Corporate Presentation

June 2, 2026

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 carrier-sparing platform and vaccine candidates, including breadth of coverage and the ability to deliver potentially better immune responses, best-in-class vaccines 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.

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 BTD 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
  - Phase 1 study in adults underway
- **VAX-GI:** Novel Shigella vaccine

ALIGNED CRITICAL RESOURCES

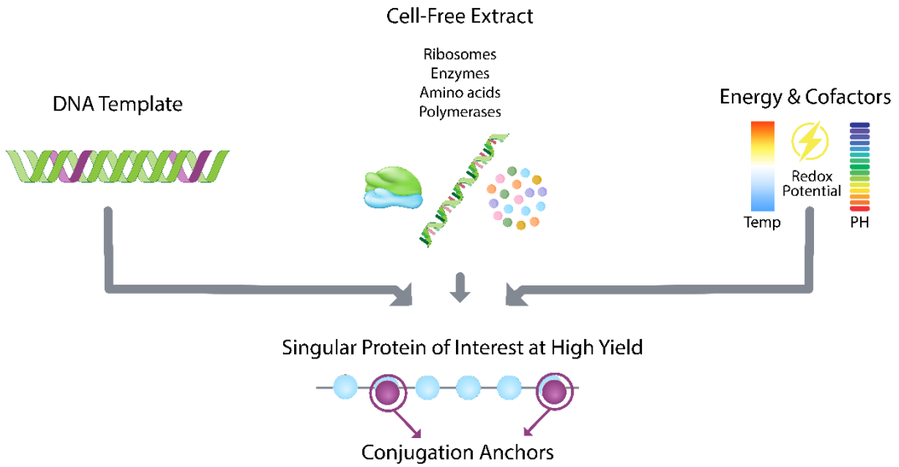
- **Strategic Manufacturing Approach**
  - Building out capacity to satisfy global PCV demand for developed markets
  - Global commercial manufacturing agreement with Lonza to produce key PCV components
  - Agreement with Thermo Fisher Scientific to establish U.S. fill-finish manufacturing; expands domestic 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

BTD = Breakthrough Therapy designation, IPD = invasive pneumococcal disease, MOA = mechanism of action.

Cell-Free Protein Synthesis Platform Unlocks Multiple Vaccine Applications

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

VAXCYTE CELL-FREE PROTEIN SYNTHESIS PLATFORM: XpressCF



- 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

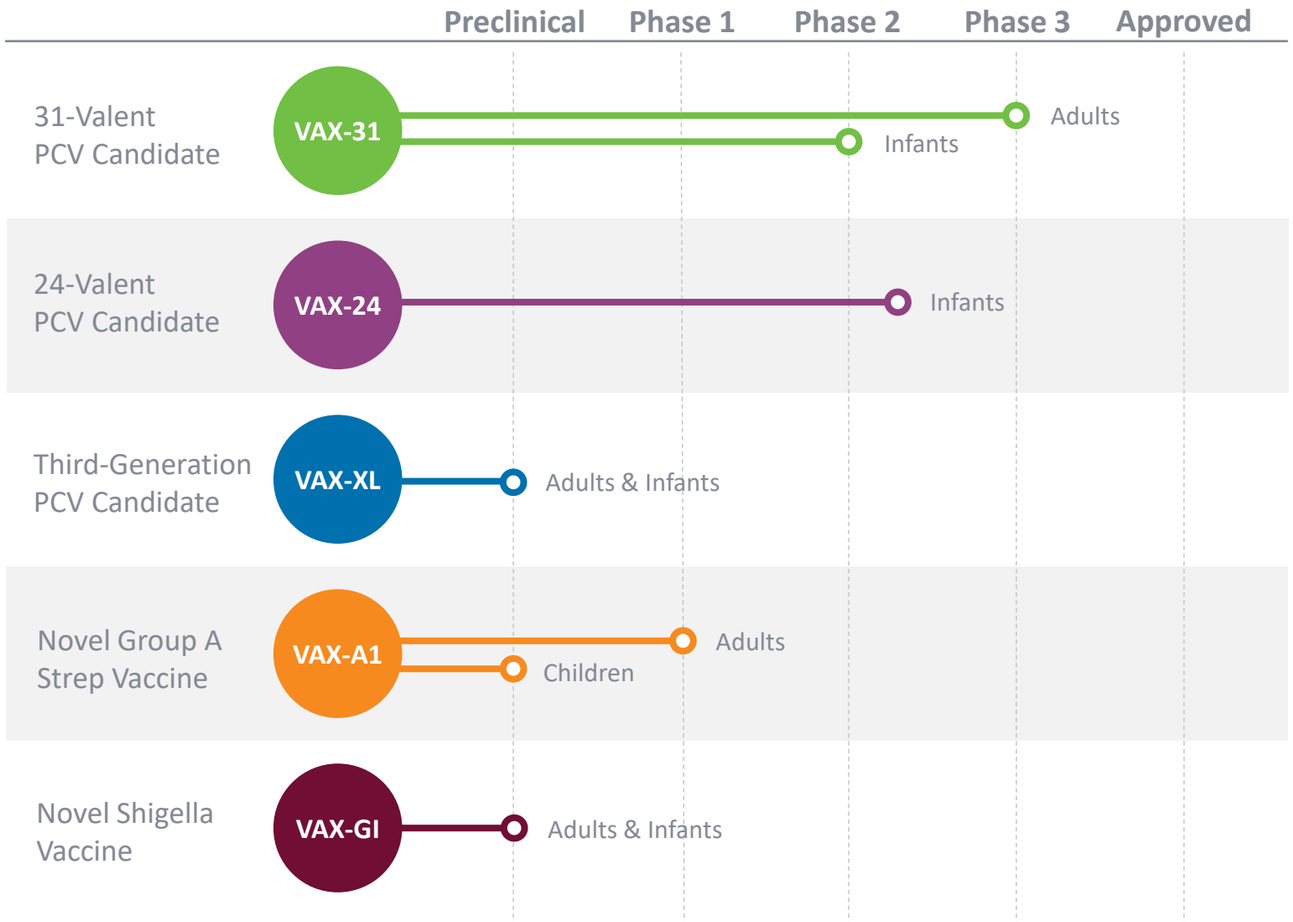
- Site-specifically attach antigens onto protein carriers designed to:
  - Enable consistent exposure of T-cell epitopes and/or B-cell epitopes on protein carrier
  - Avoid off-target effects
  - Enable use of less protein carrier without sacrificing immunogenicity
  - Enable broader-spectrum vaccines

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

VAX-31 ADULT INDICATION[1]

- 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**[2] trials in the first half of 2027

VAX-31 INFANT INDICATION[1]

- 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[3]

- Announce topline data from the Phase 1, first-in-human adult study in the second half of 2027

(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.
(3) Guidance as of June 2, 2026. VAX-A1 Phase 1, first-in-human study has the primary objective of evaluating safety and tolerability and is being conducted in Australia.

Experienced Management Team with Track Record in Vaccines and Biopharma

Grant Pickering, MBA
Chief Executive Officer & Co-Founder

KLEINER PERKINS
Dendreon
GSK
Johnson&Johnson

Andrew Guggenhime, MBA
President & Chief Financial Officer

Dermira
Calistoga Pharmaceuticals
Facet Biotech

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

Pfizer
NOVARTIS
MERCK

Mike Mullette, MBA
Chief Commercial Officer

lykos THERAPEUTICS
moderna
SANOFI

Chris Griffith, MS, MBA
Chief Business & Strategy Officer

Dermira
GILEAD
Adanate

Harp Dhaliwal, MBA
Chief Technical Operations Officer

Dermira
MEDIVATION
Biogen

Roger Nosal
Senior VP & Head of Global Regulatory & Quality

Pfizer
NGT BioPharma Consultants

Jeff Fairman, PhD
VP Research & Co-Founder

JUVARIS BIOTHERAPEUTICS, INC.
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
valentis

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[1,2]

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

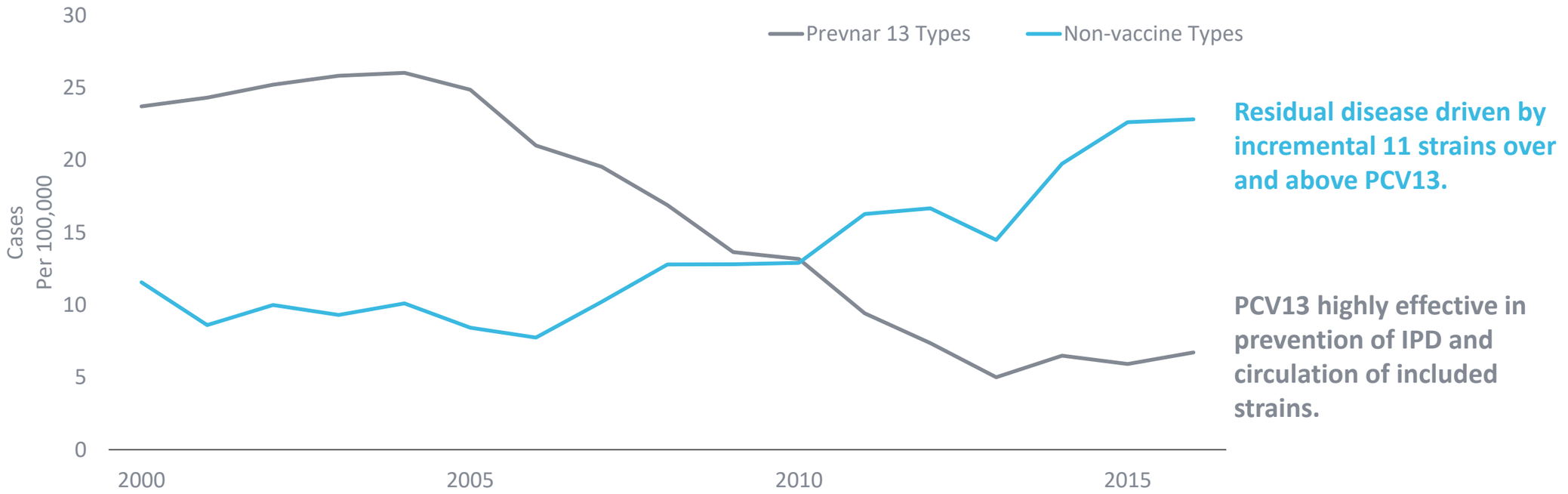
- *Streptococcus pneumoniae* is the leading cause of vaccine-preventable deaths globally in children under five[4]
- ~225K U.S. adult hospitalizations annually caused by pneumococcal pneumonia[5]
- ~300K children under five years old die annually worldwide due to *Streptococcus pneumoniae*[6]

SoC = standard of care. (1) https://www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/. (2) https://www.cdc.gov/pinkbook/hcp/table-of-contents/chapter-17-pneumococcal-disease.html. (3) https://view-hub.org/vaccine/pcv, accessed source December 2025. (4) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8677503/table/T2/. (5) https://www.cdc.gov/mmwr/volumes/74/wr/mm7401a1.htm. (6) https://www.cdc.gov/pneumococcal/php/surveillance/index.html#:~:text=Global%20trends,deaths%20occur%20in%20developing%20countries.

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.*

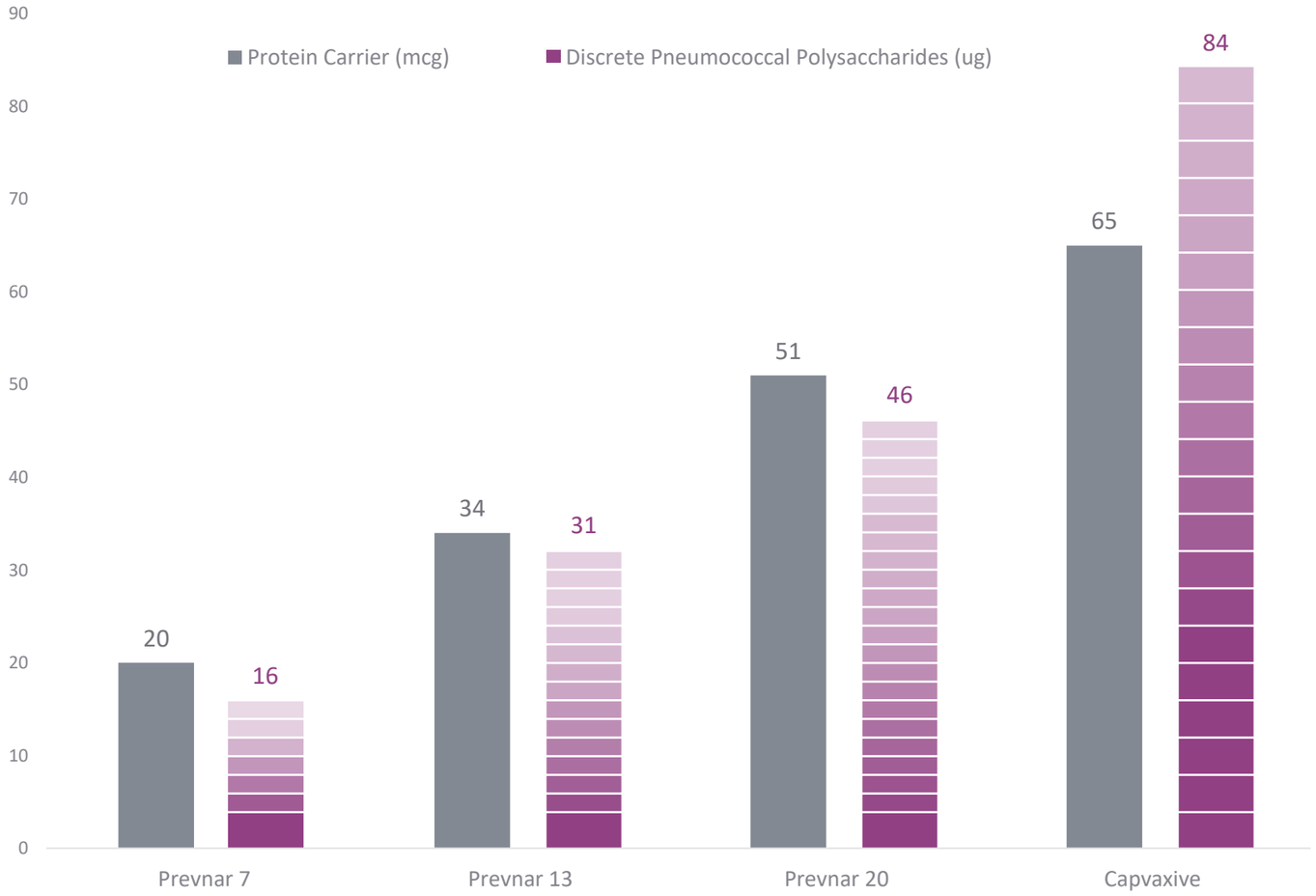
Limitations of Current PCVs

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



Sources: Prevnar 7, Prevnar 13, Prevnar 20, Vaxneuvance and Capvaxive product inserts.

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

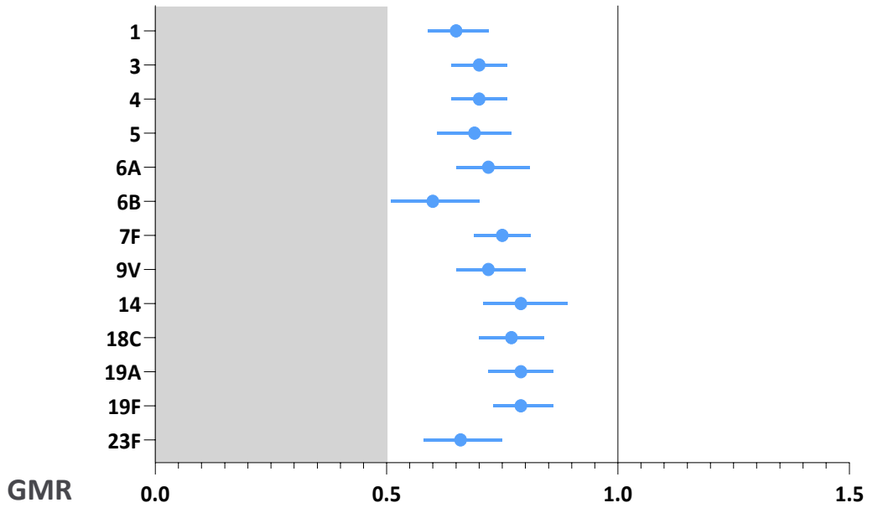
Coverage Expansion Using Conventional Chemistry Has Led to Carrier-Induced Immune Suppression

CARRIER SUPPRESSION

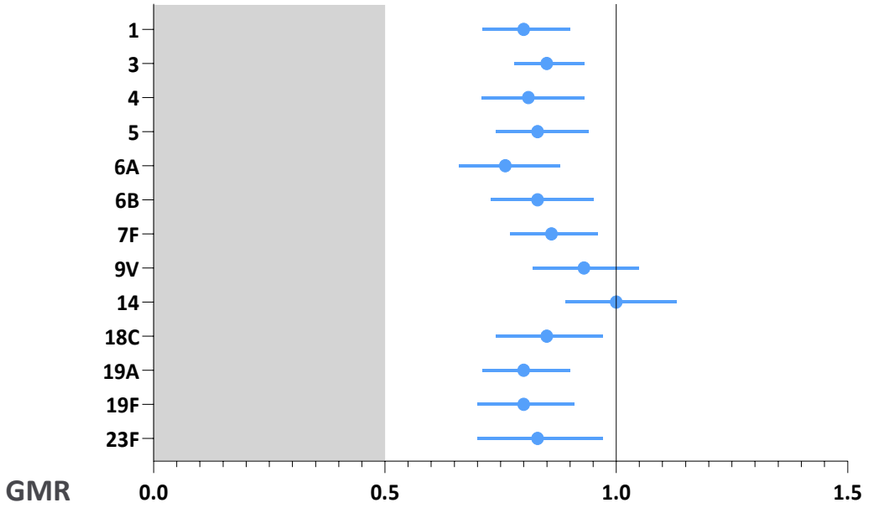
Diminished immune response to target polysaccharides due to cumulative amount of protein carrier

- 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[1]



ADULT IMMUNE RESPONSES (OPA): PCV20 VS PCV13[2]

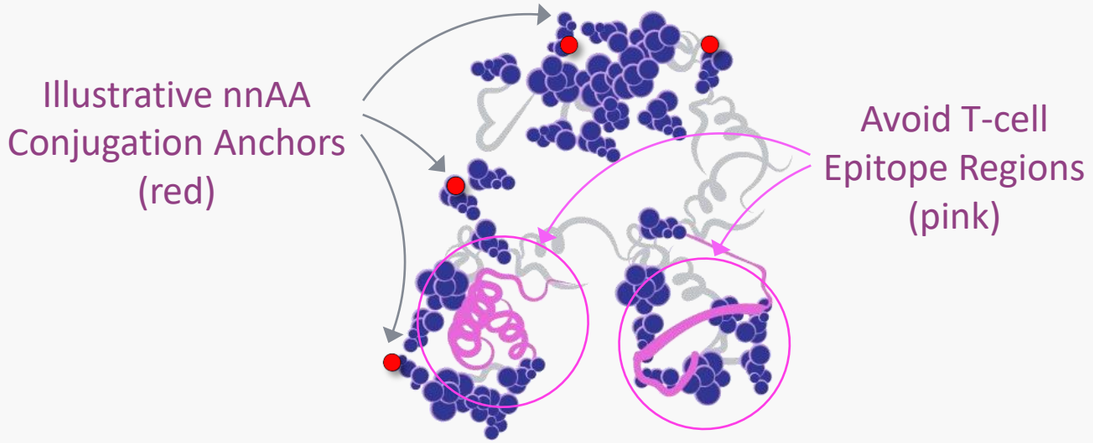


(1) Immunoglobulin G (IgG) Geometric Mean Concentrations post-dose 4 – Prevnar 20 BLA Clinical Review Memorandum by FDA (STN: 125731/189). April 27, 2023.
(2) Prevnar 20 BLA Clinical Review Memorandum. STN: 125731/0 June 8, 2021.
OPA = opsonophagocytic assay; GMR = geometric mean ratio.

