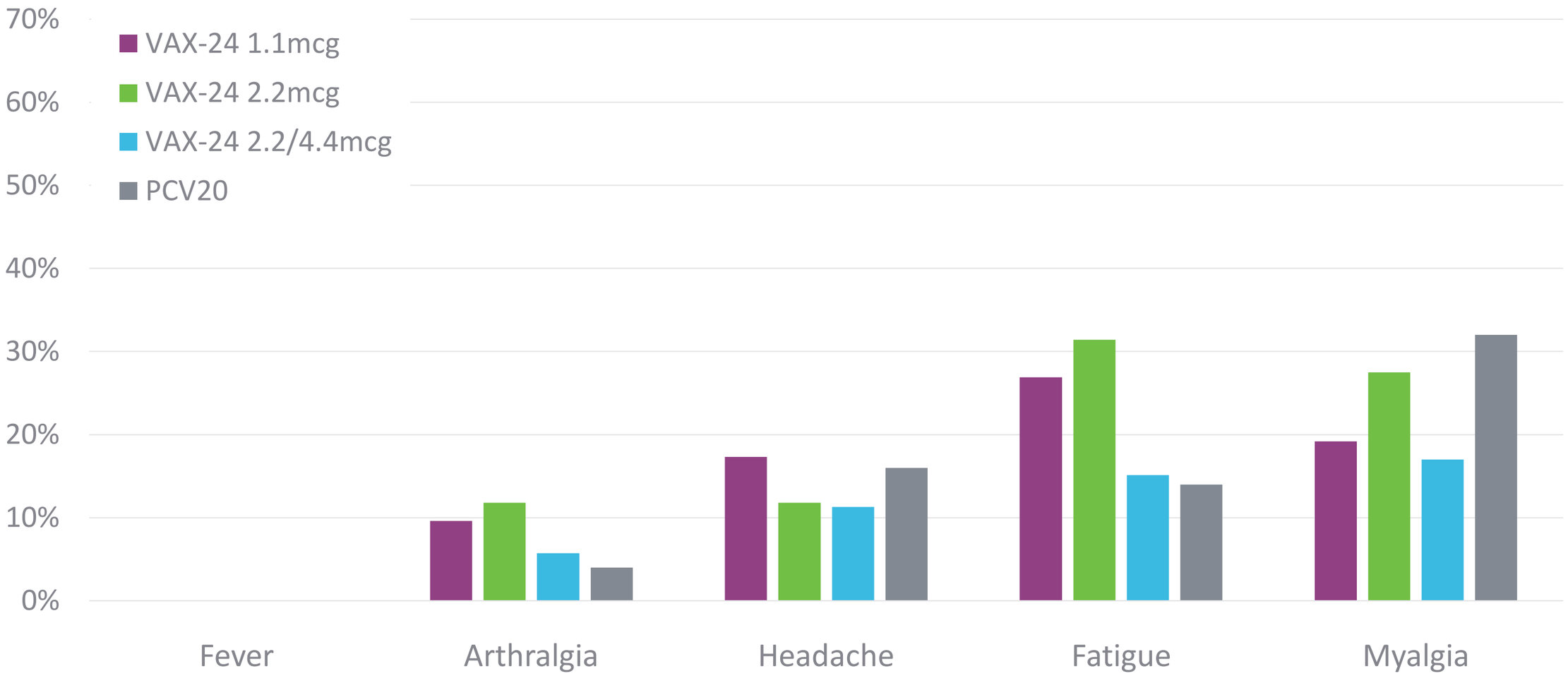
## Generally Balanced Across Cohorts and Similar for the Safety and Immunogenicity Populations

| | 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) |

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



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



# 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:

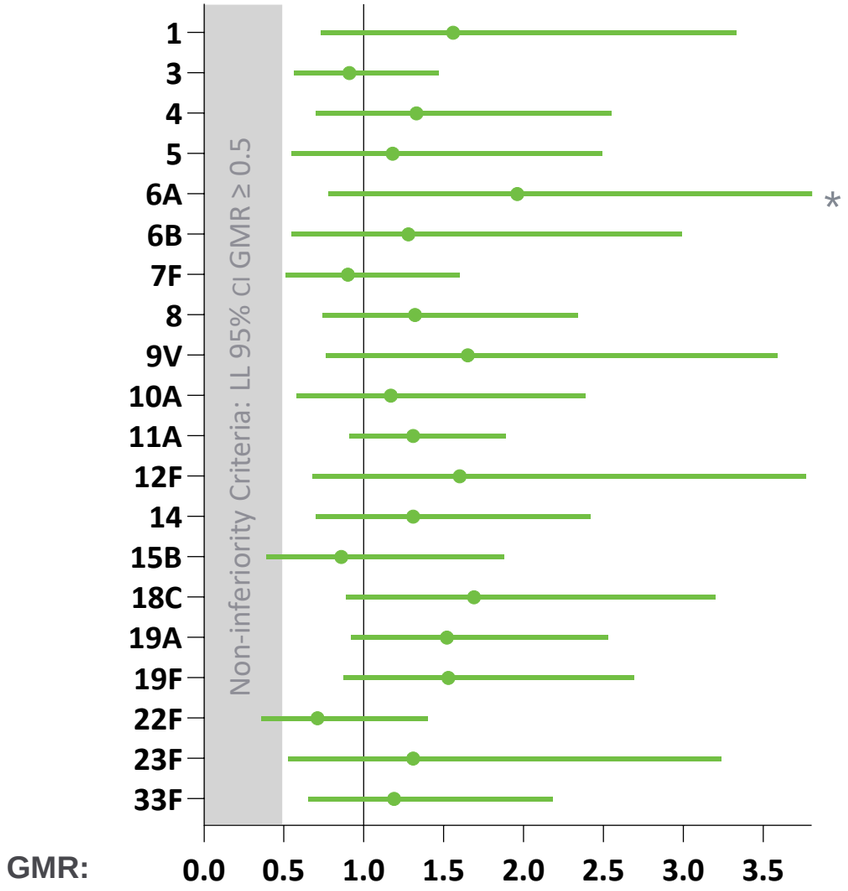
### Superiority:

