

# Corporate Presentation



May 6, 2026

**VAXCYTE**  
*protect humankind™*

# Forward-Looking Statements

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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 carrier-sparing platform and vaccine candidates, including breadth of coverage and the ability to deliver potentially better immune responses, a potentially best-in-class pneumococcal conjugate vaccine (PCV) franchise and the improvement upon the standard-of-care; demand for Vaxcyte’s vaccine candidates; the design, timing of initiation, progress and expected results of Vaxcyte’s preclinical studies, clinical trials and research and development plans; the ability of Vaxcyte’s cell-free platform to deliver the broadest-spectrum PCVs that provide protection against both currently circulating and historically prevalent strains; applicability of precedent criteria for licensure; Vaxcyte’s ability to establish global commercial manufacturing capacity for its PCV candidates; the ability of Vaxcyte to commercialize its PCV candidates and to meet the PCV franchise market demand for commercial markets; the use and availability of funds from NIH; the growth and expansion of the pneumococcal vaccine market, and the potential to address the need for broader-spectrum of coverage in such market; 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 and other statements that are not historical fact. The words “anticipate,” “believe,” “continue,” “could,” “designed,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These forward-looking statements are based on Vaxcyte’s current expectations and actual results and timing of events could differ materially from those anticipated in such forward-looking statements as a result of risks and uncertainties, including, without limitation, risks related to Vaxcyte’s product development programs, including development timelines, success and timing of chemistry, manufacturing and controls and related manufacturing activities; potential delays or inability to obtain and maintain required regulatory approvals for its vaccine candidates; the risks and uncertainties inherent with preclinical and clinical development processes; the success, cost and timing of all development activities and clinical trials; and sufficiency of cash and other funding to support Vaxcyte’s development programs and other operating expenses. 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 6, 2026 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.

A scientist in a white lab coat and safety glasses is working in a laboratory. The background is a blurred laboratory setting with various pieces of equipment and shelves.

## 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 Enrollment Completed in VAX-31 OPUS-1 Phase 3, Noninferiority Trial Designed to Establish Fulsome Coverage for Adults

## POTENTIAL BEST-IN-CLASS PCV FRANCHISE



- **Carrier-sparing, site-specific conjugation platform** enabling broader-spectrum PCVs
- **Adult Indication:**
  - **VAX-31:** Broadest-spectrum PCV in the clinic
  - Enrollment completed in OPUS-1, OPUS-2 and OPUS-3 Phase 3 trials
  - FDA BTM granted for IPD and pneumonia
  - Designed to cover ~95% of IPD while maintaining pressure on currently circulating and historically disease-causing serotypes in U.S. adults ≥ 50 years of age
- **Pediatric Indication:**
  - **VAX-24:** Announced final data from positive infant Phase 2 dose-finding study
  - **VAX-31:** Enrollment completed in Phase 2 dose-finding study, which includes multiple higher doses designed to optimize immune responses in children
- **VAX-XL: Third-generation PCV to further expand coverage**

## HIGHLY ATTRACTIVE PCV MARKET



- **Well-defined ~\$8B market segment poised for substantial growth**
  - **Age range in U.S. recently expanded to include adults ≥ 50 years of age;** and
  - Many developed countries now adopting **universal vaccination of older adults**
- Leverages established surrogate immune endpoints as basis for full approval, **negating need for field efficacy studies to support licensure**
- Serotype and disease spectrum of coverage is the **primary adoption driver**, yet incumbents **limited to partial coverage, which is driven by carrier suppression**

## EXCLUSIVE CELL-FREE PLATFORM



- **Vaxcyte PCV Franchise**
  - Leverages **site-specific conjugation** to expose protective T-cell antigens
  - Enables **carrier-sparing** conjugates that honor well-understood PCV MOA
- Permits production of **“tough-to-make” antigens**
- **Platform unlocks large market opportunities beyond PCVs**, including Group A Strep and Shigella
- **VAX-A1:** Novel Group A Strep vaccine
  - Plan to initiate Phase 1 adult study in mid-2026<sup>1</sup>
- **VAX-GI:** Novel Shigella vaccine

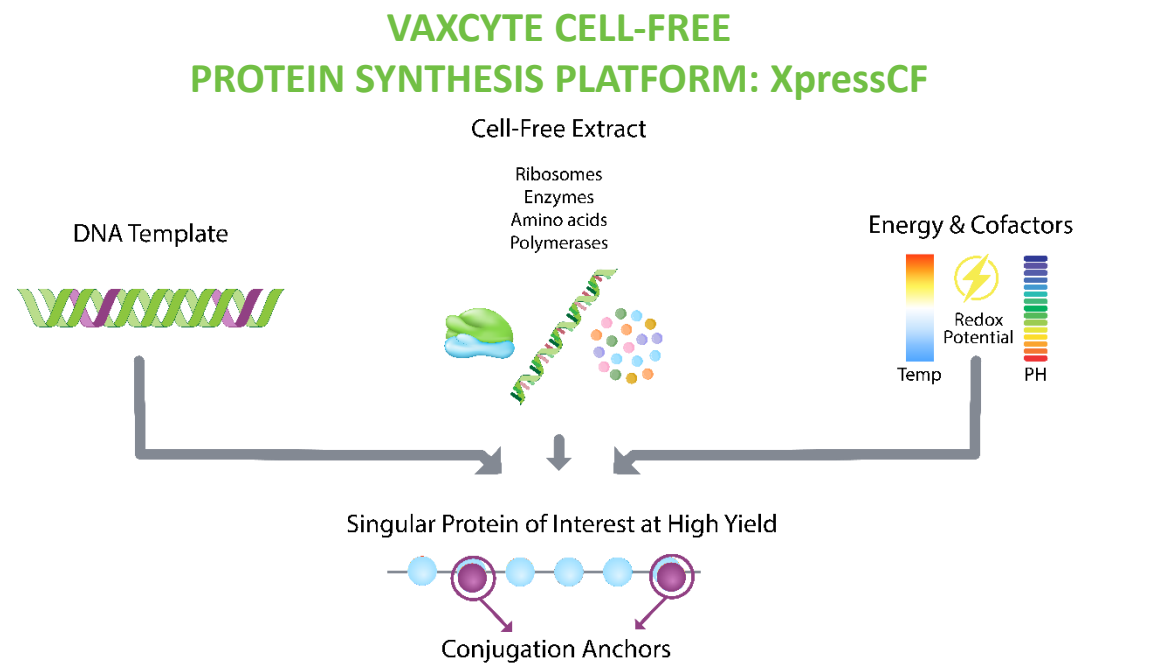
## ALIGNED CRITICAL RESOURCES



- **Strategic Manufacturing Approach**
  - Building out capacity to satisfy global PCV demand for developed markets
  - Global commercial manufacturing agreement with Lonza to produce key PCV components
  - Agreement with Thermo Fisher Scientific to establish U.S. fill-finish manufacturing; expands domestic capacity to support future commercial manufacturing
- **Seasoned management team**, directors and advisors
- **~\$2.7 billion in cash, cash equivalents and investments** as of 3/31/26

# Cell-Free Protein Synthesis Platform Unlocks Multiple Vaccine Applications

## Facilitates Design and Production of Proteins Beyond the Reach of Conventional Methods



- Transcriptional & translational (ribosomal) protein production machinery from E. coli
- 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
- Large-scale production achieved using standard equipment

### SUPERIOR CONJUGATE VACCINES

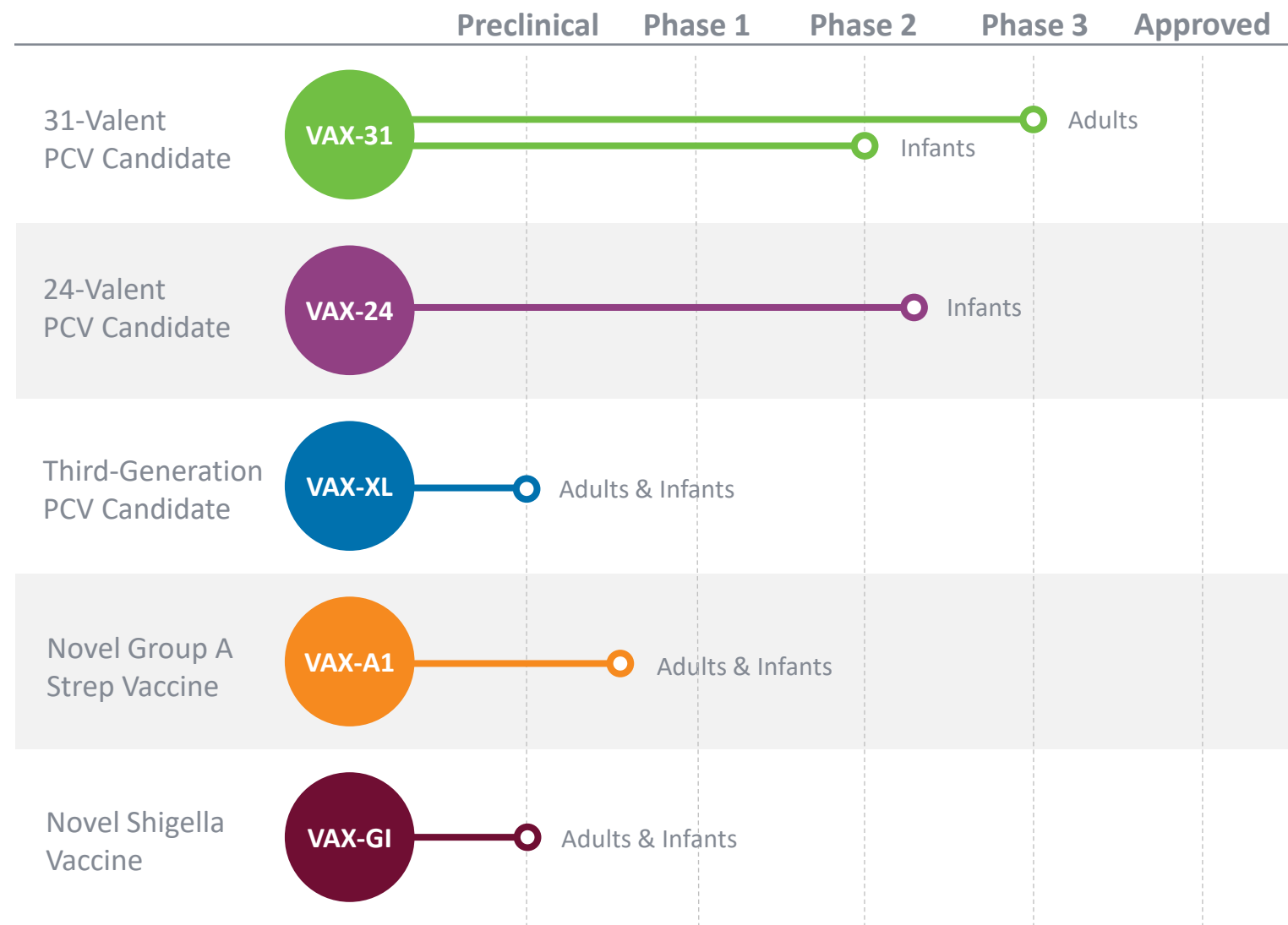
- Site-specifically attach antigens onto protein carriers designed to:
  - Enable consistent exposure of T-cell epitopes and/or B-cell epitopes on protein carrier
  - Avoid off-target effects
  - Enable use of less protein carrier without sacrificing immunogenicity
  - Enable broader-spectrum vaccines

### 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 with Multiple Near-Term Milestones

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



### Anticipated 2026 and 2027 Key Milestones<sup>1</sup>

#### VAX-31 ADULT INDICATION

- Announce safety, tolerability and immunogenicity data from the:
  - **OPUS-1** Phase 3 pivotal, noninferiority trial in the fourth quarter of 2026 (topline data)
  - **OPUS-2** and **OPUS-3<sup>2</sup>** trials in the first half of 2027

#### VAX-31 INFANT INDICATION

- Announce topline data from the ongoing Phase 2 dose-finding study from both the primary three-dose immunization series and booster dose either sequentially or together by the end of the first half of 2027

#### VAX-A1

- Initiate Phase 1 adult clinical study in mid-2026, with the primary objective of assessing safety and tolerability

(1) Guidance as of May 6, 2026.

(2) OPUS-2 is a Phase 3 trial evaluating concomitant administration of VAX-31 with a seasonal influenza vaccine; OPUS-3 is a Phase 3 trial evaluating VAX-31 in adults who have previously received pneumococcal vaccination.

# Experienced Management Team with Track Record in Vaccines and Biopharma

**Grant Pickering, MBA**  
*Chief Executive Officer  
& Co-Founder*



**Andrew Guggenime, MBA**  
*President  
& Chief Financial Officer*



**Jim Wassil, MS, MBA**  
*Executive VP  
& Chief Operating Officer*



**Mike Mullette, MBA**  
*Chief Commercial Officer*



**Chris Griffith, MS, MBA**  
*Chief Business & Strategy Officer*



**Harp Dhaliwal, MBA**  
*Chief Technical Operations Officer*



**Roger Nosal**  
*Senior VP  
& Head of Global Regulatory & Quality*



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



# PCV Opportunity

**VAXCYTE**  
*protect humankind™*



# Global Health 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 ~\$8 BILLION GLOBAL VACCINE CATEGORY

Vaccinations are recommended globally for infants and adults to prevent PD<sup>1,2</sup>

- >170 countries have officially introduced PCVs into national immunization programs<sup>3</sup>
- Routine SoC schedule in the U.S.:
  - Infants:
    - Prevnar 20<sup>®</sup> (PCV20) x 4 doses; or
    - Vaxneuvance<sup>®</sup> (PCV15) x 4 doses
  - Adults aged 50 and older (single dose):
    - PCV20 or Capvaxive<sup>™</sup> (PCV21); or
    - PCV15 & Pneumovax<sup>®</sup> 23 (PPV23)



## GLOBAL INCIDENCE & IMPACT OF PD STILL SUBSTANTIAL

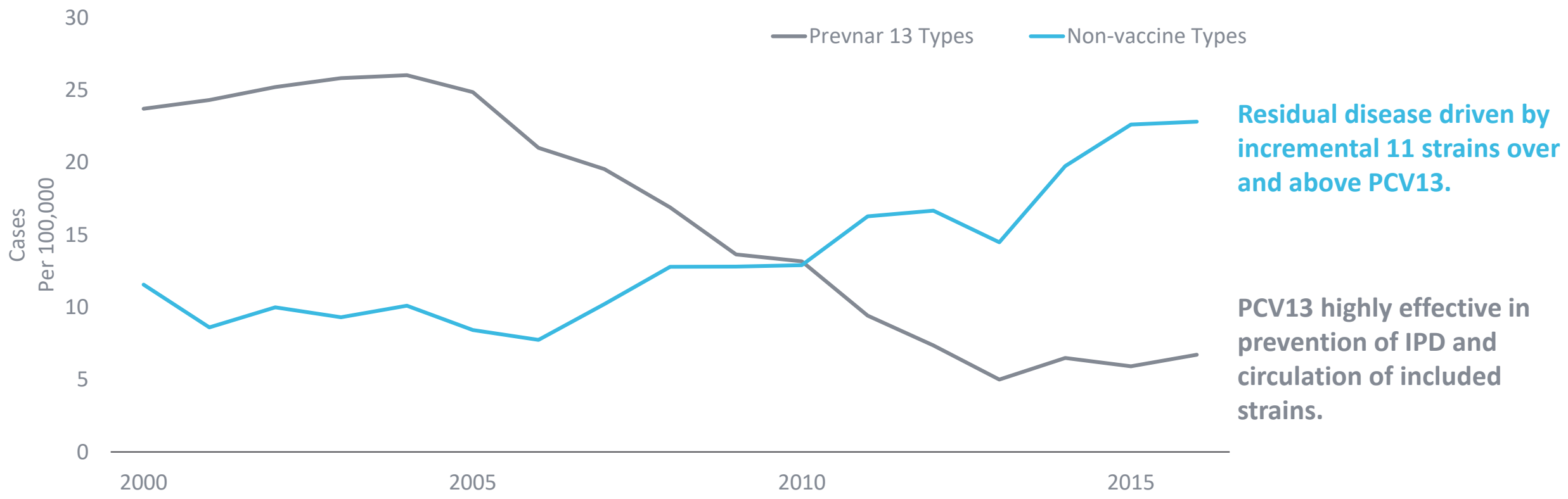
Global pneumococcal disease in children is driven by emerging serotypes not covered by currently available vaccines and in adults by not only emerging serotypes, but also fragmented coverage of today's standard of care vaccines

- *Streptococcus pneumoniae* is the leading cause of vaccine-preventable deaths globally in children under five<sup>4</sup>
- ~225K U.S. adult hospitalizations annually caused by pneumococcal pneumonia<sup>5</sup>
- ~300K children under five years old die annually worldwide due to *Streptococcus pneumoniae*<sup>6</sup>

# 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  $\geq 65$ <sup>1</sup>



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

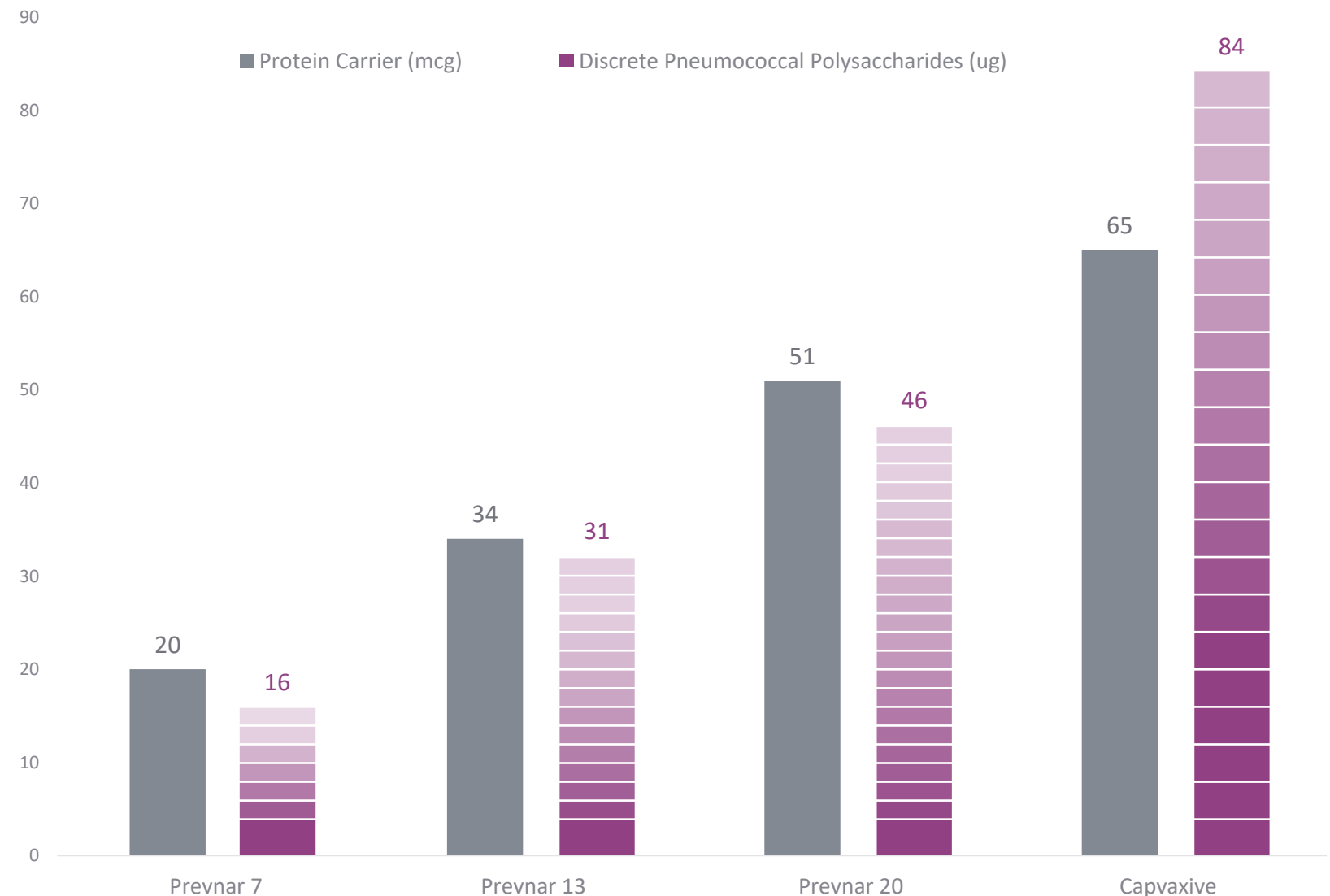
# Limitations of Current PCVs

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

## LIMITATIONS OF CONVENTIONAL CHEMISTRY

- Random conjugation masks on-target T-cell epitopes on the protein carrier
- Conventional reductive amination chemistry requires higher amounts of protein carrier than polysaccharide to form stable conjugates
- Overabundance of protein carrier exacerbates carrier suppression, due to competition for CD4+ help between disease-specific polysaccharides and non-disease specific protein carrier

## PROTEIN CARRIER DIVERTS IMMUNE RESPONSE



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

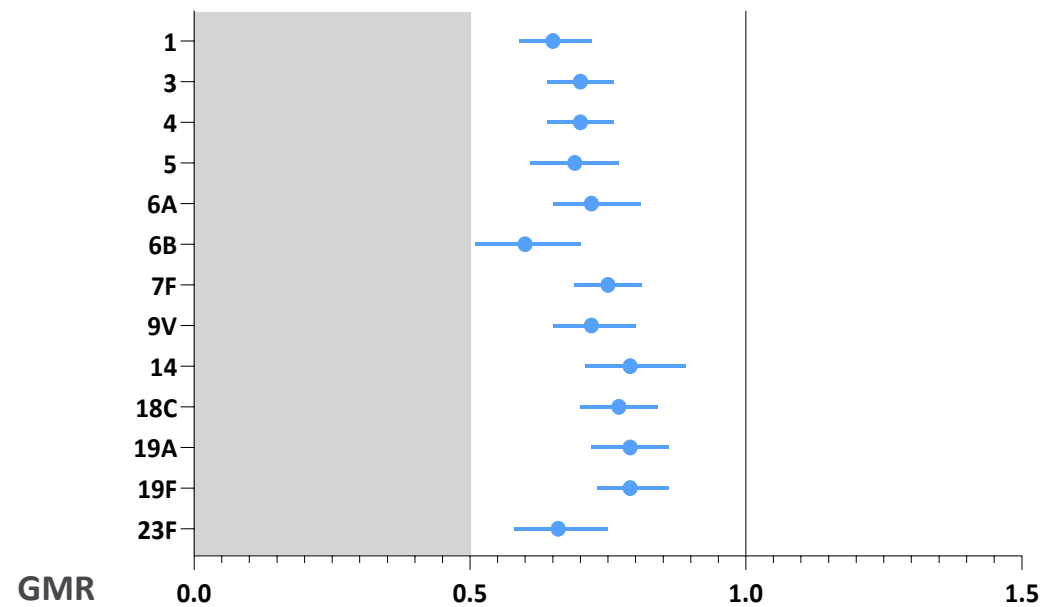
## Coverage Expansion Using Conventional Chemistry Has Led to Carrier-Induced Immune Suppression

### CARRIER SUPPRESSION

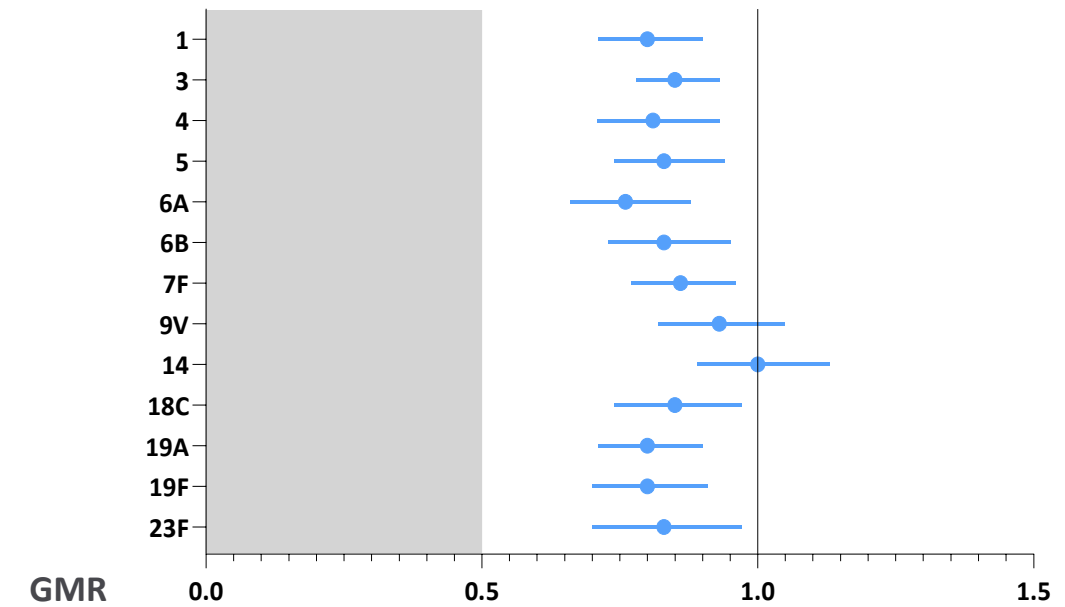
Diminished immune response to target polysaccharides due to cumulative amount of protein carrier

- 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):  
PCV20 VS PCV13<sup>1</sup>



ADULT IMMUNE RESPONSES (OPA):  
PCV20 VS PCV13<sup>2</sup>



(1) Immunoglobulin G (IgG) Geometric Mean Concentrations post-dose 4 – Prevnar 20 BLA Clinical Review Memorandum by FDA (STN: 125731/189). April 27, 2023.