Vaxcyte's PCV Franchise Employs Carrier-Sparing Conjugates

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

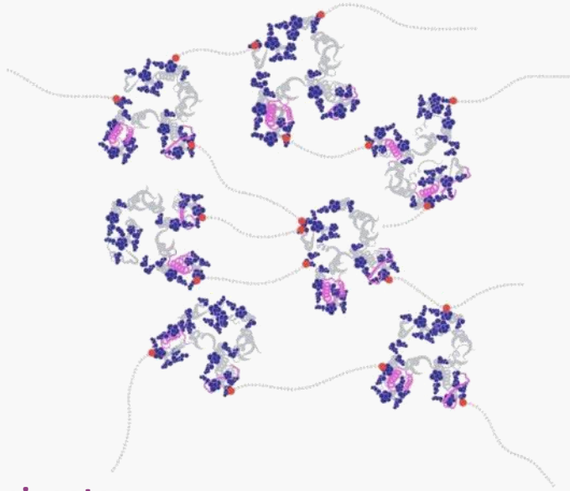
PROPRIETARY eCRM® PROTEIN CARRIER WITH PRECISE, SITE-SPECIFIC CONJUGATION SITES



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

VAXCYTE CARRIER-SPARING CONJUGATES MIMIC THE CUSTOMARY MATRIX FORM

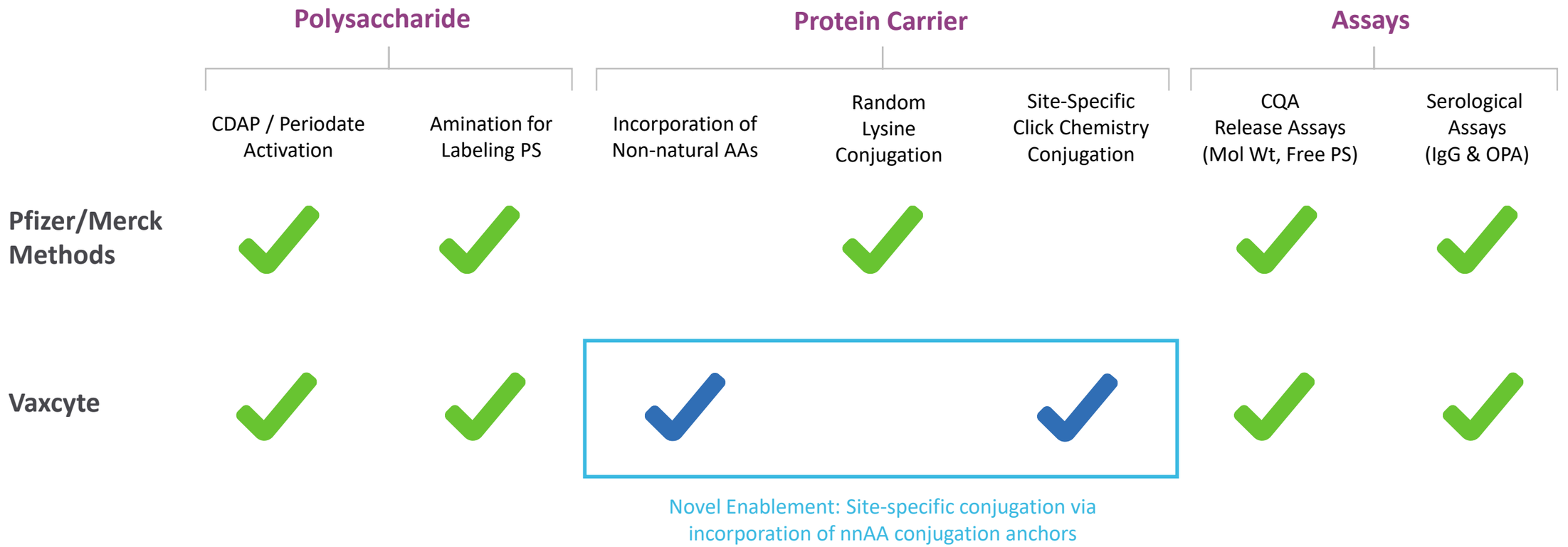


Carrier-Sparing Conjugates

- 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



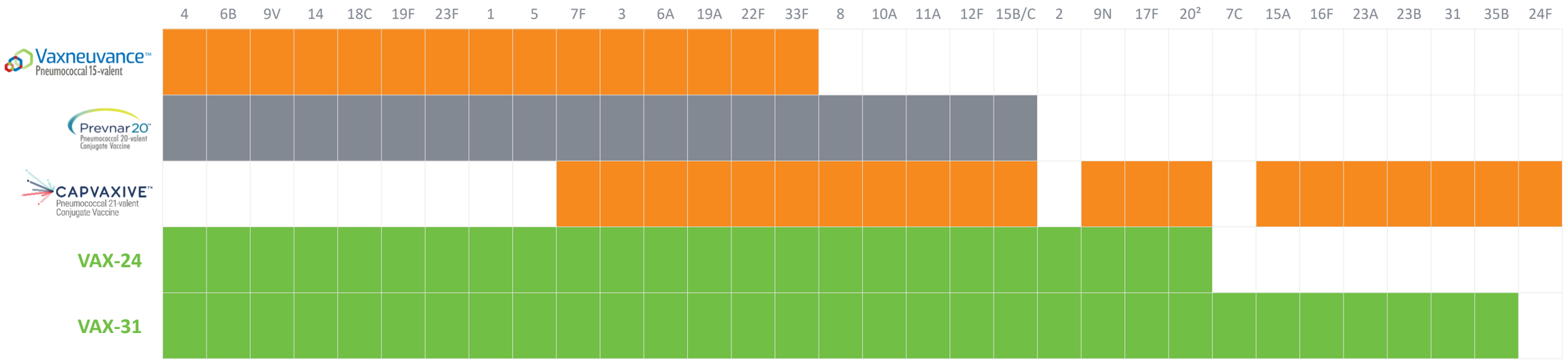
OPA = opsonophagocytic activity; IgG = immunoglobulin G.

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[1]

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)

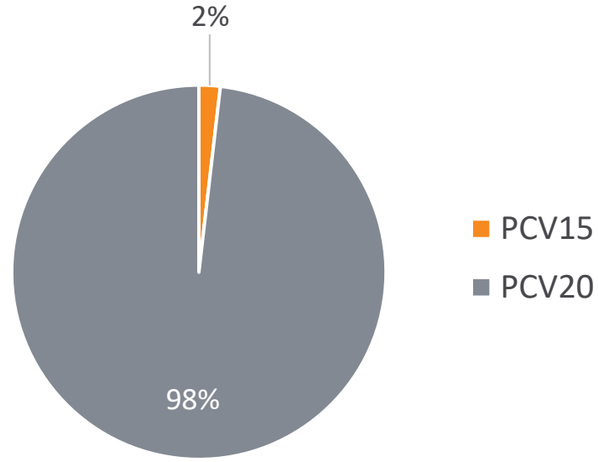
ATTRACTIVE MARGINS

- Pneumococcal vaccines are premium priced, delivering highly attractive margins
- Broader-spectrum PCVs extend premium price in the U.S.[1]
  - 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[2]

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

MOA = mechanism of action; ACIP = U.S. CDC Advisory Committee on Immunization Practices; PPSV23 = Pneumovax 23.
(1) Private Sector costs per dose of the Current CDC Vaccine Price List, VFC Program; source link (accessed April 2026).
(2) FDA safety assessment of PCV20 data presented at February 2024 ACIP meeting.

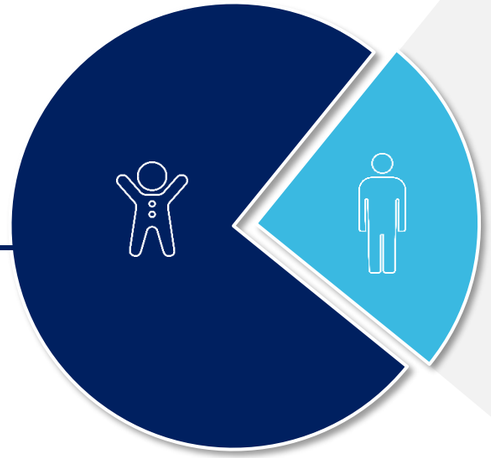
Pneumococcal Vaccine Market Poised for Significant Growth

Combined $8B Market Expected to Grow to ~$12B in 2030[1], Driven Primarily by Adult Market Expansion

Future Market

2030: ~$12B

Pediatric market highly penetrated; significant growth opportunity in adult segment



Total Market

Today: ~$8B

EXPECTED ADULT SEGMENT GROWTH DRIVERS

- PCV recommendation expanded to U.S. adults 50+ (from 65+)[2]
- "At risk" adults aged 19-49 included in U.S. recommendation
- Potential shift to adult prime-boost schedule in U.S.
- Revaccination of individuals with history of lower valency pneumococcal vaccination[3]
- Expanded OUS adult PCV recommendations

(1) *ZS Associates, Vaccine Landscape Report - Pneumococcal infections, April 2026.*
(2) *https://www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/.*
(3) *Current revaccination recommendations primarily apply to individuals previously vaccinated with lower-valency pneumococcal regimens (e.g., PCV13 ± PPSV23).*

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[1]

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[2]**

PPSV23 = Pneumovax 23.

(1) Transition from PPSV23 to PCV-only or newly introduced PCV recommendation: France, Germany, Japan, Netherlands, Spain (regional, Galicia), Switzerland, United Kingdom.

(2) Pfizer full-year 2025 earnings reporting, full-year 2024 vs. full-year 2025; Prevnar family includes revenues from Prevnar 20/Prevenar 20 (pediatric and adult) and Prevnar 13/Prevenar 13 (pediatric and adult).

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

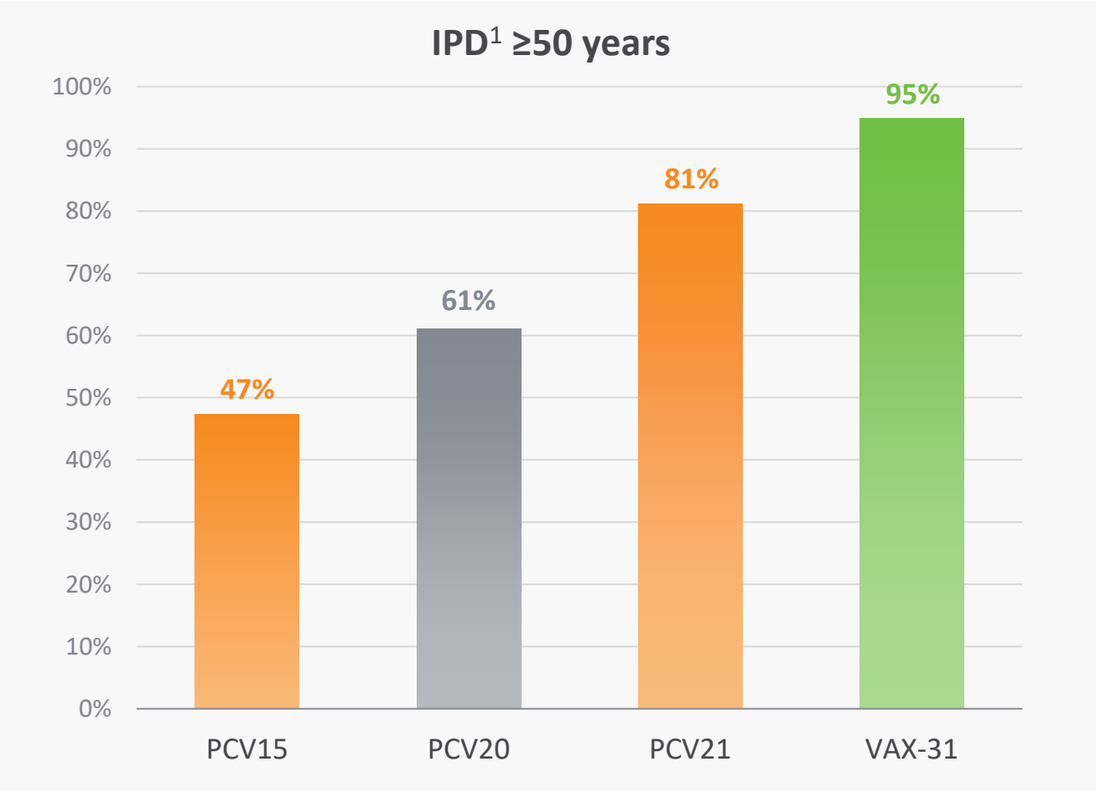
- Agreement expands domestic capacity (North Carolina)
- Supports future commercial manufacturing and deepens investment in American innovation and infrastructure

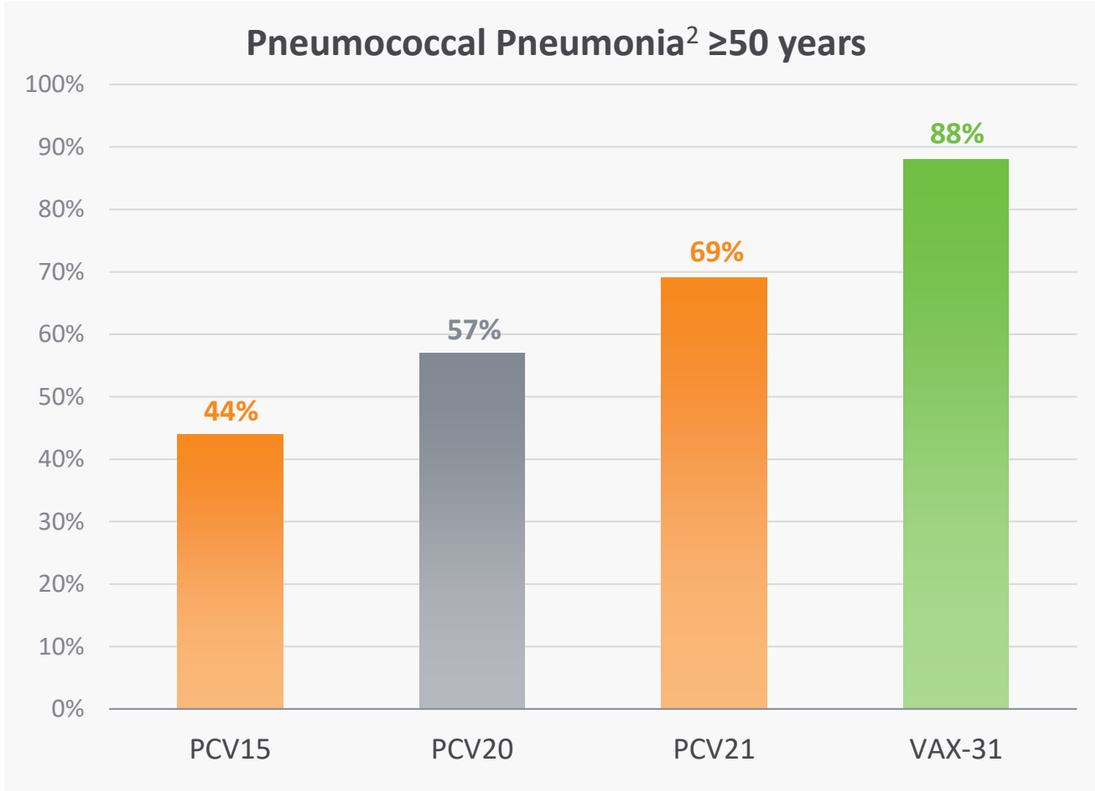
VAX-31 Adult Clinical Program

VAXCYTE
protect humankind™

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

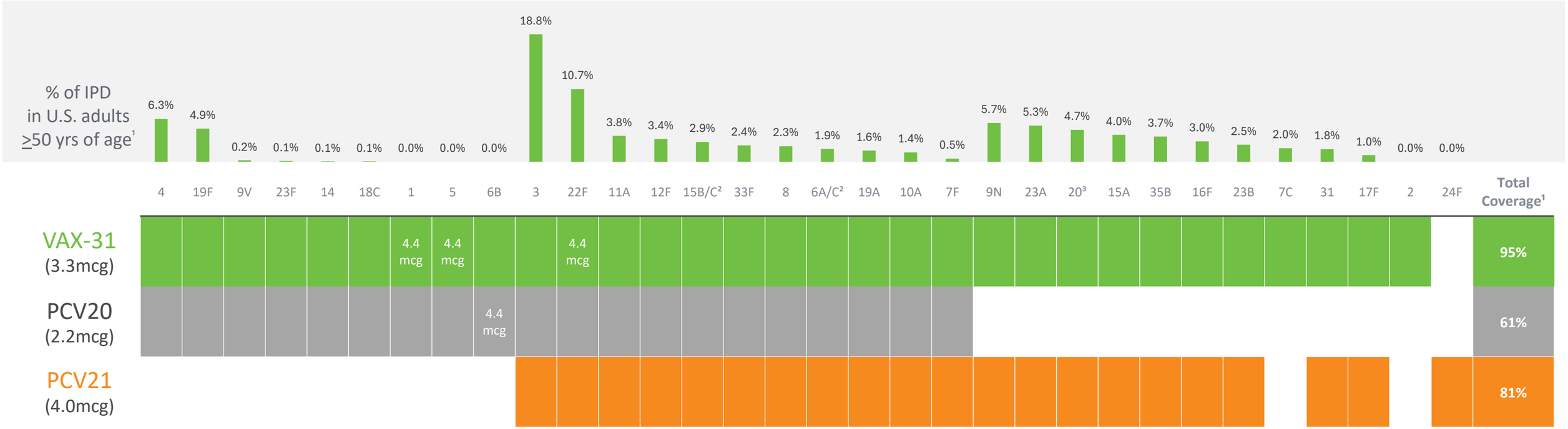




All estimates assume cross-protection between serotypes 6A and 6C and between 15B and 15C.
(1) CDC 2023 Active Bacterial Core (ABC) Surveillance data (https://data.cdc.gov/Public-Health-Surveillance/1998-2023-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p/about_data); IPD cases with missing serotype 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