- 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

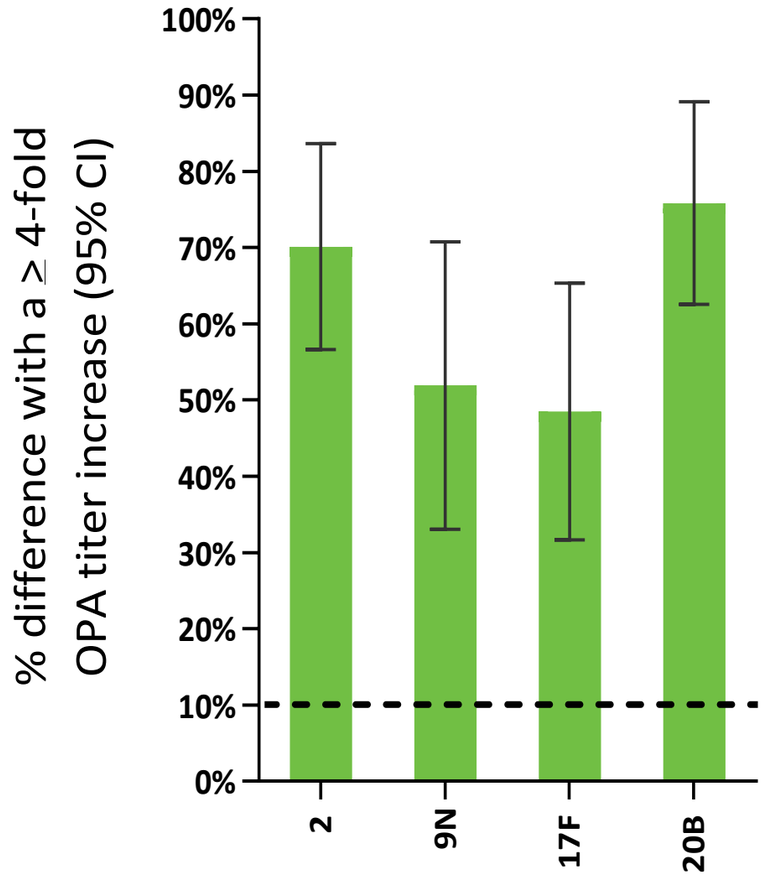
*CI = confidence interval*

# 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)**

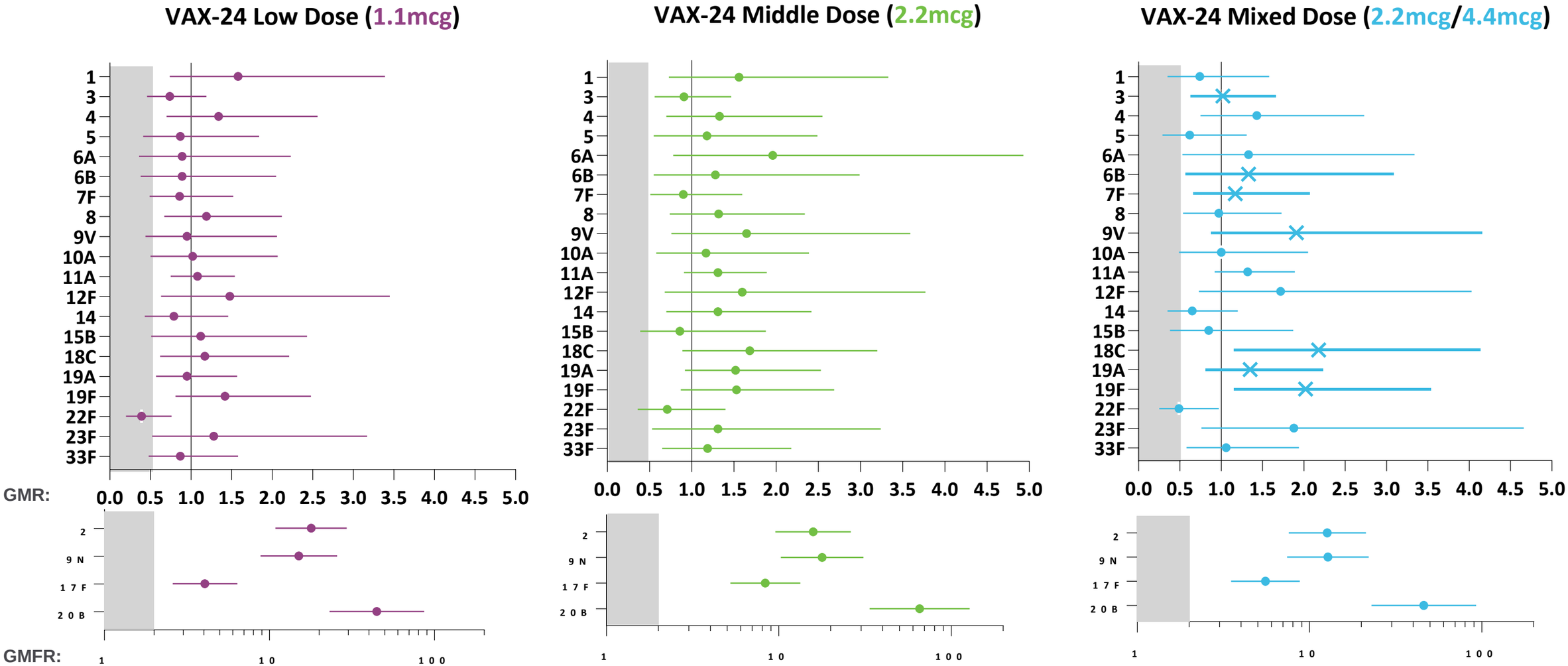



**Threshold for Superiority (LL95%CI > 10%)**

* *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.*

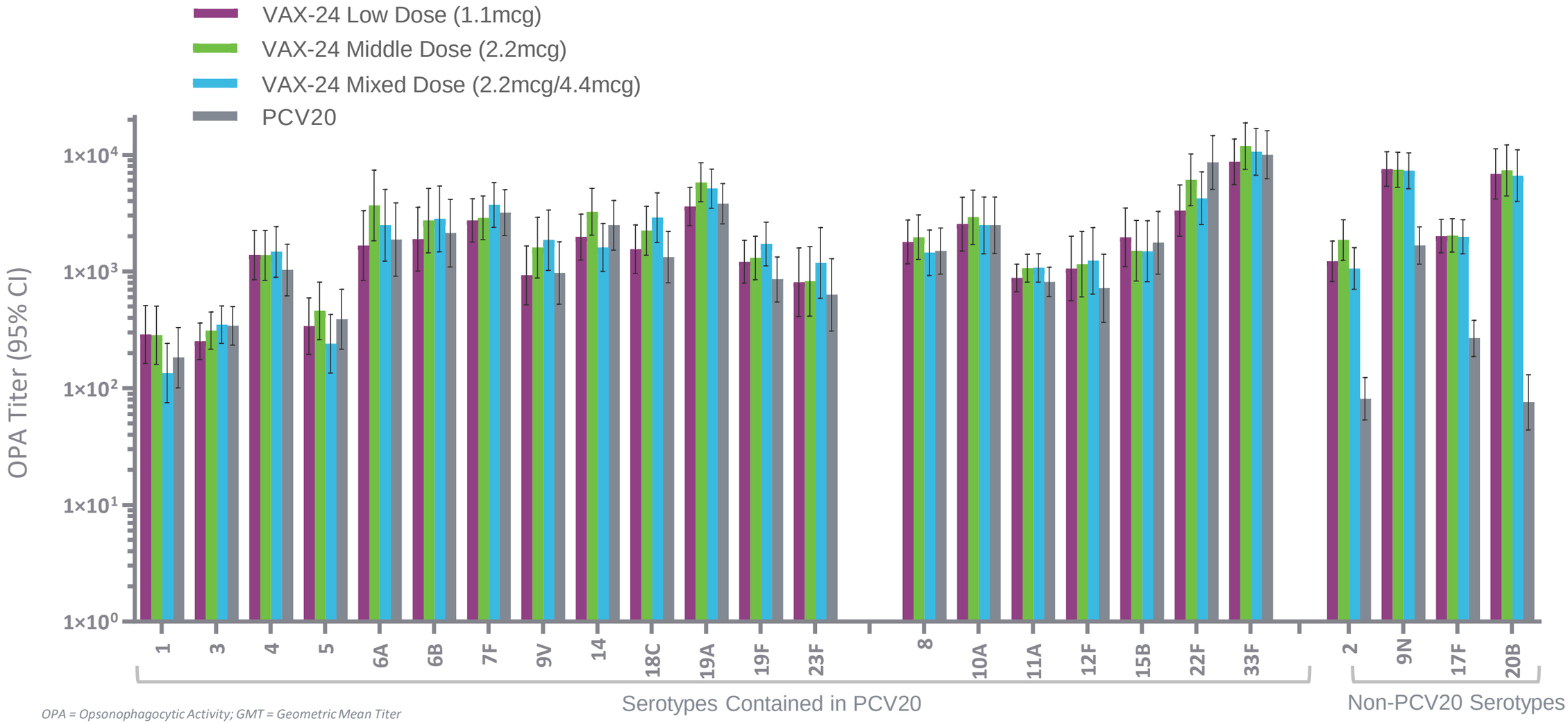
# 65+ Study Results Confirm 2.2mcg is Optimal Dose to Advance to Phase 3

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



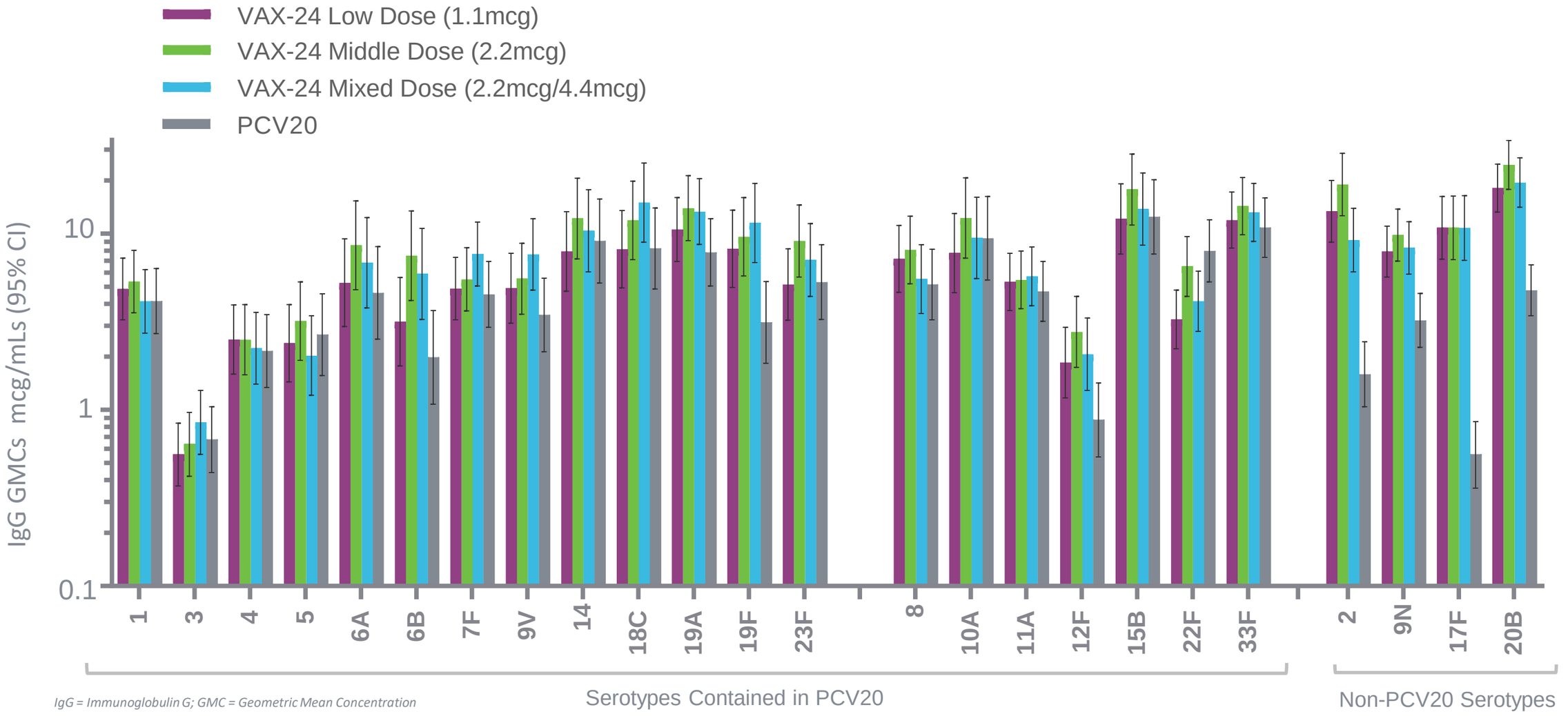

*X = 7 VAX-24 serotypes at the 4.4mcg dose; GMR = Geometric Mean Ratio; GMFR = Geometric Mean Fold Ratio*

# 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



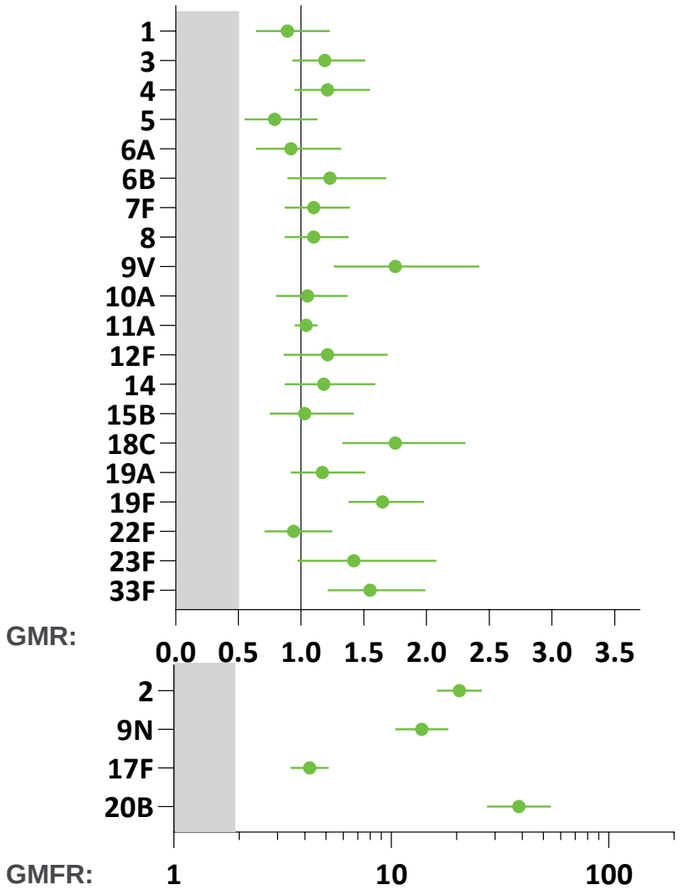

*IgG = Immunoglobulin G; GMC = Geometric Mean Concentration*

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

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

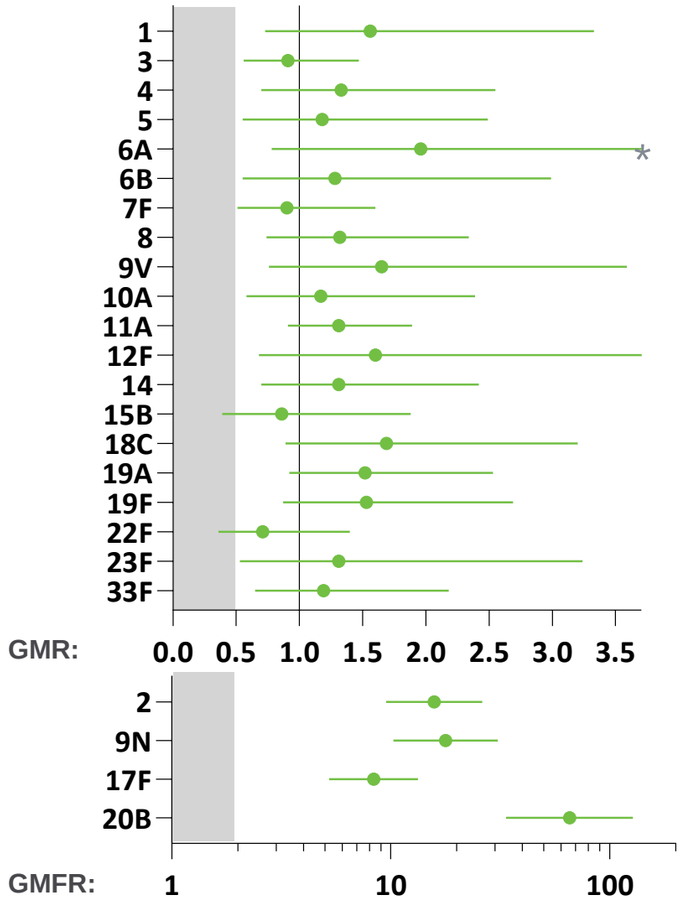
## 65+ Study Data Show Further Improvement in Overall Immune Response vs. PCV20