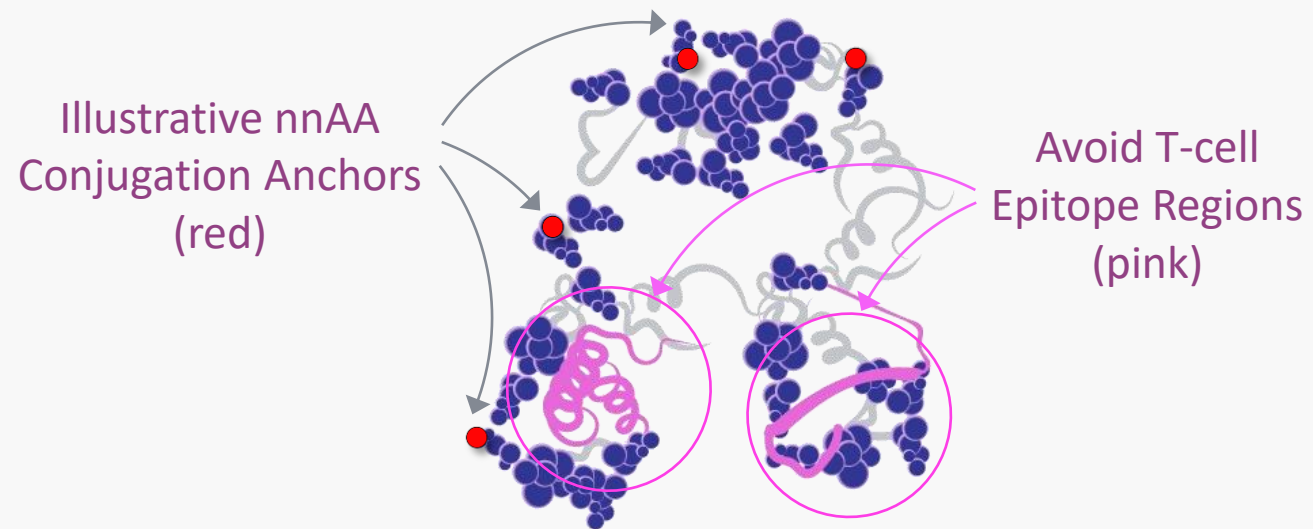
(2) Prevnar 20 BLA Clinical Review Memorandum. STN: 125731/0 June 8, 2021.

OPA = opsonophagocytic assay; GMR = geometric mean ratio.

# Vaxcyte's PCV Franchise Employs Carrier-Sparing Conjugates

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

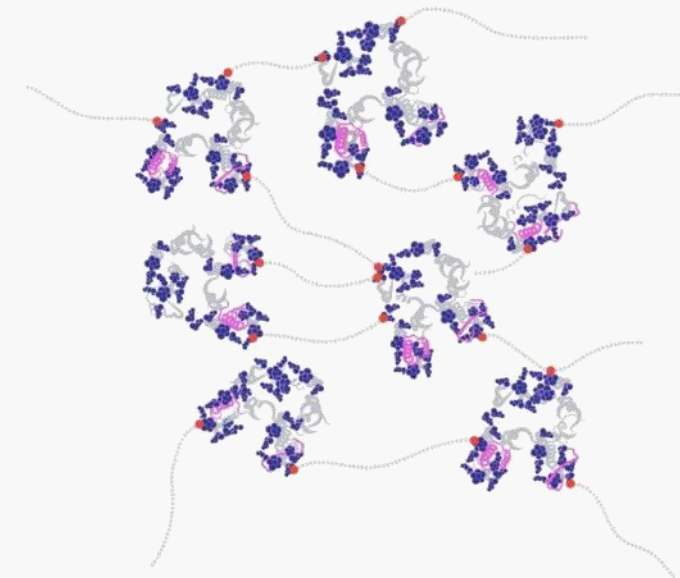
## PROPRIETARY eCRM<sup>®</sup> PROTEIN CARRIER WITH PRECISE, SITE-SPECIFIC CONJUGATION SITES



### eCRM: Enhanced Potency Potential

- Avoids masking sites on CRM<sub>197</sub> carrier responsible for T-cell help
- Optimized sites for conjugation using copper-free click chemistry
- More consistent antigenic presentation

## VAXCYTE CARRIER-SPARING CONJUGATES MIMIC THE CUSTOMARY MATRIX FORM



### Carrier-Sparing Conjugates

- Less protein carrier / conjugate may allow addition of more serotypes while minimizing carrier suppression and maintaining immunogenicity
- VAX-31 and VAX-24 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

	Polysaccharide		Protein Carrier		Assays		
	CDAP / Periodate Activation	Amination for Labeling PS	Incorporation of Non-natural AAs	Random Lysine Conjugation	Site-Specific Click Chemistry Conjugation	CQA Release Assays (Mol Wt, Free PS)	Serological Assays (IgG & OPA)
Pfizer/Merck Methods	✓	✓		✓		✓	✓
Vaxcyte	✓	✓	✓		✓	✓	✓

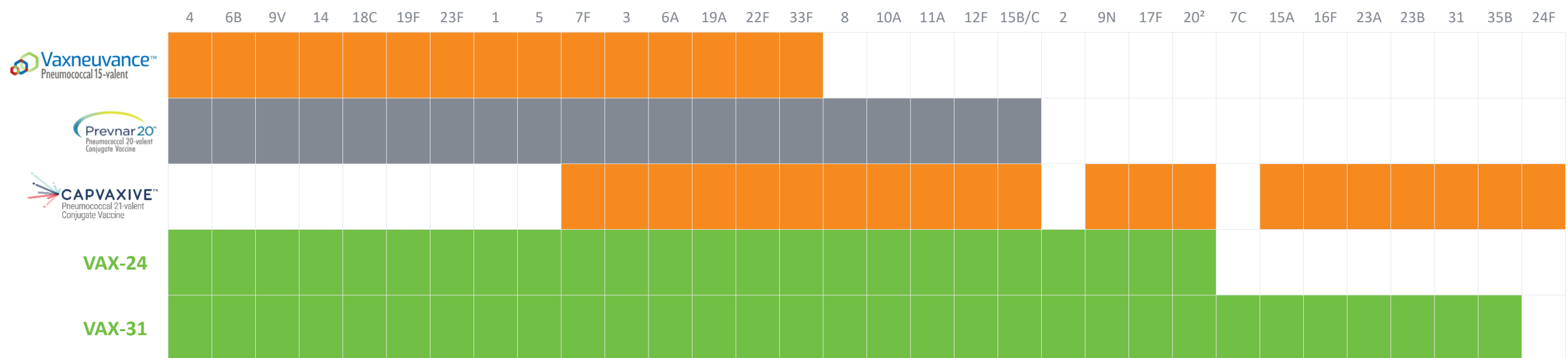
Novel Enablement: Site-specific conjugation via incorporation of nnAA conjugation anchors

# Vaxcyte's PCV Franchise Has More Fulsome Coverage Versus On-Market PCVs

Pneumococcal Vaccines Represent One of the Largest Segments of Global Vaccine Market, with Significant Growth Expected<sup>1</sup>

**VAX-31:** 31-valent PCV, the broadest-spectrum PCV in the clinic, designed to cover both currently circulating and long-established, historically disease-causing serotypes

**VAX-24:** 24-valent PCV designed to cover more serotypes than any pediatric pneumococcal vaccine on-market today



SoC = standard of care. Source: Prescribing information for Prevnar, Prevnar 13, Prevnar20, Synflorix, Vaxneuvance, Prevnar 20 and Capvaxive. Company filings for Vaxcyte. Capvaxive is approved for use in adults only.

(1) Public Company Reports: PFE, MRK, SNY, MRNA, GSK, AZN, excluding Covid-19 vaccine sales.

(2) The serogroup 20 antigen contained in VAX-24 and VAX-31, formerly known as a 20B variant, has been officially reclassified as 20C. Due to the significant structural homology between 20C and 20B, immune responses elicited by 20C have been demonstrated to be highly cross-reactive with 20B. The Company therefore expects to be able to demonstrate coverage for both serotypes, 20B and 20C, in the VAX-31 adult Phase 3 and infant Phase 2 studies. Reference: Yu J, et al.; New pneumococcal serotype 20C is a WciG O-acetyltransferase deficient variant of canonical serotype 20B. Microbiol Spectr 0:e02443-24. Within the serotype 20 group, strain 20B is the predominant circulating strain and shows greater genetic similarity to 20C compared to 20A. PCV21 includes 20A, VAX-31 includes 20C, with 20B planned to be evaluated in clinical studies to demonstrate cross protection.

# Pneumococcal Vaccine Market is Highly Attractive

Vaxcyte's PCV Franchise Has the Potential to Be Best-in-Class Due to Broader Coverage and Improved Immunogenicity

## PNEUMOCOCCAL VACCINE MARKET DYNAMICS

### PCVs ARE HIGHLY EFFECTIVE

- 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 with surrogate immune endpoints as basis for full approval, negating need for field efficacy trials

### DURABLE & RAPID REVENUE

- Prevnar Family (PCV7/PCV13/PCV20) & PPSV23 have generated >\$100B in revenues
- PCV13 and PCV20 had combined annual sales of ~\$6.5B in 2025
- PCV21 generated \$759M in 2025 (launched 3Q 2024)

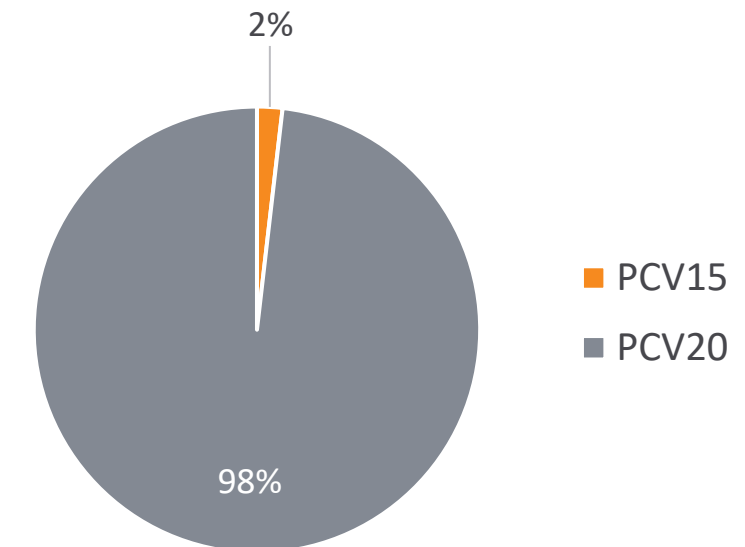
### ATTRACTIVE MARGINS

- Pneumococcal vaccines are premium priced, delivering highly attractive margins
- Broader-spectrum PCVs extend premium price in the U.S.<sup>1</sup>
  - PCV21: \$302 (adult)
  - PCV20: \$299
  - PCV15: \$239 (pediatric)

### COVERAGE & RECOMMENDING BODIES DRIVE ADOPTION

- Potential for rapid adoption, with spectrum of coverage and ACIP recommendation driving uptake
- Examples:
  - Shingrix® vs Zostavax®
  - Gardasil® vs Cervarix®
  - PCV20 vs PCV15

## SEROTYPE & DISEASE COVERAGE ADVANTAGE IS PRIMARY DRIVER OF U.S. PCV MARKET ADOPTION

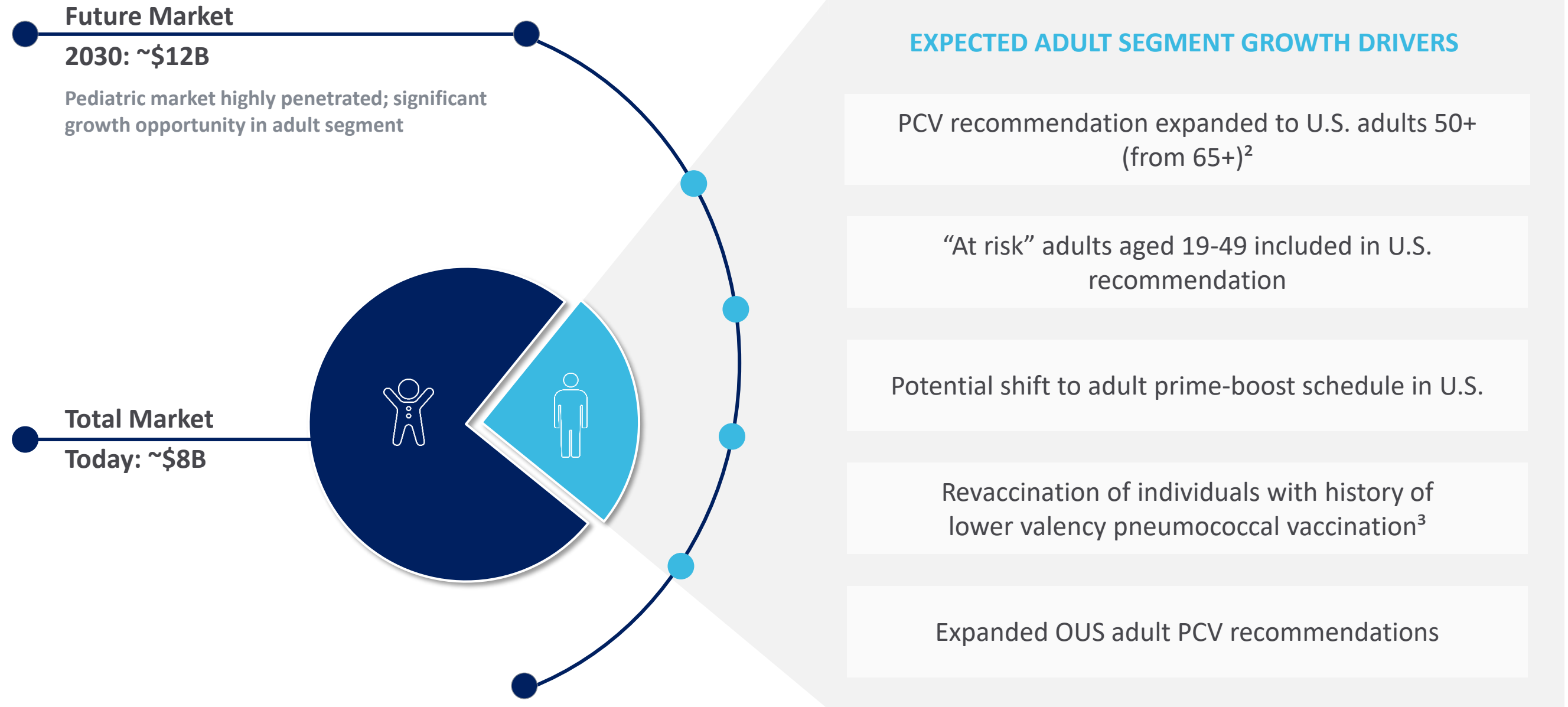


PCV VACCINATION IN ADULTS AGED ≥ 65  
JULY 2021 - NOVEMBER 2023<sup>2</sup>

- Broader-spectrum of serotype and disease coverage drove 98% adoption for PCV20 over PCV15 despite ACIP recommendation of both vaccines

# Pneumococcal Vaccine Market Poised for Significant Growth

Combined \$8B Market Expected to Grow to ~\$12B in 2030<sup>1</sup>, Driven Primarily by Adult Market Expansion



# Recent Burst of Adult PCV Recommendations Outside the U.S.

Serotype Epidemiology, Broad-Valency PCVs Driving New Recommendations and Shift from PPSV23 to PCVs

Licensure of broader-spectrum PCVs is driving adult universal recommendations internationally

Expanded Global Adult PCV Adoption

Japan

Switzerland

France

Spain (Regional)

Germany

United Kingdom

Netherlands

PCVs NOW RECOMMENDED<sup>1</sup>

**PRIOR ADULT RECOMMENDATION:**

No Prior Universal, Age-Based PCV Recommendation or PPSV23 Only

International revenues for the Prevnar vaccine family increased ~8% year-over-year<sup>2</sup>

# Establishing Manufacturing Capacity, Robust Supply Chain to Support Expected VAX-31 Adult U.S. Launch, Followed by U.S. Infant and Global Adult and Infant PCV Launches

## Global Commercial Manufacturing Agreement with Lonza



- Relationship encompasses production of key PCV components
- Dedicated large-scale facility built to provide capacity for U.S. and global demand for adults and infants

## U.S. Fill-Finish Manufacturing Agreement with Thermo Fisher



- Agreement expands domestic capacity (North Carolina)
- Supports future commercial manufacturing and deepens investment in American innovation and infrastructure

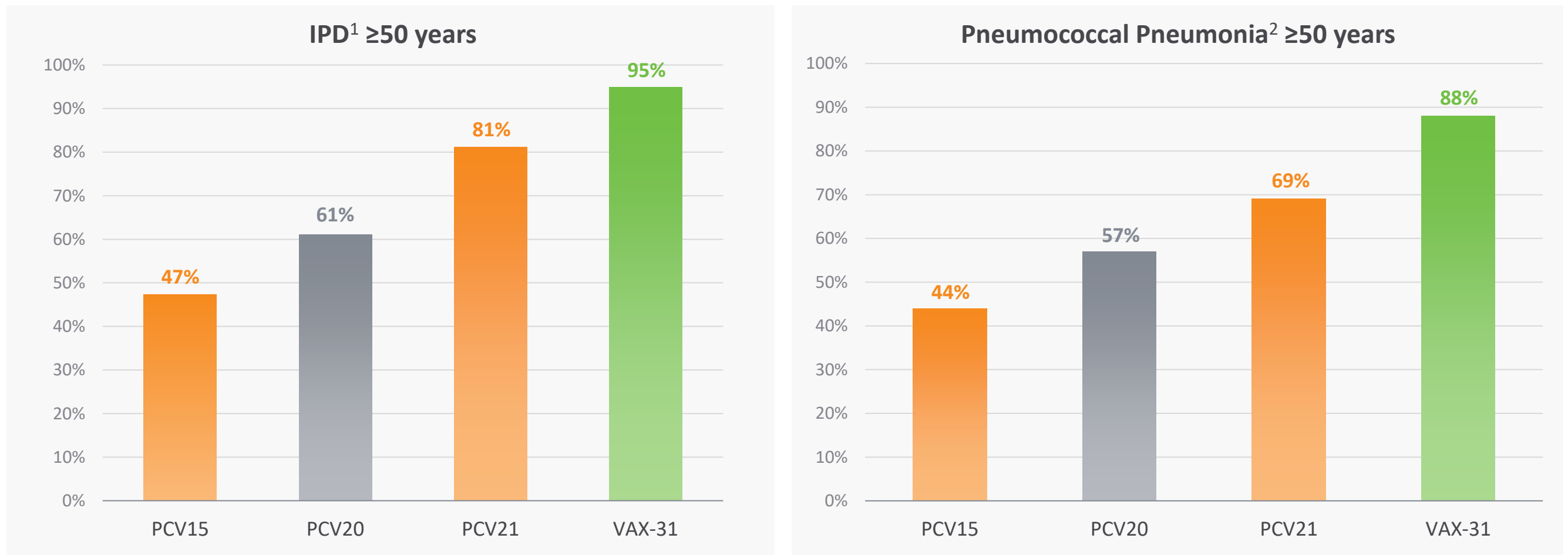
# VAX-31 Adult Clinical Program

**VAXCYTE**  
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# VAX-31 Designed to Expand Protection with Broadest Disease Coverage in Adults

## Percentage of IPD and Non-Bacteremic Pneumococcal Pneumonia Covered by PCVs in U.S. Adults



All estimates assume cross-protection between serotypes 6A and 6C and between 15B and 15C.