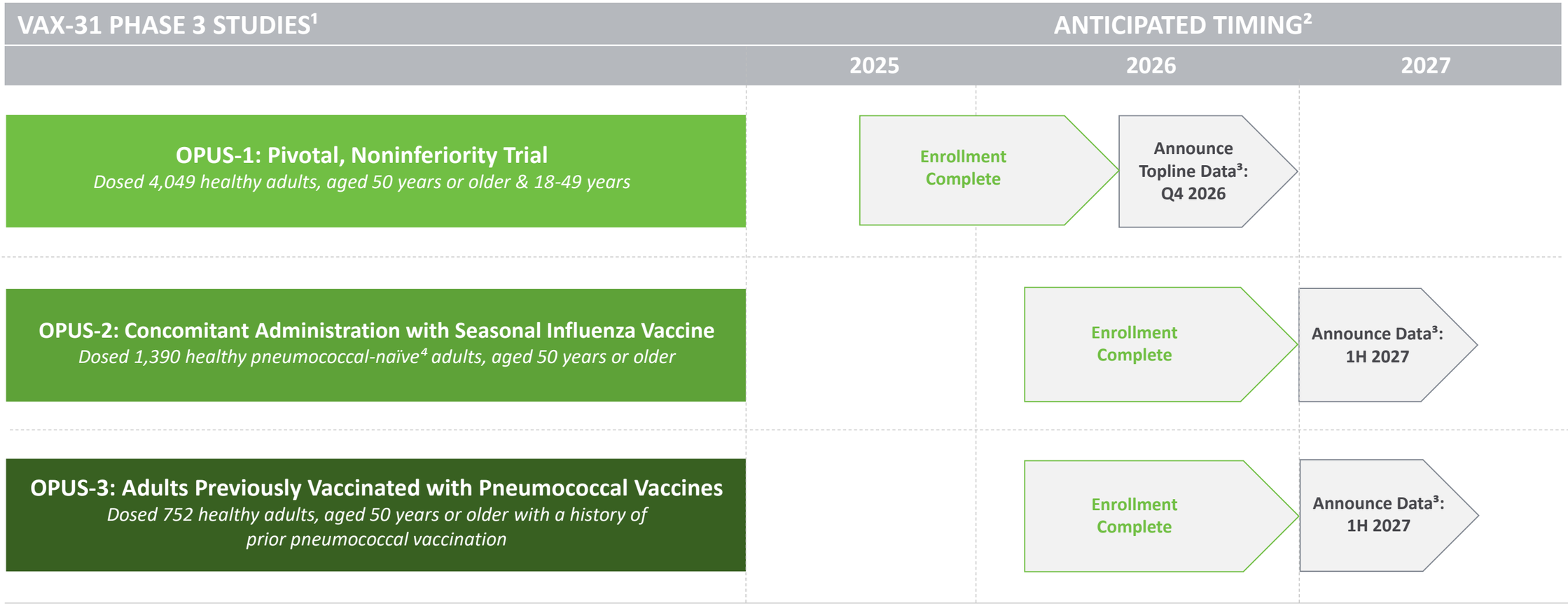


SoC = standard of care.
(1) % of IPD caused in individuals ≥50 yrs of age in the U.S. in 2023 based on ABC surveillance data (https://data.cdc.gov/Public-Health-Surveillance/1998-2023-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p/about_data).
(2) Serotypes 6A/6C and 15B/15C are closely related subtypes 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[1] with PCV21 and PCV20, the Current Standards of Care in U.S. Adults

ADULTS AGED ≥50 YEARS

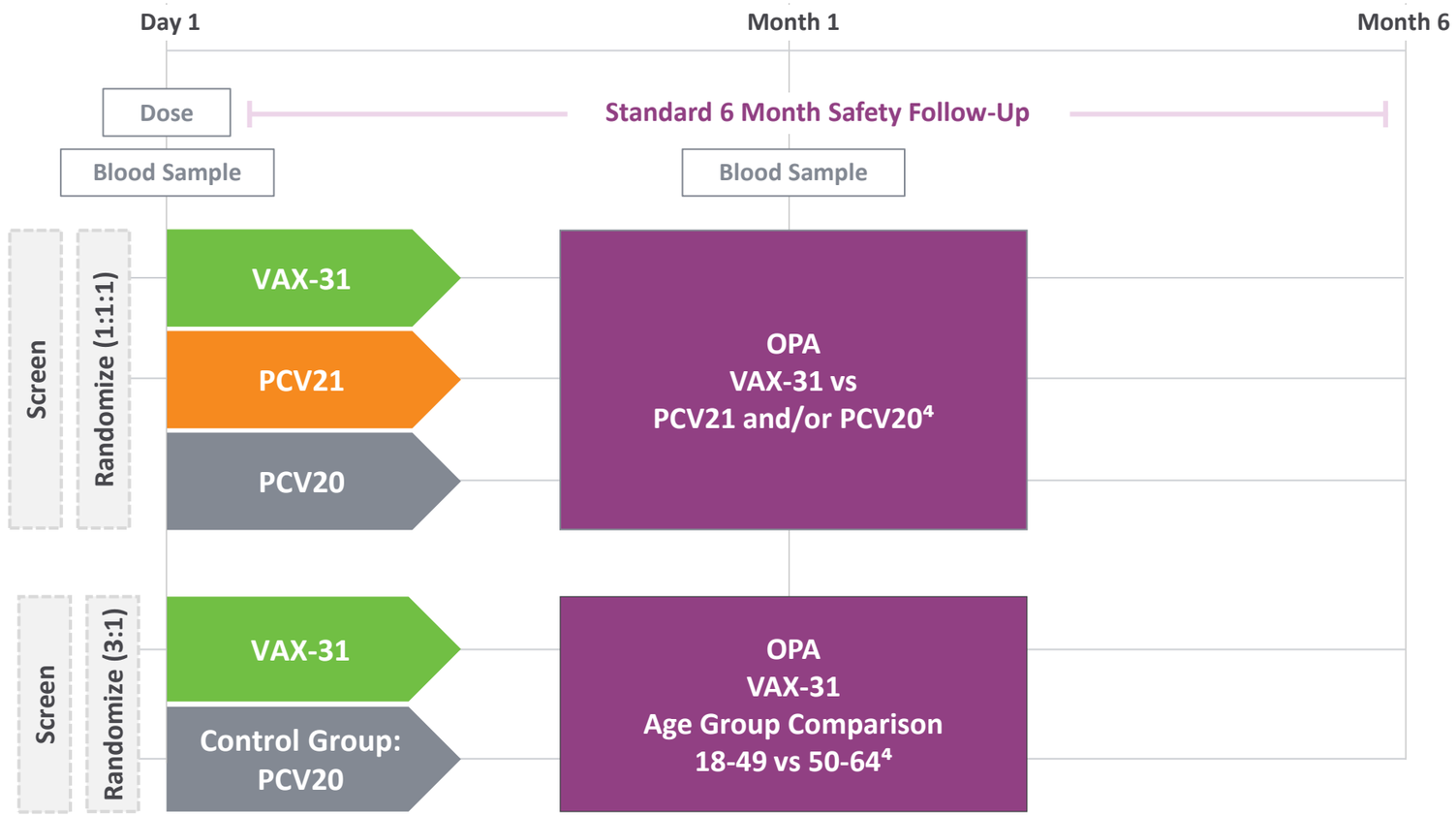
Key primary immunogenicity objectives:

- Noninferiority[2] of VAX-31 compared with PCV21 and/or PCV20 for the 28 serotypes shared with one or both comparators
- Superiority[3] 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



OPA = opsonophagocytic activity. (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) Primary Noninferiority Objective: The lower bound of the two-sided 95% confidence interval (CI) for the OPA geometric mean ratio (GMR) of VAX-31 exceeds 0.667. (3) Primary Superiority Objective: The lower bound of the two-sided 95% CI of the OPA GMR exceeds 2.0. (4) IgG comparisons of VAX-31 versus PCV21 and/or PCV20 are secondary endpoints.

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	• **Noninferiority** compared with PCV21 and/or PCV20 for the 28 serotypes (STs) shared with either or both comparator vaccines in adults 50+	**OPA GMR** LOWER BOUND OF TWO-SIDED 95% CONFIDENCE INTERVAL: **>0.667**
	• **Superiority** 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+	**>2.0**
	• **Noninferiority** of immune responses in adults aged 18-49 years compared with those in adults aged 50-64 years	**>0.667**
SECONDARY OBJECTIVES	• **Noninferiority** compared with both PCV21 and PCV20 for the 11 STs common to all three vaccines in adults 50+	**OPA GMR** LOWER BOUND OF TWO-SIDED 95% CONFIDENCE INTERVAL: **>0.5**
	• **Statistically greater immune responses** relative to PCV21 or PCV20 for the 28 shared STs in adults 50+	**>1.0**
	• **Superiority** compared with PCV20 for the 8 STs common to VAX-31 and PCV21 but not included in PCV20 in adults 50+	**>2.0**
	• **Superiority** compared with PCV21 for the 9 STs common to VAX-31 and PCV20 but not included in PCV21 in adults 50+	**>2.0**

KEY SAFETY & TOLERABILITY OBJECTIVES

- **Safety and tolerability** 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

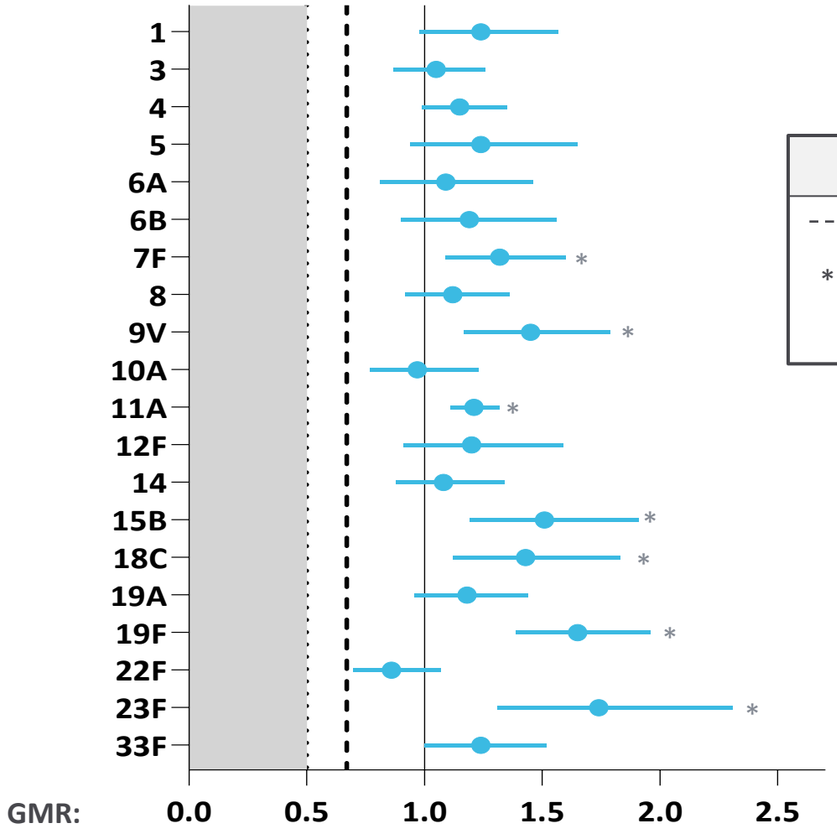
SAE = serious adverse events, NOCI = new onset of chronic illnesses, MAAE = medically attended adverse events, AE = adverse events, BLA = Biologics License Application.

Key additional considerations included in totality of data for potential BLA: Results from additional VAX-31 Ph 3 studies, magnitude of Ab responses, degree of shortfall on primary endpoints for any STs that do not hit noninferiority threshold, % of circulating disease for each ST, % of incremental disease coverage of unique STs.

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[1]

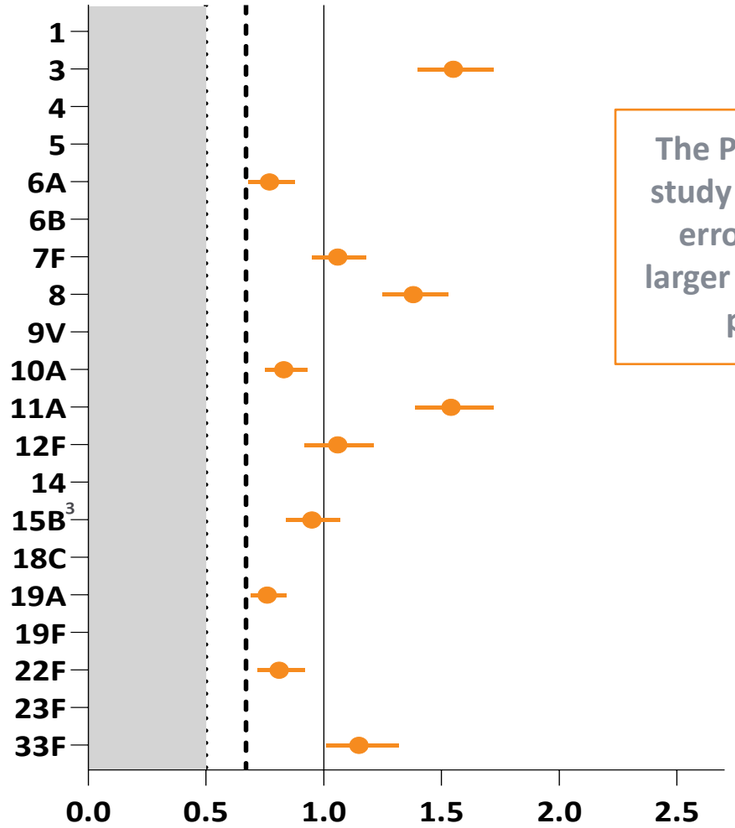
VAX-31 HIGH DOSE PHASE 2 NI STUDY VS PCV20:
20 Common STs (OPA GMRs)



Graph Key:

- GMR at 0.667
- * 7 serotypes that reached statistical significance for superiority

PCV21 PHASE 3 PIVOTAL NI STUDY VS PCV20:
11 Common STs (OPA GMRs)[2,3]



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.

Consistent with Precedent, VAX-31 Will Be Evaluated Based on Totality of Evidence, Not a Tally of Noninferiority Hits or Misses

WHAT THE FDA HAS CONSIDERED BASED ON TOTALITY OF EVIDENCE:

BREADTH OF SEROTYPE AND DISEASE COVERAGE

Incremental serotypes and circulating disease covered vs. comparator

MAGNITUDE OF IMMUNE RESPONSE

Robust titers FDA considers protective

CLINICAL RELEVANCE OF ANY MISS

Disease burden of affected serotype

OVERALL BENEFIT-RISK

Safety, tolerability, public health value

Clear Expectations Ahead of OPUS-1 Reflect Confidence in Delivering Best-in-Class Pneumococcal Vaccine

VAX-31 VS. PCV20

High confidence based on data from Phase 2 head-to-head

+11 incremental serotypes

+31-34% incremental disease coverage

+25% average improvement in GMTs across all 20 STs in Phase 2 trial for VAX-31 compared to PCV20

Base case: 1 expected ST miss (22F) [1]

Robust immune responses, exceeding threshold FDA considers protective

Upside case: No ST misses (replicating Ph2 data)

VAX-31 VS. PCV21

Expect strong performance based on triangulation of existing data

+10 additional serotypes

+14-19% incremental disease coverage

Base case: handful of expected ST misses (3, 8, 23B, 31, 35B)[1]

Robust immune responses, exceeding threshold FDA considers protective

Upside case: 3-4 ST misses (including ST 3)

GMT = geometric mean titer.

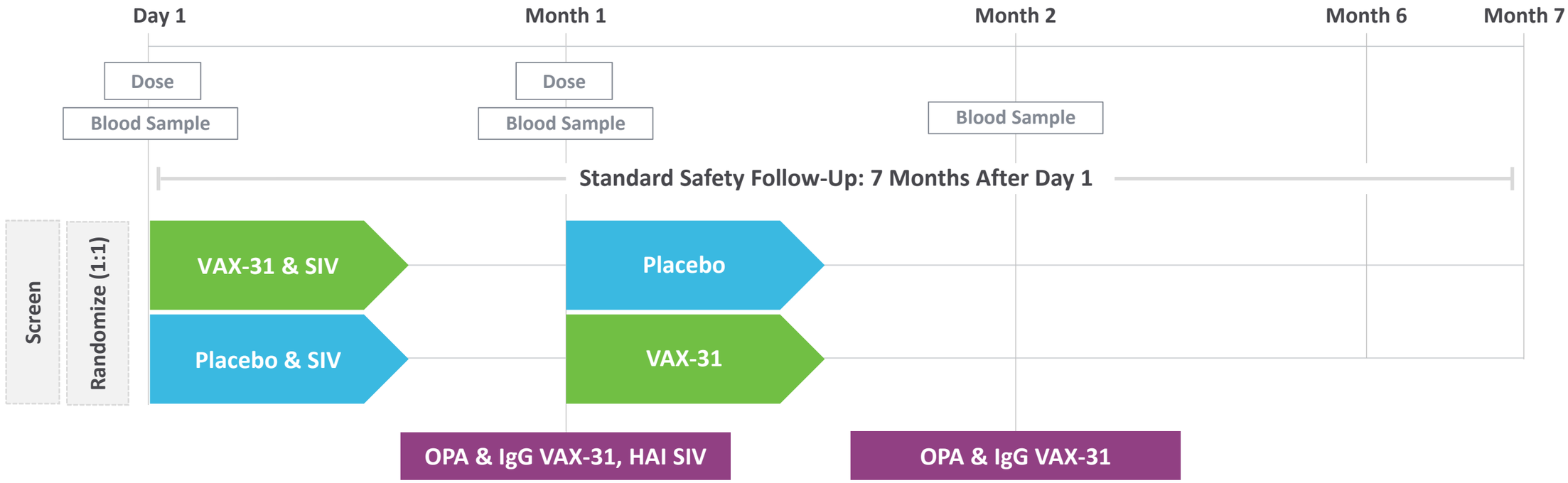
(1) STs 3, 8 and 22F are contained in all three vaccines. Under the protocol Vaxcyte submitted to FDA, achieving NI threshold against either PCV20 or PCV21 is sufficient to meet NI criteria for STs common to all three vaccines. For OPUS-1, "miss" is defined as lower bound of the two-sided 95% confidence interval of the OPA GMR is below the 0.667 noninferiority threshold.

