Corporate Presentation



November 4, 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, research and development and regulatory 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; expectations with regard to serotype cross-reactivity; the standards for review and licensure of vaccines and regulators accepting Vaxcyte's study as designed; 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 November 4, 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 presentation as a result of new information, future events or changes in its expectations.



VAXCYTE MISSION STATEMENT

We are on a global mission to engineer high-fidelity vaccines that protect humankind from the consequences of bacterial diseases.

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

VAX-31 Met All Primary Endpoints Under a More Stringent Noninferiority Standard in OPUS-1 Pivotal Phase 3 Adult Trial

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
  - Announced OPUS-1 Phase 3 topline results; trial met all prespecified primary endpoints
  - Enrollment completed in 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 ~$8.5B** 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 ongoing
- **VAX-GI:** Novel Shigella vaccine

ALIGNED CRITICAL RESOURCES

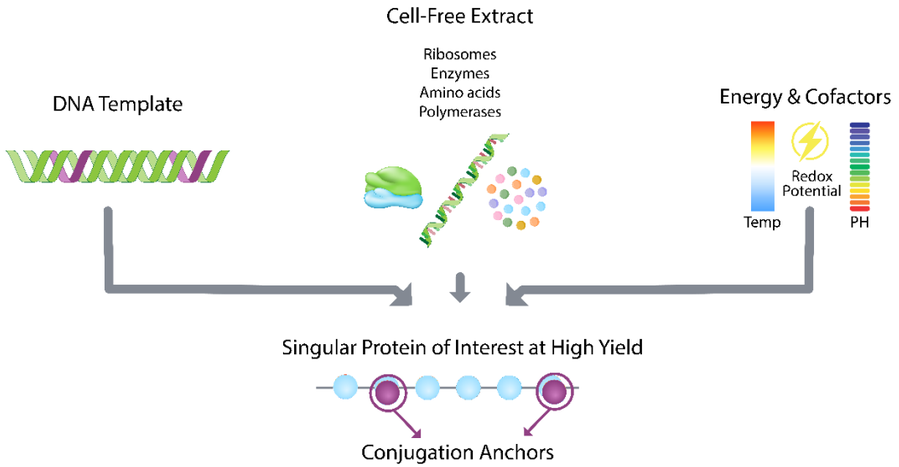
- **Strategic Manufacturing Approach**
  - Building out capacity to satisfy global PCV demand for developed markets
  - Global commercial manufacturing agreement with Lonza to produce key PCV components
  - Agreement with Thermo Fisher Scientific to establish U.S. fill-finish manufacturing; expands domestic capacity to support future commercial manufacturing
- **Seasoned management team,** directors and advisors
- **Pro forma cash, cash equivalents and investments of ~$3.4B[1]**

BTD = Breakthrough Therapy designation, IPD = invasive pneumococcal disease, MOA = mechanism of action.
(1) Reflects cash, cash equivalents and investments as of September 30, 2026 of ~$2.3B, and estimated net proceeds from October 2026 concurrent offerings of common stock, pre-funded warrants and convertible senior notes of ~$1.1B.