(1) CDC 2023 Active Bacterial Core (ABC) Surveillance data ([https://data.cdc.gov/Public-Health-Surveillance/1998-2023-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p/about\\_data](https://data.cdc.gov/Public-Health-Surveillance/1998-2023-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p/about_data));

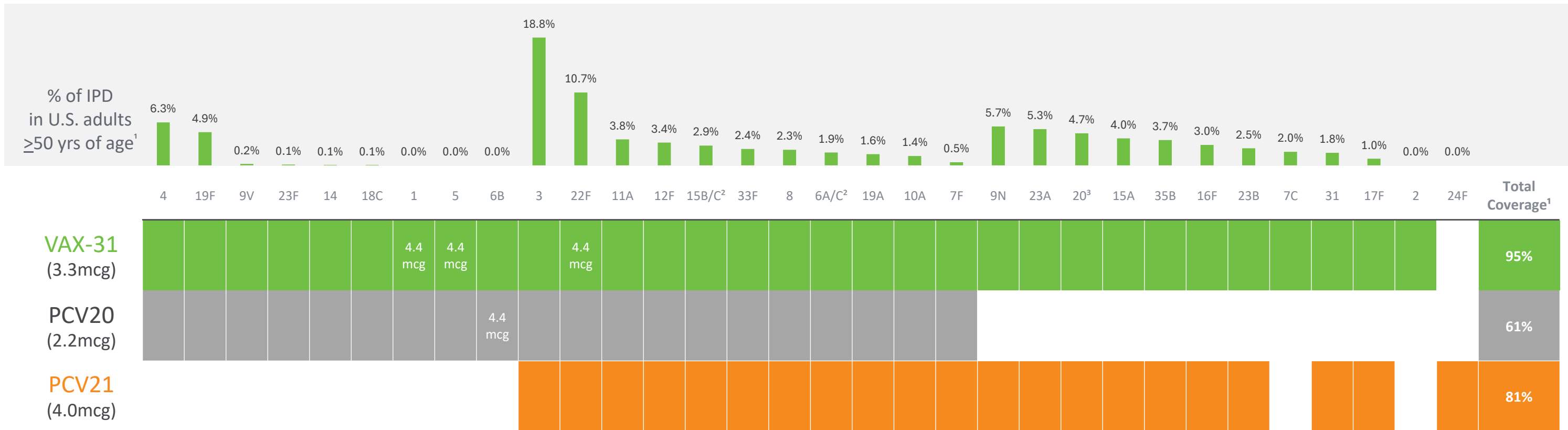
IPD cases with missing serotype data were excluded, non-typeable cases were included in the denominator.

(2) King LM et al. Pneumococcal Serotype Distribution and Coverage of Existing and Pipeline Pneumococcal Vaccines, *The Journal of Infectious Diseases*, 2025, jiaf376;

<https://doi.org/10.1093/infdis/jiaf376>; the percentage covered by PCV is based on a weighted average based on inpatient pneumonia cases (50–64 years of age, ≥65 years of age).

# VAX-31 is Designed to Provide Comprehensive Coverage, While Maintaining or Improving Immune Response, Relative to Today's SoC that Only Provides Partial Coverage

**Next Generation PCV Designed to Cover ~95% of IPD and ~88% of Pneumococcal Pneumonia in U.S. Adults Aged 50+ with Potential to Provide an Incremental 14-34% Broader IPD Coverage and 19-31% Broader Pneumonia Coverage than Standard-of-Care Vaccines**



SoC = standard of care.

(1) % of IPD caused in individuals ≥50 yrs of age in the U.S. in 2023 based on ABC surveillance data ([https://data.cdc.gov/Public-Health-Surveillance/1998-2023-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p/about\\_data](https://data.cdc.gov/Public-Health-Surveillance/1998-2023-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p/about_data)).

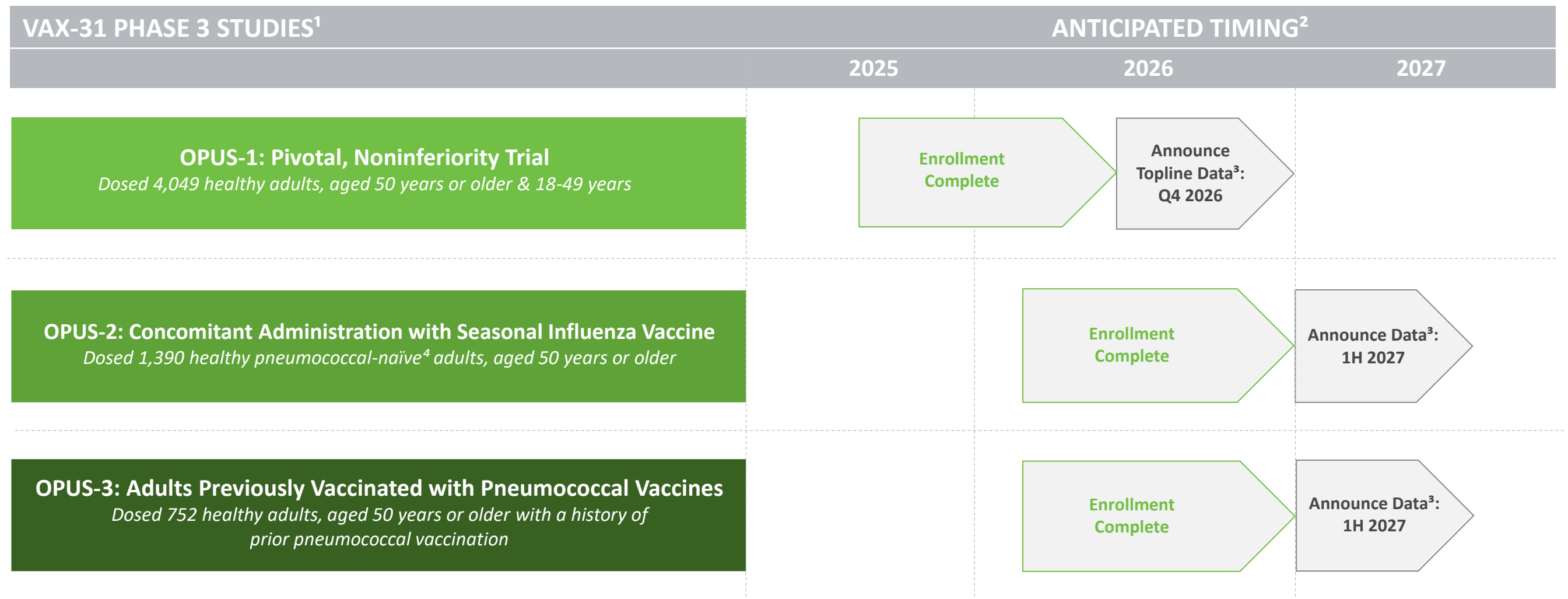
(2) Serotypes 6A/6C and 15B/15C are closely related subtypes for which cross-protection is assumed. All three—PCV21, PCV20, and VAX-31—include 6A. PCV20 and VAX-31 include the 15B antigen; PCV21 contains the 15C antigen and demonstrated cross-reactive responses against serotype 15B, supporting an indication for IPD caused by 15B and 15C.

(3) Serotype 20 comprises closely related subtypes for which cross-protection is assumed. Within the serotype 20 group, strain 20B is the predominant circulating strain and shows greater genetic similarity to 20C compared to 20A. PCV21 includes 20A, VAX-31 includes 20C, with 20B planned to be evaluated in clinical studies to demonstrate cross protection. The serogroup contained in VAX-24 and VAX-31, formerly known as a 20B variant, has been officially reclassified as 20C. For additional details on serogroup 20, please see footnote 2 on slide 15.

# VAX-31 Adult Phase 3 Program

# VAX-31 OPUS Phase 3 Adult Program Overview (Subject Enrollment: n=6,191)

OPUS Clinical Program Designed to Support Potential BLA Filing; Enrollment Completed in OPUS-1, OPUS-2, and OPUS-3 Trials



BLA = Biologics License Application.

(1) Also planning for a manufacturing consistency study (e.g., a lot-to-lot study).

(2) Guidance as of May 6, 2026.

(3) Includes safety, tolerability and immunogenicity data.

(4) No known prior history of IPD or pneumococcal pneumonia, or receipt of any licensed or investigational pneumococcal vaccine.

# OPUS-1 Phase 3 Noninferiority Trial Evaluating VAX-31 for the Prevention of Invasive Pneumococcal Disease and Pneumonia in Adults (n=4,049 Dosed)

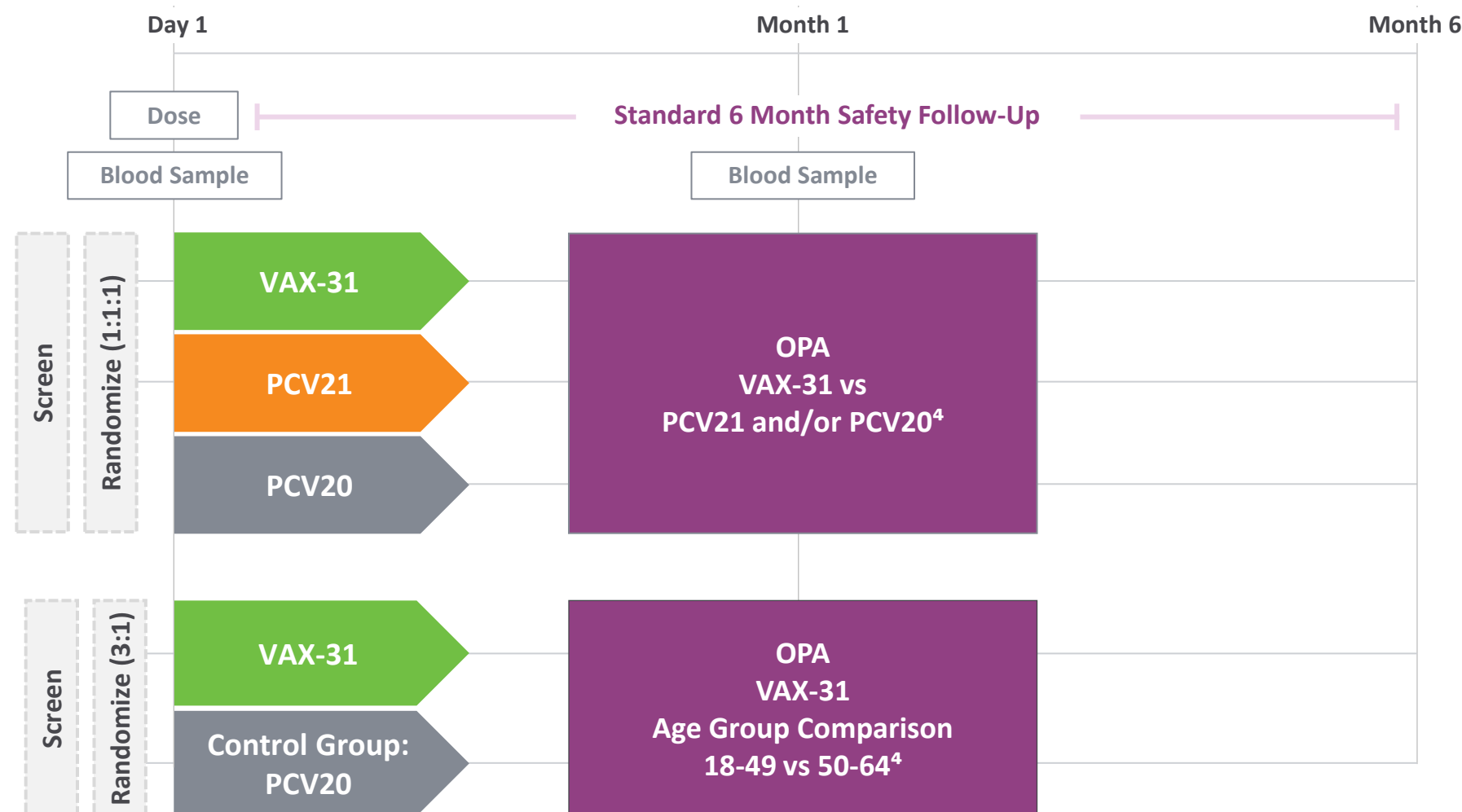
Study Designed to Establish New Standard for Adult PCVs Through Head-to-Head Safety, Tolerability and Immunogenicity Comparisons of VAX-31<sup>1</sup> with PCV21 and PCV20, the Current Standards of Care in U.S. Adults

**ADULTS AGED ≥50 YEARS**  
Key primary immunogenicity objectives:

- Noninferiority<sup>2</sup> of VAX-31 compared with PCV21 and/or PCV20 for the 28 serotypes shared with one or both comparators
- Superiority<sup>3</sup> for the three serotypes unique to VAX-31 and serotype 20B versus the comparator vaccines

**ADULTS AGED 18–49 YEARS**  
Key primary immunogenicity objective:

- Noninferiority of VAX-31 immune responses in adults 18-49 years of age compared to those in adults 50-64 years of age



# OPUS-1 Phase 3 Pivotal Noninferiority Trial Key Objectives

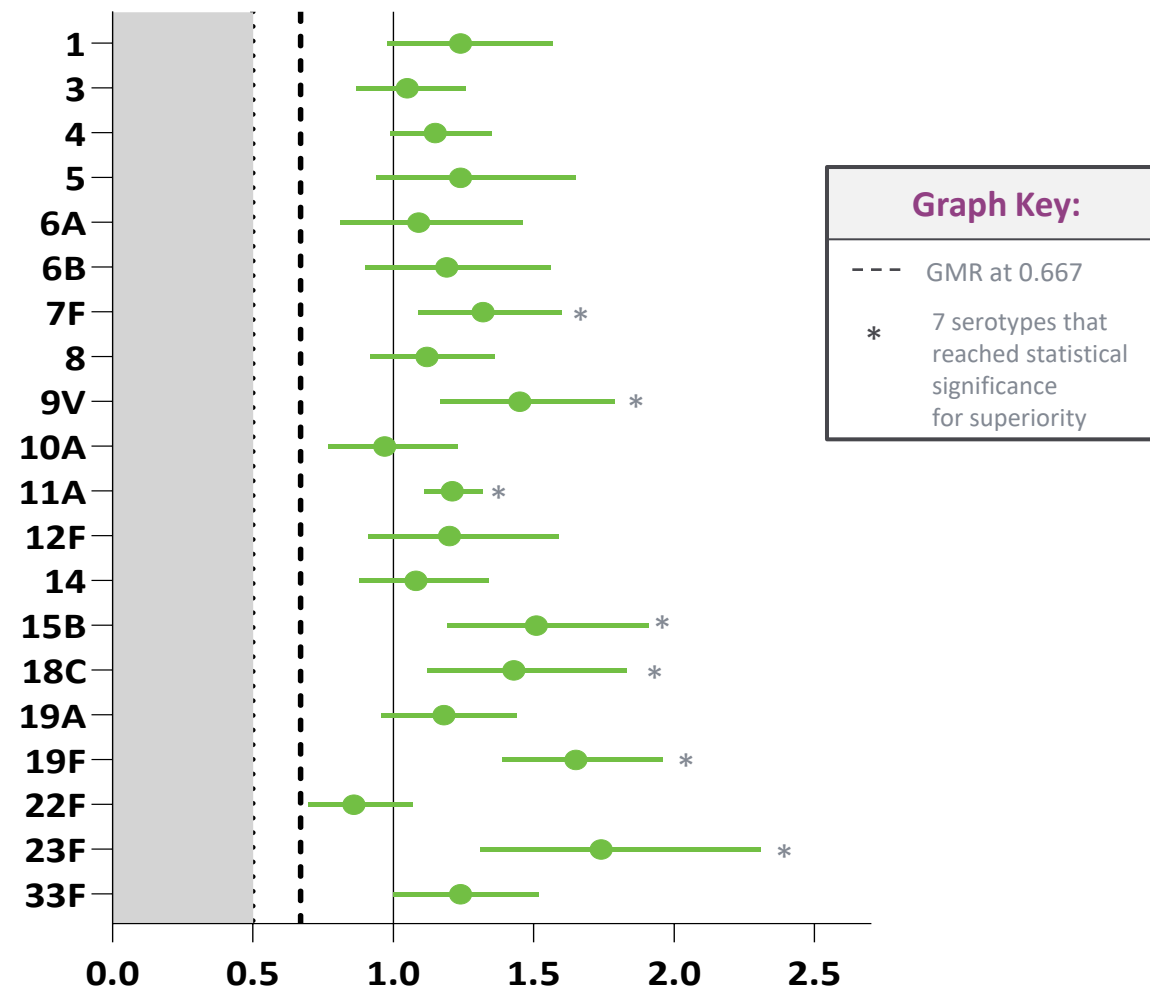
Expected to Serve as Cornerstone of BLA Package for Potential Licensure in Adults

VAX-31 IMMUNOGENICITY STUDY OBJECTIVES		EVALUATION CRITERIA
PRIMARY OBJECTIVES	<ul style="list-style-type: none"> <li><b>Noninferiority</b> compared with PCV21 and/or PCV20 for the 28 serotypes (STs) shared with either or both comparator vaccines in adults 50+</li> </ul>	>0.667
	<ul style="list-style-type: none"> <li><b>Superiority</b> of VAX-31 compared with PCV21 or PCV20 for the 3 STs unique to VAX-31 (2, 7C and 20C) and for ST 20B in adults 50+</li> </ul>	<b>OPA GMR</b> LOWER BOUND OF TWO-SIDED 95% CONFIDENCE INTERVAL >2.0
	<ul style="list-style-type: none"> <li><b>Noninferiority</b> of immune responses in adults aged 18-49 years compared with those in adults aged 50-64 years</li> </ul>	>0.667
SECONDARY OBJECTIVES	<ul style="list-style-type: none"> <li><b>Noninferiority</b> compared with both PCV21 and PCV20 for the 11 STs common to all three vaccines in adults 50+</li> </ul>	>0.5
	<ul style="list-style-type: none"> <li><b>Statistically greater immune responses</b> relative to PCV21 or PCV20 for the 28 shared STs in adults 50+</li> </ul>	>1.0
	<ul style="list-style-type: none"> <li><b>Superiority</b> compared with PCV20 for the 8 STs common to VAX-31 and PCV21 but not included in PCV20 in adults 50+</li> </ul>	<b>OPA GMR</b> LOWER BOUND OF TWO-SIDED 95% CONFIDENCE INTERVAL >2.0
	<ul style="list-style-type: none"> <li><b>Superiority</b> compared with PCV21 for the 9 STs common to VAX-31 and PCV20 but not included in PCV21 in adults 50+</li> </ul>	>2.0
KEY SAFETY & TOLERABILITY OBJECTIVES		
<ul style="list-style-type: none"> <li><b>Safety and tolerability</b> will be evaluated for 6 months following initial vaccination, including SAE, NOCI, and MAAE; Day 1 to Day 7, solicited local reactions and solicited systemic events will be evaluated; Day 1 to Month 1, all unsolicited AEs will be evaluated</li> </ul>		

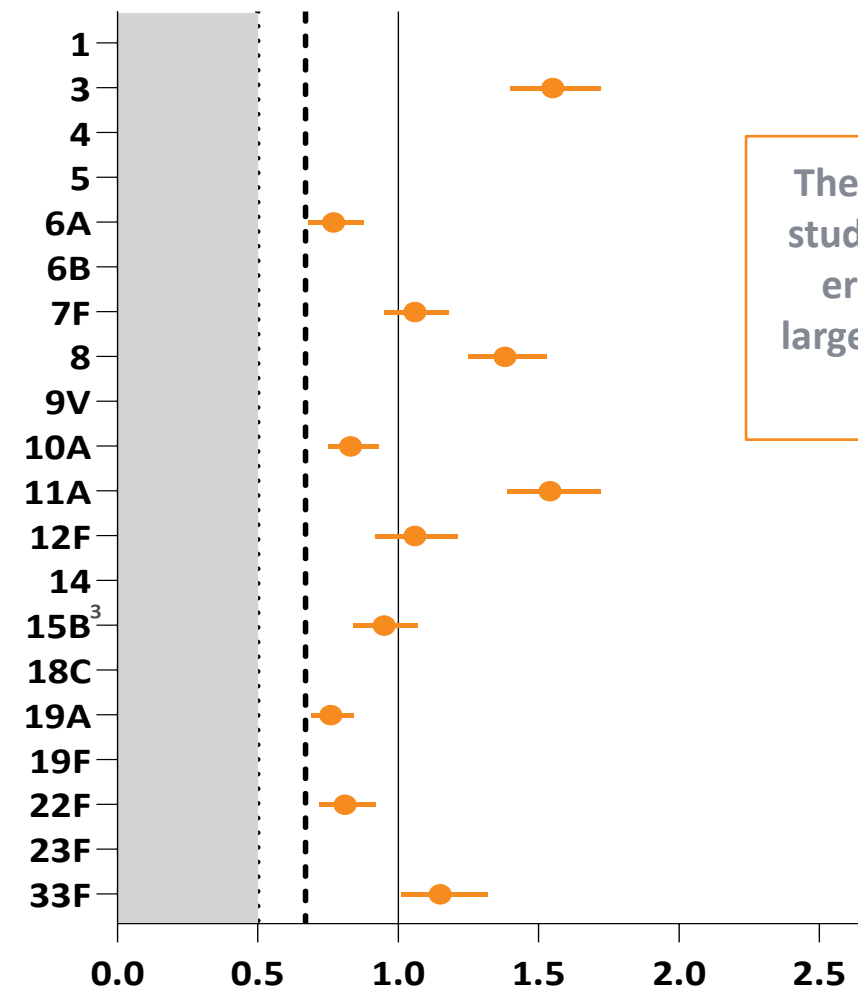
# OPA GMR Responses for VAX-31 (Phase 2) and PCV21 (Phase 3) vs PCV20

VAX-31 GMRs Higher on 18 of 20 Common STs and 7 STs Achieved Statistically Higher Immune Responses<sup>1</sup>

VAX-31 HIGH DOSE PHASE 2 NI STUDY VS PCV20:  
20 Common STs (OPA GMRs)



PCV21 PHASE 3 PIVOTAL NI STUDY VS PCV20:  
11 Common STs (OPA GMRs)<sup>2,3</sup>



The PCV21 Phase 3 study shows tighter error bars given larger study size and powering

ST = serotypes. NI = noninferiority; OPA = opsonophagocytic activity; GMR = geometric mean ratio.