OPUS-1 Readout Approaches from a Position of Strength

STRENGTHENED COMPETITIVE SETUP AND SUBSTANTIALLY MORE ST AND DISEASE COVERAGE THAN CURRENT STANDARD-OF-CARE PCVs			
VAX-31 is the **only** high-valent, next-generation **adult PCV in late-stage development**	Across the industry, **four adult pneumococcal vaccine programs** were recently **discontinued and/or data have not delivered a compelling clinical profile**	The **0.67 noninferiority threshold** in OPUS-1 Phase 3 trial has the **potential to create a more difficult path for any followers**	OPUS-1, OPUS-2, and OPUS-3 are **fully enrolled;** OPUS-1 **on track for topline data in fourth quarter 2026**

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[1] when Administered Either Concomitantly with or One Month Following Administration of a Licensed Seasonal Influenza Vaccine in Healthy Pneumococcal-Naïve[2] Adults Aged ≥50 Years



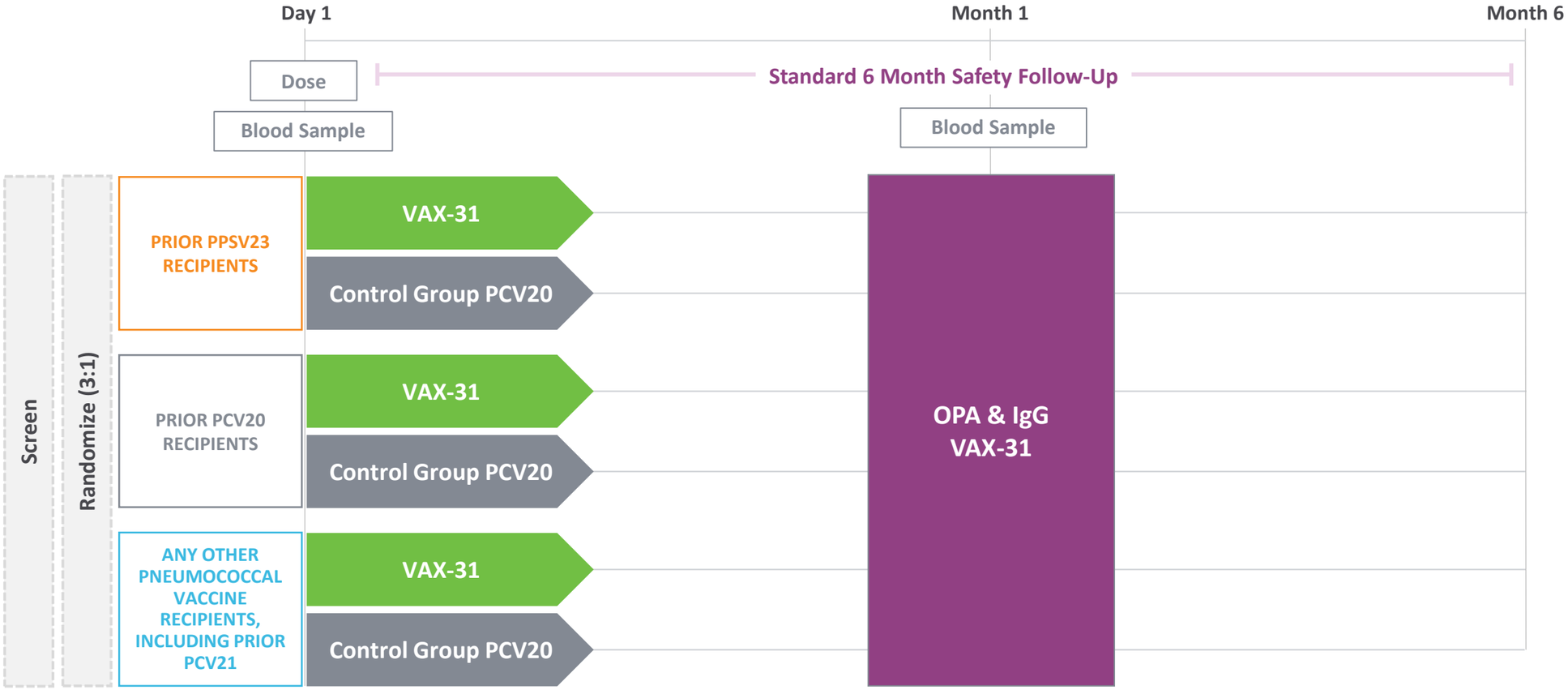
OPA = opsonophagocytic activity, IgG = immunoglobulin G, HAI = hemagglutination inhibition, SIV = seasonal influenza vaccine.

(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[1] in Healthy U.S. Adults Aged 50 Years and Older with a History of Prior Pneumococcal Vaccination[2]



OPA = opsonophagocytic activity, IgG = immunoglobulin G, PPSV23 = Pneumovax 23.

(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) Prior pneumococcal vaccination defined as previously receiving PPSV23, PCV20 or any other licensed pneumococcal vaccine ≥6 months prior to administration of the first VAX-31 dose.

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

OPA = opsonophagocytic activity, HAI = hemagglutination inhibition, GMTs = geometric mean titers, IgG = immunoglobulin G, GMCs = geometric mean concentrations, GMFRs = geometric mean fold rises, SAE = serious adverse events, NOCI = new onset of chronic illnesses, MAAE = medically attended adverse events, AE = adverse events, SIV = seasonal influenza vaccine.

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

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

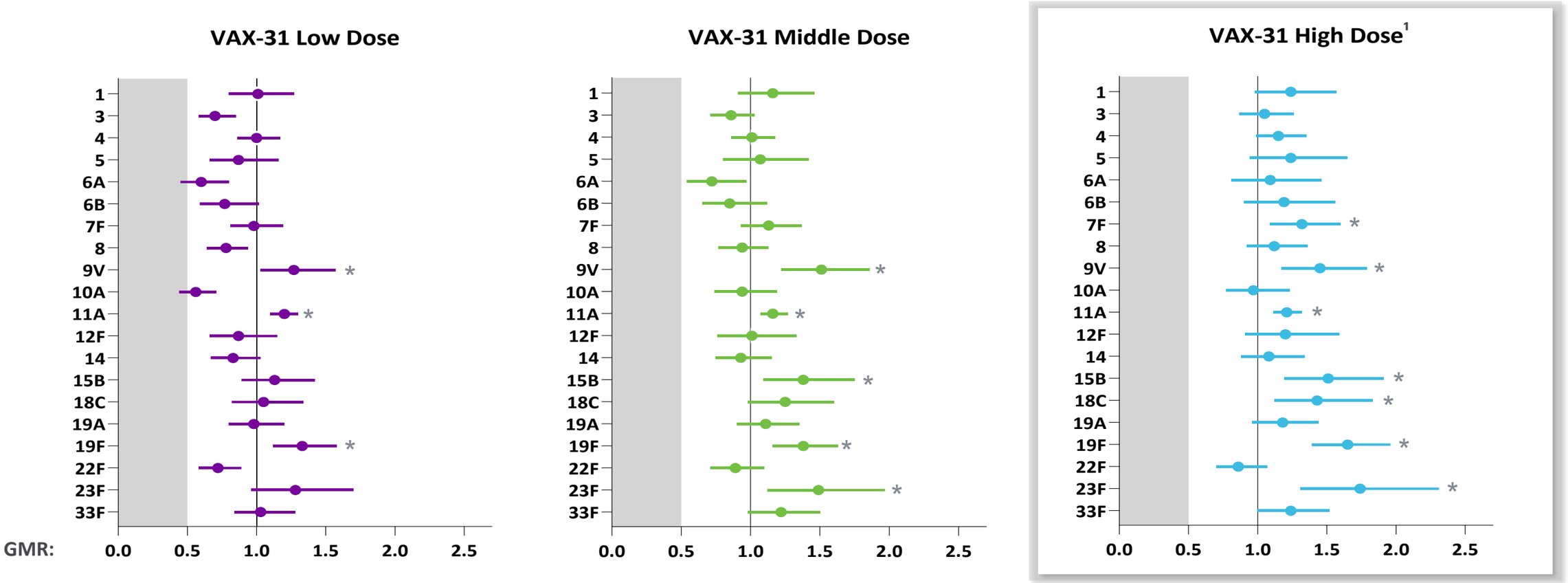
Unprecedented Results Support Potential Best-in-Class PCV With Broadest Serotype and Disease Coverage

- **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**

OPA = opsonophagocytic activity; ST = serotype; IgG = immunoglobulin G.

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

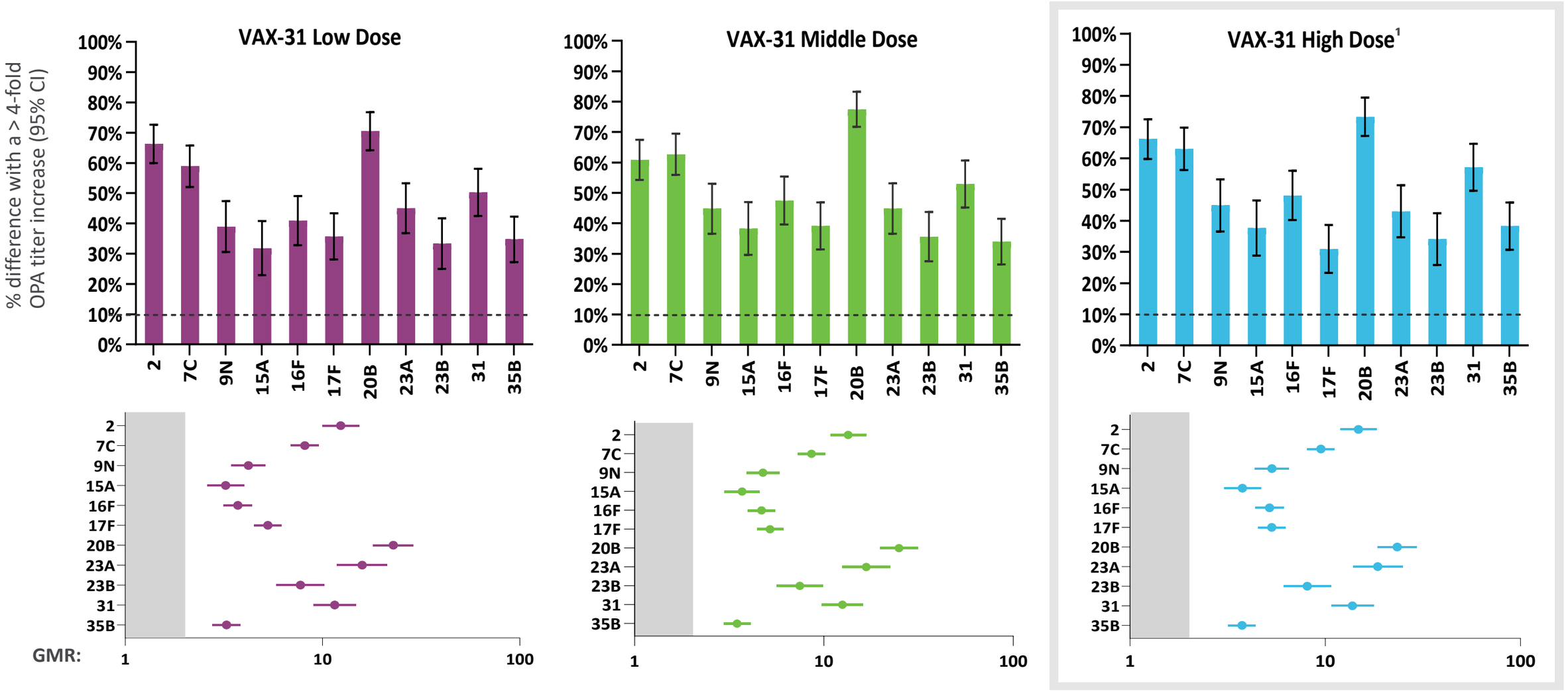
** Reached statistical significance for superiority.*

(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.

OPA = opsonophagocytic activity; GMR = geometric mean ratio.

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

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



(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.
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.
OPA = opsonophagocytic activity; GMR = geometric mean ratio; ST = serotype.

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

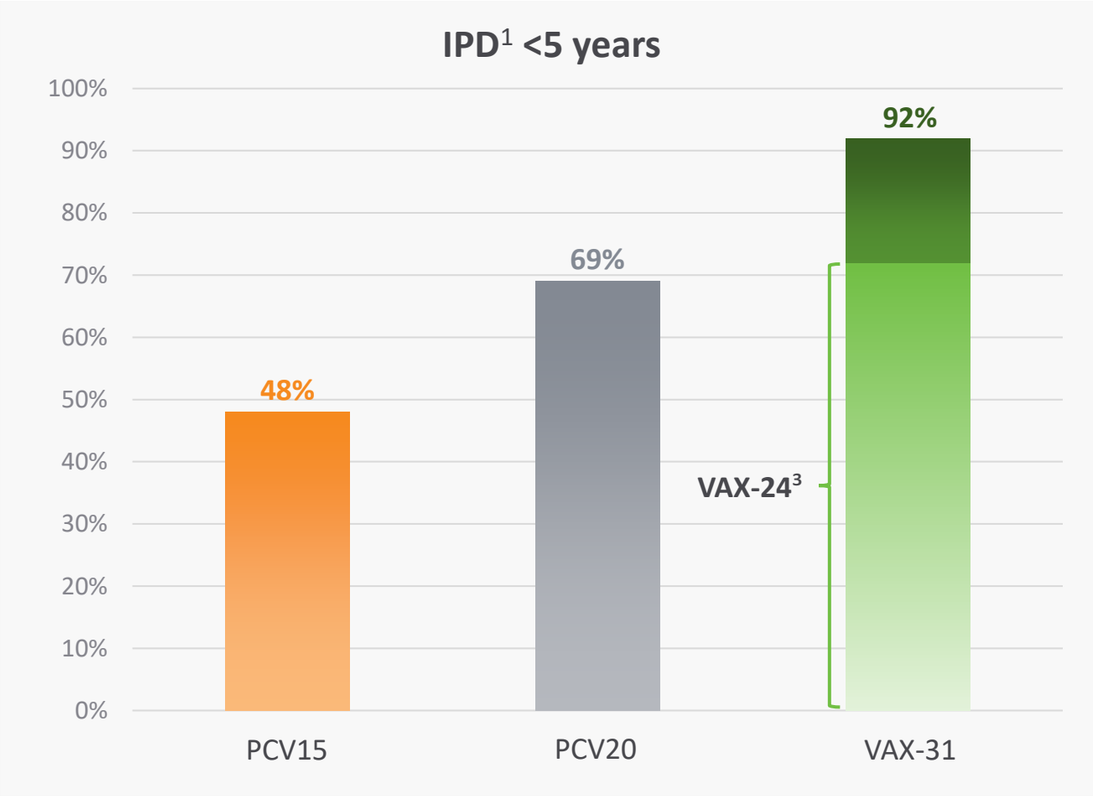
(1) VAX-31 High Dose (all serotypes dosed at 3.3mcg, except serotypes 1, 5, and 22F which are dosed at 4.4mcg) selected to advance to Phase 3.
TEAE = treatment emergent adverse events, MAAE = medically attended adverse events, NOCI = new onset of chronic illnesses, SAE = serious adverse events. Excludes Solicited AEs.

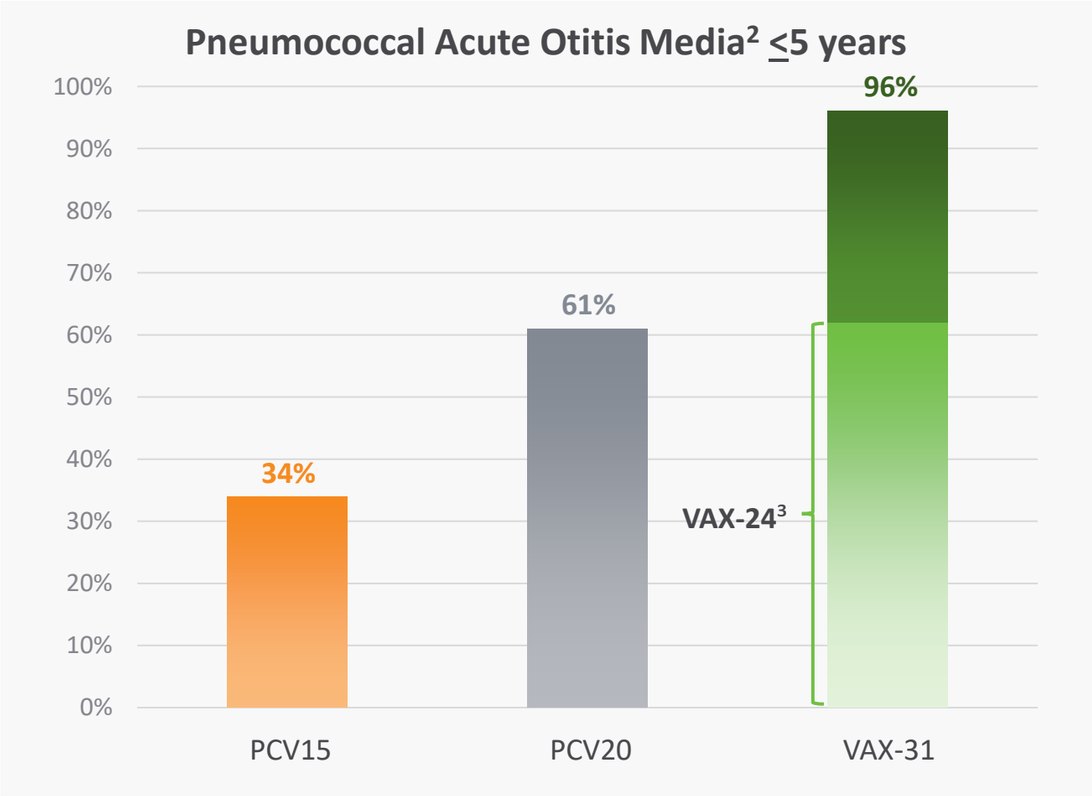
PCV Infant Clinical Program

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

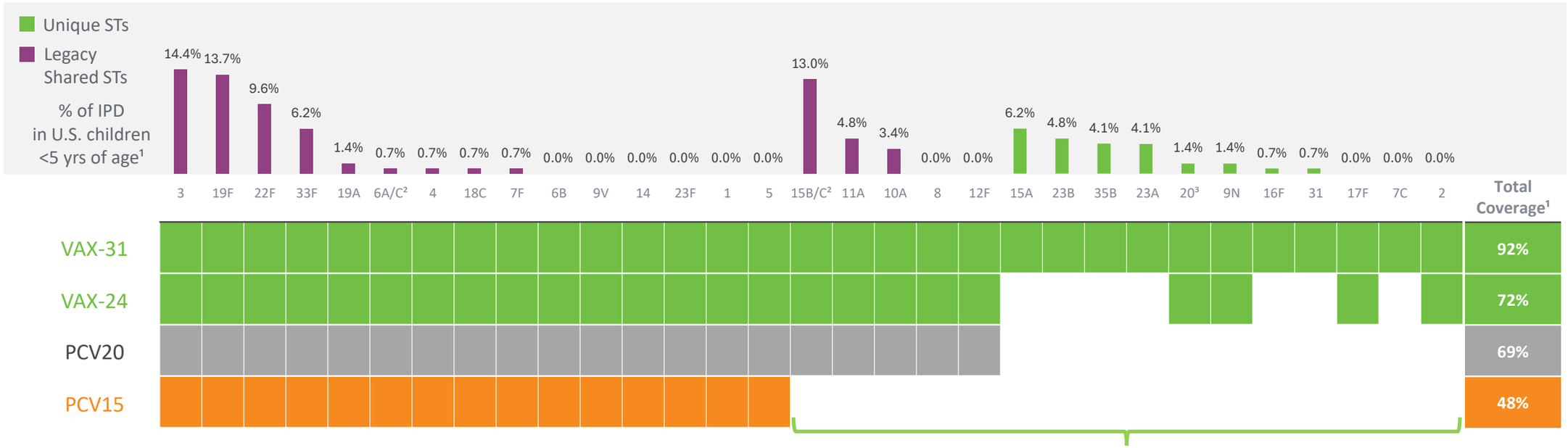




All estimates assume cross-protection between serotypes 6A and 6C and between 15B and 15C.
(1) CDC 2023 Active Bacterial Core (ABC) Surveillance data (https://data.cdc.gov/Public-Health-Surveillance/1998-2023-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p/about_data); IPD cases with missing serotype 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[1]

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

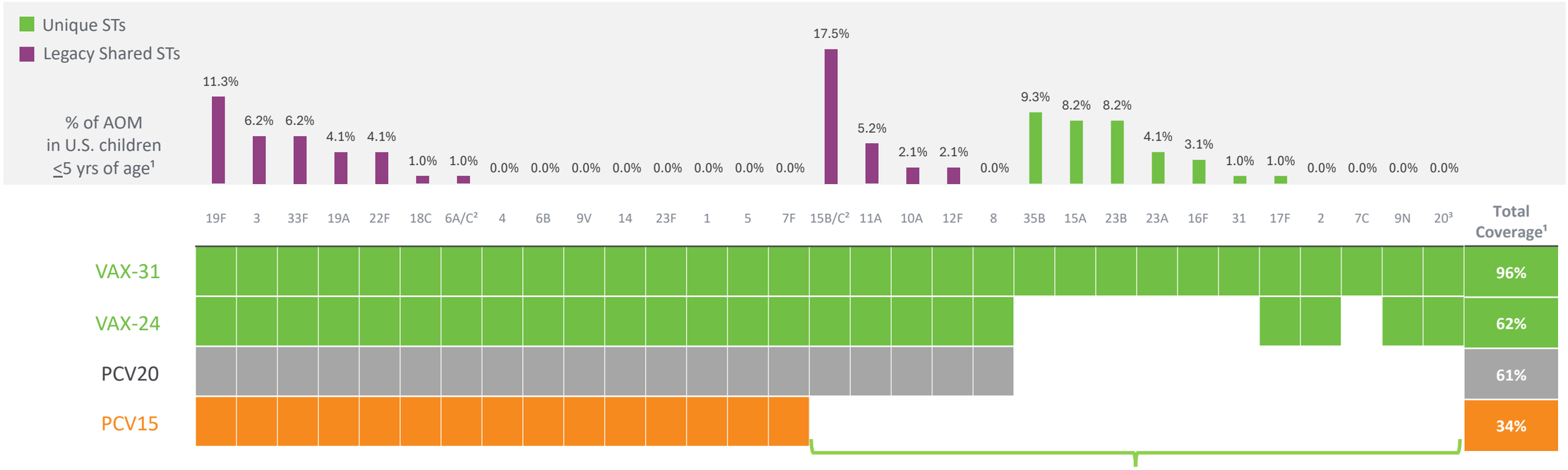
LEGACY SHARED 20 STs: In the infant study, VAX-24 had higher responses on the highest circulating STs (3 & 19F) and while there were some lower relative responses compared to PCV20, they were restricted to a small subset of shared STs with limited residual disease.