### 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 |

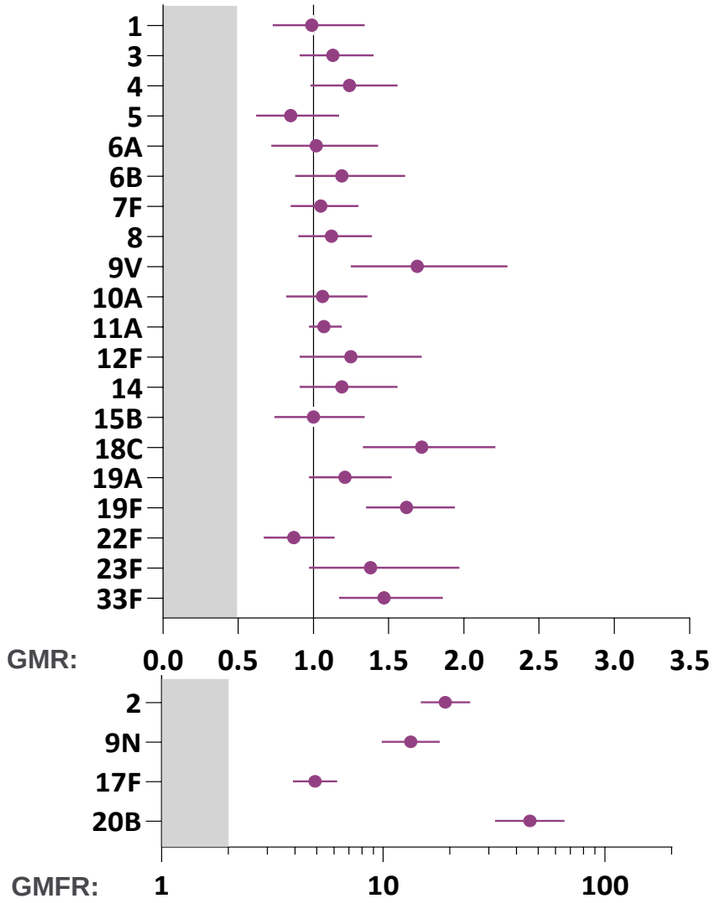
VAXCYTE

* *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.*

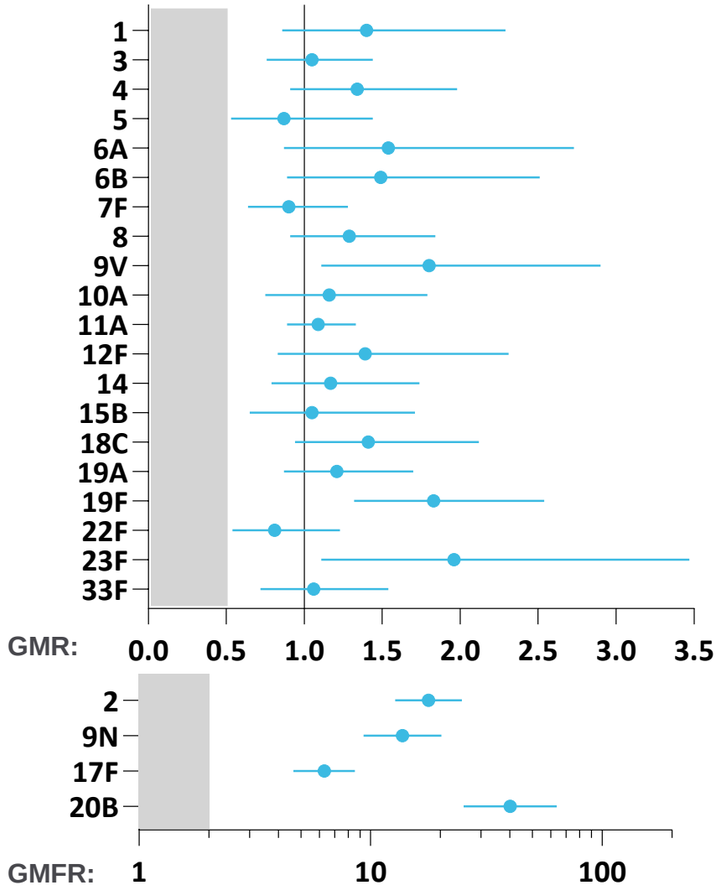
# Prespecified Pooled Analyses Support Advancement of VAX-24 to Phase 3

## 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*

# 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

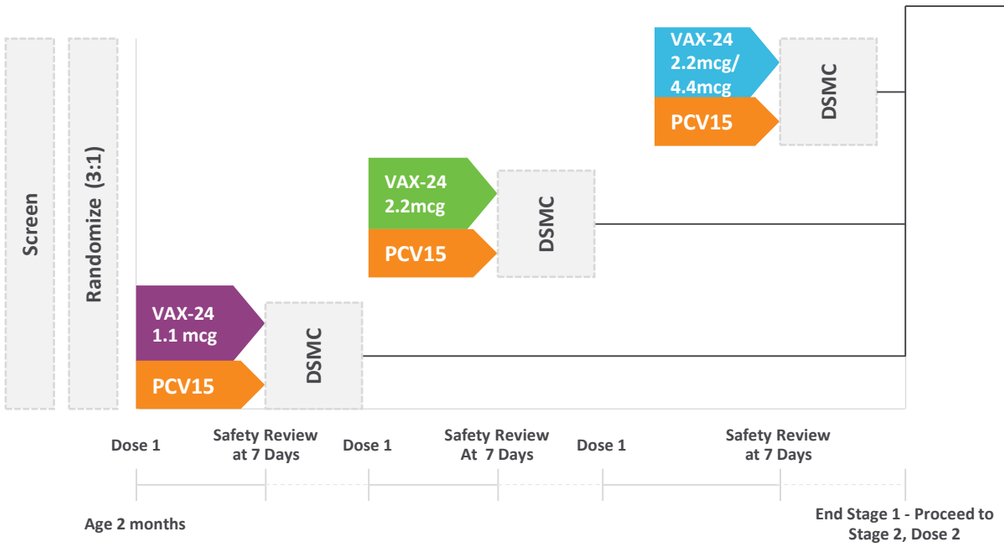
- Well-established regulatory pathway, with multiple precedents of approval based on surrogate immune endpoints
- Historically, consistent study design and endpoints across Phase 2 and pivotal Phase 3 programs
- Precedent Phase 3 programs and VAX-24 Phase 2 data support flexibility of choice in ultimate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

# VAX-24 Phase 2 Infant Study

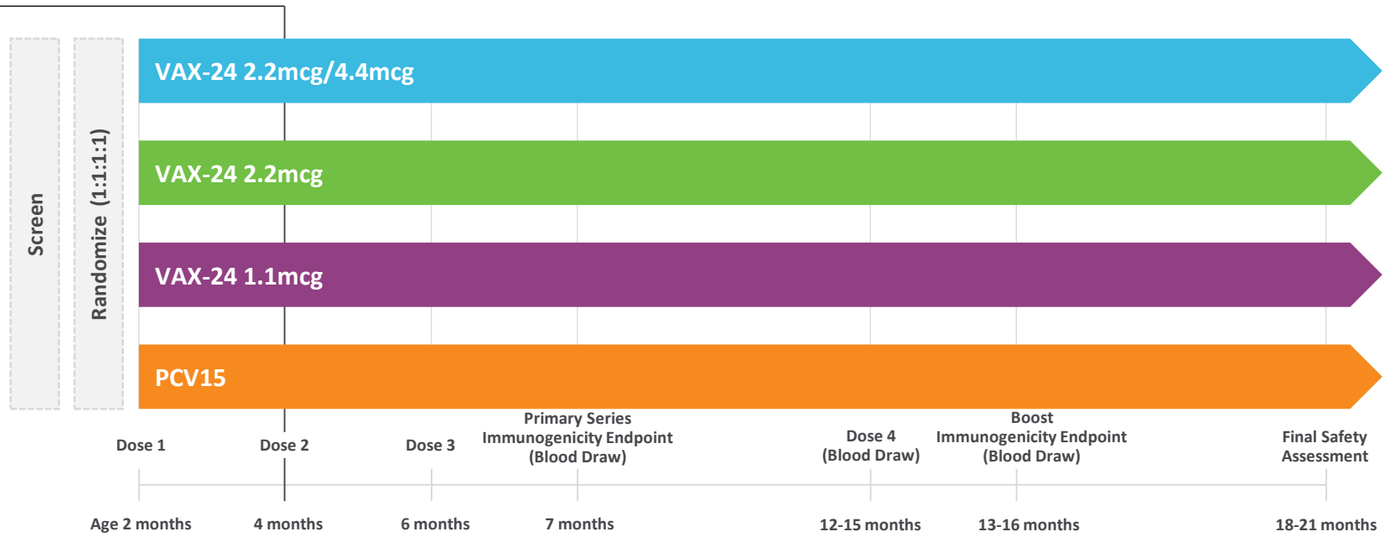
# Design of VAX-24 Phase 2 Clinical Study in Infants

## Randomized, Observer-Blind, Active-Controlled, Dose-Finding, Clinical Study to Evaluate Safety, Tolerability & Immunogenicity of VAX-24 vs SOC in Healthy Infants

### Stage 1: Dose Escalation (n~48)




### Stage 2: Main Study (n~750)




### STAGE 1 OVERVIEW

- Stage 1 is evaluating safety and tolerability of a single injection of VAX-24 at three dose-escalating levels and compared to PCV15 in ~48 healthy infants.
- Infants will be enrolled and dosed at two months of age and evaluated seven days post-dose. Following satisfactory Data Safety Monitoring Committee (DSMC) review of safety data, the study will proceed to the next dose.
- If DSMC approves moving forward, all participants from Stage 1 will be part of the Stage 2 study starting at dose two (four months).

*SOC = standard-of-care*
*ACIP = Advisory Committee on Immunization Practices*

### STAGE 2 OVERVIEW

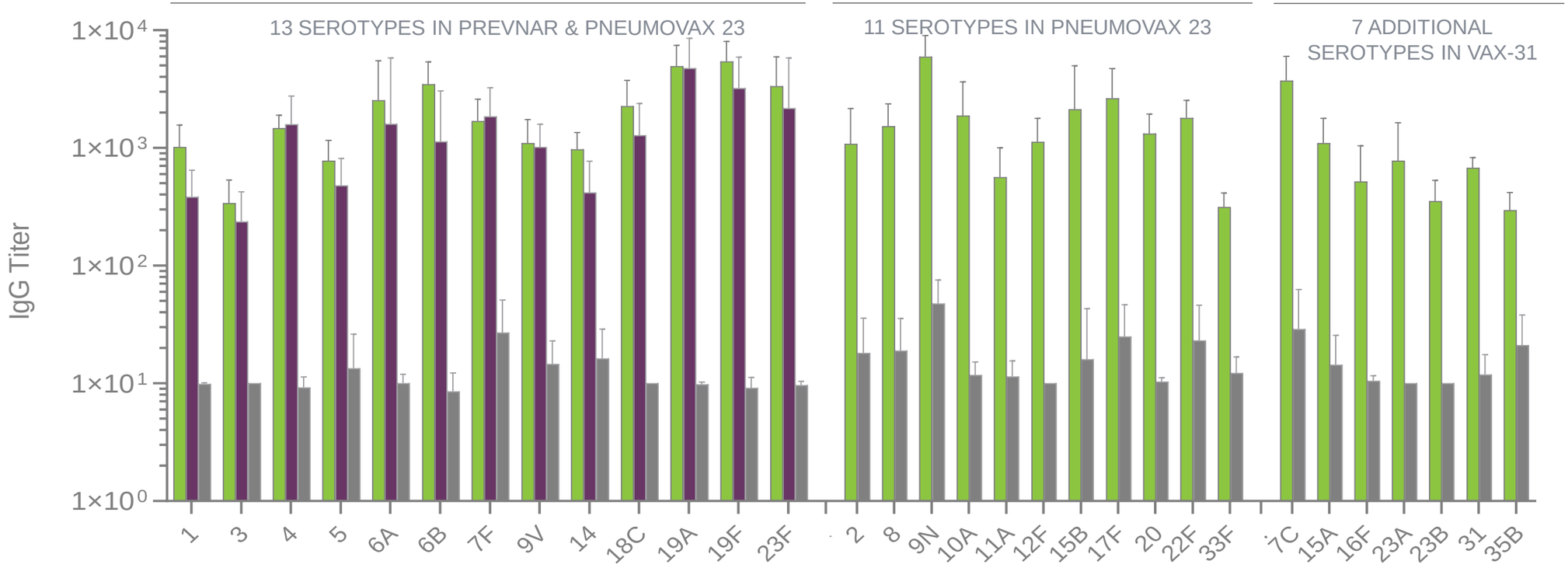
- Stage 2 will evaluate safety, tolerability and immunogenicity of VAX-24 at three dose levels and compared to PCV15 in ~750 healthy infants. Per ACIP guideline, the primary immunization series includes three doses given at two months, four months and six months of age, followed by a booster dose at 12-15 months of age.
- The key prespecified immunogenicity study endpoints include an assessment of the induction of immunoglobulin G (IgG) antibody responses 30 days post-dose three (proportion of participants achieving accepted IgG threshold of ≥0.35ug/ml) and IgG geometric mean titer ratios 30 days post-dose 4 on a serotype-by-serotype basis for all three VAX-24 dose levels and compared to PCV15.
- All participants will be evaluated for safety six months following the booster dose at 12-15 months of age.