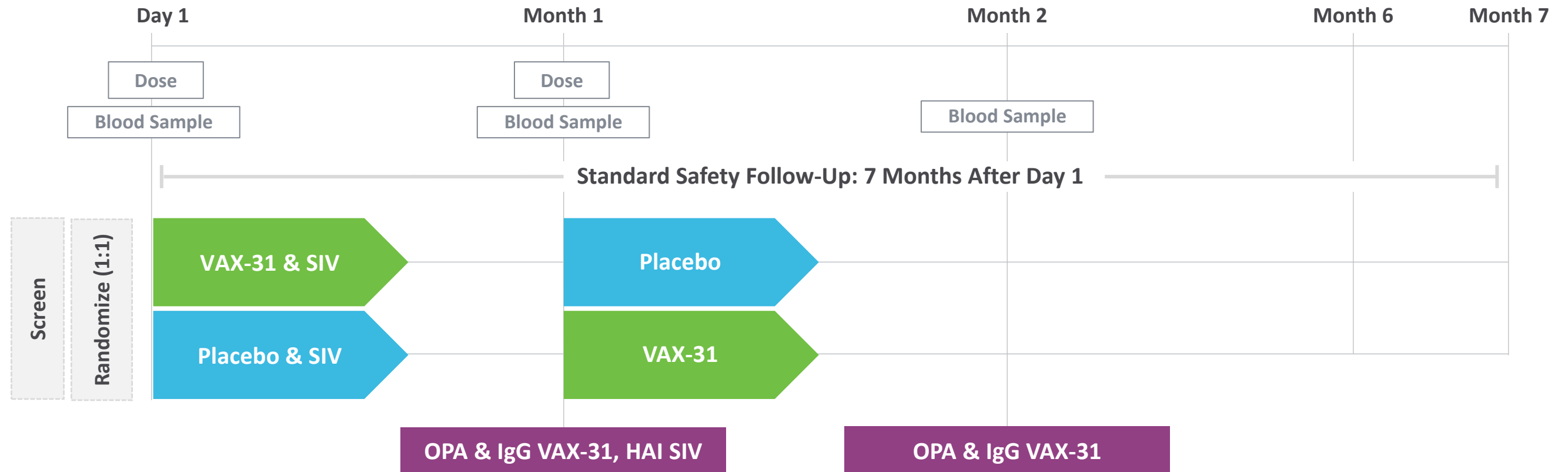
(1) 95% CI lower bound >1.0.

(2) Source: package insert Capvaxive.

(3) Common serotypes are those in VAX-31 shared with PCV20 and PCV21 per product labeling. PCV21 is indicated for the prevention of IPD caused by serotypes 15B and 15C but contains only the 15C antigen; however, 15B responses were evaluated.

# OPUS-2 Phase 3 Clinical Trial Evaluating VAX-31 Concomitantly Administered with Seasonal Influenza Vaccine (n=1,390 Dosed)

Descriptive Study Evaluating Safety, Tolerability and Immunogenicity of VAX-31<sup>1</sup> when Administered Either Concomitantly with or One Month Following Administration of a Licensed Seasonal Influenza Vaccine in Healthy Pneumococcal-Naïve<sup>2</sup> Adults Aged ≥50 Years



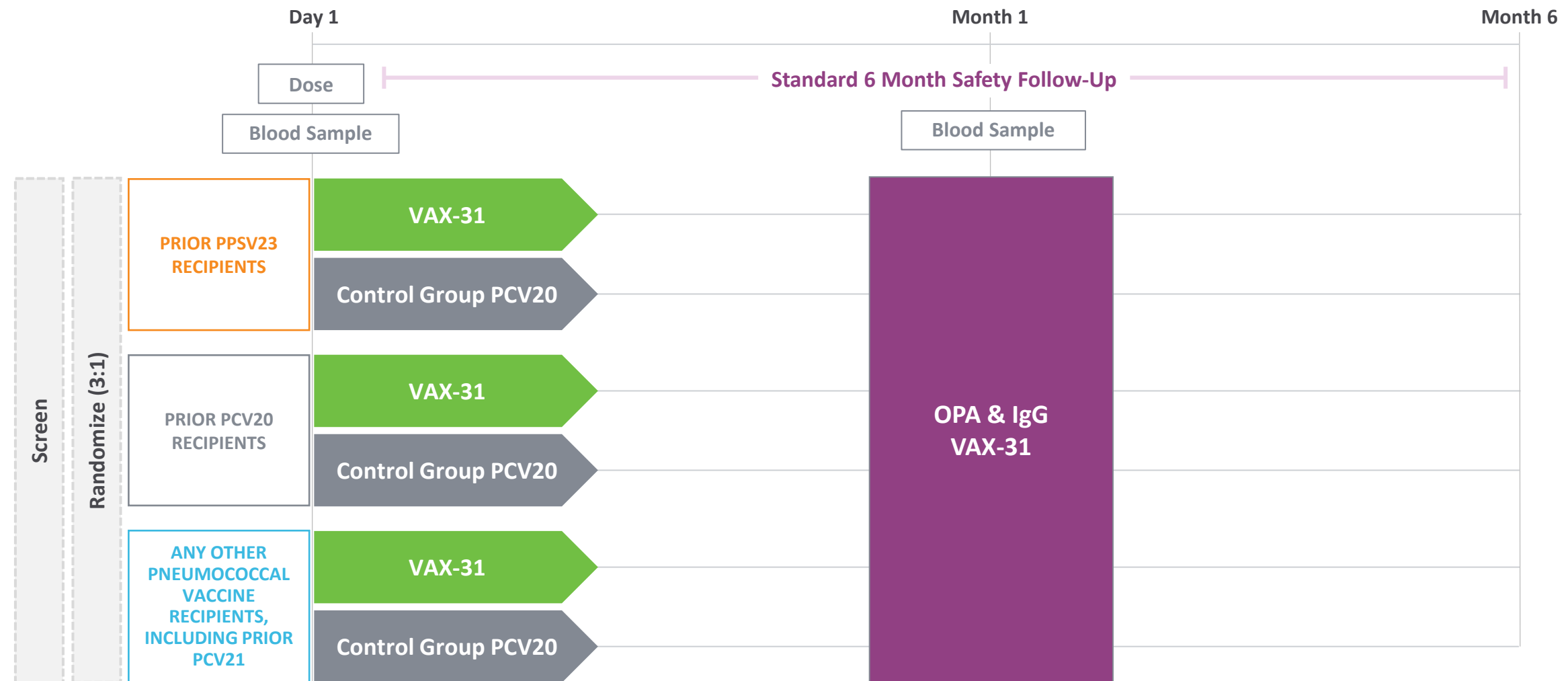
OPA = opsonophagocytic activity, IgG = immunoglobulin G, HAI = hemagglutination inhibition, SIV = seasonal influenza vaccine.

(1) VAX-31 High Dose (all serotypes dosed at 3.3mcg, except serotypes 1, 5, and 22F which are dosed at 4.4mcg) selected to advance to Phase 3.

(2) No known prior history of IPD or pneumococcal pneumonia, or receipt of any licensed or investigational pneumococcal vaccine.

# OPUS-3 Phase 3 Clinical Trial Evaluating VAX-31 in Healthy Adults Who Have Previously Received a Pneumococcal Vaccine (n=752 Dosed)

## Descriptive Study Evaluating Safety, Tolerability and Immunogenicity of a Single Dose Of VAX-31<sup>1</sup> in Healthy U.S. Adults Aged 50 Years and Older with a History of Prior Pneumococcal Vaccination<sup>2</sup>



# OPUS-2 and OPUS-3 Phase 3 Clinical Trial Key Objectives

## Descriptive Phase 3 Studies Designed to Demonstrate VAX-31's Performance in Real-World Adult Use

### OPUS-2: PHASE 3 TRIAL EVALUATING VAX-31 CONCOMITANTLY ADMINISTERED WITH SEASONAL INFLUENZA VACCINE

#### KEY IMMUNOGENECITY OBJECTIVES

- **Primary Objective:** Assessing serotype-specific immune responses (OPA GMTs and GMFRs) elicited by VAX-31 across all 31 serotypes and serotype 20B in healthy pneumococcal-naïve adults aged 50 years and older
- **Primary Objective:** Comparing strain-specific immune responses (HAI GMTs) elicited by a SIV when co-administered with VAX-31 to those elicited by a SIV alone
- **Secondary Objective:** Comparing IgG antibody responses (IgG GMCs) elicited by VAX-31 across all 31 serotypes and serotype 20B when VAX-31 is co-administered with a SIV to those elicited by VAX-31 alone

#### KEY SAFETY & TOLERABILITY OBJECTIVES

- Participants will be followed for safety through Month 7 after Dose 1, including SAE, NOCI, and MAAE; Day 1 to Day 7, solicited adverse events will be evaluated; Day 1 to Month 1, all unsolicited AEs will be evaluated

### OPUS-3: PHASE 3 TRIAL EVALUATING VAX-31 IN HEALTHY ADULTS WHO HAVE PREVIOUSLY RECEIVED A PNEUMOCOCCAL VACCINE

#### KEY IMMUNOGENECITY OBJECTIVES

- **Primary Objective:** Assessing serotype-specific immune responses (OPA GMTs and GMFRs) elicited by VAX-31 across all 31 serotypes and serotype 20B in adults who have previously received PPSV23, PCV20 or other prior licensed pneumococcal vaccines or combinations thereof
- **Secondary Objective:** Describing serotype-specific IgG antibody responses (IgG GMCs and GMFRs) elicited by VAX-31 across all 31 serotypes and serotype 20B

#### KEY SAFETY & TOLERABILITY OBJECTIVES

- Participants will be followed for safety through Month 6 after Dose 1, including SAE, NOCI, and MAAE; Day 1 to Day 7, solicited adverse events will be evaluated; Day 1 to Month 1, all unsolicited AEs will be evaluated

# Overview: VAX-31 Adult Phase 1/2 Study Results

# Positive VAX-31 Phase 1/2 Adult Data Published in *Lancet Infectious Diseases*

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



Overall study results positive and met objectives



Well tolerated, demonstrating a safety profile similar to PCV20



At all doses studied, VAX-31 demonstrated robust OPA and IgG immune responses for all 31 STs, all three doses advanceable to Phase 3



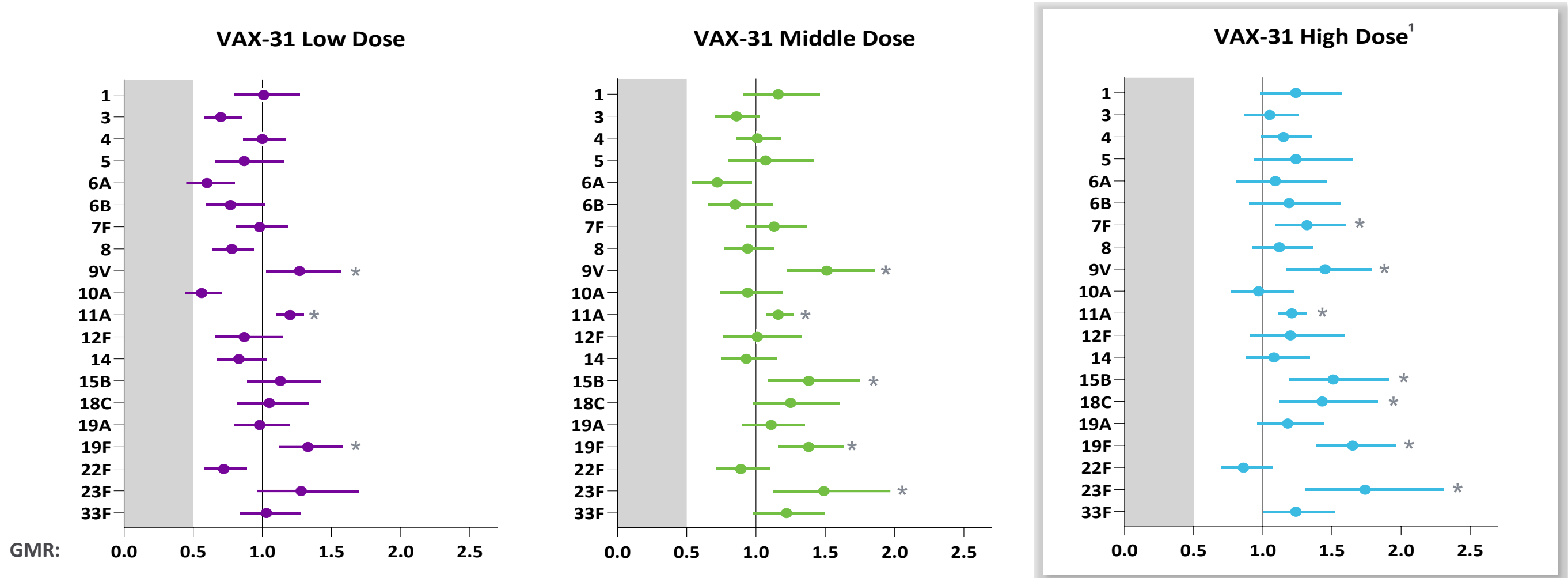
VAX-31 data further validate the potential of Vaxcyte's carrier-sparing platform to deliver best-in-class PCVs



VAX-31 High Dose selected to advance to Phase 3

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

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



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

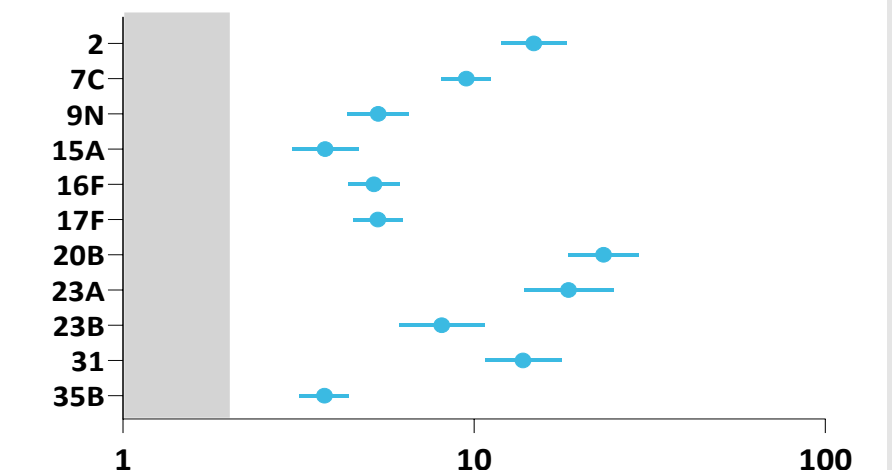
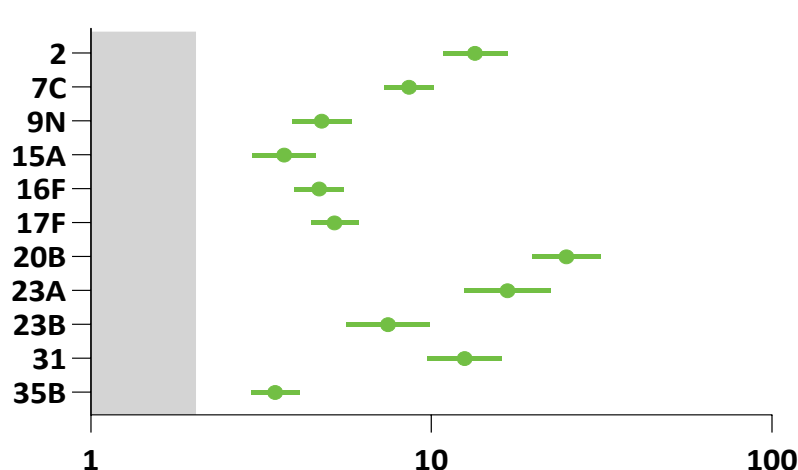
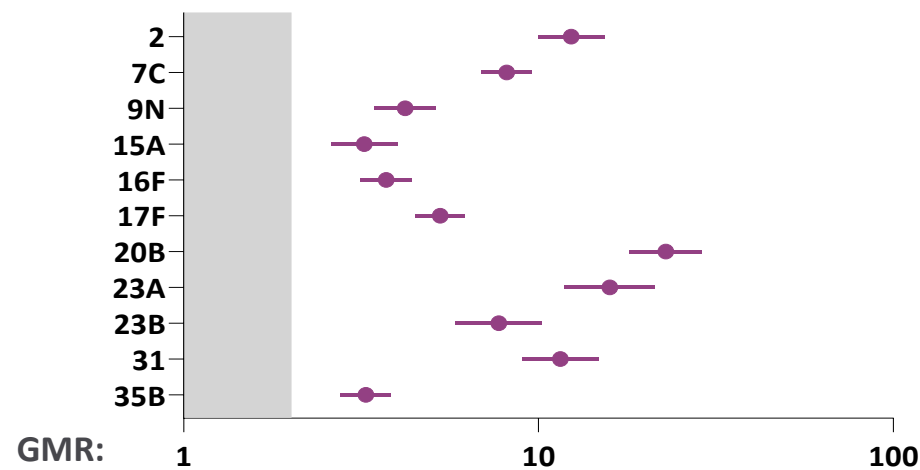
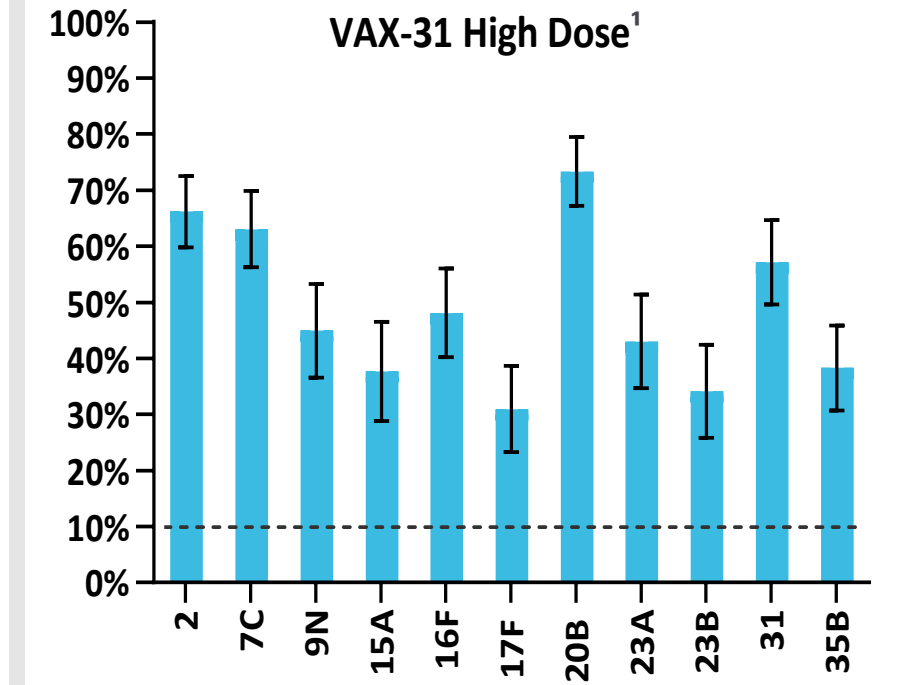
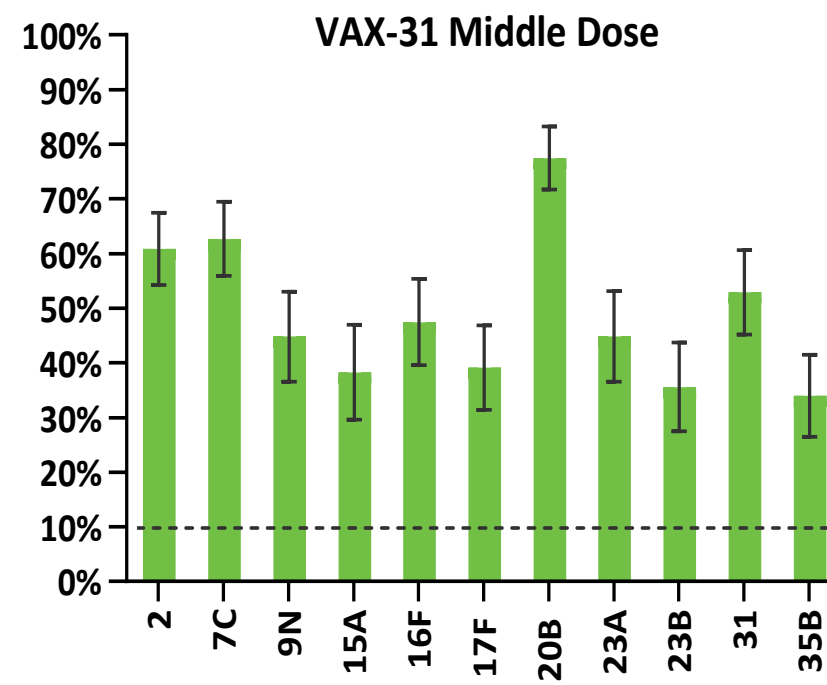
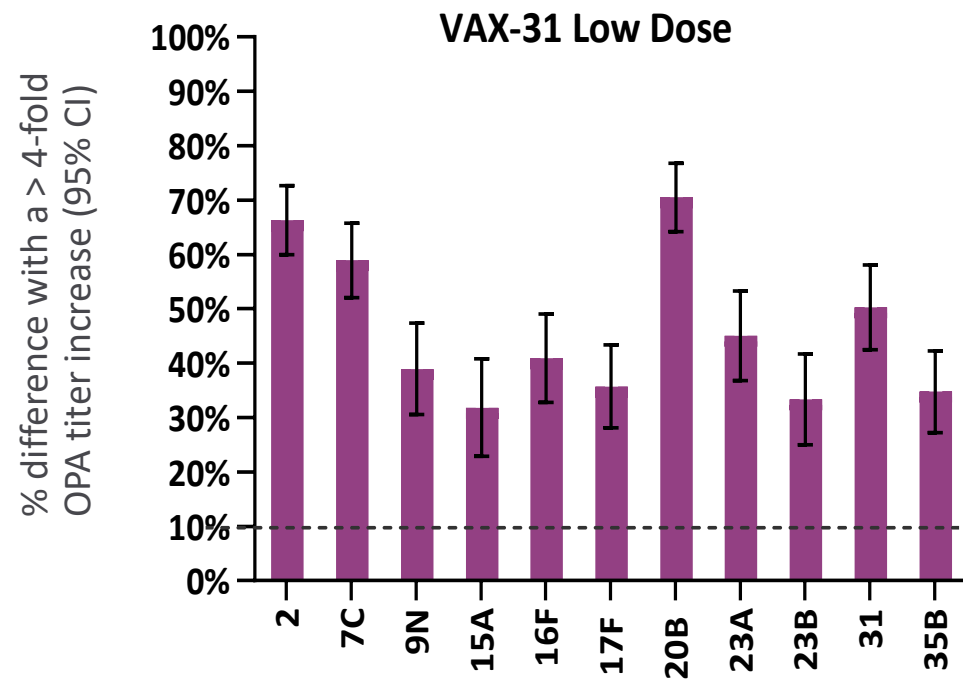
**Middle Dose:** 13 of 20 STs had a GMR greater than 1.0 and 5 STs achieved statistically higher immune responses

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

\* Reached statistical significance for superiority.