(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).
(2) Serotypes 6A/6C and 15B/15C are closely related subtypes for which cross-protection is assumed. PCV20 and VAX-31 include 15B, and all three—PCV15, PCV20, and VAX-31— include 6A. % of IPD caused in individuals <5 yrs of age is 0.7% for 6C, 0% for 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.

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

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.[1]

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

HCP = healthcare provider.

(1) Cross-sectional web survey conducted by Pfizer in October-November 2022; sponsor-affiliated and conducted prior to policy finalization, reflects stated intentions rather than observed behavior and does not represent real-world uptake https://www.tandfonline.com/doi/full/10.1080/14760584.2025.2585808#abstract.

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

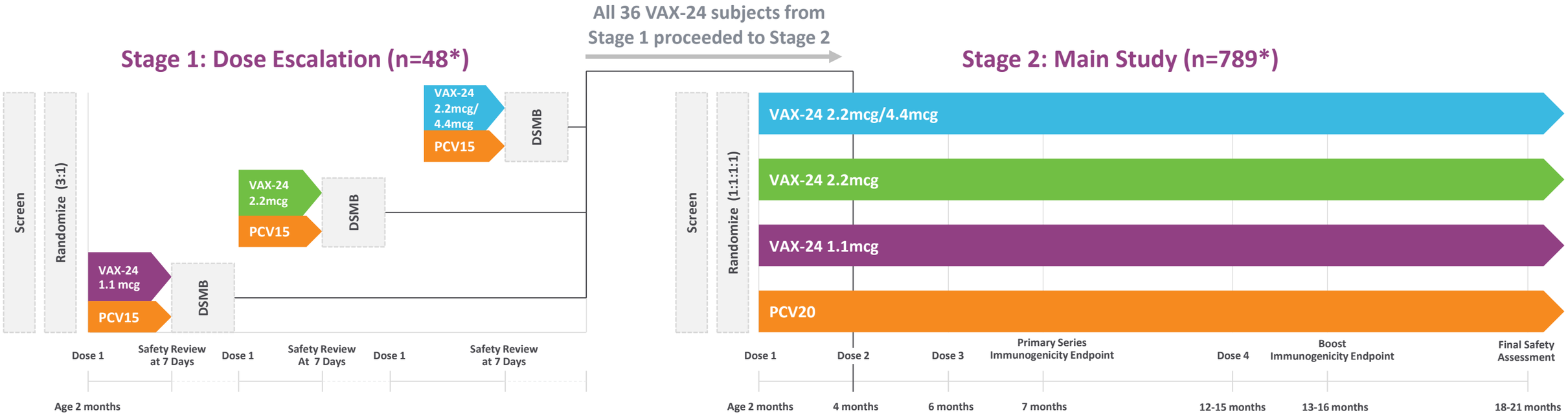
Final VAX-24 Phase 2 Infant Study Results and Platform Demonstrate Potential to Achieve Broadest Coverage of Any Infant PCV On-Market

- **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**

OPA = opsonophagocytic activity; IgG = immunoglobulin G.

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

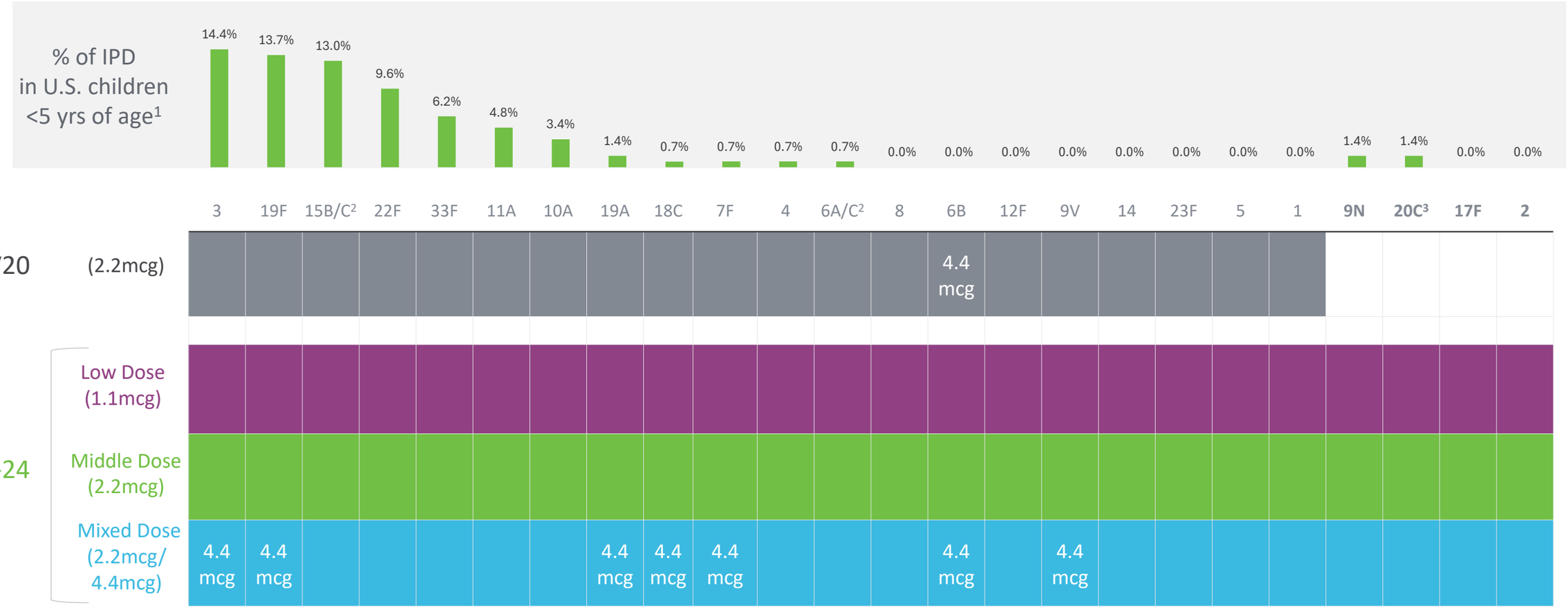
Randomized, Observer-Blind, Active-Controlled, Dose-Finding, Clinical Study to Evaluate Safety, Tolerability and Immunogenicity of VAX-24 vs. Standard-of-Care (PCV20) in 803 Healthy Infants



(*) The 36 subjects from the three VAX-24 cohorts in Stage 1 proceeded to Stage 2 of the study. The 12 subjects who received PCV15 in Stage 1 were given PCV20 in Stage 2 and followed separately; they are not included in the safety or immunogenicity evaluable populations. Two (2) subjects withdrew after being randomized in Stage 2.

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.

(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).
(2) Serotypes 6A/6C and 15B/15C are closely related subtypes for which cross-protection is assumed.
(3) 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.

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

Safety Results Similar to PCV20 and Across Cohorts

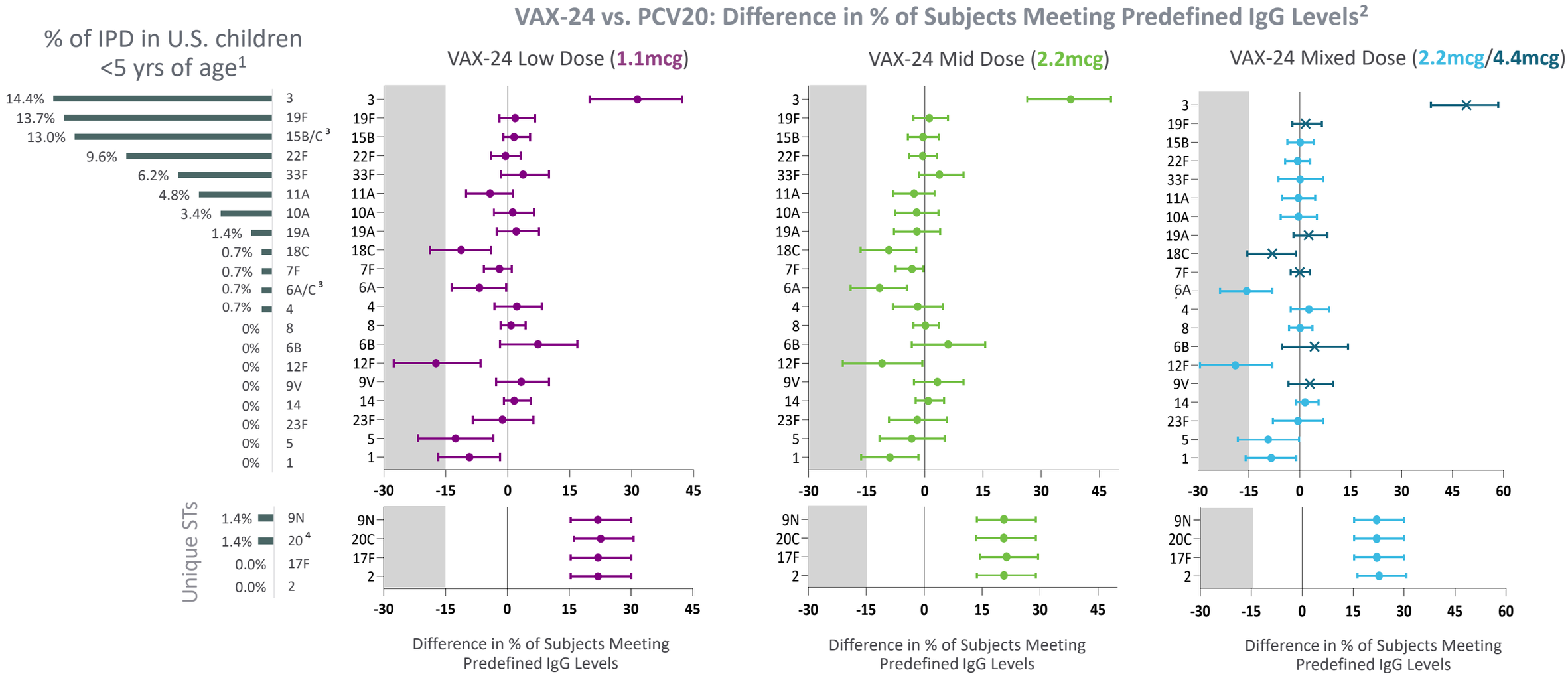
	VAX-24 Low Dose	VAX-24 Mid Dose	VAX-24 Mixed Dose	PCV20
NUMBER OF SUBJECTS	195	186	191	185
Unsolicited TEAE, n (%)	167 (85.6)	161 (86.6)	163 (85.3)	169 (91.4)
Related Unsolicited TEAE, n (%)	6 (3.1)	13 (7.0)	13 (6.8)	6 (3.2)
MAAE, n (%)	172 (88.2)	155 (83.3)	167 (87.4)	161 (87.0)
Related MAAE, n (%)	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)[1]	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)[2]
Related Death, n (%)	0	0	0	0

TEAE = treatment emergent adverse events, NOCI = new onset of chronic illnesses, MAAE = medically attended adverse events, SAE = serious adverse events.
(1) Related NOCI = mild nasal congestion.
(2) One sudden infant death syndrome (SIDS) case occurred in the PCV20 cohort 7 weeks after the first and only dose was administered; following a thorough investigation, case was found to be unrelated to study vaccine.

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



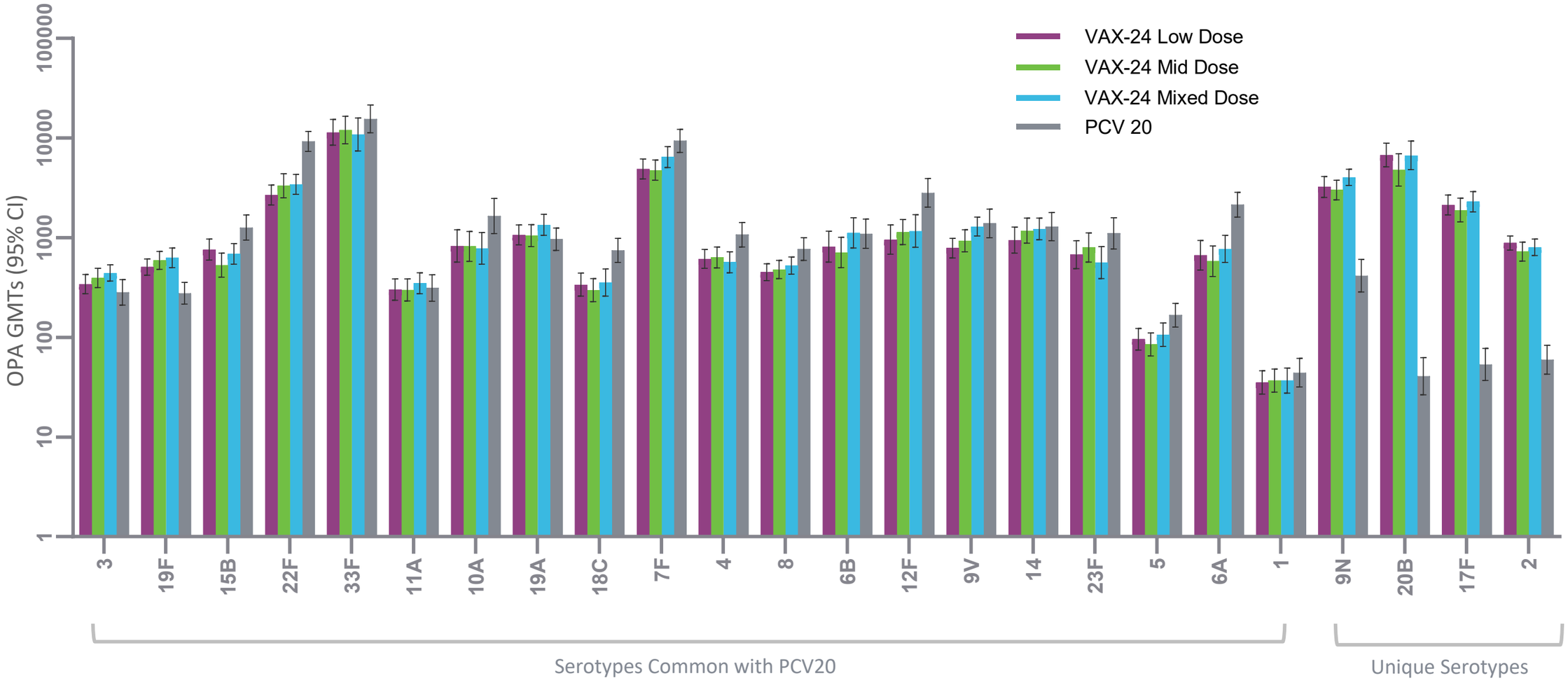
NI = noninferiority; ST = serotype; IgG = immunoglobulin G.

● = Point Estimate. **X** = STs dosed at 4.4mcg.

(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 ≥0.35mcg/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).
(3) Serotypes 6A/6C and 15B/15C are closely related subtypes for which cross-protection is assumed.
(4) 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



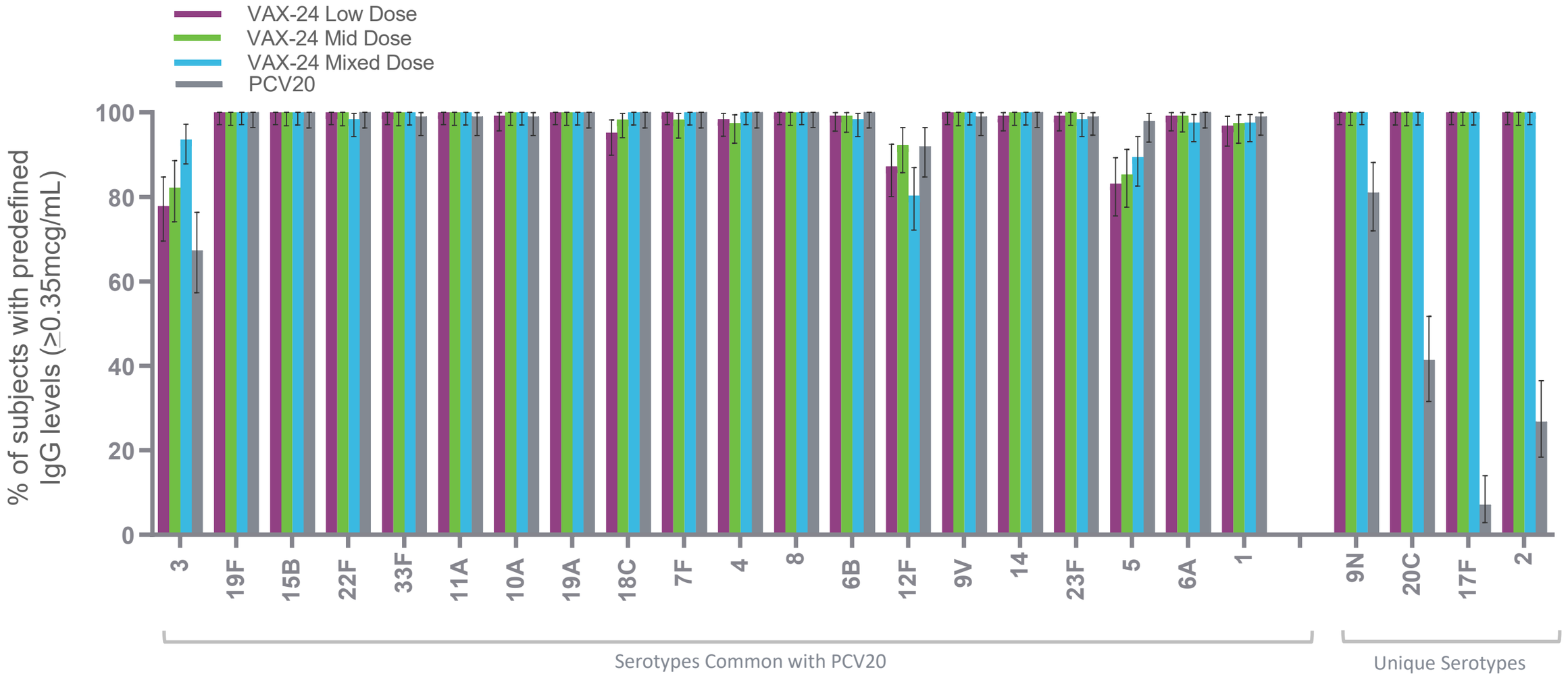
OPA = opsonophagocytic activity; GMT = geometric mean titer; IgG = immunoglobulin G.