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

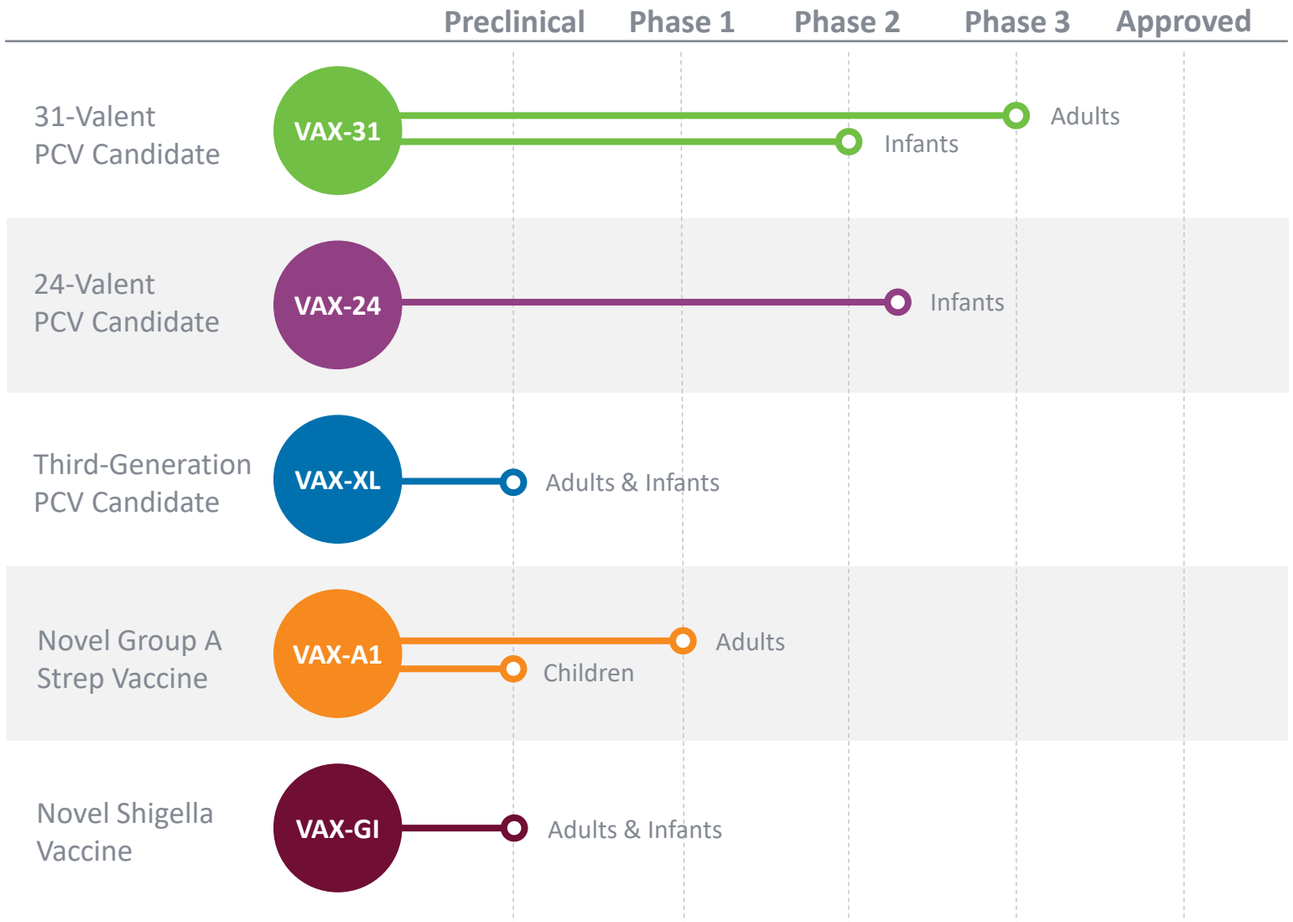
- Site-specifically attach antigens onto protein carriers designed to:
  - Enable consistent exposure of T-cell epitopes and/or B-cell epitopes on protein carrier
  - Avoid off-target effects
  - Enable use of less protein carrier without sacrificing immunogenicity
  - Enable broader-spectrum vaccines

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



Key Milestones Anticipated by End of 2027[1]

VAX-31 ADULT INDICATION

- Announce safety, tolerability and immunogenicity data from the **OPUS-2** and **OPUS-3**[2] 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

- Announce topline data from the Phase 1, first-in-human adult study[3] in the second half of 2027

(1) Guidance as of November 4, 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) 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, Director & 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 & Chief Scientific Officer

Pfizer
NOVARTIS
MERCK

Mike Mullette, MBA
Chief Commercial Officer

lykos THERAPEUTICS
moderna
SANOFI

Luis Jodar, PhD
Chief Medical Officer

Pfizer
World Health Organization
International Vaccine Institute

Chris Griffith, MS, MBA
Chief Business & Strategy Officer

Dermira
GILEAD
Adanate

Harp Dhaliwal, MBA
Chief Technical Operations Officer

Dermira
MEDIVATION
Biogen

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 ~$8.5 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