# VAX-31 Preclinical Study

# VAX-31 Preclinical Data: Further Evidence of Potential for Platform

## IgG Responses for VAX-31 Comparable to Prevnar 13 & Superior to Polysaccharide-only Serotypes

- VAX-31 incorporates VAX-24 strains plus emerging serotypes responsible for significant IPD & antibiotic resistance.
- Demonstrates spectra scalability of platform and reproducibility of VAX-31 POC data with conjugates produced at larger scale.




*Note: +/- 95% confidential interval.*

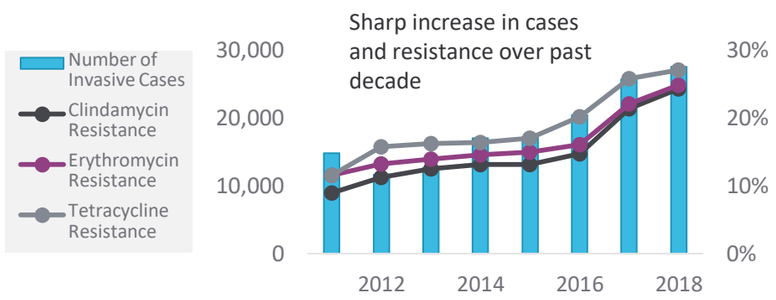
# Non-PCV Pipeline

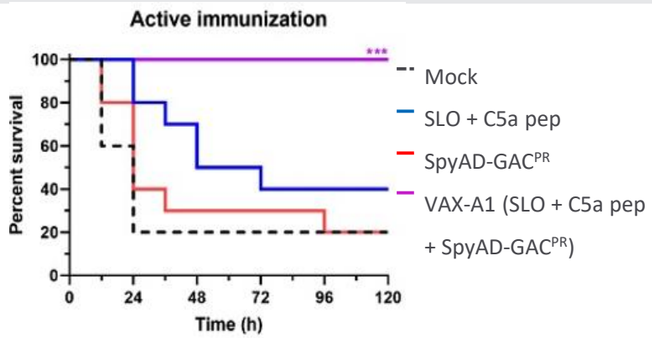
# VAX-A1: Group A Strep Conjugate Vaccine Program

## Novel Conjugate Vaccine Designed to Provide Universal Protection

| | |
|---|---|
| **UNMET NEED** | • Group A Strep results in 700M cases of illness annually worldwide, including pharyngitis, or strep throat, and certain severe invasive infections such as sepsis, necrotizing fasciitis and toxic shock syndrome.<br>• Upgraded CDC threat given significant source of antibiotic Rxs driving resistance which has nearly tripled in past decade<br>• Responsible for post-infectious immune-mediated rheumatic heart disease leading to over 300K deaths in 2015<br>• Highly prevalent in children and rate of invasive disease in adults > 65 has more than doubled (exceeding IPD rate in adults) |
| **VAX-A1: BROAD-SPECTRUM, MONOVALENT CONJUGATE VX** | • Designed to confer robust, boostable and durable protection against a broad spectrum of subtypes of Group A Strep<br>• Leverages site-specific conjugation to disease-specific carrier to expose mapped T- and B-cell epitopes<br>• Proprietary conserved antigen – Polyrhamnose – conjugated to an immunogenic disease-specific carrier along with two conserved virulence factors |
| **PROGRAM STATUS** | • Partially funded by grant from CARB-X (consortium of BMGF, Wellcome Trust, US Biodefense Agency (BARDA)); received $6.6M to date, with total potential funding of up to $14.6M inclusive of grants to date<br>• Initiated IND-enabling activities in 2H:21<br>• Development of VAX-A1 continues to advance and further information about the anticipated timing of an IND application will be provided as the program progresses |

**KEY DATA**




*CDC. Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: US Department of Health and Human Services, CDC; 2019.*
*BMGF = Bill & Melinda Gates Foundation.*

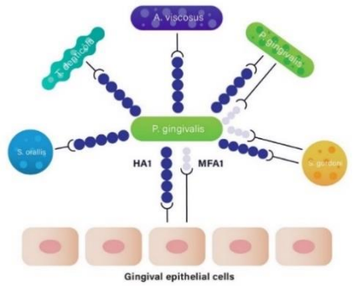
# VAX-PG: Periodontitis Vaccine Program

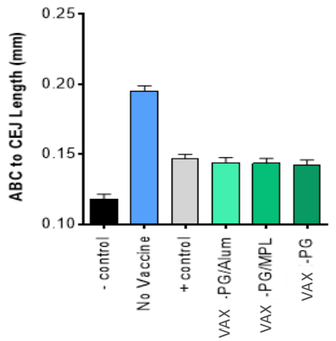
## Therapeutic Vaccine Targeting Gingipains to Address Large, Underserved Market

| | |
|---|---|
| **UNMET NEED** | • Periodontal disease is a chronic oral inflammatory disease leading to destruction of soft & hard tissues supporting the teeth<br>• Highly prevalent: estimated 65 million US adults afflicted<br>• Periodontal disease caused an estimated loss of $330.6 billion in the US and Europe in 2018, with the direct costs exceeding $6 billion<br>• Associated with increased risk of heart attack, stroke, cardiovascular disease and Alzheimer's Disease |
| **VAX-PG: MULTIVALENT THERAPEUTIC VACCINE** | • Incorporates proprietary combination of known virulence factors of keystone pathogen<br>• Preclinical model demonstrated protein-specific IgG response following immunization and protected mice from P. gingivalis-elicited oral bone loss<br>• Initial goal to develop therapeutic vaccine that slows or stops disease progression |
| **PROGRAM STATUS** | • Preclinical proof of concept published in Journal of Clinical Periodontology<br>• A final vaccine candidate for VAX-PG was nominated in Q4 2022 and the program continues to advance |
| **MOA & KEY DATA** | • Restoration of balanced microbiota by interrupting underlying inflammatory condition |








**Challenge Study Results**

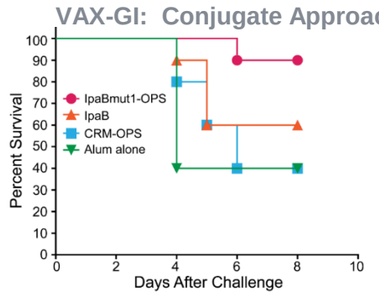
Immunization with all formulations of VAX-PG provided significant protection against oral bone loss compared to the unvaccinated control ($p<0.01$)

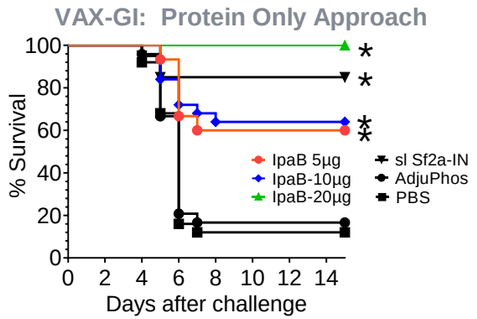
*Huang et.al. J Clin Periodontol. 2019 Feb;46(2):197-205.*

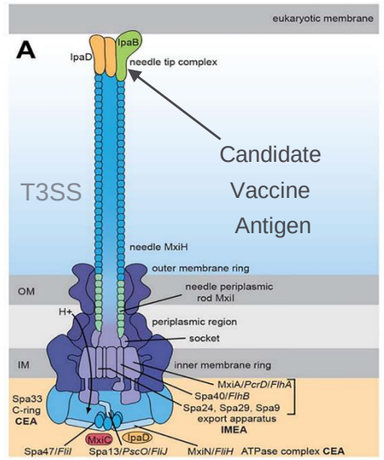
# VAX-GI: Shigella Vaccine Program

## Novel Shigella Vaccine

| | |
|---|---|
| **UNMET NEED** | • Shigella is a bacterial illness with no available preventative treatment<br>• Affects an estimated 180 million people worldwide each year and results in approximately 164,000 deaths annually, mostly among children under five years of age in low-income and middle-income settings[1]<br>• With the aim of reducing morbidity and mortality due to the disease, the World Health Organization's lists Shigella vaccine development as a priority goal[2] |
| **VAX-GI: NOVEL SHIGELLA VACCINE** | • Development collaboration with the University of Maryland, Baltimore; supported with funding by two NIH R01 grants for five years<br>• Will pursue conjugate and protein-only approaches simultaneously<br>• Conjugate approach: IpaB-LPS/IpaH/VirG; Protein-only approach: IpaB/IpaH/VirG |
| **PROGRAM STATUS** | • New program added to preclinical pipeline<br>• Decision on final candidate to be determined by a human challenge study conducted at the University of Maryland, Baltimore<br>• Currently optimizing process for scale-up and production |
| **MOA & KEY DATA** | • Targeting IpaB inhibits assembly of T3SS and toxin delivery to immune cells<br>• Opsonophagocytosis and killing of bacteria |





(1) *Lancet. 2018 Feb 24;391(10122):801-812.*
(2) *https://www.who.int/publications/i/item/9789240036741.*

# Key Corporate Highlights

VAXCYTE
protect humankind™

- Large Market Opportunity for Lead PCV Franchise
- Cell-Free Protein Synthesis Platform
- Disciplined Target Selection
- Robust Pipeline with Multiple Novel Vaccines
- Aligned Critical Resources