Serotypes 6A/6C and 15B/15C are closely related subtypes for which cross-protection is assumed.
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. Serotype 20B was studied in this OPA analysis.

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

OPA = opsonophagocytic activity; IgG = immunoglobulin G.

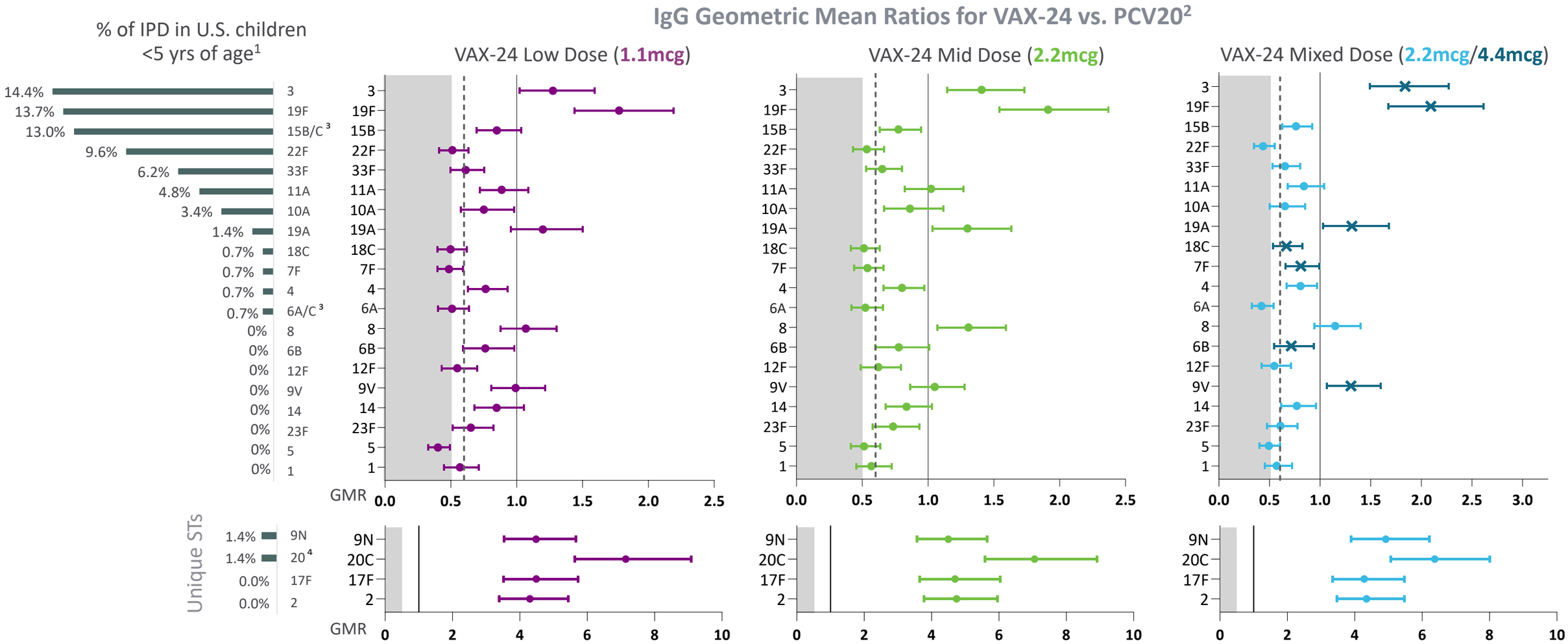
VAX-24 Demonstrated High Overall Seroconversion Rates Across All Doses PD4



Serotypes 6A/6C and 15B/15C are closely related subtypes for which cross-protection is assumed.
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.
IgG = immunoglobulin G.

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



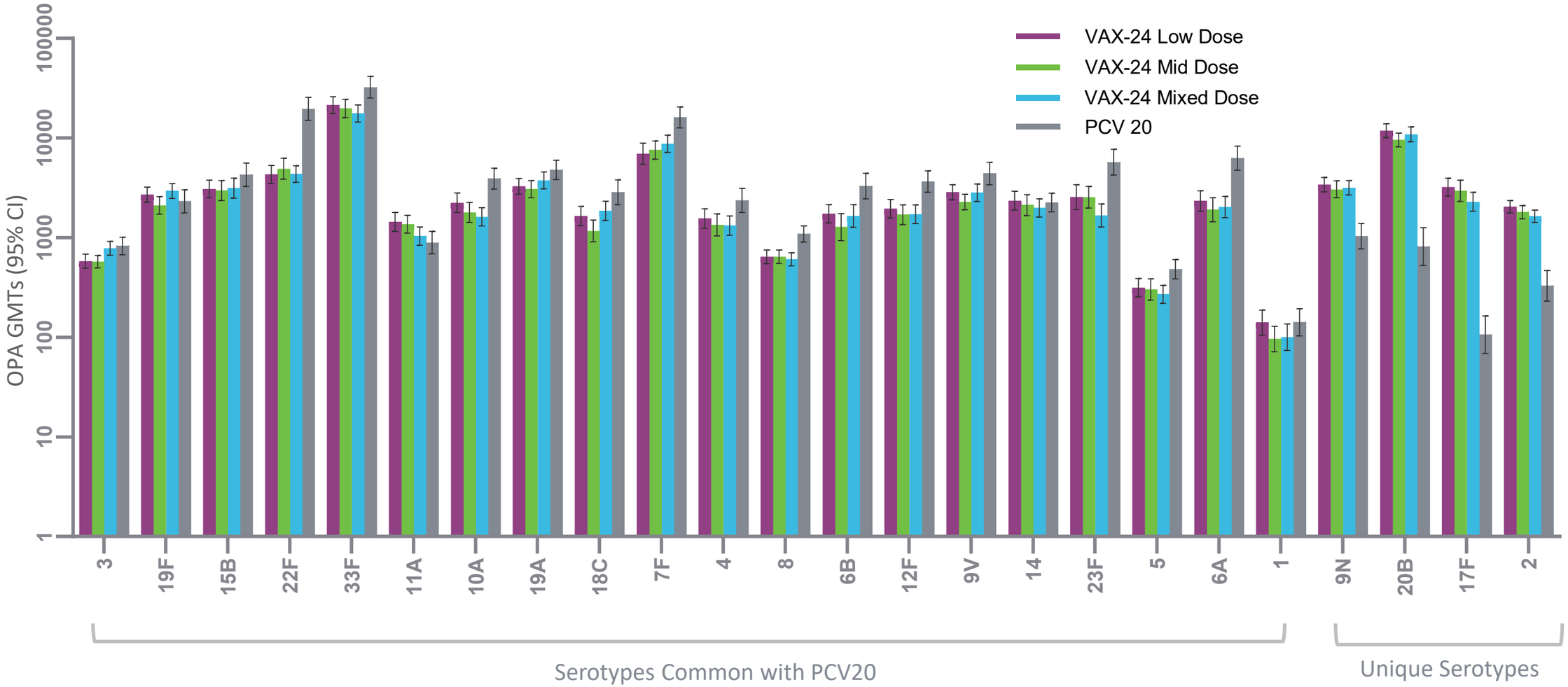
GMR = geometric mean ratio; IgG = immunoglobulin G; ST = serotype.

● = Point Estimate. **X** = STs dosed at 4.4mcg.

(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).
(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).
(3) Serotypes 6A/6C and 15B/15C are closely related subtypes for which cross-protection is assumed.
(4) 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

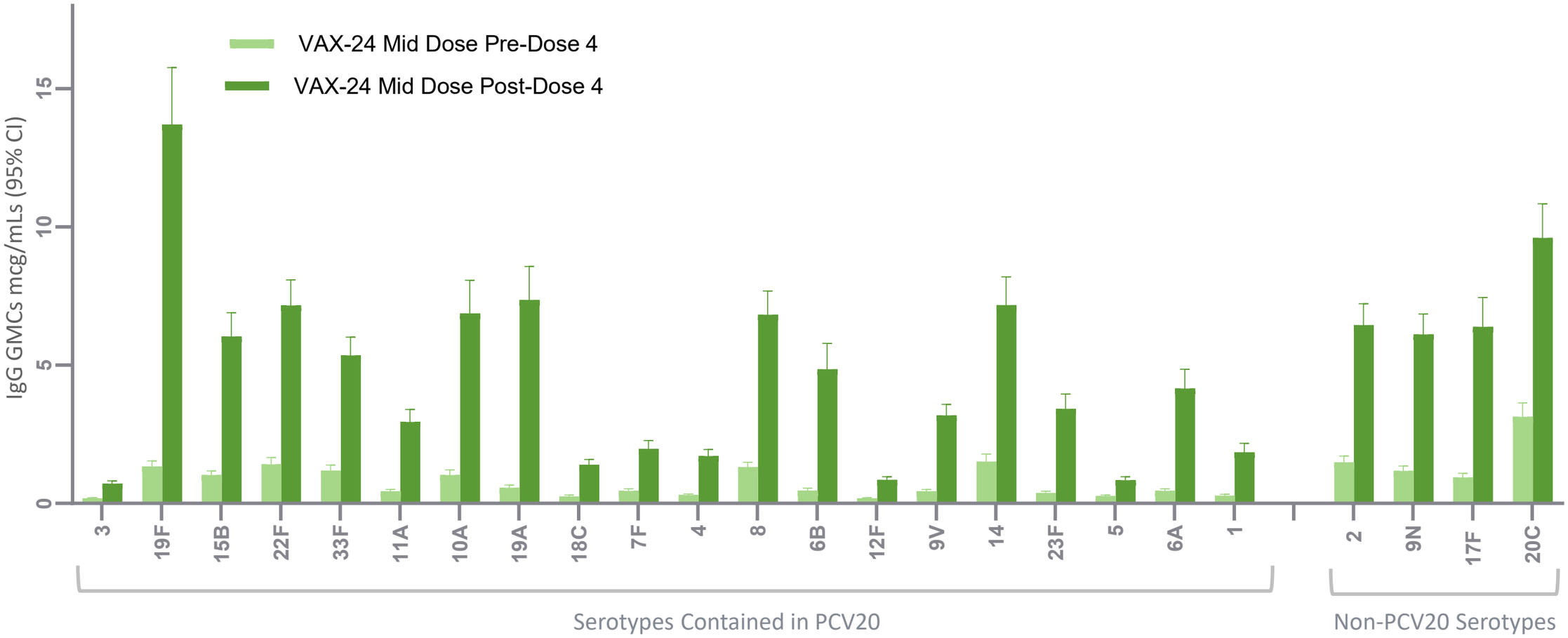
Demonstrated Robust OPA Titers, Generally Consistent with IgG Responses



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

Serotypes 6A/6C and 15B/15C are closely related subtypes for which cross-protection is assumed.
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. Serotype 20B was studied in this OPA analysis.

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



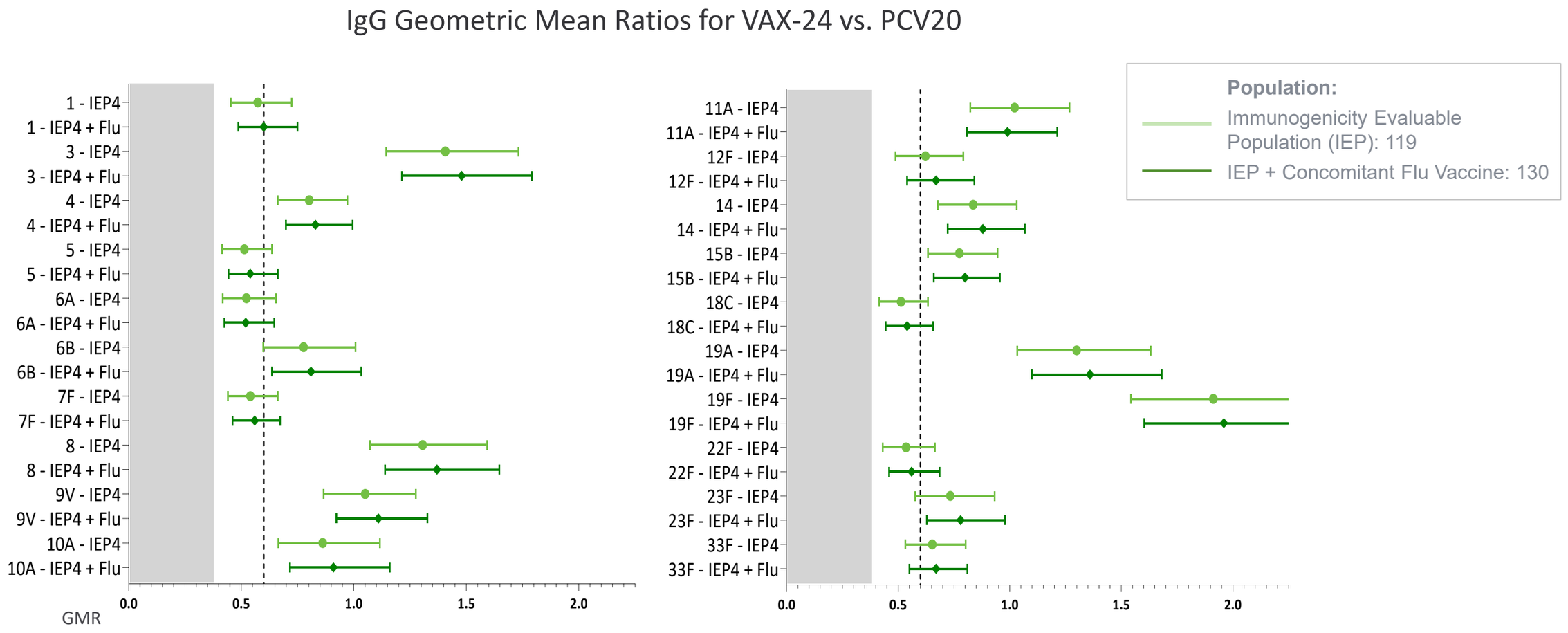
GMT = geometric mean concentration; IgG = immunoglobulin.

Serotypes 6A/6C and 15B/15C are closely related subtypes for which cross-protection is assumed.
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. IgG = immunoglobulin G.

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

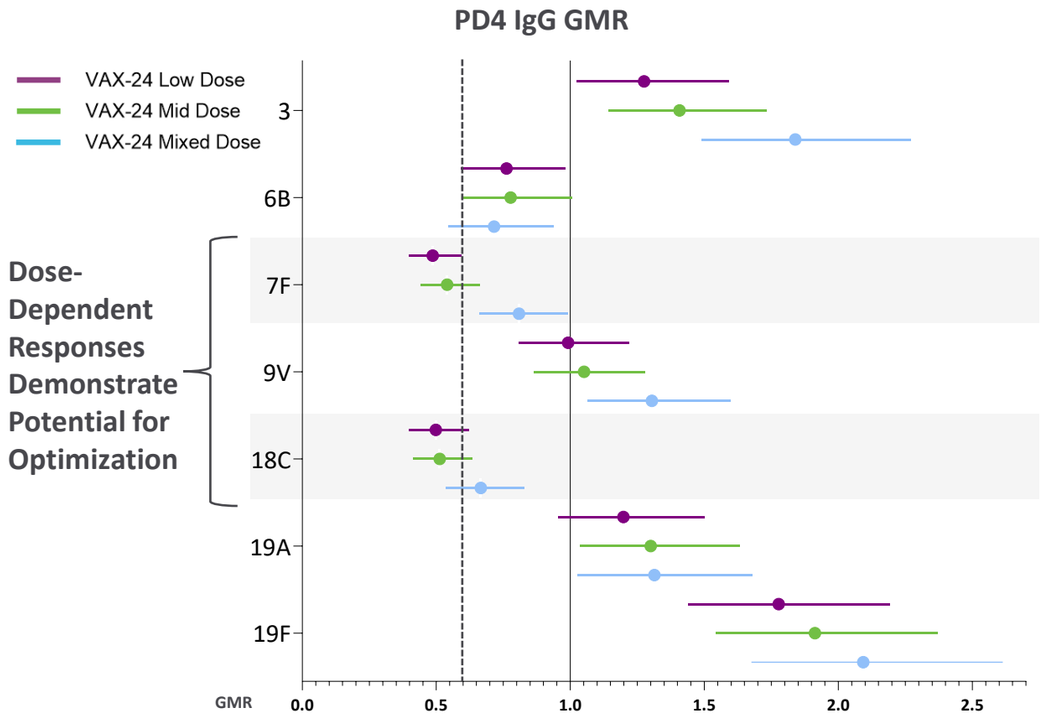


GMR = geometric mean ratio; IgG = immunoglobulin.
The IEP4 includes eligible subjects who received the same vaccine across all 4 doses, with valid PD4 IgG or OPA assay results based on blood sample collected within protocol-defined window, and without protocol deviations that may interfere with PD4 immune 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.