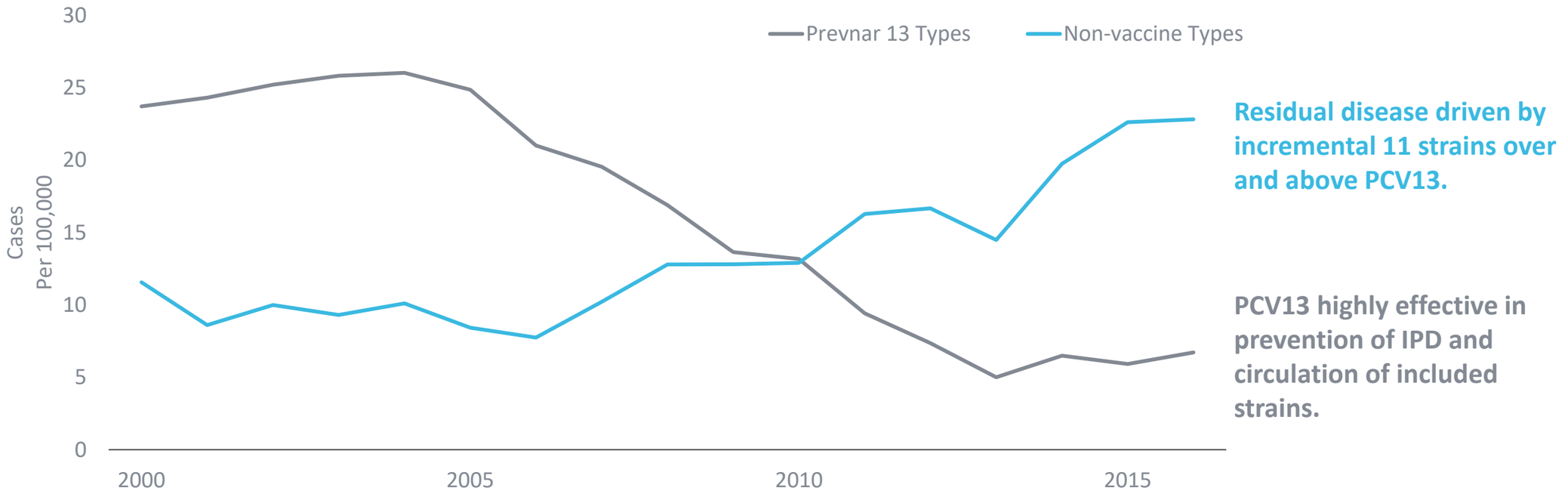
- *Streptococcus pneumoniae* is the leading cause of vaccine-preventable deaths globally in children under five[4]
- ~225K U.S. adult hospitalizations annually caused by pneumococcal pneumonia[5]
- ~300K children under five years old die annually worldwide due to *Streptococcus pneumoniae*[6]

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.