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

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



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

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

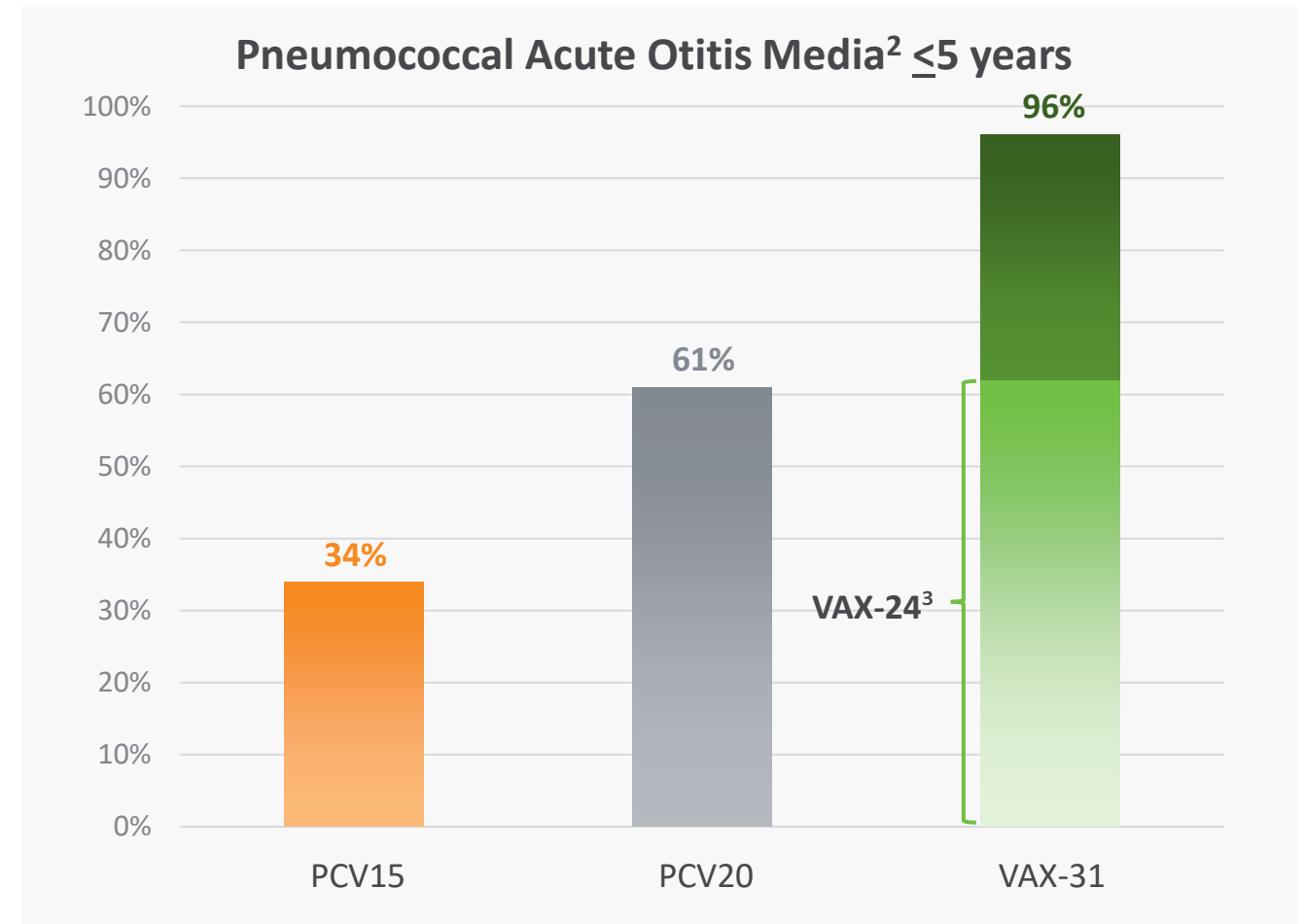
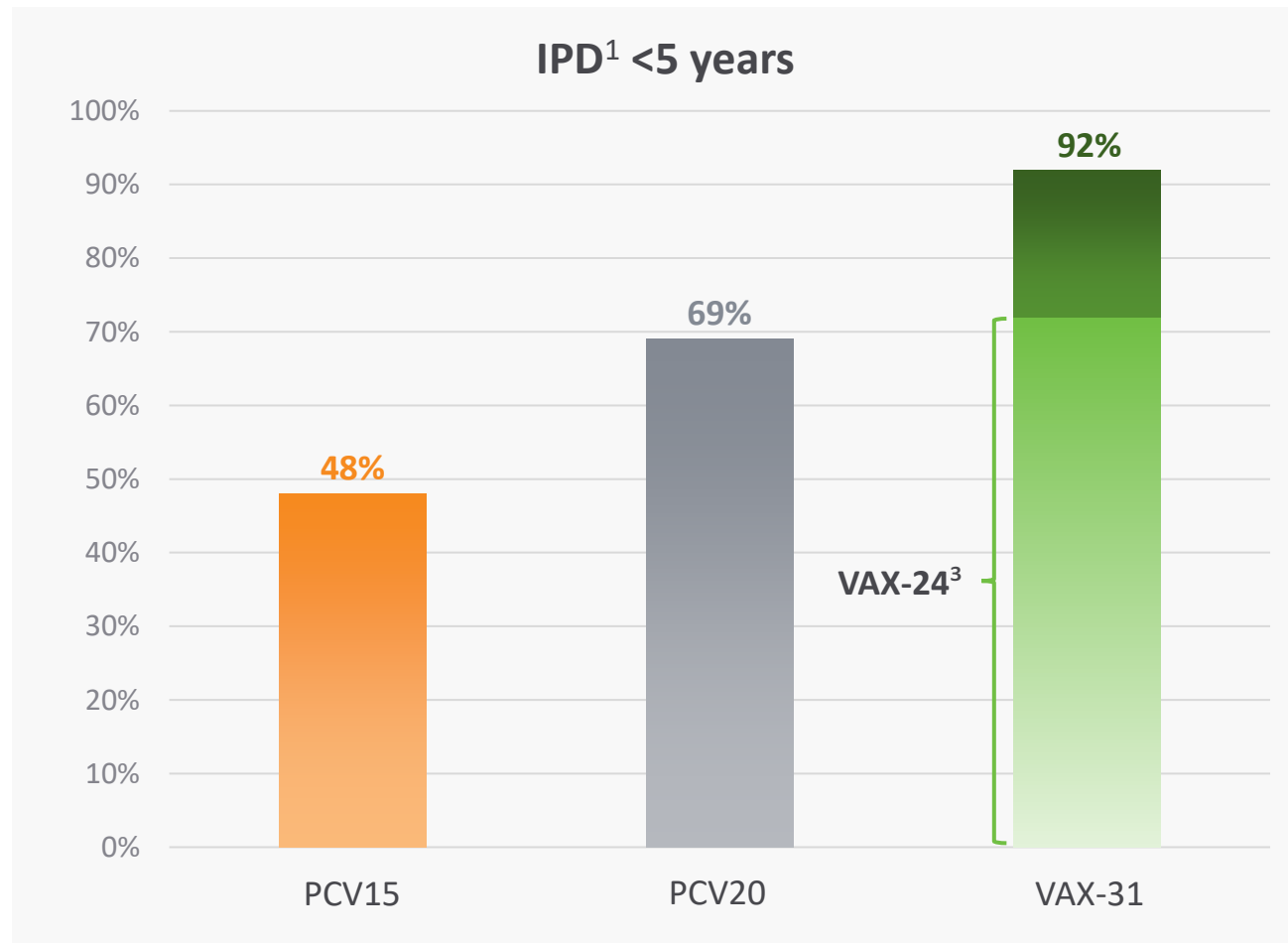
# PCV Infant Clinical Program

**VAXCYTE**  
*protect humankind™*



# VAX-31 Designed to Expand Protection with Broadest Disease Coverage in Children

## Percentage of IPD and Pneumococcal Acute Otitis Media Covered by PCVs in U.S. Children



All estimates assume cross-protection between serotypes 6A and 6C and between 15B and 15C.

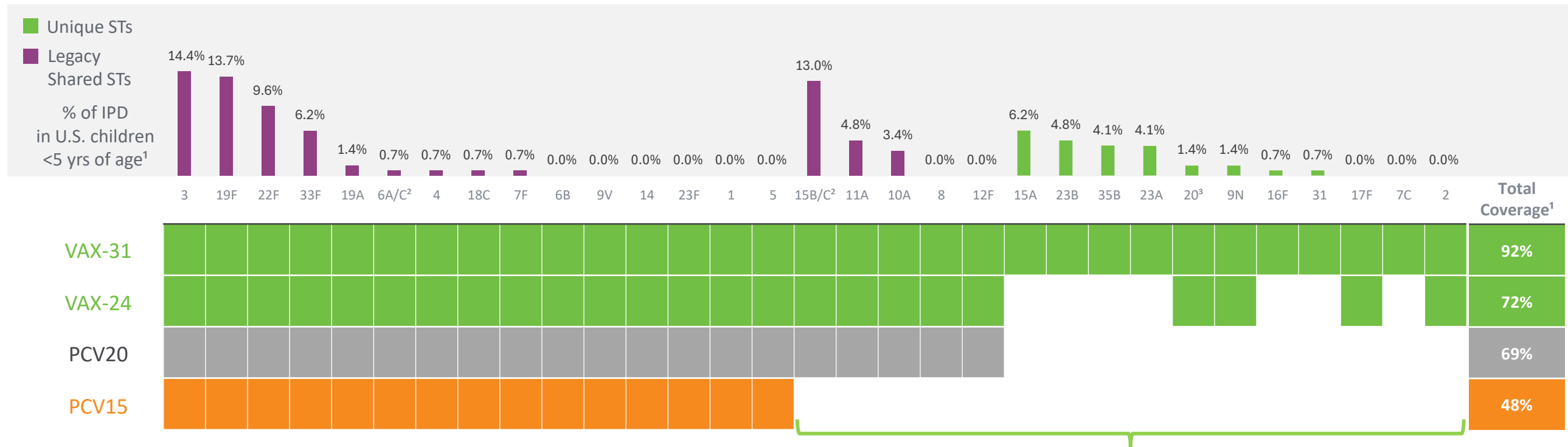
(1) CDC 2023 Active Bacterial Core (ABC) Surveillance data ([https://data.cdc.gov/Public-Health-Surveillance/1998-2023-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p/about\\_data](https://data.cdc.gov/Public-Health-Surveillance/1998-2023-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p/about_data)); IPD cases with missing serotype data were excluded, non-typeable cases were included in the denominator.

(2) In U.S. children five years of age or under, VAX-31 is estimated to address ~96% of AOM: Grant LR et al., *FrontPediatr*.2024;12:1383748. Serotype percentages reflect 2017–2021 data (Supplemental Table 1).

(3) VAX-31 includes all serotypes covered by VAX-24, plus an additional 7 serotypes; VAX-24 coverage is depicted in light green and covers 72% of IPD cases in U.S. children <5 years and 62% of AOM cases in U.S. children ≤5 years.

# VAX-31 Designed to Deliver Broadest Disease and Serotype Coverage in Infants, Including ~92% of Invasive Pneumococcal Disease (IPD) in U.S. Children<sup>1</sup>

**VAX-31's UNIQUE 11 STs:** Across multiple adult and infant studies, Vaxcyte's PCVs have shown strong immune responses across all incremental STs relative to PCV20. VAX-31, in particular, could significantly increase coverage versus today's standard-of-care.



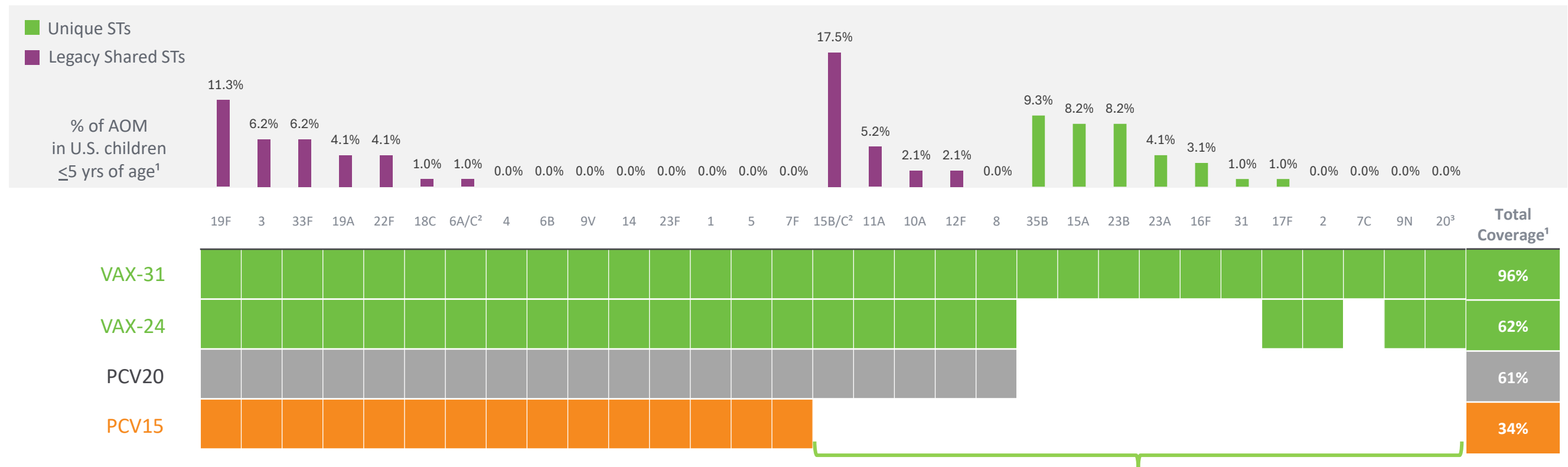
**VAX-31'S UNIQUE STs HAVE POTENTIAL TO PROVIDE 23-44% MORE IPD COVERAGE COMPARED TO CURRENT STANDARD-OF-CARE INFANT PCVs**

**LEGACY SHARED 20 STs:** In the infant study, VAX-24 had higher responses on the highest circulating STs (3 & 19F) and while there were some lower relative responses compared to PCV20, they were restricted to a small subset of shared STs with limited residual disease.

# VAX-31 Designed to Deliver Broadest Disease and Serotype Coverage in Infants, Including ~96% of Pneumococcal Acute Otitis Media (AOM) in U.S. Children<sup>1</sup>

## VAX-31's UNIQUE STs VS STANDARD-OF-CARE INFANT PCVs:

Potential to Provide 35-62% Increase in AOM Coverage Compared to Current Standards-of-Care Infant PCVs



## VAX-31'S UNIQUE STs COMPARED TO CURRENT INFANT STANDARD-OF-CARE PCVs

(1) In children five years of age or under, VAX-31 is estimated to address ~96% of AOM: Grant LR et al., *FrontPediatr*.2024;12:1383748. Serotype percentages reflect 2017–2021 data (Supplemental Table 1).

(2) Serotypes 6A/6C and 15B/15C are closely related subtypes for which cross-protection is assumed. PCV20 and VAX-31 include 15B, and PCV15 and VAX-31 include 6A.

(3) Serotype 20 comprises closely related subtypes for which cross-protection is assumed. Within the serotype 20 group, strain 20B is the predominant circulating strain and shows greater genetic similarity to 20C compared to 20A. PCV21 includes 20A, VAX-31 includes 20C, with 20B planned to be evaluated in clinical studies to demonstrate cross protection. The serogroup 20 antigen contained in VAX-24 and VAX-31, formerly known as a 20B variant, has been officially reclassified as 20C. For additional details on serogroup 20, please see footnote 2 on slide 15.

# Healthcare Providers Confirm: Broader Coverage Wins in PCV Selection

U.S. pediatric and family medicine providers overwhelmingly favor broader-coverage PCVs and would take action to expand protection for infants.<sup>1</sup>

**BROAD PROTECTION  
DRIVES HCP ADOPTION**



**93%**

of HCPs prefer higher coverage PCVs, and 80% agree higher coverage will reduce IPD

**PROVIDERS WOULD  
SWITCH MID-SERIES**



**76%**

would switch infants to broader-coverage PCV even mid-series to maximize protection

**WILLINGNESS TO  
PRESCRIBE “CATCH UP”**



**60%**

would prescribe another dose of broader-coverage PCV for already-vaccinated children under 5

**OTITIS MEDIA  
PREVENTION MATTERS**



**84%**

say protection against acute otitis media is an important vaccine feature

# VAX-24 Infant Phase 2 Dose-Finding Study Final Results

# Final VAX-24 Phase 2 Infant Study Results and Platform Demonstrate Potential to Achieve Broadest Coverage of Any Infant PCV On-Market



**Overall study results positive and met objectives**



**Well tolerated, demonstrating a safety profile similar to PCV20**



**VAX-24 elicited substantial IgG, OPA and memory responses and performed particularly well against currently circulating serotypes contained in the vaccine**



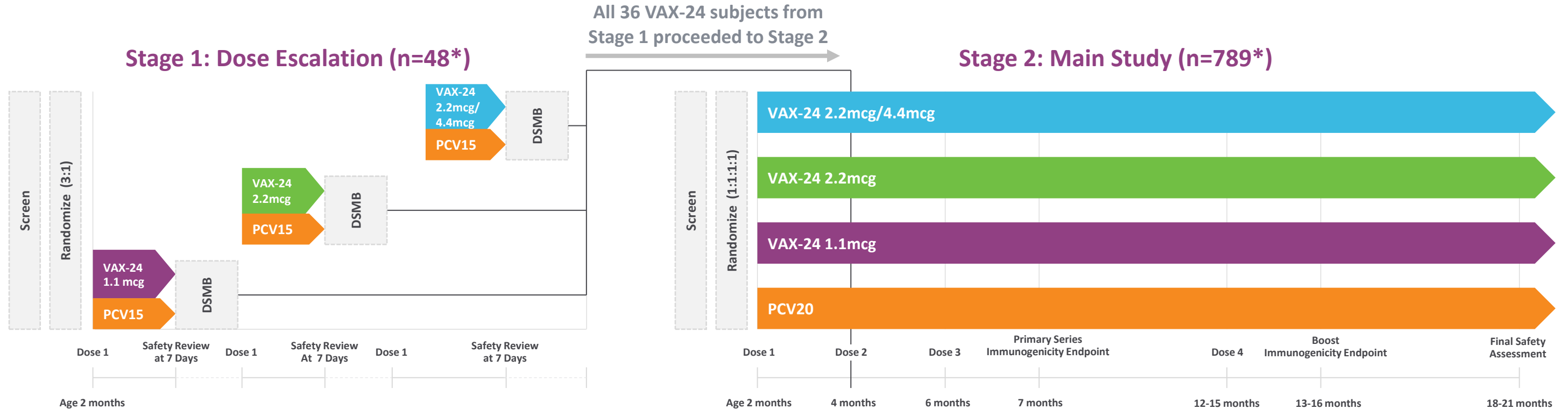
**Substantial, dose-dependent immune responses and little to no evidence of carrier suppression observed**



**Results consistent with previously reported positive interim results; provide additional evidence validating rationale for exploring higher doses in ongoing VAX-31 infant Phase 2 dose-finding study**

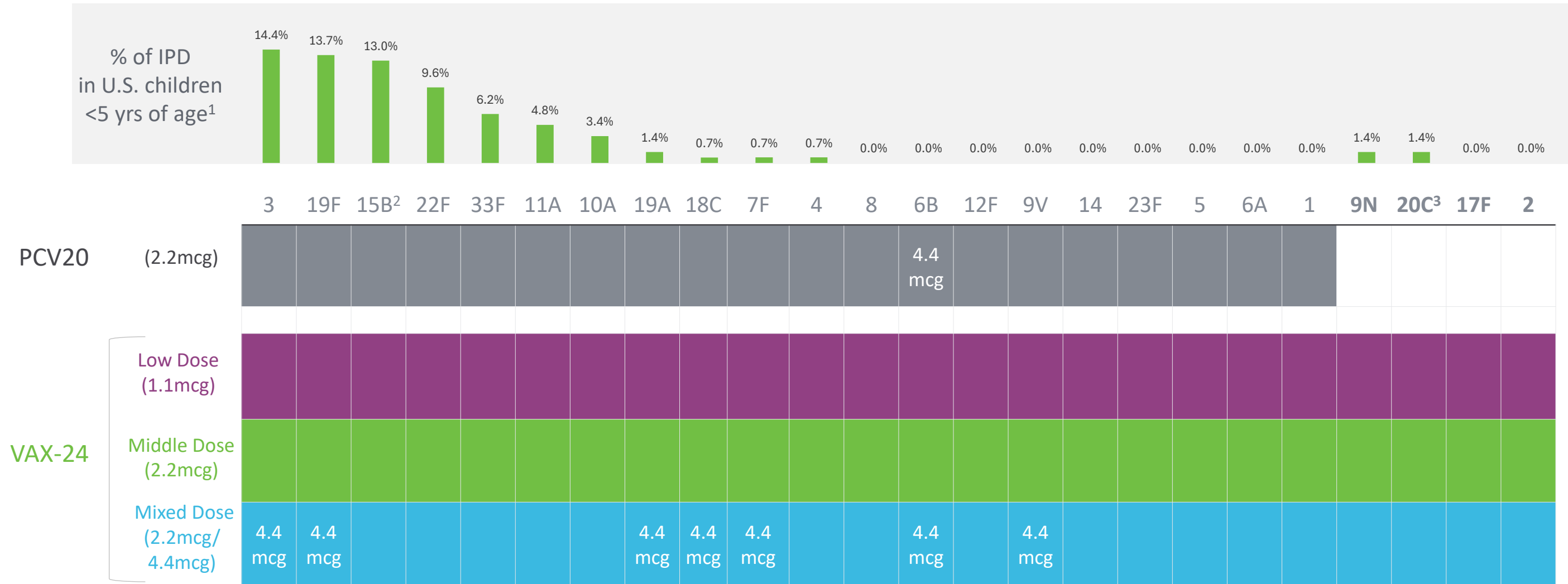
# VAX-24 Infant Phase 2 Dose-Finding Clinical Study (N=803)

Randomized, Observer-Blind, Active-Controlled, Dose-Finding, Clinical Study to Evaluate Safety, Tolerability and Immunogenicity of VAX-24 vs. Standard-of-Care (PCV20) in 803 Healthy Infants



# Three VAX-24 Doses Evaluated in Infant Phase 2 Dose-Finding Study

## Identical to Doses Evaluated in VAX-24 Adult Program



• Mixed dose included 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.