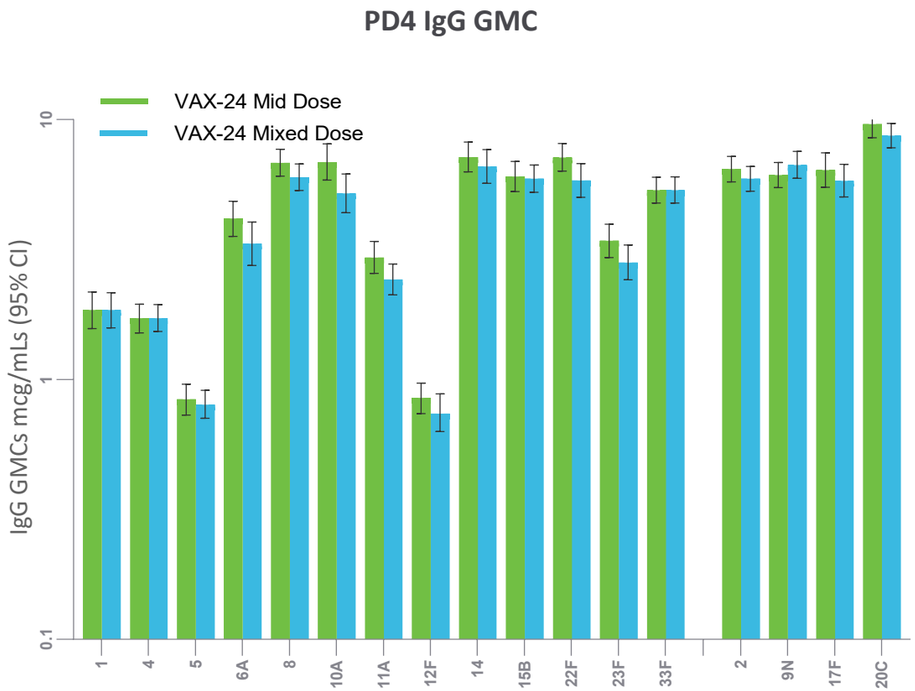
Dose Response Evidenced PD4 Across Most Serotypes

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

DOSE-DEPENDENT IMMUNOGENICITY OBSERVED ACROSS DOSE RANGE[1]



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



17 STs dosed at 2.2 mcg at both Mid and Mixed Doses[2]

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

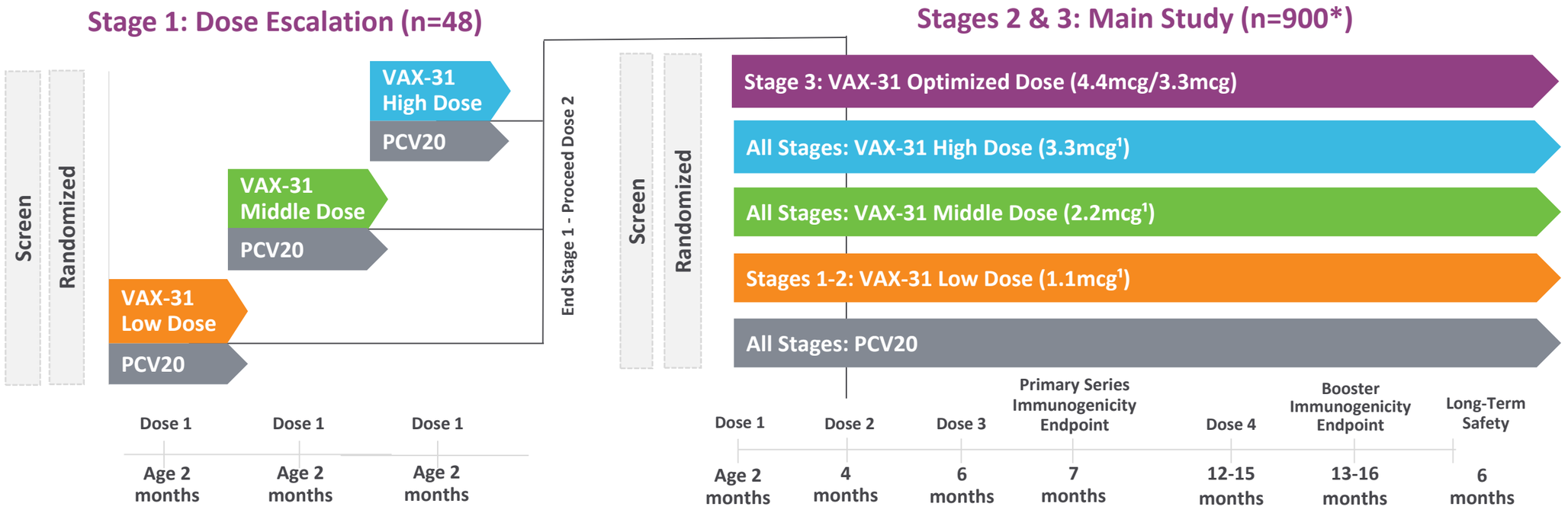
(1) Data represent 7 STs dosed at 1.1, 2.2 and 4.4 mcg.
(2) Serotypes 6A/6C and 15B/15C are closely related subtypes for which cross-protection is assumed. The serogroup 20 antigen contained in VAX-24 and VAX-31, formerly known as a 20B variant, has been officially reclassified as 20C. For additional details on serogroup 20, please see footnote 2 on slide 15.

VAX-31 Infant Clinical Program

VAXCYTE
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.

(*) n=900, inclusive of the 48 subjects from Stage 1.
(1) Except serotypes 1, 5 and 22F, which were dosed at 1.65mcg, 3.3mcg, and 4.4mcg, respectively.

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	• Solicited local reactions • Solicited systemic events	• Unsolicited adverse events (AE) • Serious adverse events (SAE), new onset of chronic illnesses (NOCI) and medically attended adverse events (MAAE)	• SAE, NOCI and MAAE	• SAE, NOCI and MAAE
IMMUNOGENICITY OUTCOME MEASURES		• % of subjects achieving Immunoglobulin G (IgG) antibody concentration ≥0.35 mcg/mL • IgG Geometric Mean Concentration (GMC) • Opsonophagocytic activity (OPA) Geometric Mean Titer (GMT)	• IgG GMC • % of subjects achieving IgG antibody concentration ≥.35 mcg/mL • % of subjects achieving IgG concentration ≥1.0 mcg/mL • OPA GMT • IgG and OPA Geometric Mean Fold Rise (GMFR) from pre-dose 4 to 1-month post-dose 4 • % of subjects achieving a 4-fold rise in IgG and OPA from pre-dose 4 to 1-month post-dose 4	

Group A Strep Opportunity & VAX-A1 Clinical Program

VAXCYTE
protect humankind™

Group A Strep: Among the World's Most Significant Bacterial Pathogens

Streptococcus pyogenes, or **Group A Strep, is a pathogen that causes a wide array of disease** from common acute infections to chronic conditions, resulting in a **significant public health burden**

GROUP A STREP IS A GRAM (+) BACTERIUM THAT IS RESPONISIBLE FOR…

Acute infections: pharyngitis, also known as strep throat, and superficial skin infections (e.g., impetigo)

Invasive and toxin-mediated disease: necrotizing fasciitis, sepsis, meningitis, pneumonia, cellulitis, scarlet fever and streptococcal toxic shock syndrome

Immune-mediated conditions: acute rheumatic fever, rheumatic heart disease and post-streptococcal glomerulonephritis (a form of kidney inflammation)

PUBLIC HEALTH BURDEN

Group A Strep is responsible for ~800M cases of illness and **more than 600K deaths annually worldwide**[1], yet no approved vaccine for Group A Strep exists

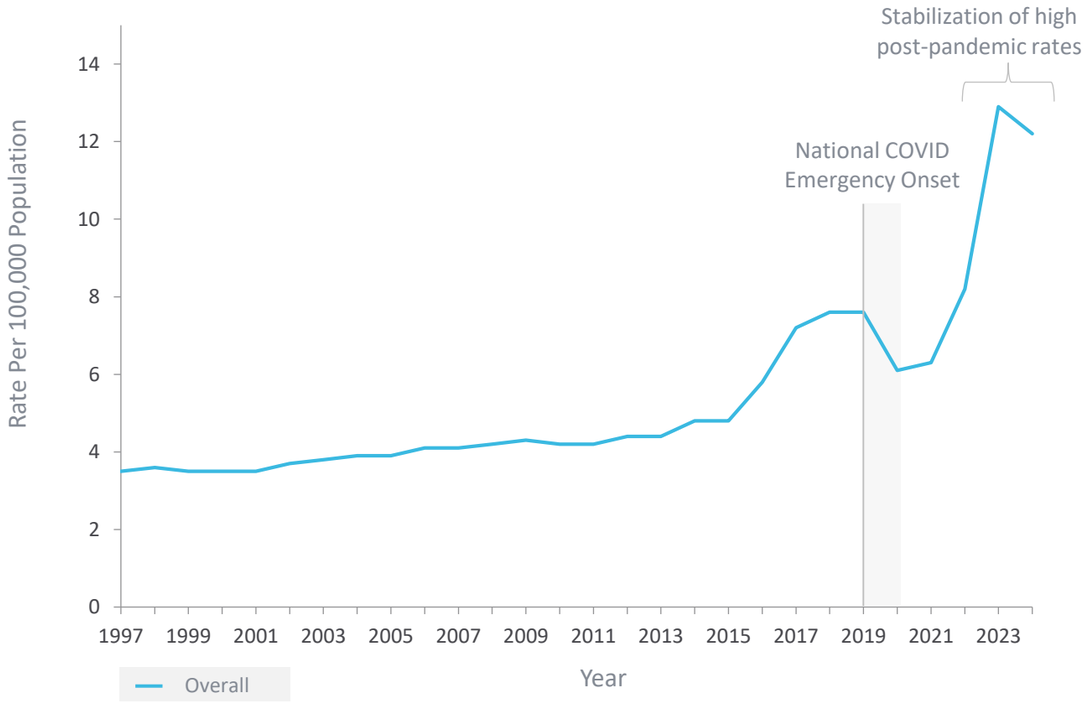
The annual **U.S. economic burden of Group A Strep is estimated to exceed $6B**, with hospitalizations due to invasive disease accounting for ~$2B annually[2]

(1) https://academic.oup.com/cid/article/77/6/917/7180116.
(2) https://academic.oup.com/cid/article/74/6/983/6311854?login=false.

Group A Strep Infection Rates Have Increased Substantially

HIGH RATES OF INVASIVE GROUP A STREP POST-COVID PANDEMIC IN THE U.S.

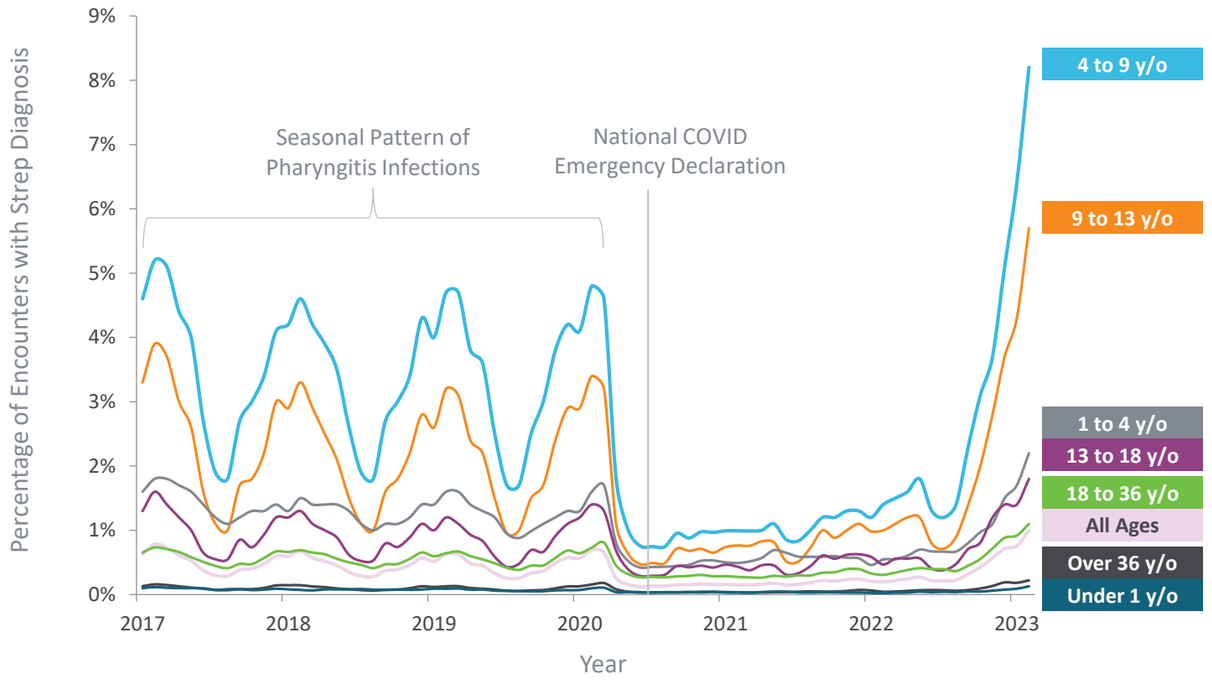
Annual Rates of Invasive Group A Strep Infections in the U.S.[1]



Currently available CDC data demonstrates pre- and post-COVID-19 pandemic Invasive Group A Strep rates, with the most recent 2024 data indicating early stabilization[3]

SIGNFICANT INCREASE IN PHARYNGITIS RATES POST-COVID PANDEMIC IN THE U.S.[2]

Percentage of Encounters for Pharyngitis by Age in the U.S.[2]



(1) https://www.cdc.gov/abcs/bact-facts/data-dashboard.html (accessed April 2026).
(2) Percentage of office visit and emergency encounters with a strep pharyngitis or strep tonsillitis diagnosis; Percentage of Encounters for Strep Throat by Age, 2023; EpicResearch.org.
(3) https://pmc.ncbi.nlm.nih.gov/articles/PMC12388776/.

Growing Threat of Antibiotic Resistance Against Group A Strep

Group A Strep Drives Significant Antibiotic Use, Especially Among Children, Contributing to Rising Antimicrobial Resistance

RISING ANTIBIOTIC RESISTANCE

Antibiotic resistance to Group A Strep has increased over the past decade[1], leading the CDC to categorize the disease as a concerning threat[2]

~1 in 3 invasive Group A Strep infections are now caused by bacteria that are resistant to erythromycin and clindamycin[3]

FALLING TREATMENT CAPACITY

Group A Strep drives an estimated **18.5M antibiotic courses annually worldwide**[4], yet antimicrobial development in biopharma industry has **dropped 35% in five years**[5]

Penicillin remains the preferred antibiotic treatment for Group A Strep but **mutations in penicillin binding protein are beginning to manifest globally, showing early signs of reduced susceptibility**[6]

(1) https://jamanetwork.com/journals/jama/fullarticle/2832277.
(2) https://www.cdc.gov/antimicrobial-resistance/media/pdfs/gas-508.pdf.
(3) https://www.cdc.gov/group-a-strep/php/surveillance/index.html.
(4) https://pmc.ncbi.nlm.nih.gov/articles/PMC10663680/.
(5) Based on an assessment of seven large research-based pharmaceutical companies; https://accesstomedicinefoundation.org/medialibrary/antimicrobial-resistance-benchmark-2026-1773667785.pdf.
(6) https://pubmed.ncbi.nlm.nih.gov/31996443/.

VAX-A1, a Potential Best-in-Class Vaccine Candidate Designed to Provide Broad Protection Against Disease Caused by Group A Strep

VAX-A1 IS DESIGNED TO:

Provide broad, strain-independent protection via a disease-specific protein carrier combined with a universal, species-defining polysaccharide (PS) to enable protection across a wide range of Group A Strep subtypes

Leverage cell-free protein synthesis platform to enable site-specific conjugation of the PS to disease-specific carrier to maintain exposure of its mapped T- and B-cell epitopes

Disarm key pathogen defense mechanisms via three conserved anti-virulence antigens that engender immune responses to the pathogen's virulence factors themselves to enhance pathogen clearance and reduce disease severity

Address a large, underserved global opportunity, with the total Group A Strep vaccine market estimated at **~$3-4B annually**[1]

VAX-A1:	STREPTOLYSIN O (SLO)	+	C5a PEPTIDASE (ScpA)	+	SPYAD & UNIVERSAL POLYSACCHARIDE (GAC^{PR})[2]
THREE DISEASE-SPECIFIC PROTEINS					

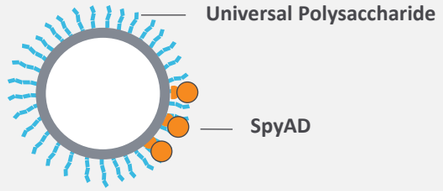
(1) https://www.nature.com/articles/s41541-023-00690-2.pdf.
(2) *SpyAD = S. pyogenes adhesion and division protein; GAC^{PR} = modified Group A carbohydrate.*

VAX-A1: Conjugate Vaccine with Multiple Modes of Action

Protein-Polysaccharide Conjugate

SpyAD & Universal Polysaccharide (GAC^{PR})[1]

SpyAD, a surface-expressed highly-conserved antigen needed for adhesion and division to host cell membranes, site-selectively conjugated to the Universal Polysaccharide (GAC^{PR}) to generate a novel conjugate vaccine

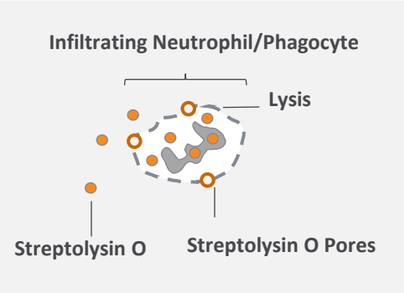


GAC^{PR} is comprised of a Polyrhamnose (PR) backbone, which has been designed to remove potentially cross-reactive epitopes associated with autoimmune complications

Protein Components

Streptolysin O (SLO)

A pore-forming cytolysin; included in VAX-A1 in detoxified form to neutralize and clear a key anti-phagocytic mechanism of bacterial defense



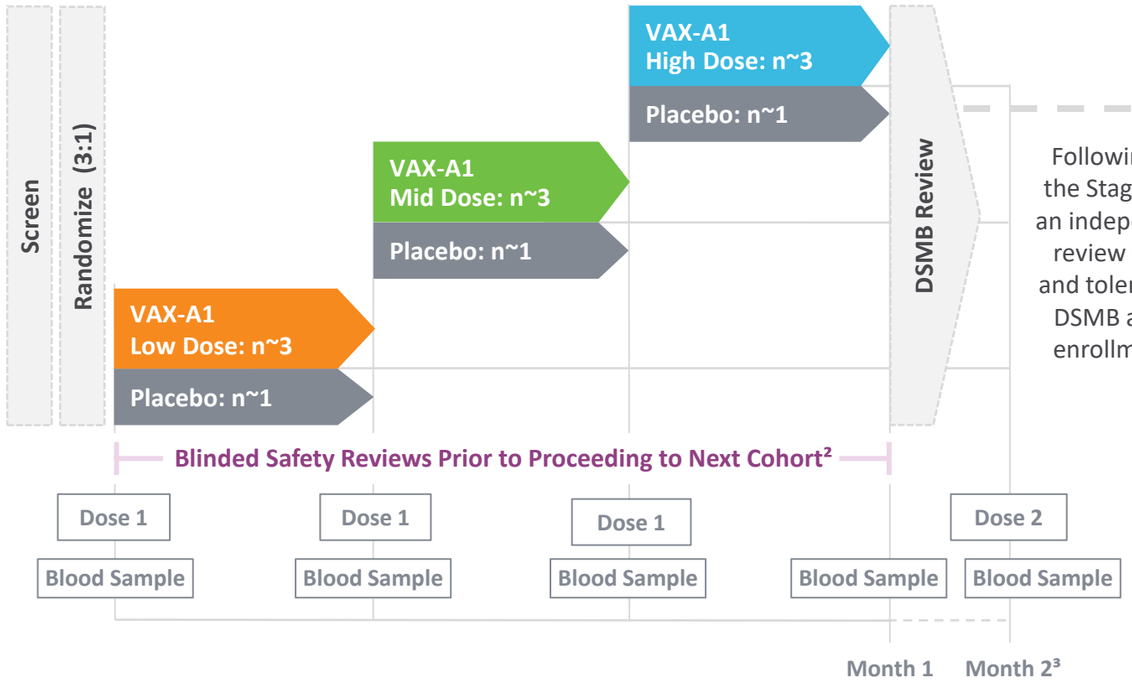
C5a Peptidase (ScpA)

Surface-expressed antigen that cleaves human C5a complement protein, which delays recruitment of phagocytes to the site of infection and alters clearance and trafficking of Group A Strep

(1) SpyAD = S. pyogenes adhesion and division protein; GAC^{PR} = modified Group A carbohydrate.