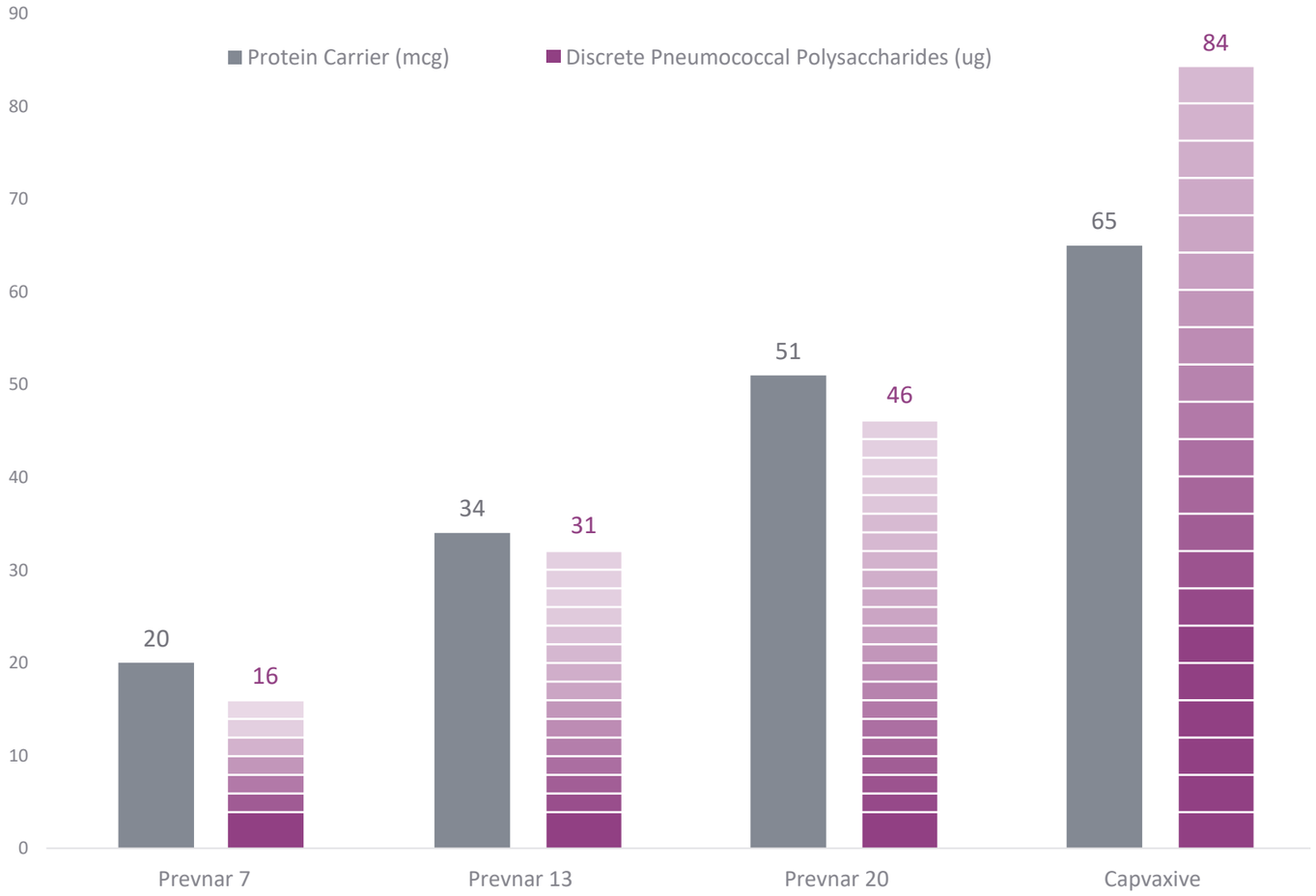
Limitations of Current PCVs

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

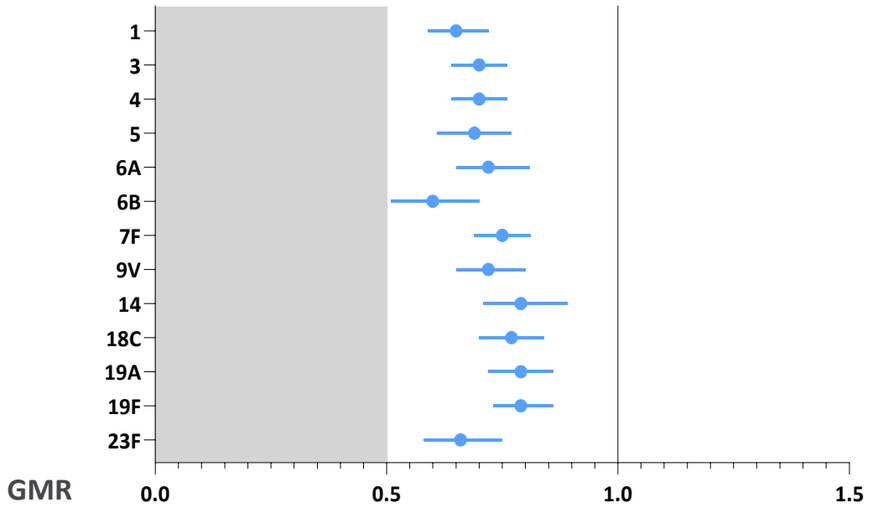
Coverage Expansion Using Conventional Chemistry Has Led to Carrier-Induced Immune Suppression