# Final 6-Month Safety Data from VAX-24 Phase 2 Study

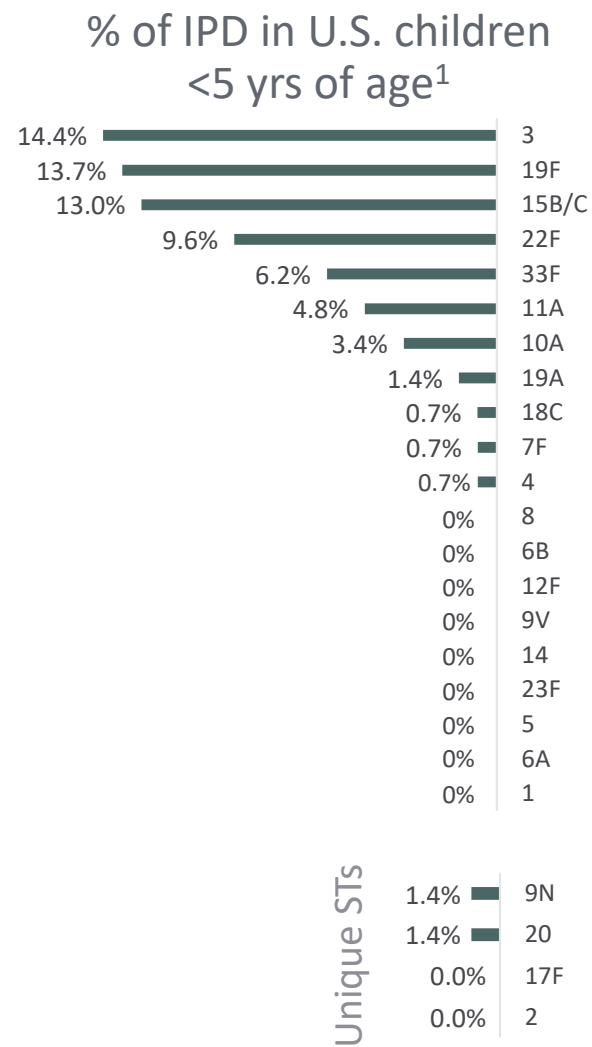
## Safety Results Similar to PCV20 and Across Cohorts

	VAX-24 Low Dose	VAX-24 Mid Dose	VAX-24 Mixed Dose	PCV20
NUMBER OF SUBJECTS	195	186	191	185
Unsolicited TEAE, n (%)	167 (85.6)	161 (86.6)	163 (85.3)	169 (91.4)
Related Unsolicited TEAE, n (%)	6 (3.1)	13 (7.0)	13 (6.8)	6 (3.2)
MAAE, n (%)	172 (88.2)	155 (83.3)	167 (87.4)	161 (87.0)
Related MAAE, n (%)	3 (1.5)	3 (1.6)	3 (1.6)	1 (0.5)
NOCI, n (%)	12 (6.2)	12 (6.5)	15 (7.9)	10 (5.4)
Related NOCI, n (%)	0	1 (0.5) <sup>1</sup>	0	0
SAE, n (%)	10 (5.1)	7 (3.8)	11 (5.8)	11 (5.9)
Related SAE, n (%)	0	0	0	0
Death, n (%)	0	0	0	1 (0.5) <sup>2</sup>
Related Death, n (%)	0	0	0	0

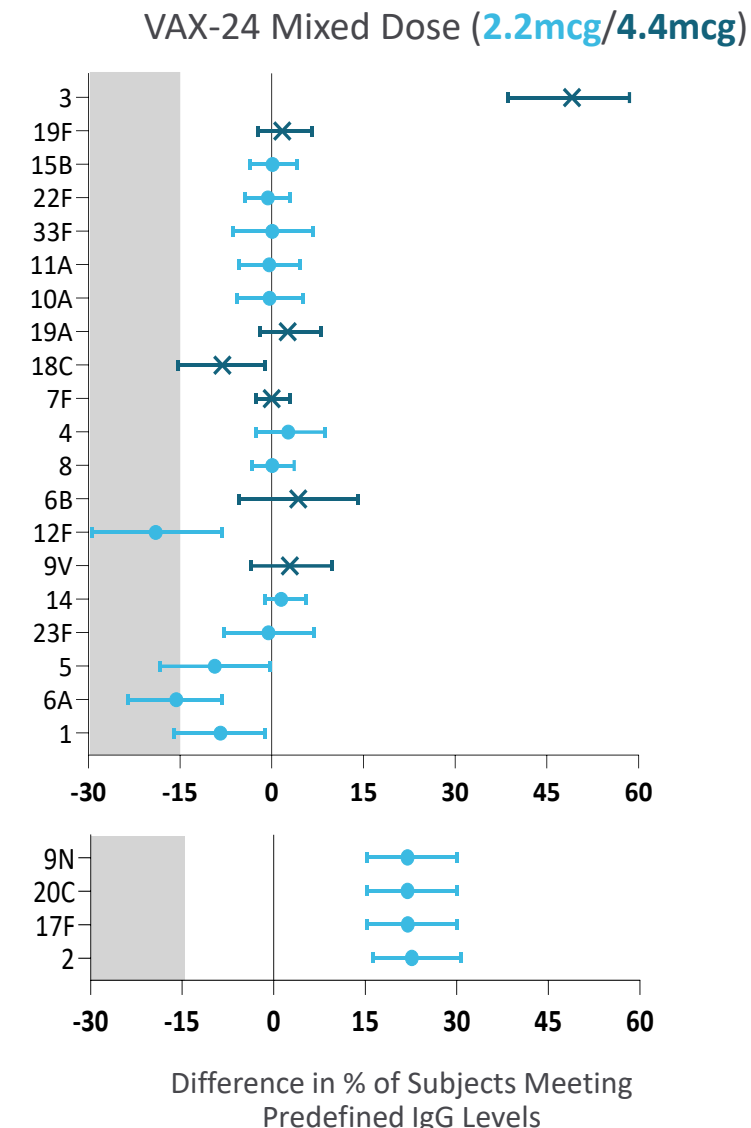
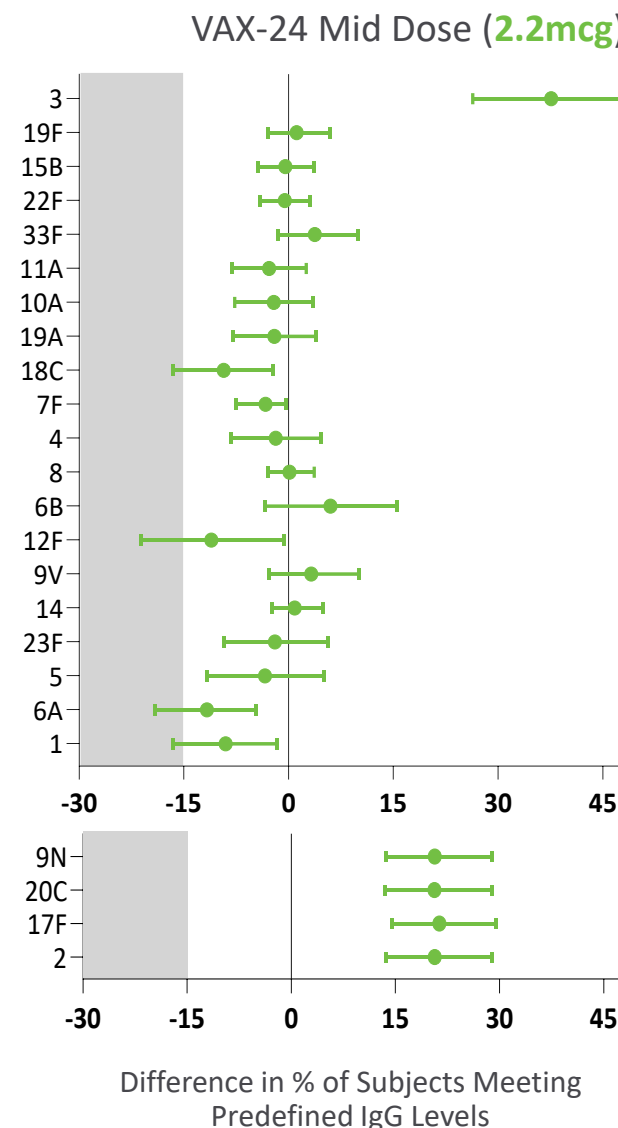
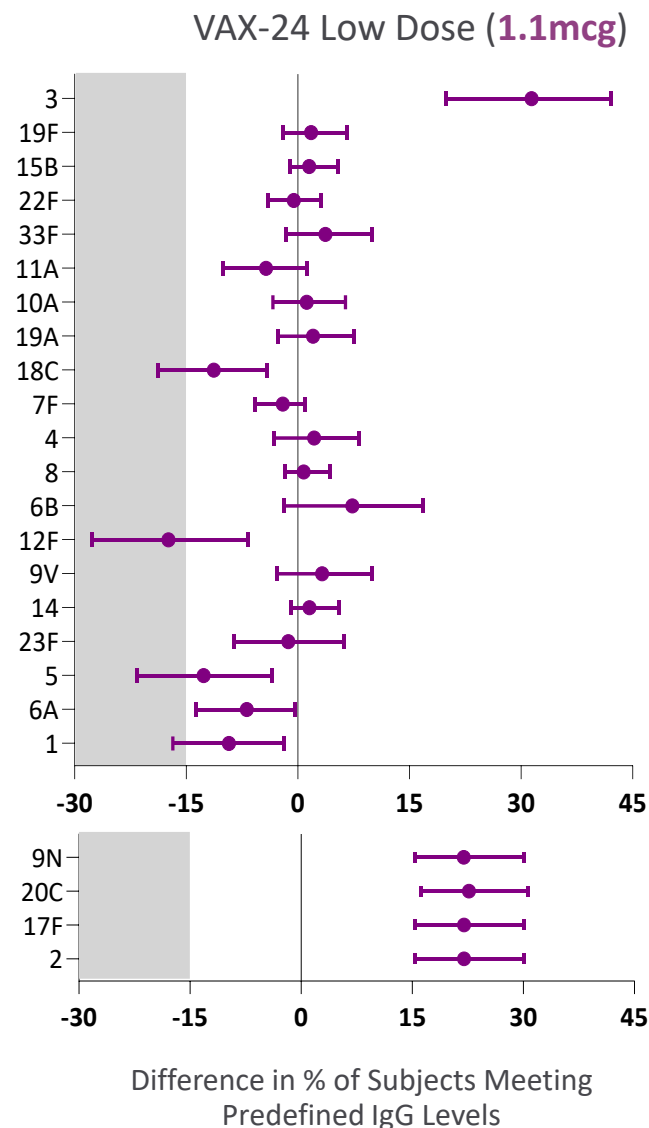
# Final Post-Dose 3 (PD3) IgG and OPA Immunogenicity Data Results

# VAX-24 PD3 Seroconversion Rates Compared to PCV20

Met Precedent Phase 2 Noninferiority Criteria for 20 of 24 STs at Low and Mid Doses and 19 of 24 STs at Mixed Dose



## VAX-24 vs. PCV20: Difference in % of Subjects Meeting Predefined IgG Levels<sup>2</sup>



NI = noninferiority; ST = serotype; IgG = immunoglobulin G.



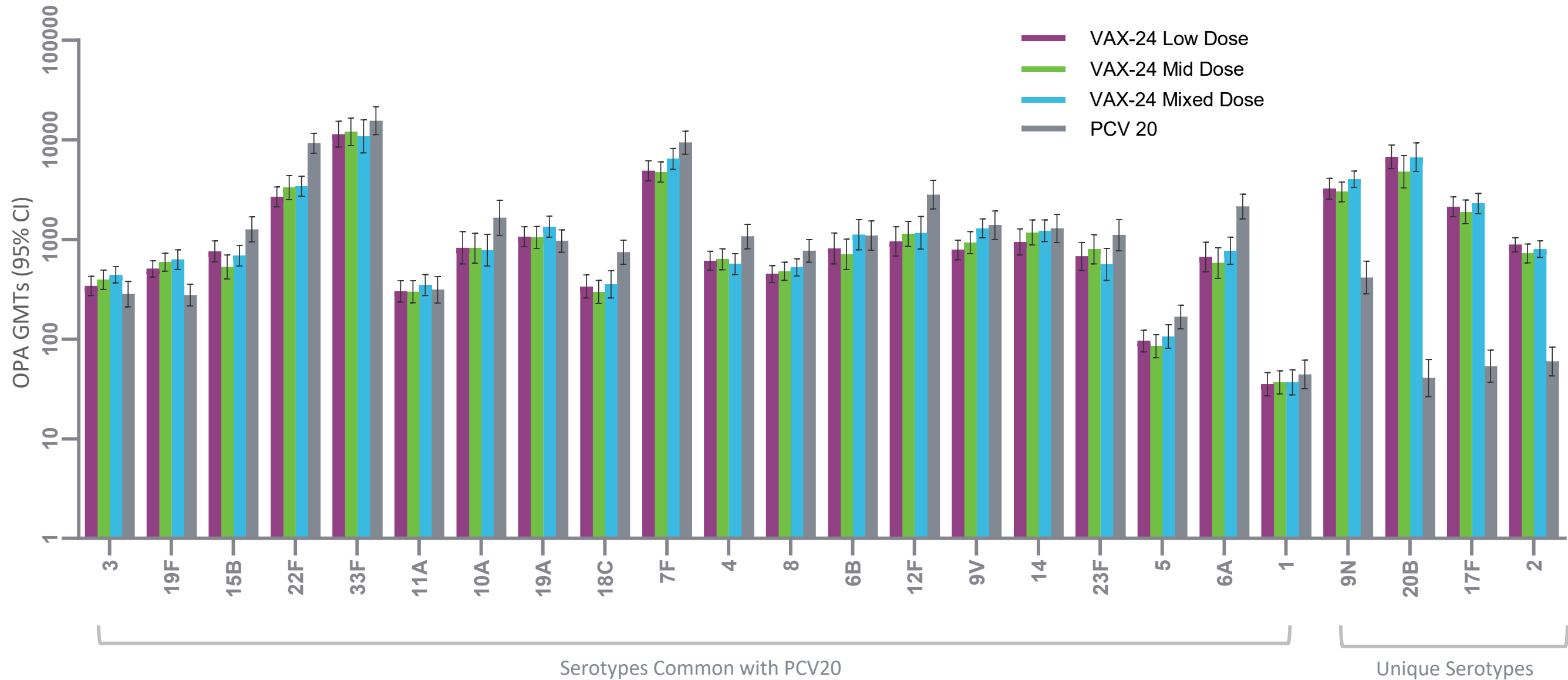
(1) % of IPD caused in individuals <5 yrs of age in the U.S. in 2023 based on ABC surveillance data.

(2) % of subjects meeting  $\geq 0.35\text{mcg/mL}$  for unique STs were calculated compared to ST 6B, which is the ST in PCV20 with the lowest seroconversion rate Post-Dose 3 (excluding ST 3 or lower responding STs). 15C coverage due to cross protection against 15B.

The serogroup 20 antigen contained in VAX-24 and VAX-31, formerly known as a 20B variant, has been officially reclassified as 20C. For additional details on serogroup 20, please see footnote 2 on slide 15.

# VAX-24 PD3 OPA GMT Immune Responses

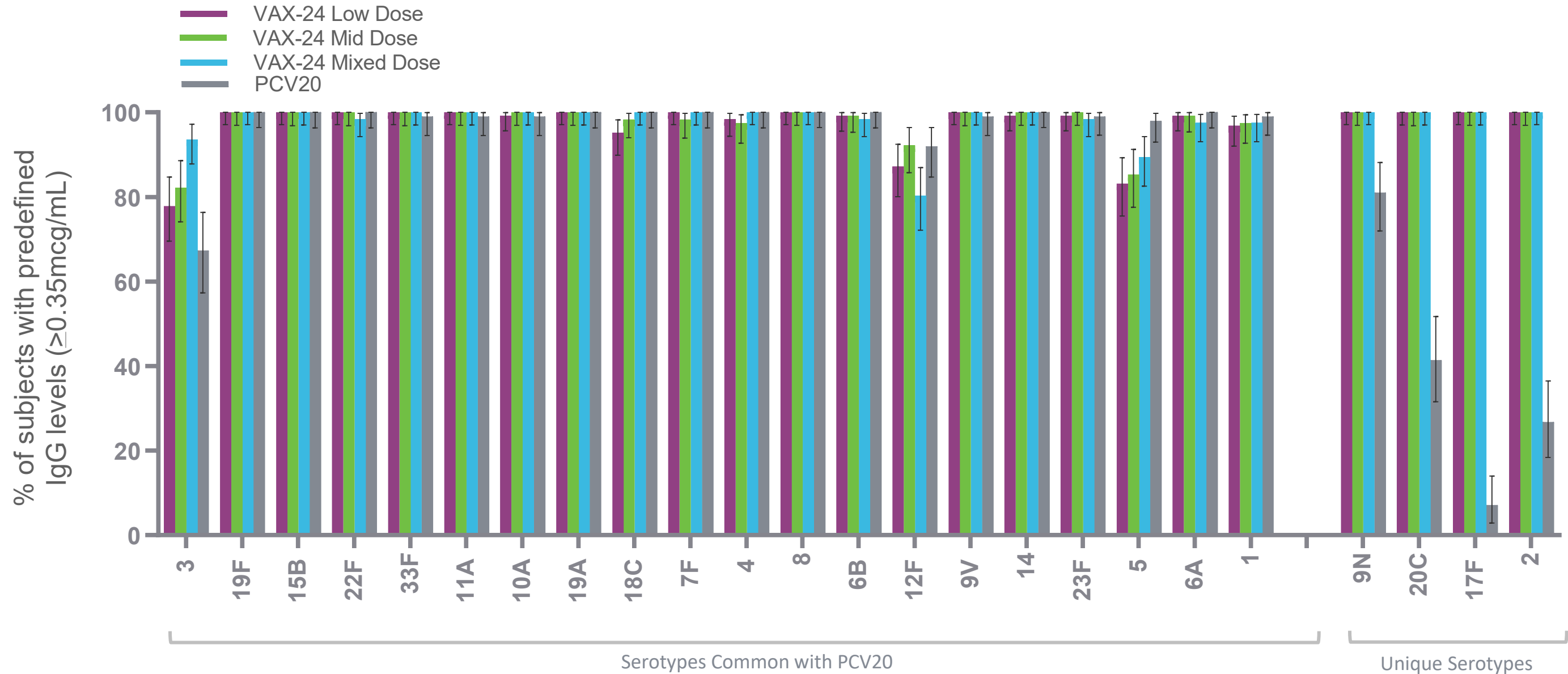
Demonstrated Robust OPA Titers, Generally Consistent with IgG Responses



OPA = opsonophagocytic activity; GMT = geometric mean titer; IgG = immunoglobulin G.