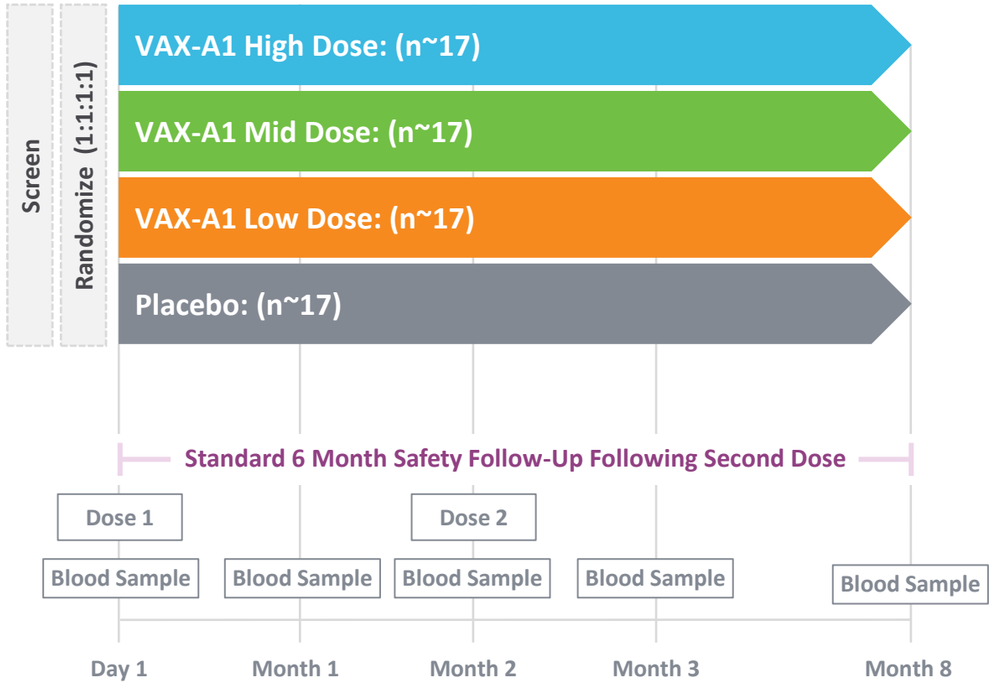
Phase 1 Two-Stage, Dose-Escalation Study Evaluating VAX-A1 in Adults: Currently Enrolling 18-40 yr olds (n~80)

Stage 1: Dose Escalation (n~12)



Following completion of the Stage 1 Month 1 visit, an independent DSMB[1] will review unblinded safety and tolerability data; upon DSMB approval, Stage 2 enrollment will proceed

Stage 2: Main Study (n~68)



Key Study Objectives: the primary objective is to assess safety and tolerability, along with the secondary objective to evaluate initial immunogenicity data

Study Site: the study is being conducted at an investigative site in Australia, where Group A Strep has been especially problematic and where there are experienced investigator networks with expertise in Group A Strep

(1) *DSMB = Data Safety Monitoring Board.*
(2) *Dose escalation for each cohort is based on a review of blinded safety and tolerability data by the Company's Internal Safety Team prior to proceeding with enrolling the next cohort.*
(3) *Following DSMB review, Stage 1 participants will receive Dose 2 at Month 2 and then follow the same protocol as Stage 2 through Month 8.*

VAX-A1 Phase 1 Study Key Objectives

Primarily Designed to Assess Safety and Tolerability, with Secondary Objective to Assess Immune Responses

	PRIOR TO EACH DOSE	DAY 7 (AFTER EACH DOSE)	1 MONTH (AFTER EACH DOSE)	8 MONTHS (AFTER DOSE 1)	ENTIRE DURATION OF STUDY
PRIMARY OUTCOME MEASURES: SAFETY AND TOLERABILITY		• Solicited local reactions • Solicited systemic adverse events (AE) • AE	• Unsolicited AE	• Medically attended adverse events (MAAE) • New onset chronic illness (NOCI) • Serious adverse events (SAE) • AE of special interest[1]	• MAAE • NOCI • SAE • AE of special interest
SECONDARY OUTCOME MEASURES: ANTIGEN-SPECIFIC IMMUNE RESPONSES	For each VAX-A1 antigen[2]: • Serum IgG geometric mean titer (GMT) • Serum IgG geometric mean fold rise (GMFR) from baseline • Percentage of participants with serum Immunoglobulin G (IgG) ≥ Lower Limit of Quantification (LLOQ) of the assay	• Standard safety laboratory parameters (hematology, coagulation, and clinical chemistry median values and median change from baseline)	For each VAX-A1 antigen: • Serum IgG GMT • Serum IgG GMFR from baseline • Percentage of participants achieving serum IgG ≥2-fold increase from baseline • Percentage of participants with serum IgG ≥ LLOQ of the assay	For each VAX-A1 antigen: • Serum IgG GMT • Serum IgG GMFR from baseline • Percentage of participants achieving serum IgG ≥2-fold increase from baseline • Percentage of participants with serum IgG ≥ LLOQ of the assay	

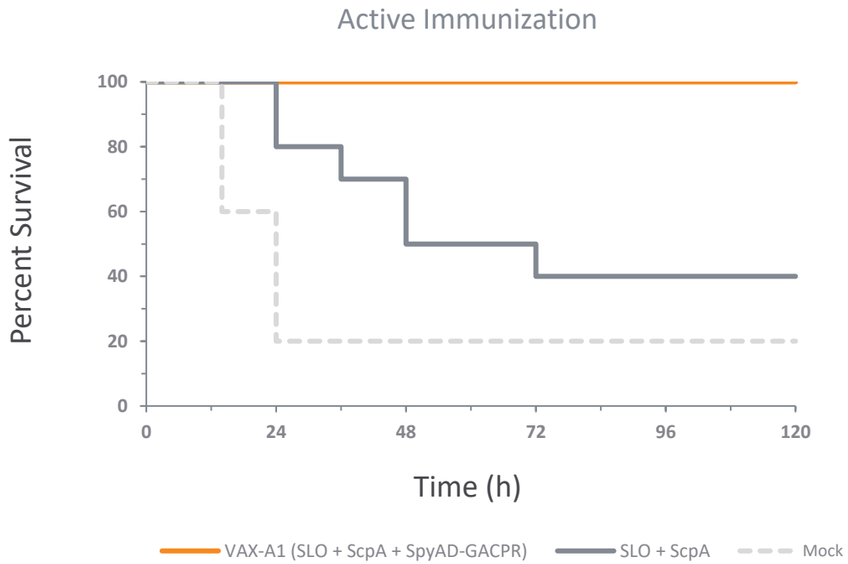
(1) Includes acute rheumatic fever, acute carditis and acute glomerulonephritis.
(2) VAX-A1 antigens include SLO, ScpA, SpyAD and GAC^{PR}.

VAX-A1 Preclinical Data Published in *Infectious Microbes & Diseases*[1] Supported Advancement into the Clinic

In This Study, VAX-A1 Demonstrated Protective Immunity Against Group A Strep in Preclinical Systemic and Skin Infection Models

OBJECTIVE	• The study examined the efficacy of a novel polysaccharide protein conjugate for a vaccine covering all serotypes of Group A Strep
RESULTS	• The vaccine elicited antibodies that were protective in systemic and soft tissue mouse models of infection • In preclinical testing, mice immunized with VAX-A1 yielded 100% survival against lethal challenge • Broad-based cross-reactivity with multiple M protein serotypes of Group A Strep was observed • No evidence of cross-reactivity to human heart or brain antigens

MICE IMMUNIZED WITH VAX-A1 YIELDED 100% SURVIVAL AGAINST LETHAL CHALLENGE



(1) https://pmc.ncbi.nlm.nih.gov/articles/PMC11501091/.

Shigella: VAX-GI Preclinical Program

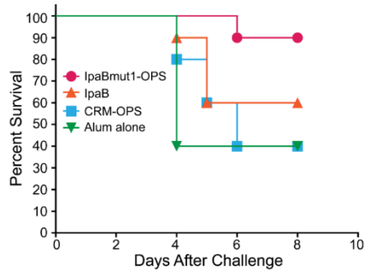
VAXCYTE
protect humankind™

VAX-GI: Shigella Vaccine Program

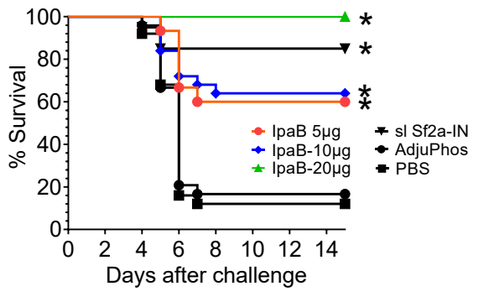
Novel Shigella Vaccine to Prevent Widespread Global Morbidity & Mortality, Particularly in Children

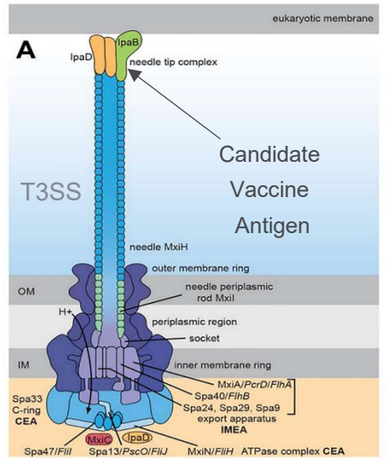
UNMET NEED	• Shigella is a bacterial illness with no available preventative treatment • Estimated to cause 80-165 million cases of disease and 600,000 deaths annually, and most cases and deaths are among children[1] • With the aim of reducing morbidity and mortality due to the disease, the World Health Organization 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 National Institutes of Health grants with total potential funding of up to $5.1M • Plan to pursue conjugate and protein-only approaches simultaneously • Conjugate approach: IpaB-LPS/IpaH/VirG; Protein-only approach: IpaB/IpaH/VirG
PROGRAM STATUS	• Decision on final candidate to be determined by a human challenge study conducted at the University of Maryland, Baltimore
MOA & KEY DATA	• Targeting IpaB inhibits assembly of T3SS and toxin delivery to immune cells • Opsonophagocytosis and killing of bacteria

VAX-GI: Conjugate Approach



VAX-GI: Protein Only Approach





(1) *Shigellosis: CDC Yellow Book 2024.*
(2) *https://www.who.int/publications/i/item/9789240036741.*

Key Corporate Highlights

VAXCYTE

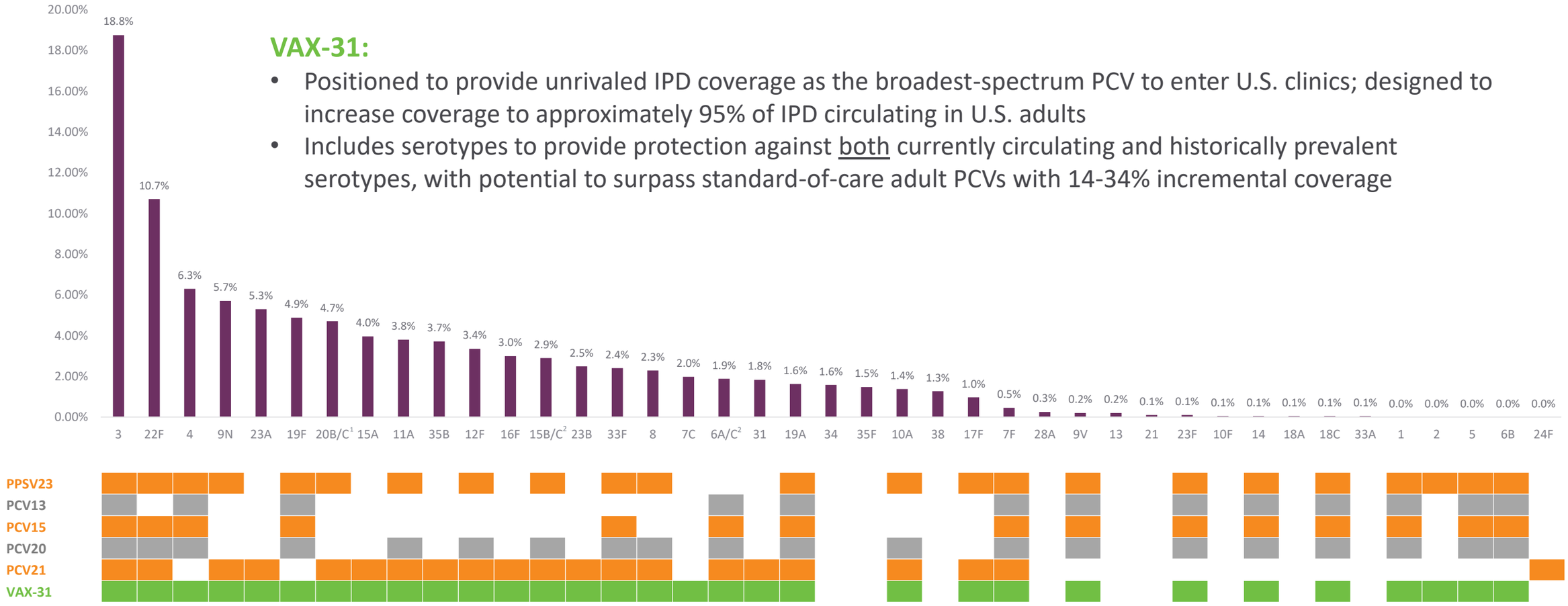
protect humankind™

- 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 <u>both</u> currently circulating and historically prevalent serotypes, with potential to surpass standard-of-care adult PCVs with 14-34% incremental coverage

Total IPD Coverage (U.S. %)[3]
71%
34%
47%
61%
81%
95%

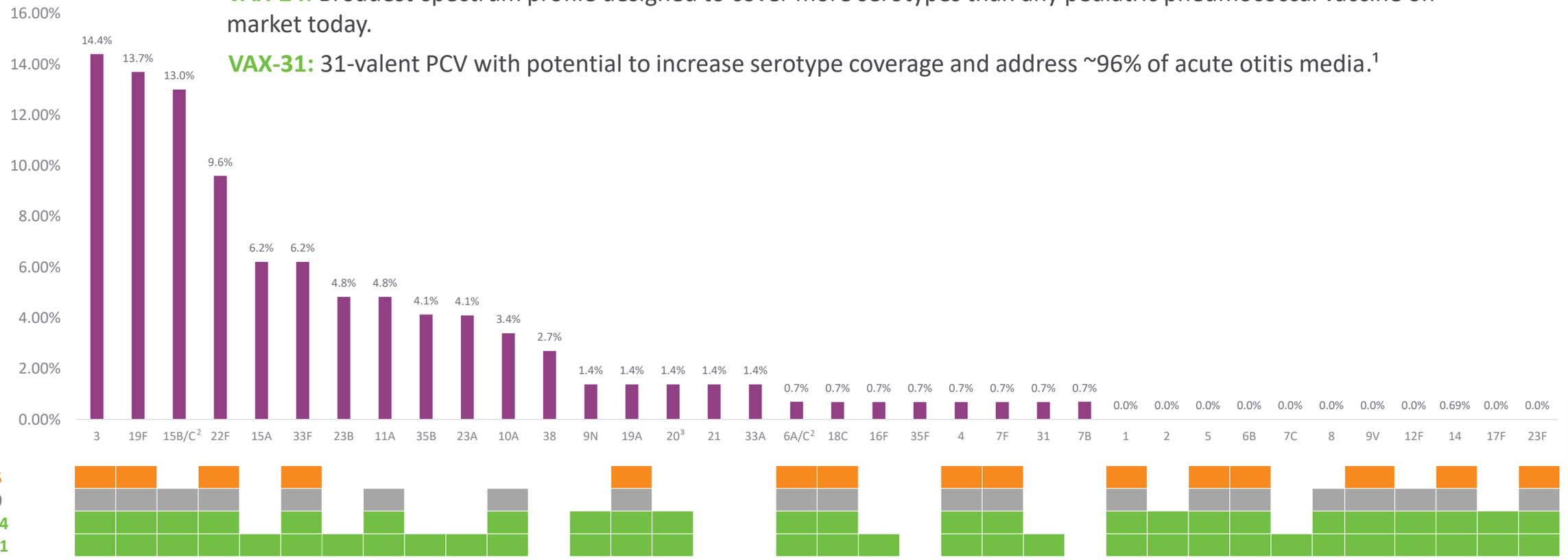
(1) The serogroup 20 antigen contained in VAX-24 and VAX-31, formerly known as a 20B variant, has been officially reclassified as 20C. For additional details on serogroup 20, please see footnote 2 on slide 15.
(2) 15C coverage due to cross-reaction against 15B. 6C coverage due to cross-protection by 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.

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.[1]

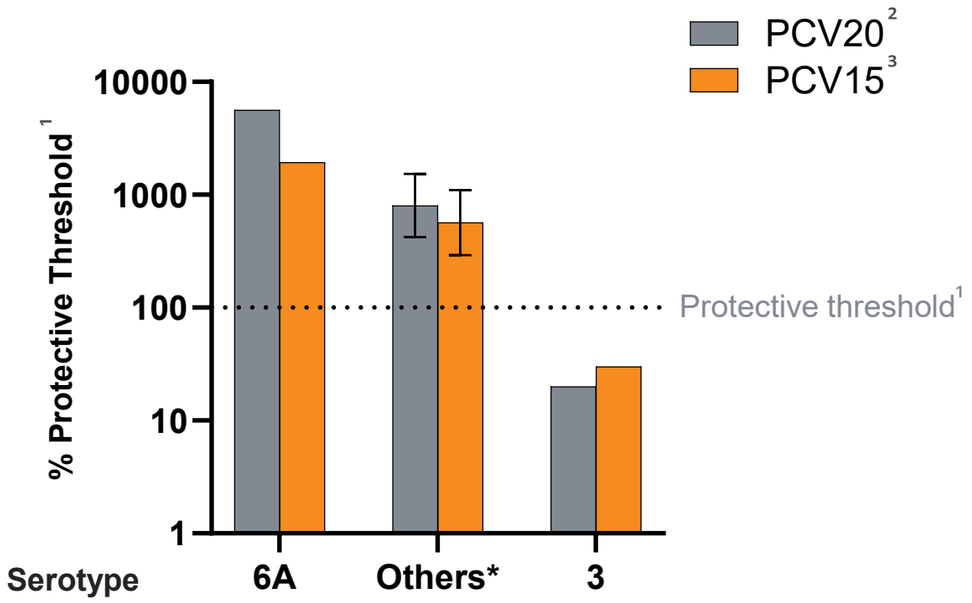


Total IPD Coverage (U.S. %)[4]
48%
69%
72%
92%

(1) 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).
(2) 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.
(3) 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.
(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.

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

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



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

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

(1) Lancet Infect Dis. 2014 Sep;14(9): 839-846.
(2) PCV20 product insert – Table 11.
(3) PCV15 product insert – Table 11.

** = 1, 4, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F.*

VAXCYTE

protect humankind™

Contact:

Jeff Macdonald, Executive Director, Investor Relations
investors@vaxcyte.com