# Appendix

# VAX-24 Adult Phase 1/2 Study Topline Results

# Phase 1/2 Adult Proof-of-Concept Study Topline Data Key Take-Aways

## 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 in adults aged 18-64**

**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 in adults 50-64 years of age**

- 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**

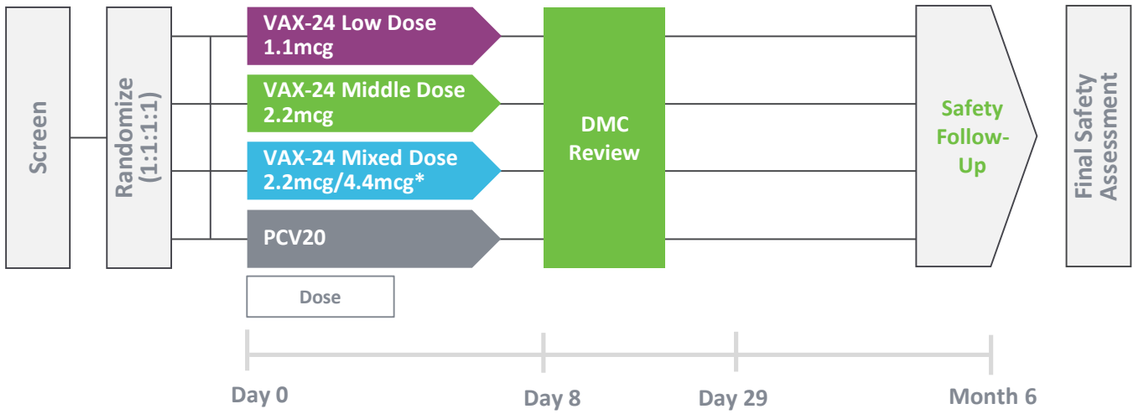
**PCV FRANCHISE: VAX-31, a 31-valent PCV candidate, advancing as follow-on to VAX-24**

- Learnings from Phase 1/2 study to inform optimal design for VAX-31 clinical program given ability to add STs without sacrificing overall immune responses

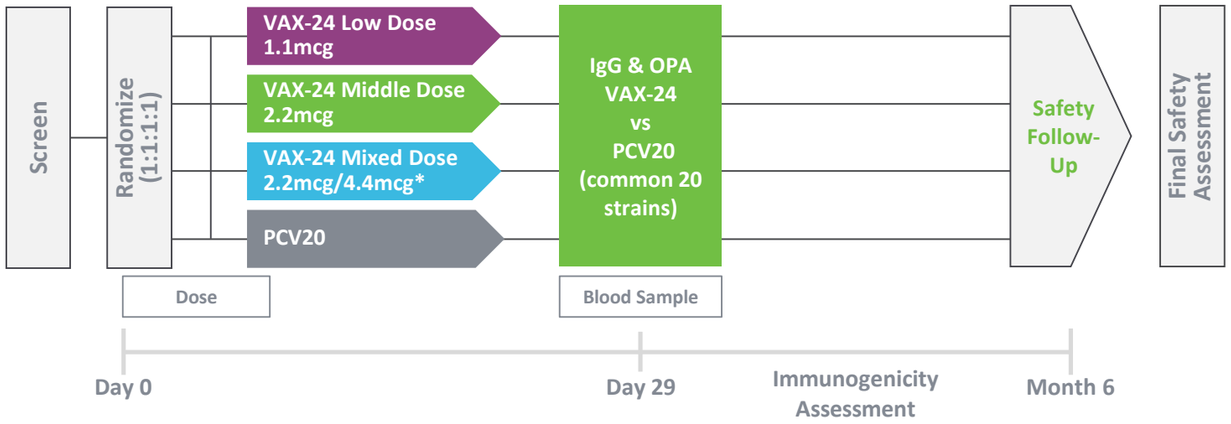
# VAX-24 Phase 1/2 Clinical Proof-of-Concept Study Design

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

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



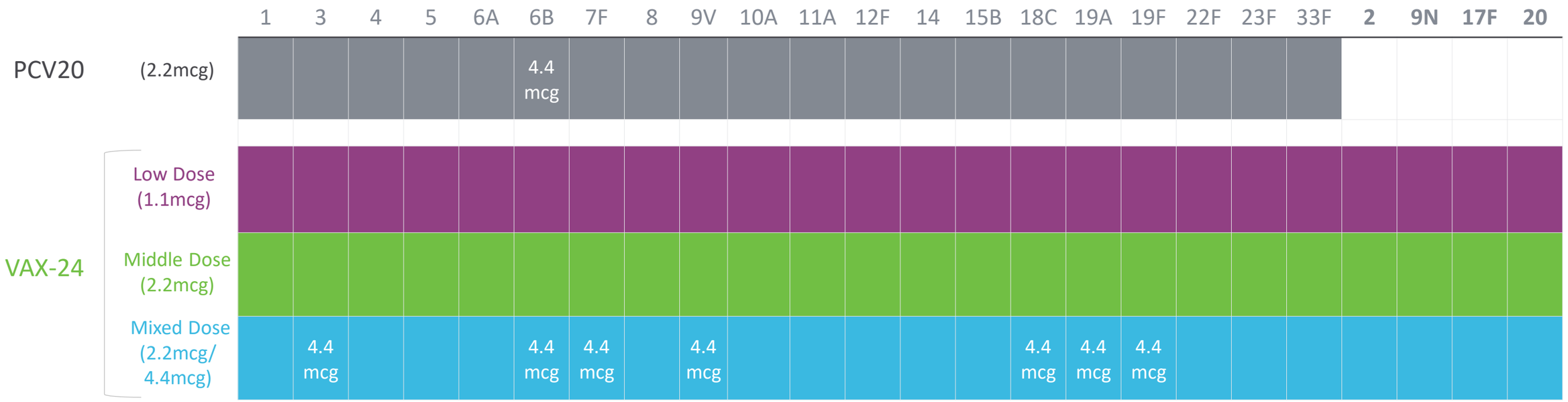

**Clinical POC Phase 2 Study**
Healthy Adults 50 to 64 (n=771)




** 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.

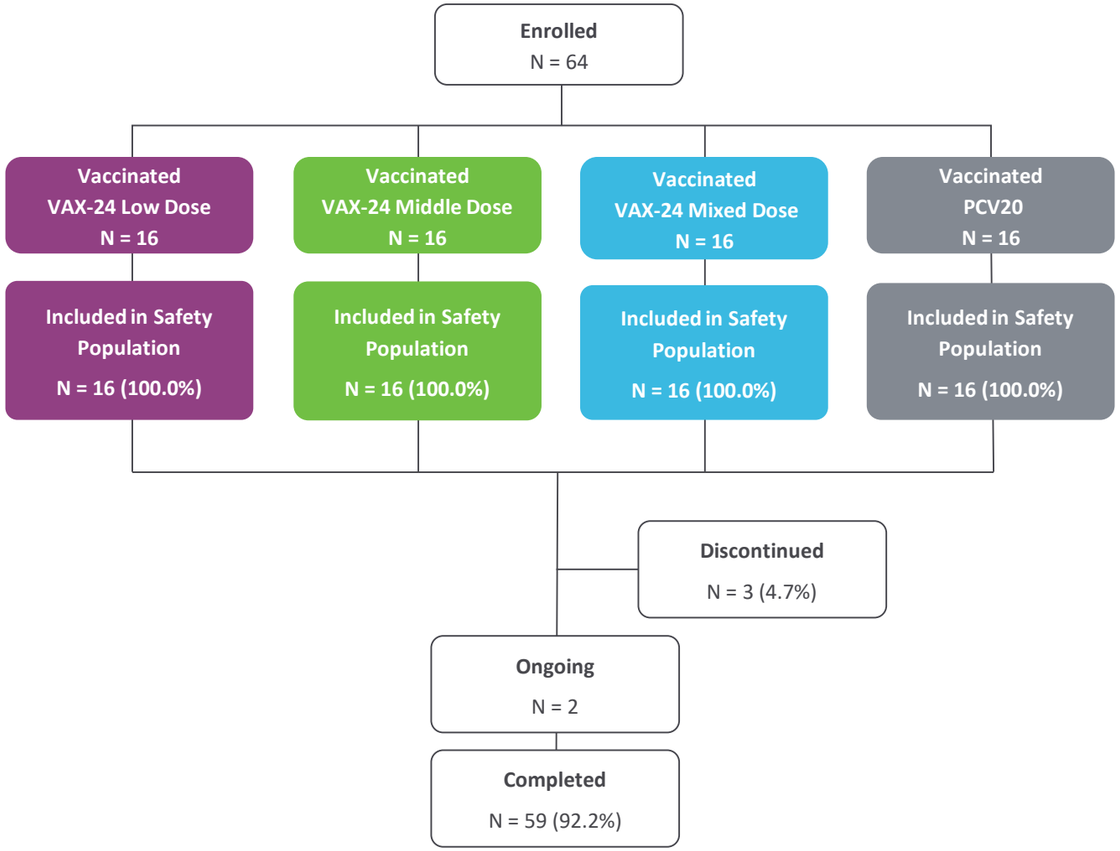
# Study Safety, Tolerability and Immunogenicity Key Outcome Measures