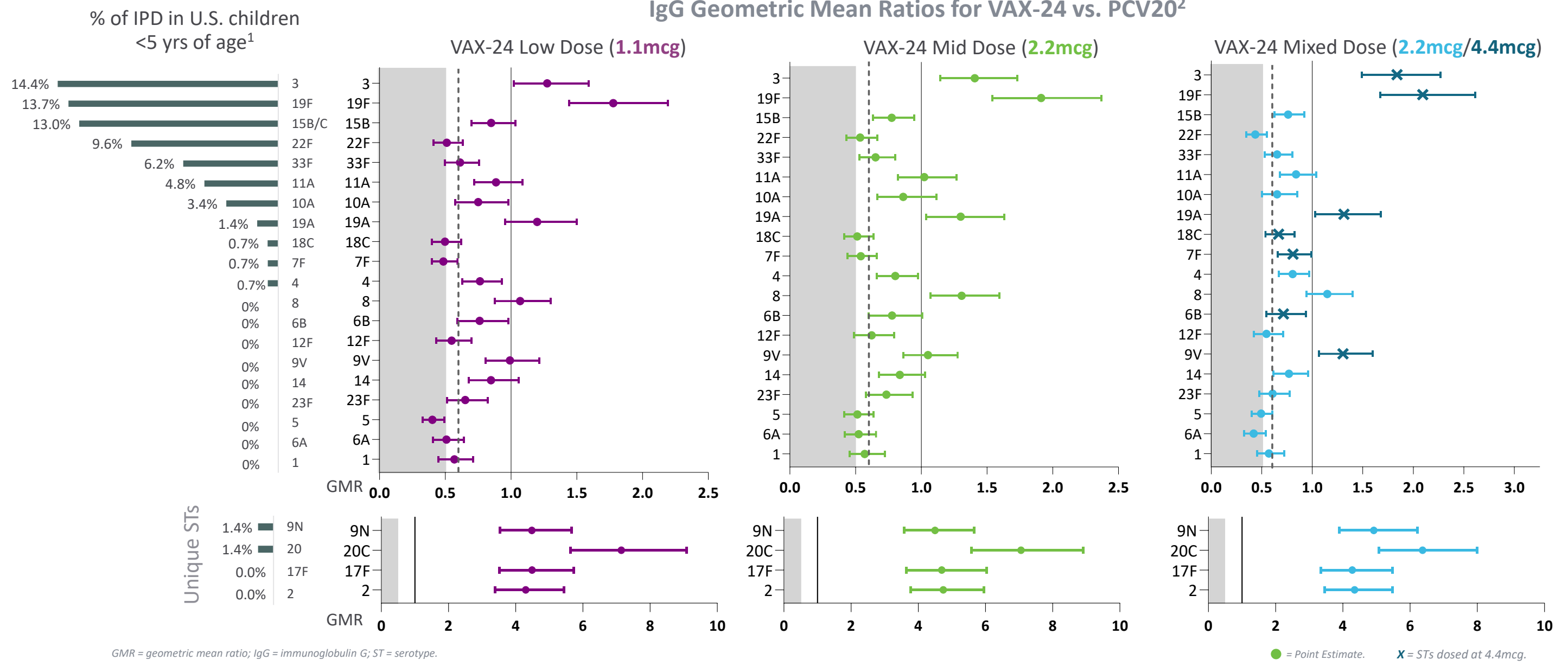
# Final Post-Dose 4 (PD4) IgG and OPA Immunogenicity Data Results

# VAX-24 Demonstrated High Overall Seroconversion Rates Across All Doses PD4



# VAX-24 PD4 IgG GMRs Compared to PCV20

Met Target Ph2 Noninferiority Criteria for Point Estimate of >0.6 on 19 of 24 STs at Mixed Dose and 18 of 24 STs at Mid Dose



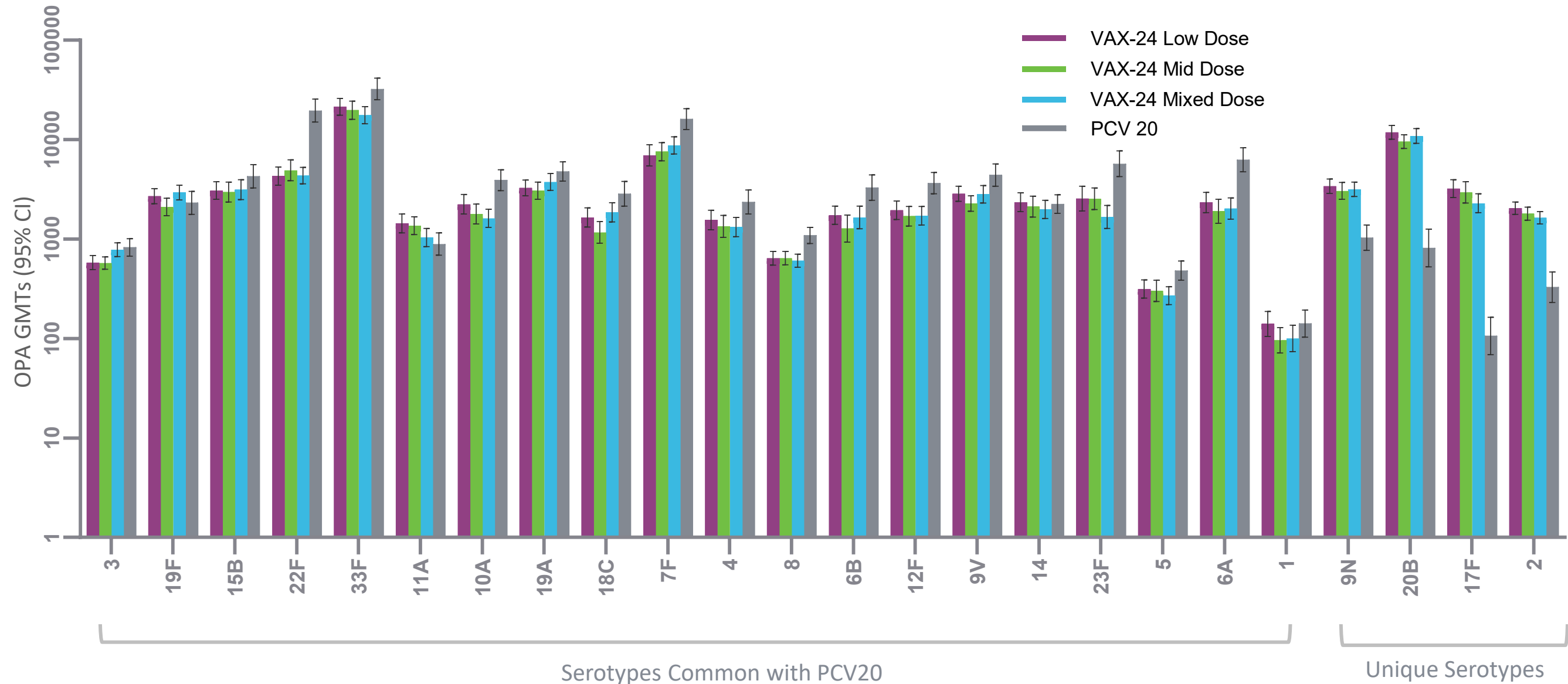
GMR = geometric mean ratio; IgG = immunoglobulin G; ST = serotype.



(1) % of IPD caused in individuals <5 yrs of age in the U.S. in 2023 based on ABC surveillance data ([https://data.cdc.gov/Public-Health-Surveillance/1998-2023-Serotype-Data-for-Invasive-Pneumococcal-qvzb-qs6p/about\\_data](https://data.cdc.gov/Public-Health-Surveillance/1998-2023-Serotype-Data-for-Invasive-Pneumococcal-qvzb-qs6p/about_data)).  
 (2) GMRs for unique STs were calculated compared to ST 12F, which is the ST in PCV20 with the lowest GMC Post-Dose 3 (excluding ST 3 or lower responding STs).  
 15C coverage due to cross protection against 15B.  
 The serogroup 20 antigen contained in VAX-24 and VAX-31, formerly known as a 20B variant, has been officially reclassified as 20C. For additional details on serogroup 20, please see footnote 2 on slide 15.

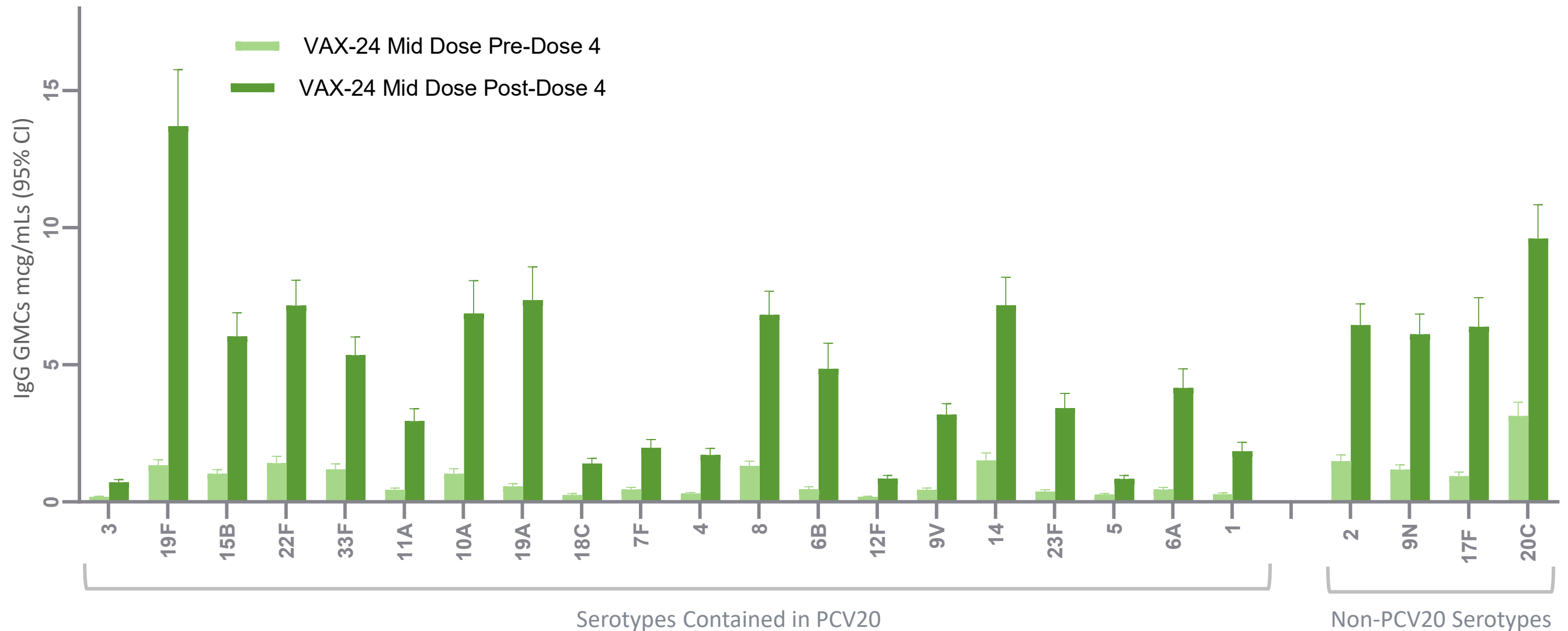
# VAX-24 PD4 OPA GMT Immune Responses

Demonstrated Robust OPA Titers, Generally Consistent with IgG Responses



OPA = opsonophagocytic activity; GMT = geometric mean titer; IgG = immunoglobulin.

# VAX-24 Demonstrated Robust Memory Responses Pre- vs Post-Dose 4 IgG GMCs



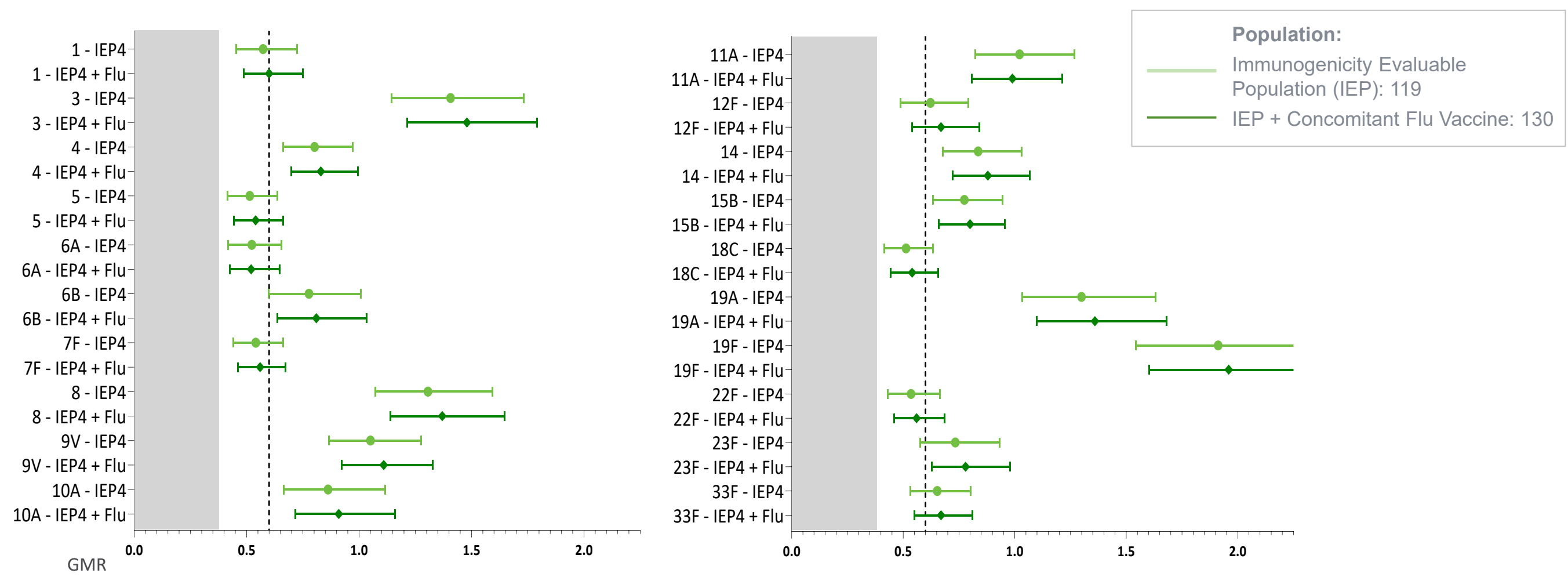
GMT = geometric mean concentration; IgG = immunoglobulin.

# Expanded Analysis of Concomitant Flu Vaccination & Dose-Dependent Immune Responses

# VAX-24 PD4 IgG GMRs Compared to PCV20 Including Subjects Who Received Flu Vaccination

## Consistently Improved Immunogenicity Responses Evidenced in Mid Dose

IgG Geometric Mean Ratios for VAX-24 vs. PCV20

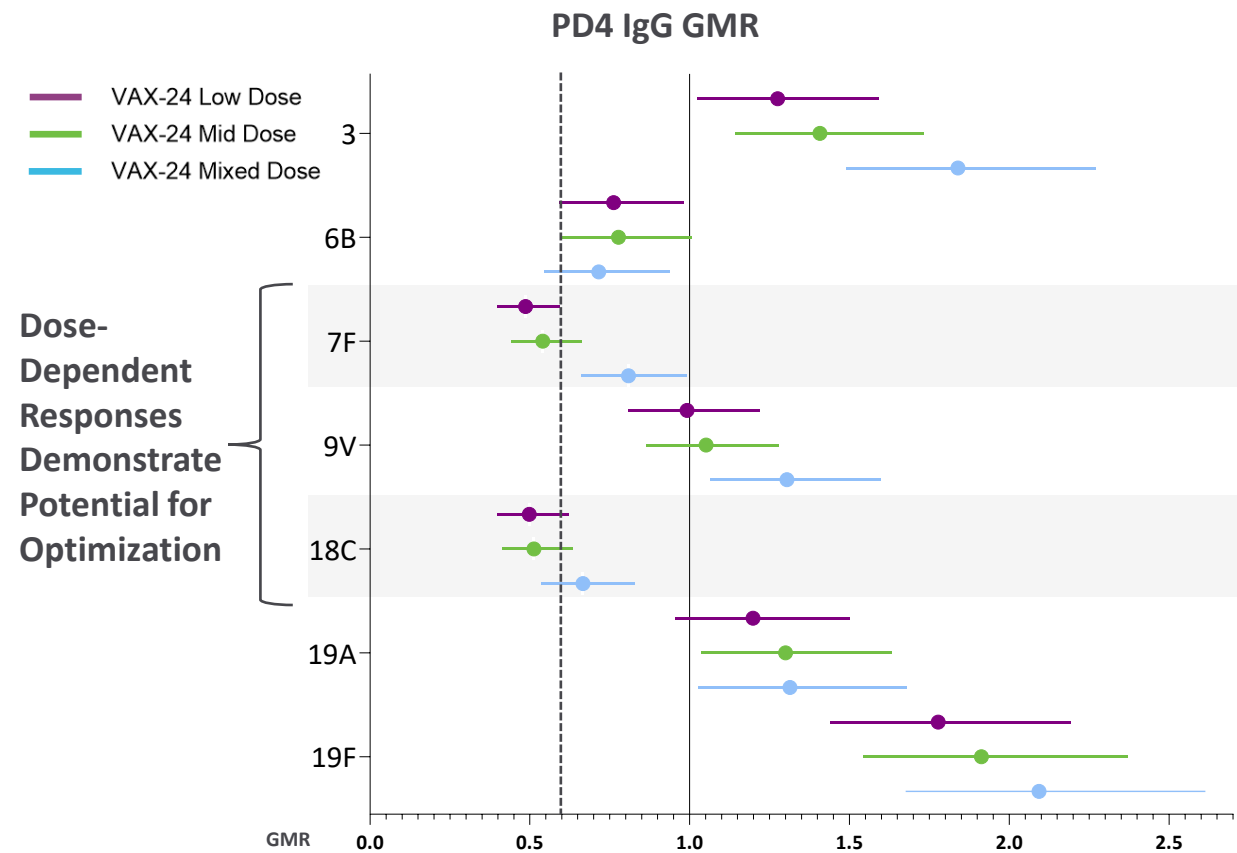


GMR = geometric mean ratio; IgG = immunoglobulin.  
 The IEP4 includes eligible subjects who received the same vaccine across all 4 doses, with valid PD4 IgG or OPA assay results based on blood sample collected within protocol-defined window, and without protocol deviations that may interfere with PD4 immune response.  
 The IEP4 + Flu population includes all eligible subjects from the IEP4 population and an additional 12 participants who followed protocol and received a flu vaccine.  
 This is not a complete study evaluating the concomitant administration of VAX-24 with other vaccines. The findings presented are limited in scope and are not necessarily indicative of how VAX-24 would perform in studies designed to assess concomitant administration.

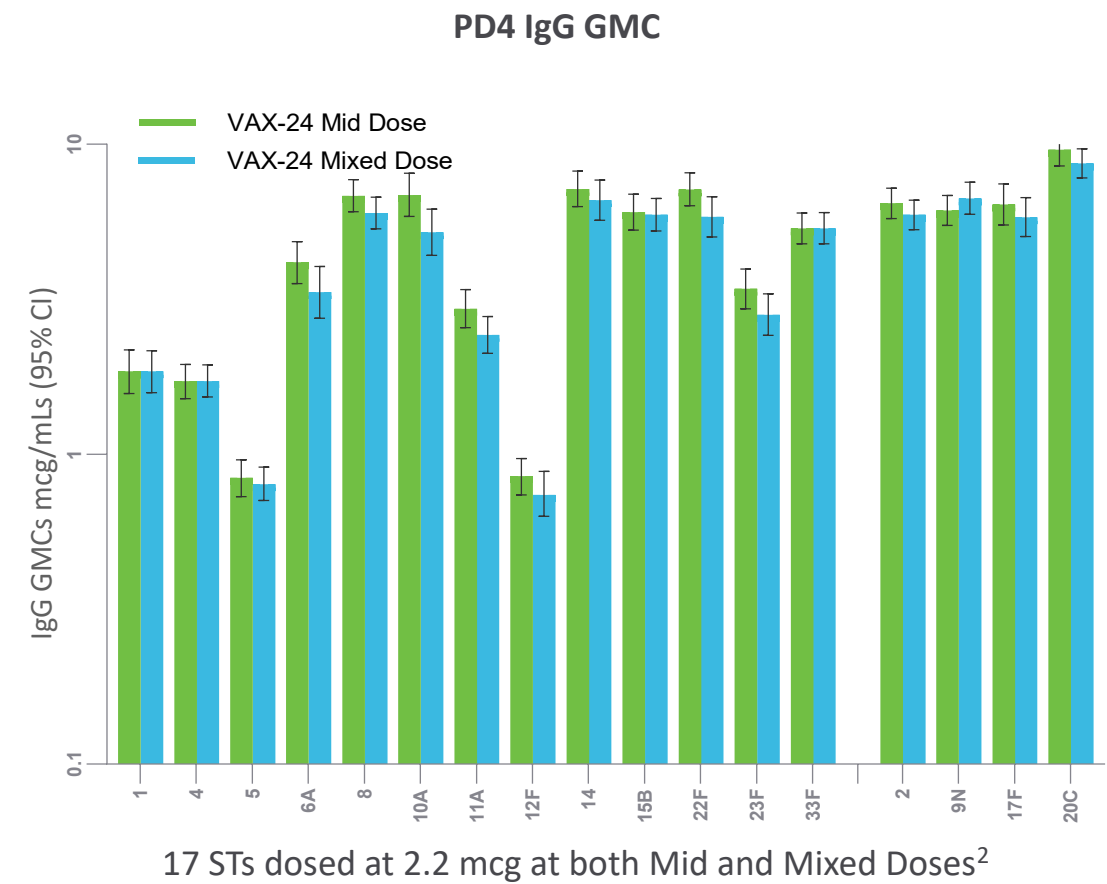
# Dose Response Evidenced PD4 Across Most Serotypes

Supports Dosing Strategy for Ongoing VAX-31 Infant Phase 2 Study

## DOSE-DEPENDENT IMMUNOGENICITY OBSERVED ACROSS DOSE RANGE<sup>1</sup>



## LITTLE TO NO CARRIER SUPPRESSION EVIDENCED BY SIMILAR PERFORMANCE ACROSS DIFFERENT LEVELS OF PROTEIN CARRIER CONTENT



GMR = geometric mean ratio; GMC = geometric mean concentration; IgG = immunoglobulin.

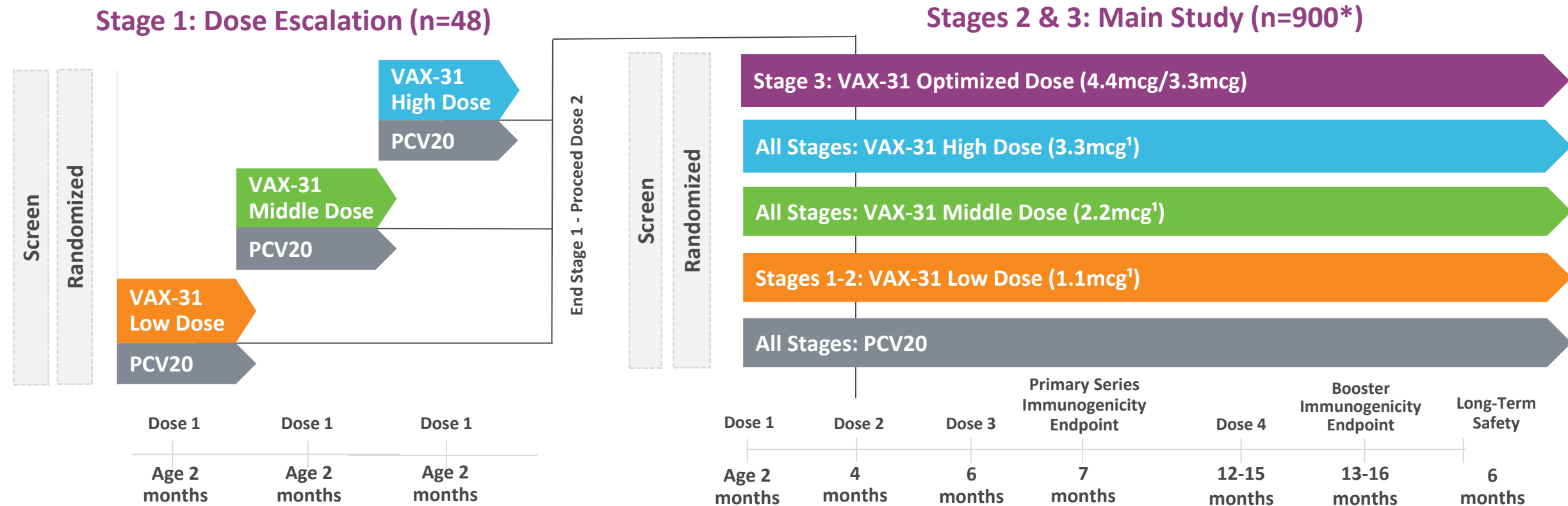
VAX-31  
Infant  
Clinical  
Program

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*protect humankind™*



# Enrollment Completed in VAX-31 Infant Phase 2 Study

3-Stage, Dose-Finding Study Evaluating Safety, Tolerability and Immunogenicity vs PCV20 in 900 Participants



**Stage 1 (safety review; completed):** The safety and tolerability of VAX-31 was evaluated at three dose levels (Low, Middle and High) and compared to PCV20 in 48 infants in a dose-escalation approach.