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

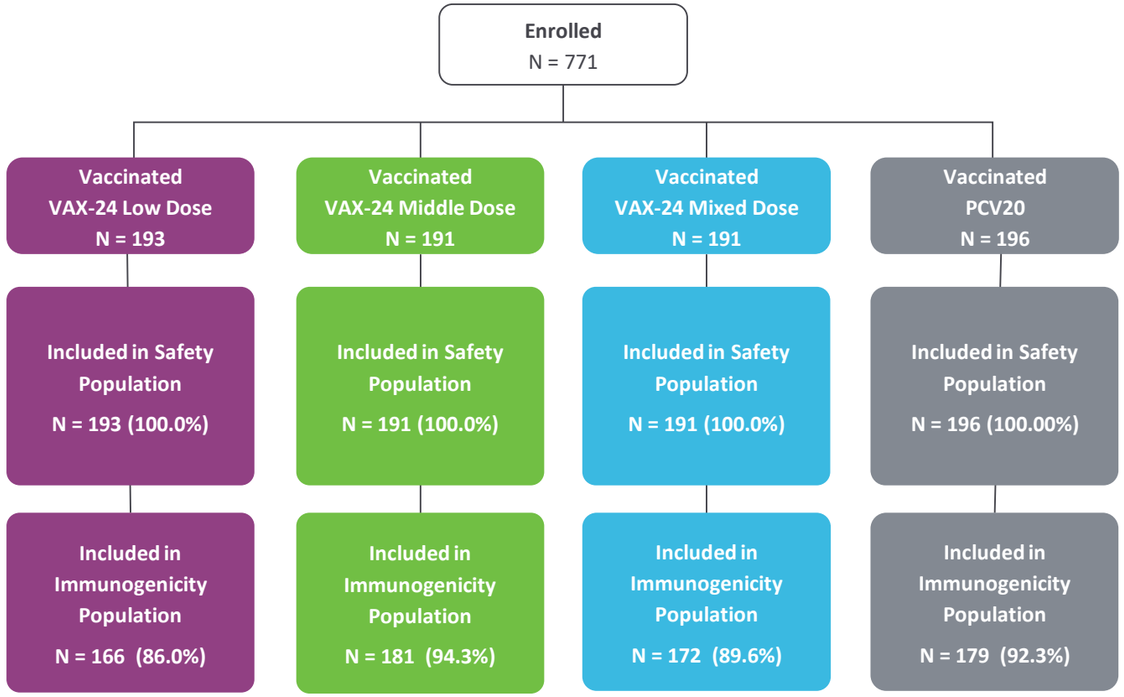
# Phase 1/2 Study Disposition

## 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)



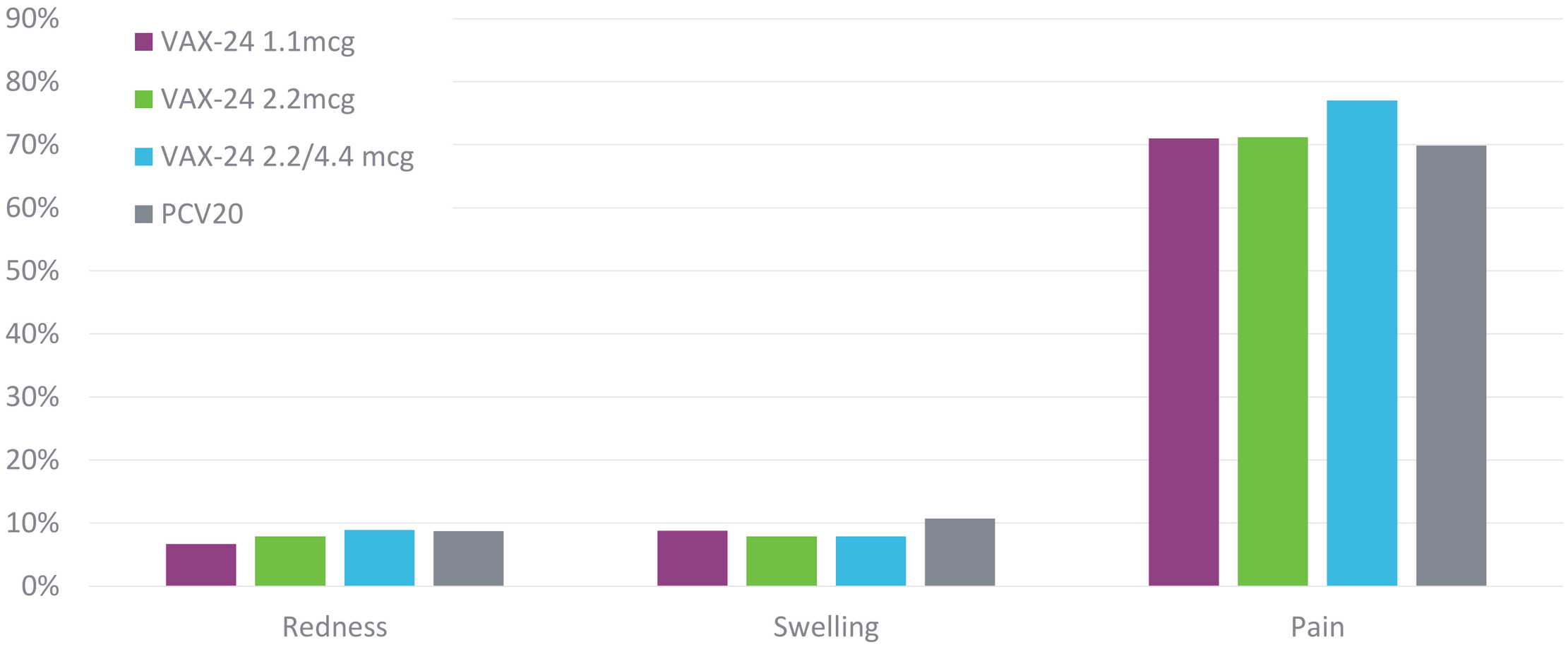

*9 subjects were lost to follow-up in Phase 2*

# Phase 2 Demographic Population

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

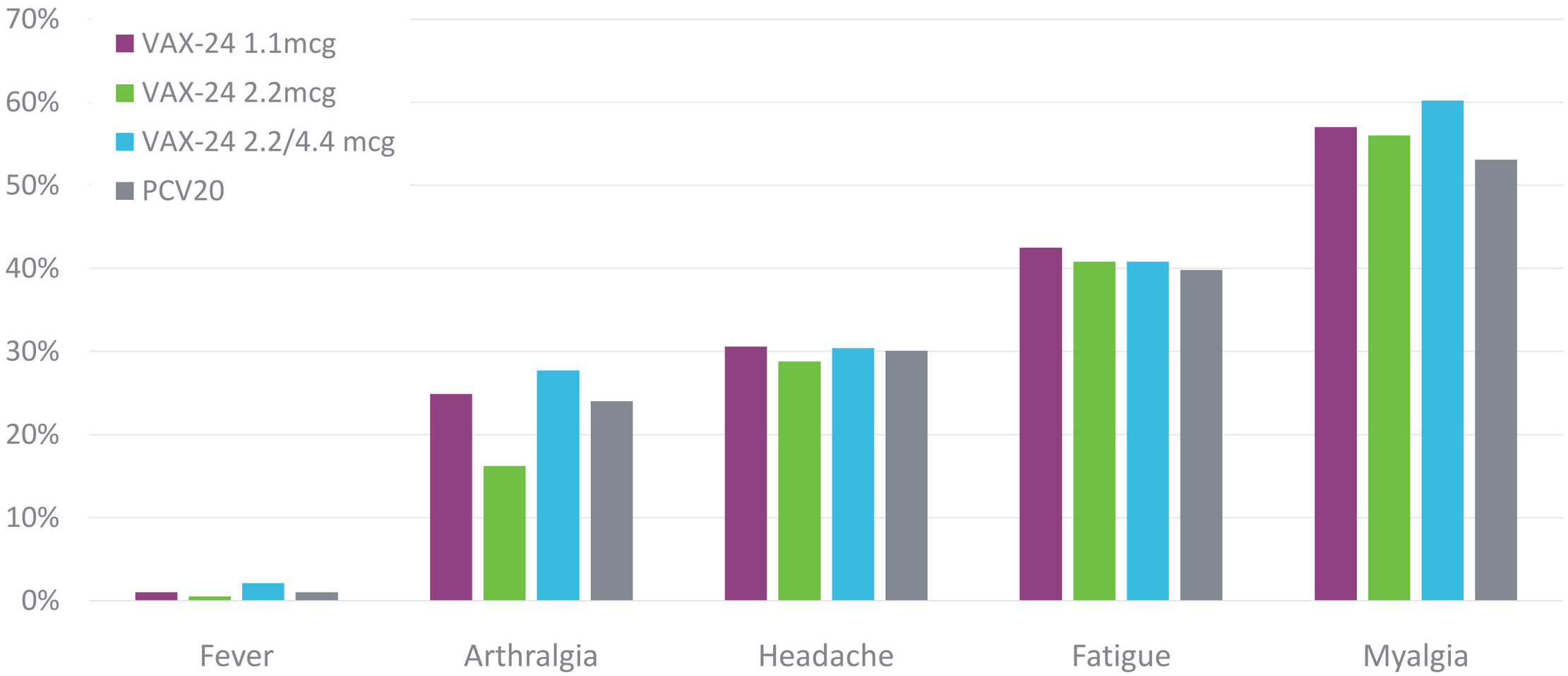
| | VAX-24 – Low Dose (1.1mcg) | | VAX-24 – Middle Dose (2.2mcg) | | VAX-24 – Mixed Dose (2.2mcg/4.4mcg) | | PCV20 | |
|---|---|---|---|---|---|---|---|---|
| | Safety | Immunogenicity | Safety | Immunogenicity | Safety | Immunogenicity | Safety | Immunogenicity |
| **Number of Subjects** | 193 | 166 | 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) |

# 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.*

# 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

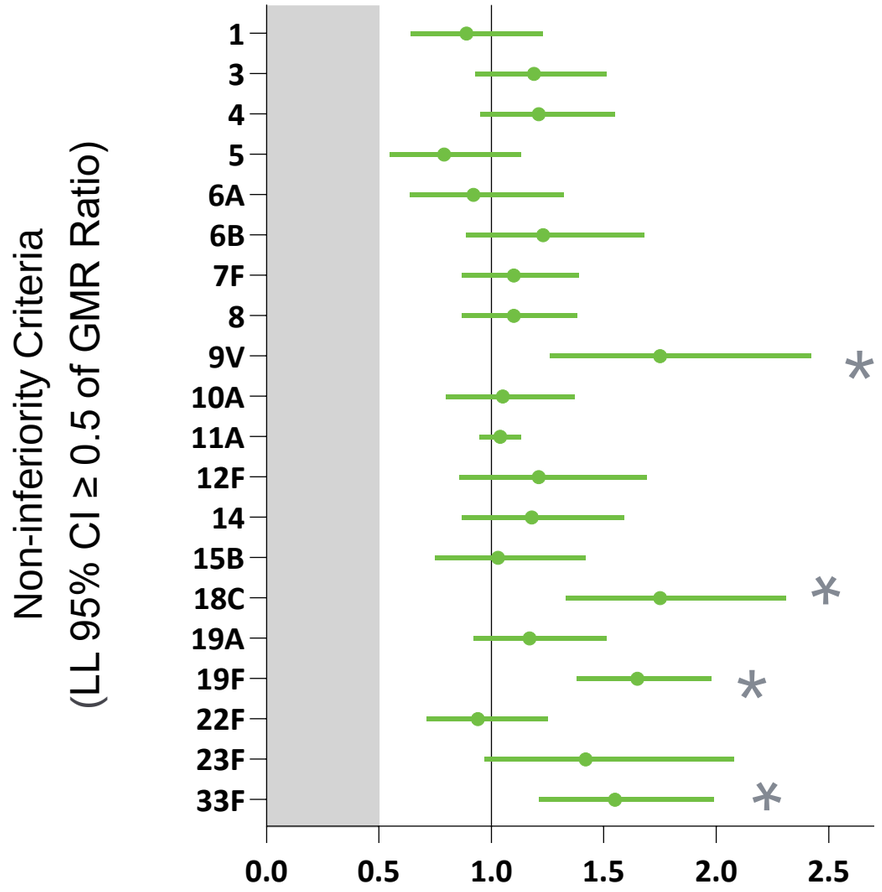
## CRITERIA FOR 4 INCREMENTAL SEROTYPES IN VAX-24:

### Superiority Standard:

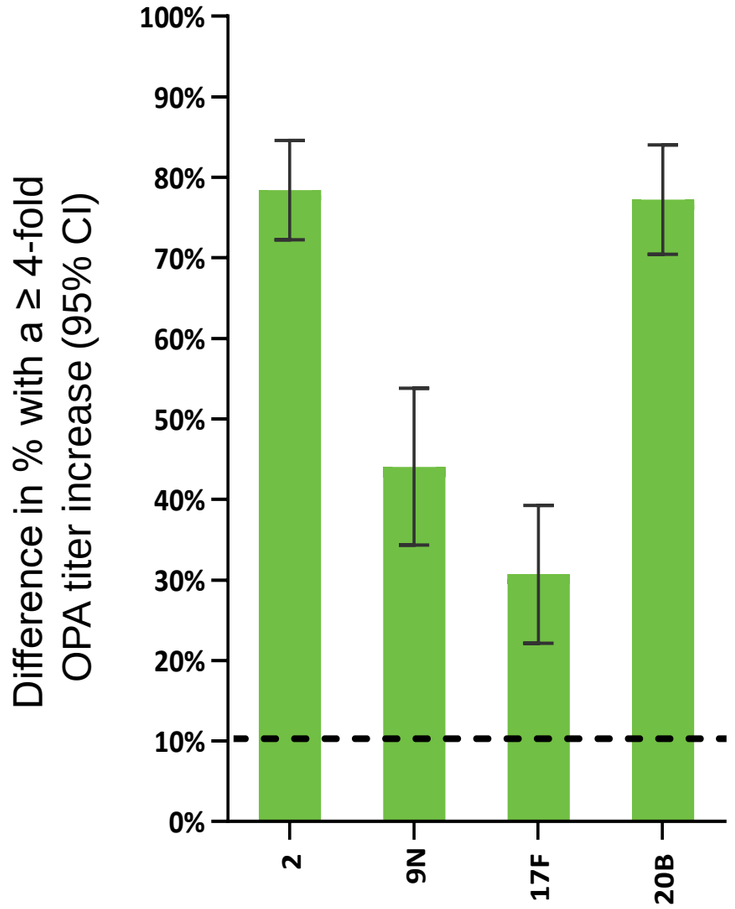
- Lower bound of the 2-sided 95% CI of the difference in the proportions of participants with a ≥4-fold increase from Day 1 to Day 29 is greater than 10%
- Lower bound of the 2-sided 95% CI of the OPA GMT ratio is greater than 2.0

# 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]**




**Regulatory Threshold for Superiority (LL95%CI > 10%)**

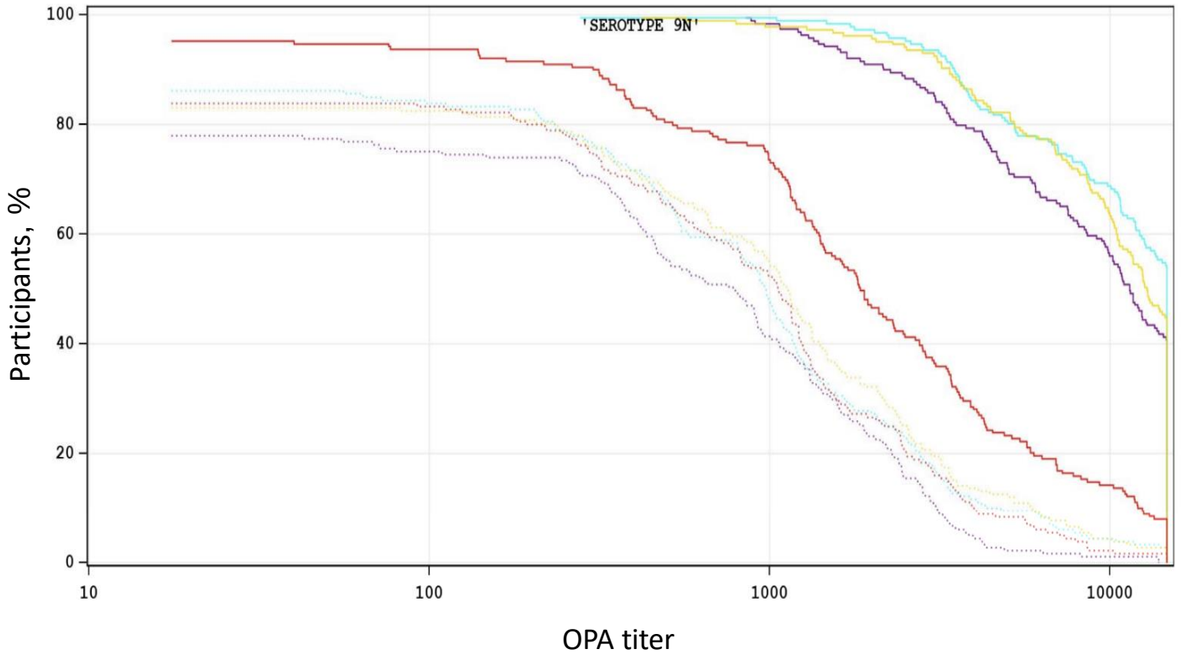
VAXCYTE

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

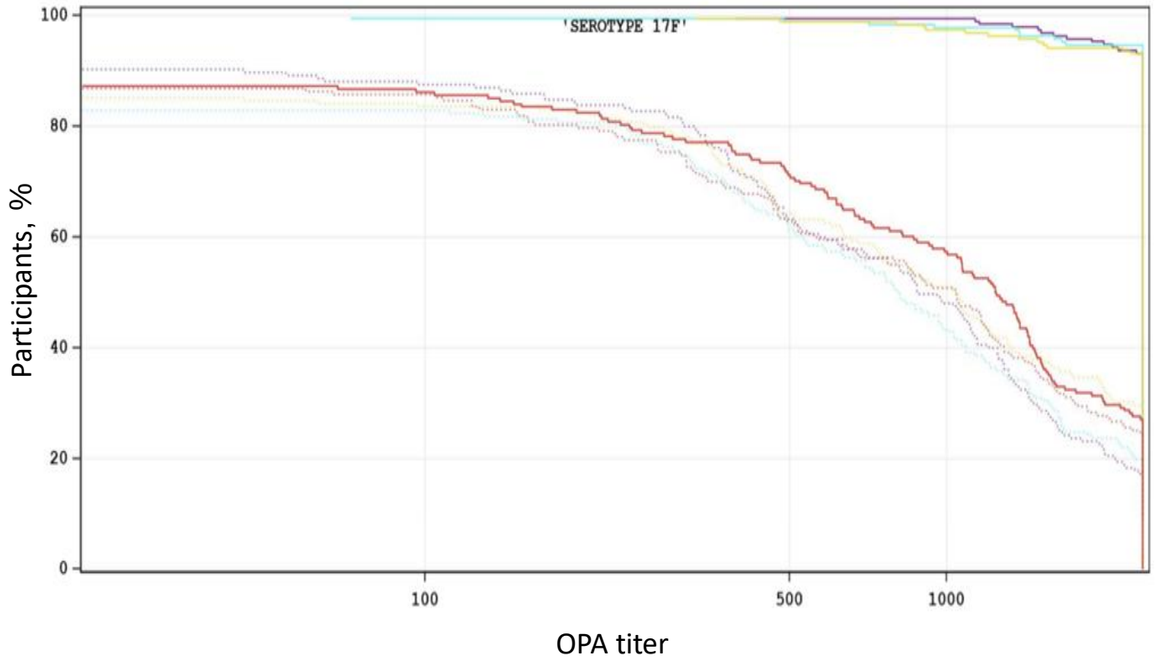
* *Reached statistical significance for superiority.*

# Serotypes 9N and 17F Had Higher Baseline Titers, yet VAX-24 Cohorts Still Showed Substantial Improvement Exceeding Regulatory Threshold

**SEROTYPE 9N:**
**OPA REVERSE CUMULATIVE DISTRIBUTION CURVE**




**SEROTYPE 17F:**
**OPA REVERSE CUMULATIVE DISTRIBUTION CURVE**

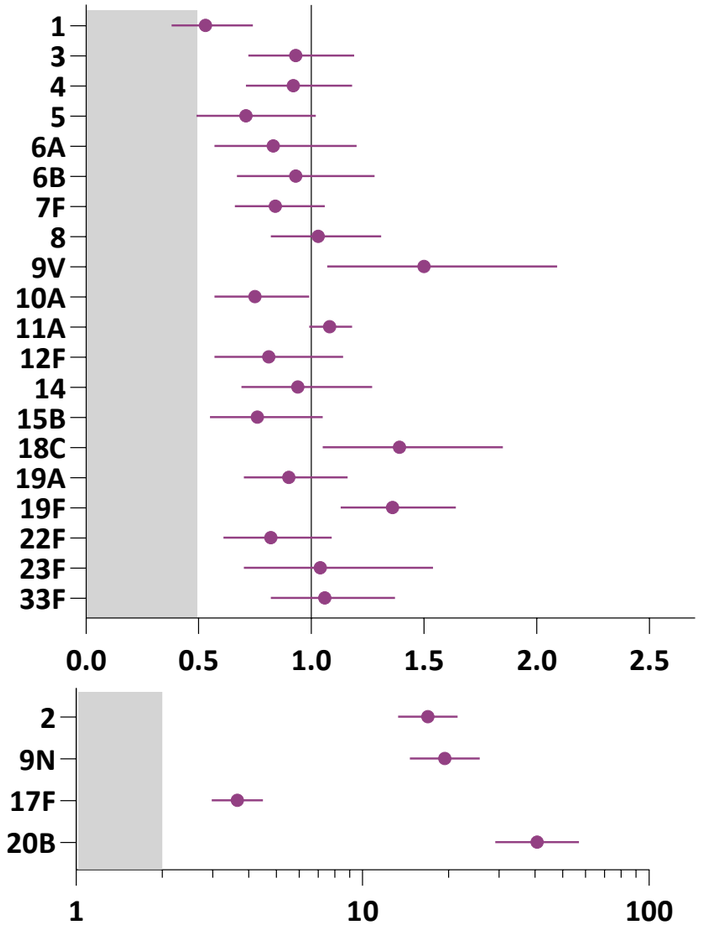



VAX-24, 1.1mcg – Day 1
VAX-24, 2.2mcg – Day 1
VAX-24, 2.2mcg/4.4mcg – Day 1
PCV20 – Day 1
VAX-24, 1.1mcg – Day 29
VAX-24, 2.2mcg – Day 29
VAX-24, 2.2mcg/4.4mcg – Day 29
PCV20 – Day 29

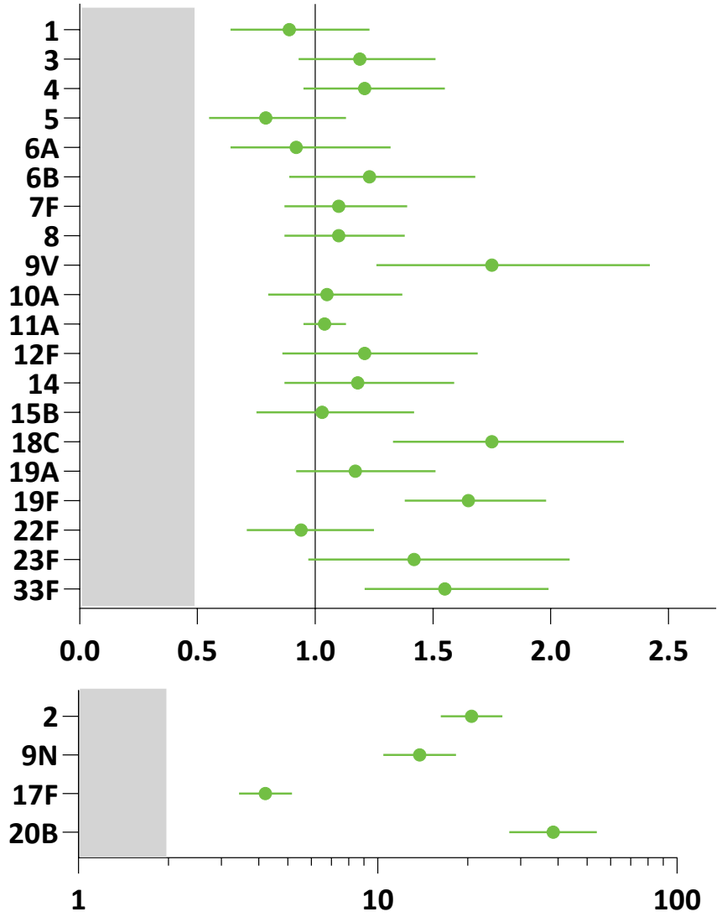
# All 3 Doses Induced Immune Responses Sufficient to Move to Phase 3