**Stage 2 (modified and incorporated into Stage 3):** Evaluating the safety, tolerability and immunogenicity of VAX-31 at the same three dose levels and compared to PCV20. The study includes a primary immunization series with doses given at two, four and six months of age, followed by a booster dose at 12-15 months of age.

**Stage 3 (enrollment completed):** The modified study, including the VAX-31 Optimized Dose arm, has completed enrollment in the third and final stage of the study. The Middle and High Dose arms are continuing in Stage 3 as planned. All participants will be evaluated for safety through six months after the booster dose.

# Study Safety, Tolerability and Immunogenicity Key Outcome Measures

	DAY 7 AFTER EACH DOSE	1 MONTH POST-DOSE 3	1 MONTH POST-DOSE 4	6 MONTHS POST-DOSE 4
SAFETY AND TOLERABILITY OUTCOME MEASURES	<ul style="list-style-type: none"> <li>Solicited local reactions</li> <li>Solicited systemic events</li> </ul>	<ul style="list-style-type: none"> <li>Unsolicited adverse events (AE)</li> <li>Serious adverse events (SAE), new onset of chronic illnesses (NOCI) and medically attended adverse events (MAAE)</li> </ul>	<ul style="list-style-type: none"> <li>SAE, NOCI and MAAE</li> </ul>	<ul style="list-style-type: none"> <li>SAE, NOCI and MAAE</li> </ul>
IMMUNOGENICITY OUTCOME MEASURES		<ul style="list-style-type: none"> <li>% of subjects achieving Immunoglobulin G (IgG) antibody concentration <math>\geq 0.35</math> mcg/mL</li> <li>IgG Geometric Mean Concentration (GMC)</li> <li>Opsonophagocytic activity (OPA) Geometric Mean Titer (GMT)</li> </ul>	<ul style="list-style-type: none"> <li>IgG GMC</li> <li>% of subjects achieving IgG antibody concentration <math>\geq 0.35</math> mcg/mL</li> <li>% of subjects achieving IgG concentration <math>\geq 1.0</math> mcg/mL</li> <li>OPA GMT</li> <li>IgG and OPA Geometric Mean Fold Rise (GMFR) from pre-dose 4 to 1-month post-dose 4</li> <li>% of subjects achieving a 4-fold rise in IgG and OPA from pre-dose 4 to 1-month post-dose 4</li> </ul>	

# Non-PCV Pipeline

**VAXCYTE**  
*protect humankind™*



# Initiation of Phase 1 Adult Clinical Study for VAX-A1, a Vaccine Candidate to Prevent Group A Strep, Expected in Mid-2026<sup>1</sup>

**Phase 1 Adult Study Includes Primary Objective of Assessing Safety and Tolerability and Secondary Objective of Evaluating Initial Immunogenicity Data of VAX-A1, a Novel Conjugate Vaccine Designed to Deliver Universal Protection Against a High-Priority Pathogen**

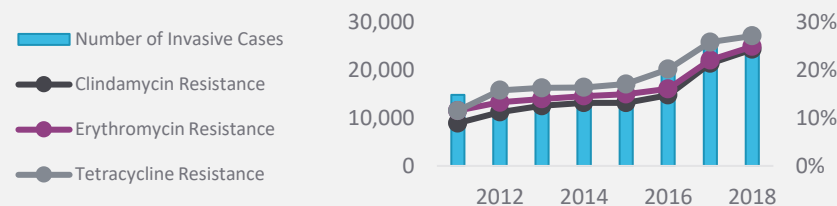
**TOTAL ANNUAL MARKET FOR GROUP A STREP VACCINES IS ESTIMATED AT ~\$3 BILLION TO \$4 BILLION GLOBALLY<sup>2</sup>**



**Group A Strep remains a global cause of morbidity and mortality in adults and children:**

- Group A Strep results in an estimated **800M cases of illness annually worldwide**, including pharyngitis, or strep throat, and an array of severe invasive infections and sequelae<sup>3</sup>
- Annual economic burden of Group A Strep disease in the U.S. population is estimated to **exceed \$6 billion<sup>4</sup>**
- Studies have indicated that antibiotic resistance to Group A Strep has been increasing over the past decade, leading the CDC to categorize Group A Strep as a concerning threat<sup>5</sup>

**Sharp increase in cases and resistance over a decade:**



## VAX-A1: BROAD-SPECTRUM, MONOVALENT CONJUGATE VX



Conjugate vaccine combining a disease-specific protein carrier and a universal species-defining PS designed to confer robust, boostable and durable protection against a broad-spectrum of subtypes of Group A Strep

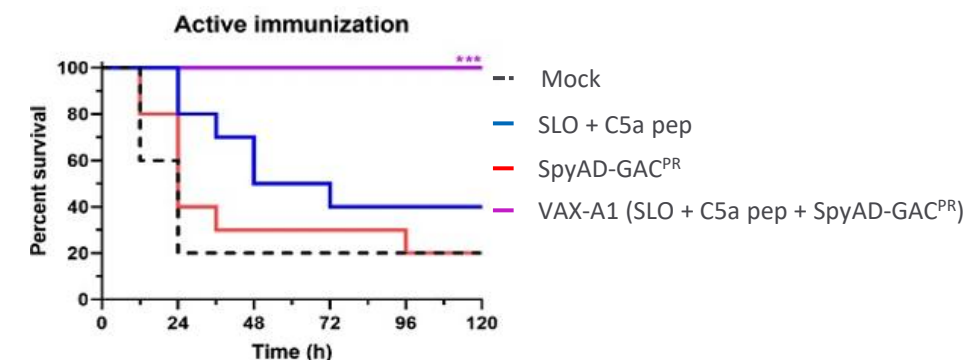


Leverages site-specific conjugation to disease-specific carrier to expose mapped T- and B-cell epitopes



Proprietary conserved antigen – Polyrhamnose – conjugated to an immunogenic disease-specific carrier along with two conserved anti-virulence factors designed to disarm the pathogen’s defense mechanisms

**KEY DATA:**



# VAX-GI: Shigella Vaccine Program

## Novel Shigella Vaccine to Prevent Widespread Global Morbidity & Mortality, Particularly in Children

<b>UNMET NEED</b>	<ul style="list-style-type: none"> <li>Shigella is a bacterial illness with no available preventative treatment</li> <li>Estimated to cause 80-165 million cases of disease and 600,000 deaths annually, and most cases and deaths are among children<sup>1</sup></li> <li>With the aim of reducing morbidity and mortality due to the disease, the World Health Organization lists Shigella vaccine development as a priority goal<sup>2</sup></li> </ul>																																																																																	
<b>VAX-GI: NOVEL SHIGELLA VACCINE</b>	<ul style="list-style-type: none"> <li>Development collaboration with the University of Maryland, Baltimore; supported with funding by two National Institutes of Health grants with total potential funding of up to \$5.1M</li> <li>Plan to pursue conjugate and protein-only approaches simultaneously</li> <li>Conjugate approach: IpaB-LPS/IpaH/VirG; Protein-only approach: IpaB/IpaH/VirG</li> </ul>																																																																																	
<b>PROGRAM STATUS</b>	<ul style="list-style-type: none"> <li>Decision on final candidate to be determined by a human challenge study conducted at the University of Maryland, Baltimore</li> </ul>																																																																																	
<b>MOA &amp; KEY DATA</b>	<ul style="list-style-type: none"> <li>Targeting IpaB inhibits assembly of T3SS and toxin delivery to immune cells</li> <li>Opsonophagocytosis and killing of bacteria</li> </ul> <div style="display: flex; justify-content: space-around;"> <div data-bbox="800 1189 1278 1571"> <p><b>VAX-GI: Conjugate Approach</b></p> <table border="1"> <caption>VAX-GI: Conjugate Approach Survival Data</caption> <thead> <tr> <th>Days After Challenge</th> <th>IpaBmut1-OPS (%)</th> <th>IpaB (%)</th> <th>CRM-OPS (%)</th> <th>Alum alone (%)</th> </tr> </thead> <tbody> <tr> <td>0</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> </tr> <tr> <td>4</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> </tr> <tr> <td>6</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> </tr> <tr> <td>8</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> </tr> </tbody> </table> </div> <div data-bbox="1447 1189 2017 1588"> <p><b>VAX-GI: Protein Only Approach</b></p> <table border="1"> <caption>VAX-GI: Protein Only Approach Survival Data</caption> <thead> <tr> <th>Days after challenge</th> <th>IpaB 5µg (%)</th> <th>IpaB-10µg (%)</th> <th>IpaB-20µg (%)</th> <th>sl Sf2a-IN (%)</th> <th>AdjuPhos (%)</th> <th>PBS (%)</th> </tr> </thead> <tbody> <tr> <td>0</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> </tr> <tr> <td>4</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> </tr> <tr> <td>6</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> </tr> <tr> <td>8</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> </tr> <tr> <td>10</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> </tr> <tr> <td>12</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> </tr> <tr> <td>14</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> <td>100</td> </tr> </tbody> </table> </div> </div> <div data-bbox="2233 1058 2710 1614"> <p><b>A</b></p> <p>Labels: eukaryotic membrane, IpaD, IpaB, needle tip complex, Candidate Vaccine Antigen, T3SS, needle MxiH, outer membrane ring, needle periplasmic rod MxiI, OM, H<sub>2</sub>O, periplasmic region, socket, IM, inner membrane ring, MxiA/PcrD/FliA, Spa40/FliH, Spa24, Spa29, Spa9, export apparatus, IMEA, Spa33, C-ring, CEA, Spa47/FliI, Spa13/PscO/FliJ, MxiN/FliH, ATPase complex, CEA.</p> </div>	Days After Challenge	IpaBmut1-OPS (%)	IpaB (%)	CRM-OPS (%)	Alum alone (%)	0	100	100	100	100	4	100	100	100	100	6	100	100	100	100	8	100	100	100	100	Days after challenge	IpaB 5µg (%)	IpaB-10µg (%)	IpaB-20µg (%)	sl Sf2a-IN (%)	AdjuPhos (%)	PBS (%)	0	100	100	100	100	100	100	4	100	100	100	100	100	100	6	100	100	100	100	100	100	8	100	100	100	100	100	100	10	100	100	100	100	100	100	12	100	100	100	100	100	100	14	100	100	100	100	100	100
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# Key Corporate Highlights



Large Market Opportunity for Broadest-Spectrum PCV

Cell-Free Protein Synthesis Enabled Pipeline

Aligned Critical Commercial Manufacturing  
and Supply Chain Resources

Robust Pipeline with Multiple Novel Vaccines

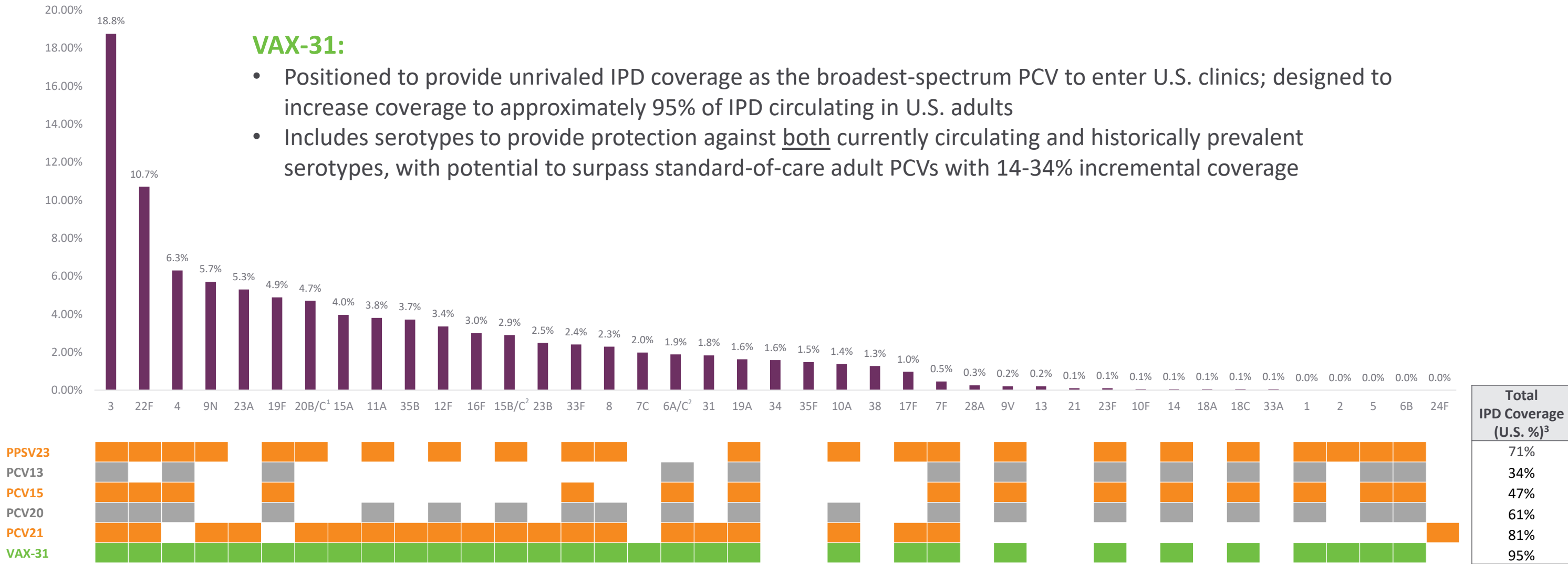
# Appendix

# Spectrum of Coverage Drives Adoption in PCV Segment

## VAX-31 Designed to Increase Coverage to ~95% of IPD Circulating in U.S. Adults

### VAX-31:

- Positioned to provide unrivaled IPD coverage as the broadest-spectrum PCV to enter U.S. clinics; designed to increase coverage to approximately 95% of IPD circulating in U.S. adults
- Includes serotypes to provide protection against both currently circulating and historically prevalent serotypes, with potential to surpass standard-of-care adult PCVs with 14-34% incremental coverage



(1) The serogroup 20 antigen contained in VAX-24 and VAX-31, formerly known as a 20B variant, has been officially reclassified as 20C. For additional details on serogroup 20, please see footnote 2 on slide 15.

(2) 15C coverage due to cross-reaction against 15B. 6C coverage due to cross-protection by 6A.

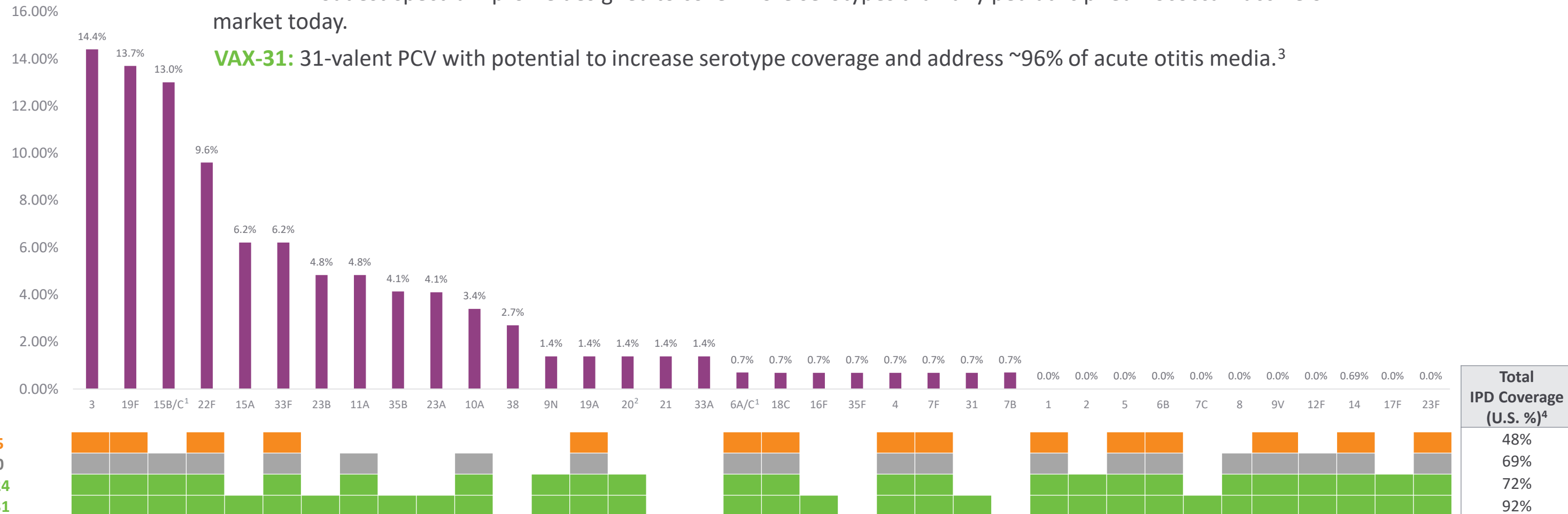
(3) % of IPD caused in individuals ≥50 yrs of age in the U.S. in 2023 based on ABC surveillance data: [https://data.cdc.gov/Public-Health-Surveillance/1998-2023-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p/about\\_data](https://data.cdc.gov/Public-Health-Surveillance/1998-2023-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p/about_data).

# Spectrum of Coverage Drives Adoption in Vital Pediatric Population

Pediatric Segment Represents Majority of ~\$8B Pneumococcal Vaccine Market

**VAX-24:** Broadest-spectrum profile designed to cover more serotypes than any pediatric pneumococcal vaccine on-market today.

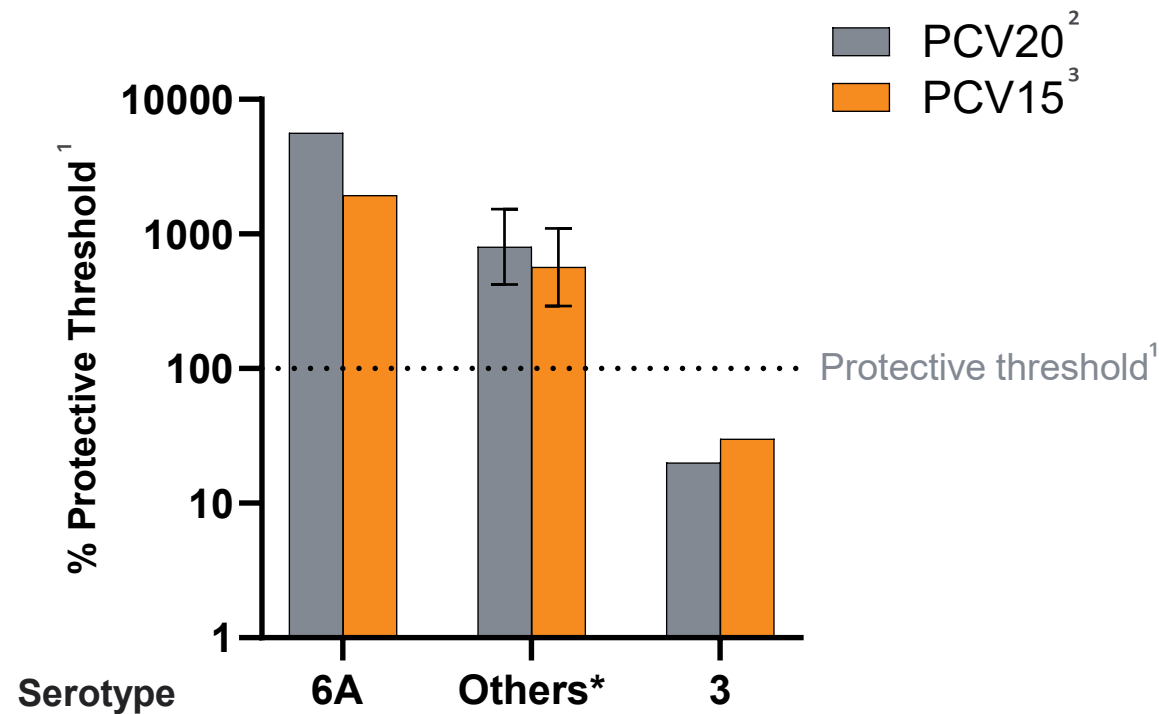
**VAX-31:** 31-valent PCV with potential to increase serotype coverage and address ~96% of acute otitis media.<sup>3</sup>



(1) 15C coverage due to cross-reaction against 15B. 6C coverage due to cross-protection by 6A. % of IPD caused in individuals <5 yrs of age is 0.7% for 6C, 0% for 6A.  
 (2) The serogroup 20 antigen contained in VAX-24 and VAX-31, formerly known as a 20B variant, has been officially reclassified as 20C. For additional details on serogroup 20, please see footnote 2 on slide 15.  
 (3) In U.S. children five years of age or under, VAX-31 is estimated to address ~96% of AOM: Grant LR et al., FrontPediatr.2024;12:1383748. Serotype percentages reflect 2017–2021 data (Supplemental Table 1).  
 (4) % of IPD caused in individuals <5 yrs of age in the U.S. in 2023 based on ABC surveillance data: [https://data.cdc.gov/Public-Health-Surveillance/1998-2023-Serotype-Data-for-Invasive-Pneumococcal/qvzb-qs6p/about\\_data](https://data.cdc.gov/Public-Health-Surveillance/1998-2023-Serotype-Data-for-Invasive-Pneumococcal/qvzb-qs6p/about_data).

# On-Market PCVs Elicit Antibodies for Disease Protection With Range of Results

## Serotype 3 (ST3) Conjugate Elicits Weakest Antibody Response Among All Conjugates



### KEY FACTORS DETERMINE WHY ST3 REQUIRES HIGHER LEVEL OF PROTECTIVE ANTIBODY



**Thick Polysaccharide Capsule:** forms a robust physical barrier that impairs opsonization and phagocytosis, requiring higher antibody levels for effective coating



**Capsule Shedding and Antibody Neutralization:** releases free polysaccharides that bind and neutralize antibodies before they reach the bacterial surface



**Reduced Opsonophagocytic Efficiency:** mucoid capsule limits complement (C3b) deposition and phagocyte recognition, making ST3 less susceptible to immune clearance

**ST3 REMAINS AN OUTLIER AS CIRCULATION HAS NOT BEEN EFFECTIVELY CONTROLLED BY VACCINATION**

# VAXCYTE

*protect humankind™*

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