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

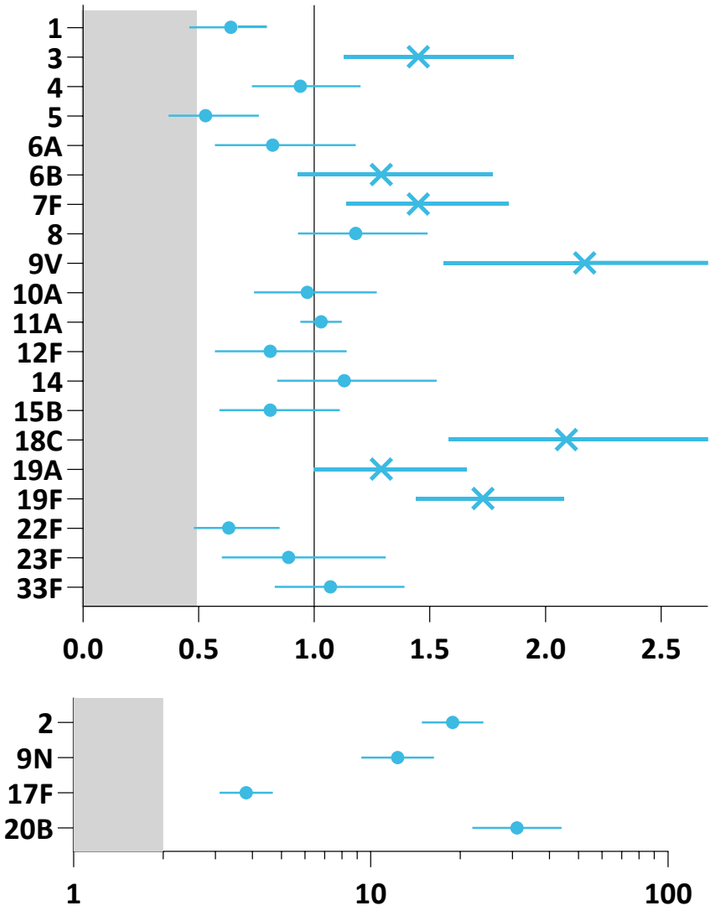
**VAX-24 Low Dose (1.1mcg)**




**VAX-24 Middle Dose (2.2mcg)**

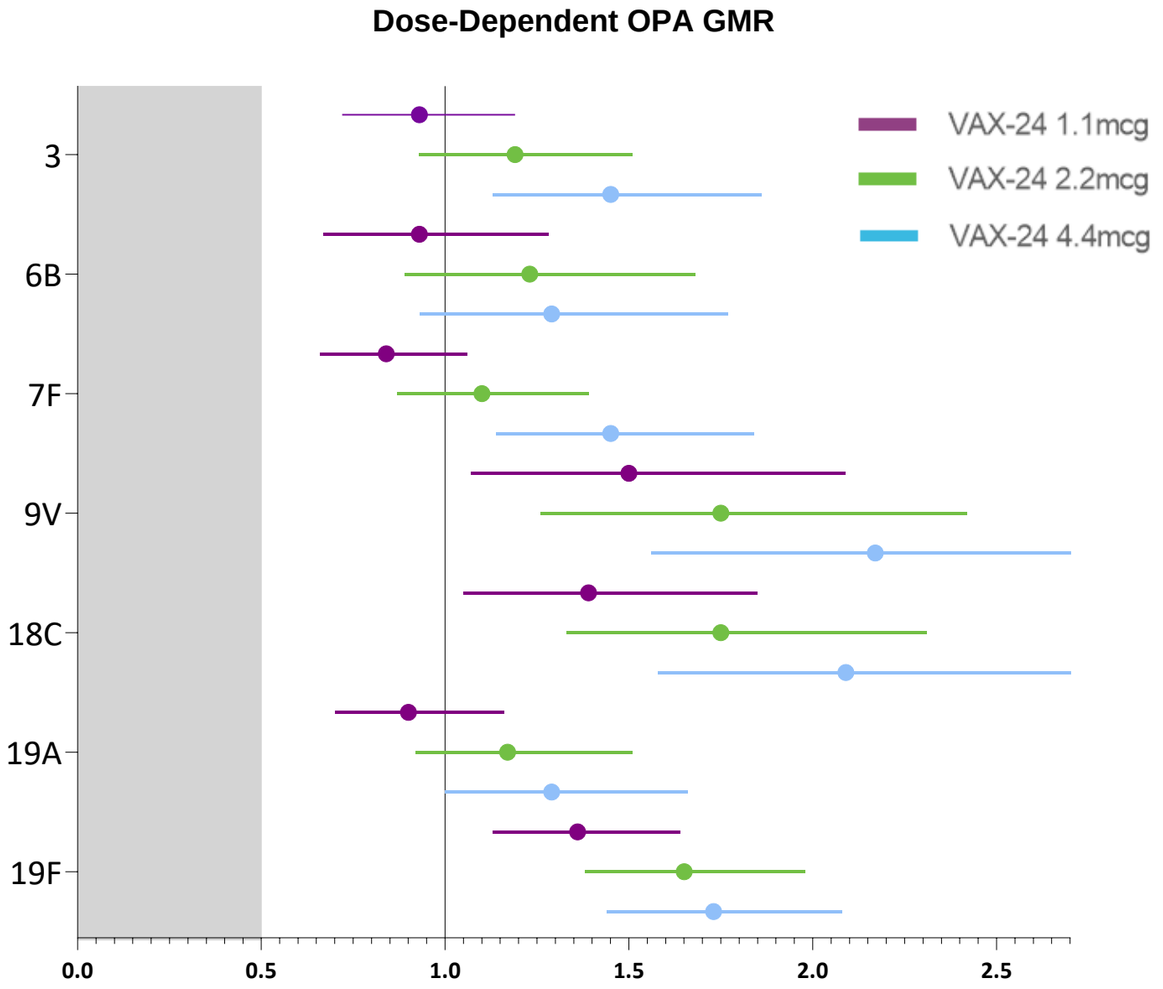



**VAX-24 Mixed Dose (2.2mcg/4.4mcg)**




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

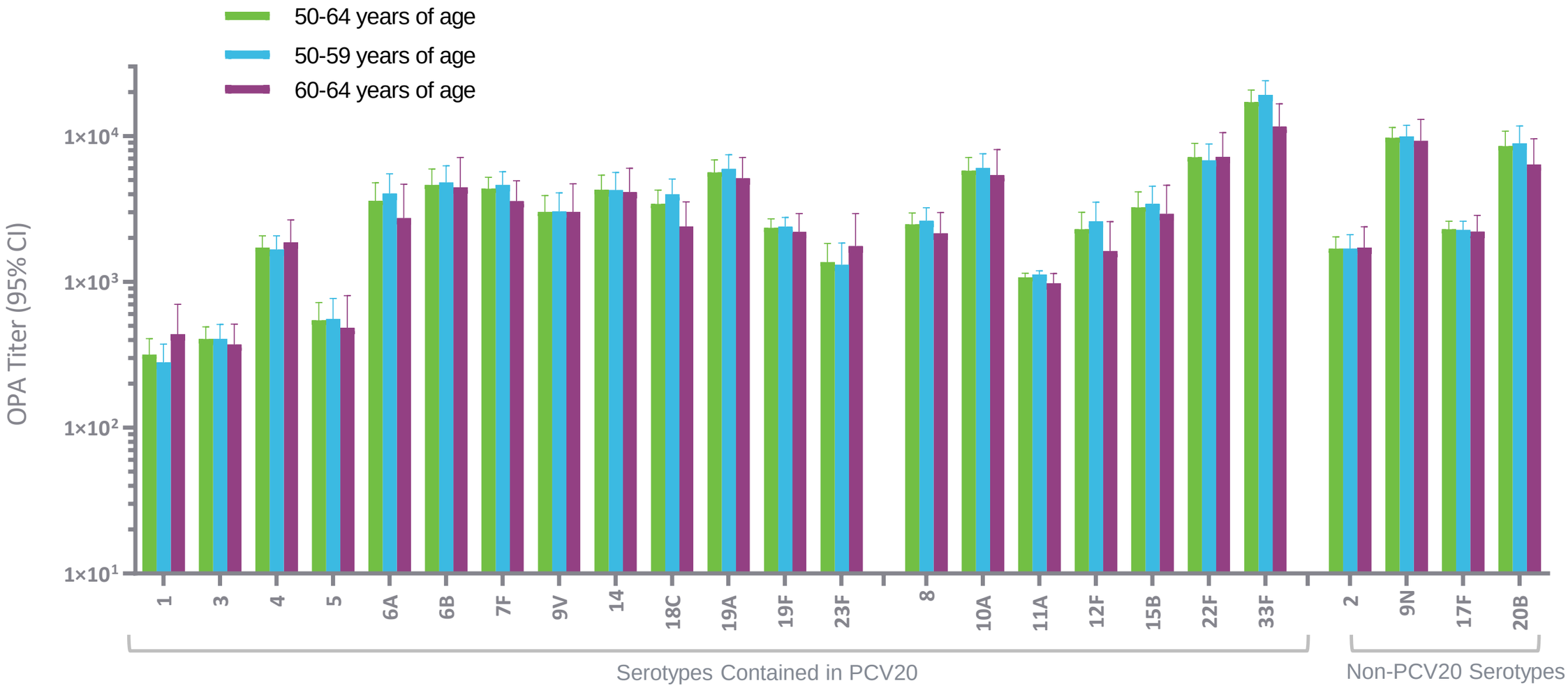
# Strong Evidence of a Dose-Dependent Response for the 7 VAX-24 Serotypes Tested at 1.1mcg, 2.2mcg and 4.4mcg




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

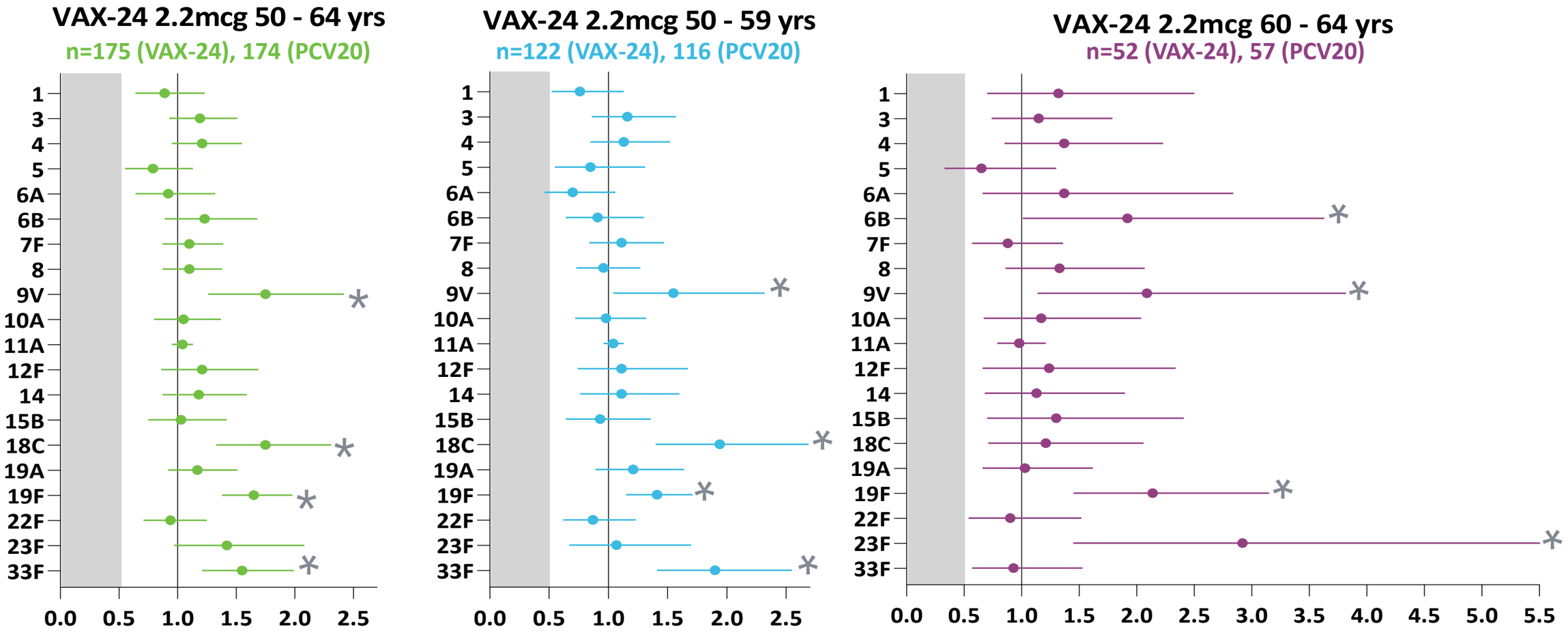
# VAX-24 2.2mcg OPA Geometric Mean Titers by Serotype and Age

## As Expected, Absolute Mean Titers Generally Lower in Older Population Due to Immunosenescence



# Age Stratified OPA GMR for 2.2mcg VAX-24 Dose Compared to PCV20

## Similar Results Between Age Groups With Higher Variability in Older Population Due to Smaller Sample Size




*Reached statistical significance for superiority.

*Note: n represents the lowest number of evaluable subjects among all serotypes.*