CARRIER SUPPRESSION

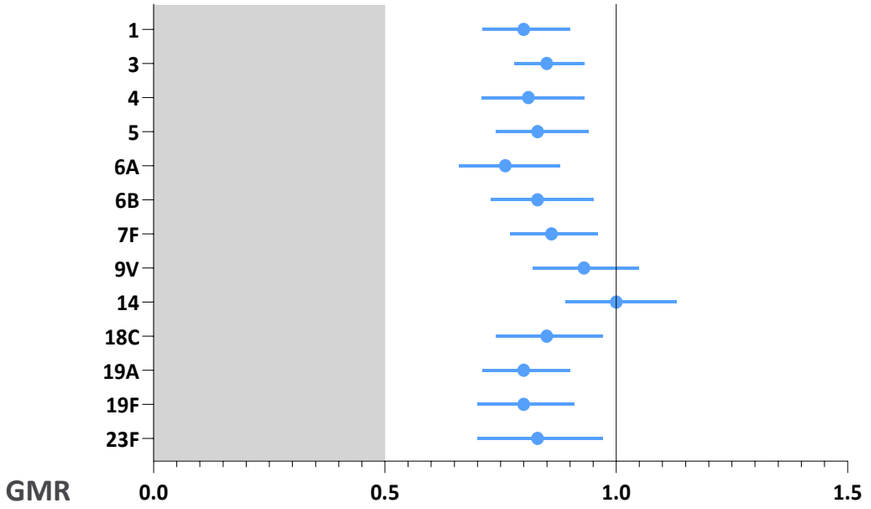
Diminished immune response to target polysaccharides due to cumulative amount of protein carrier

- 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]

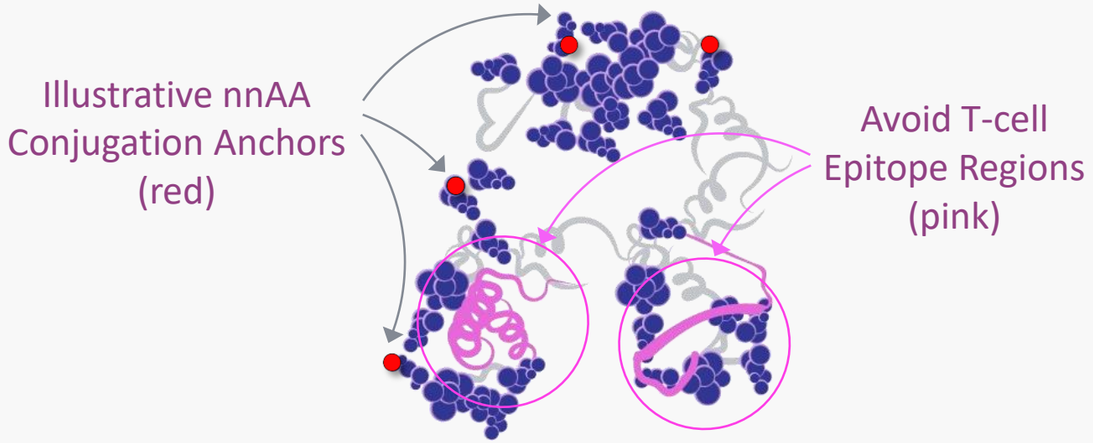


(1) Immunoglobulin G (IgG) Geometric Mean Concentrations post-dose 4 – Prevnar 20 BLA Clinical Review Memorandum by FDA (STN: 125731/189). April 27, 2023.
(2) Prevnar 20 BLA Clinical Review Memorandum. STN: 125731/0 June 8, 2021.
OPA = opsonophagocytic activity; GMR = geometric mean ratio.

Vaxcyte's PCV Franchise Employs Carrier-Sparing Conjugates

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

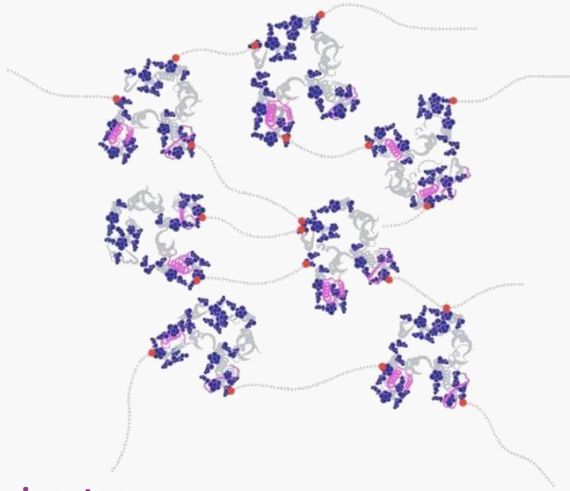
PROPRIETARY eCRM® PROTEIN CARRIER WITH PRECISE, SITE-SPECIFIC CONJUGATION SITES



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

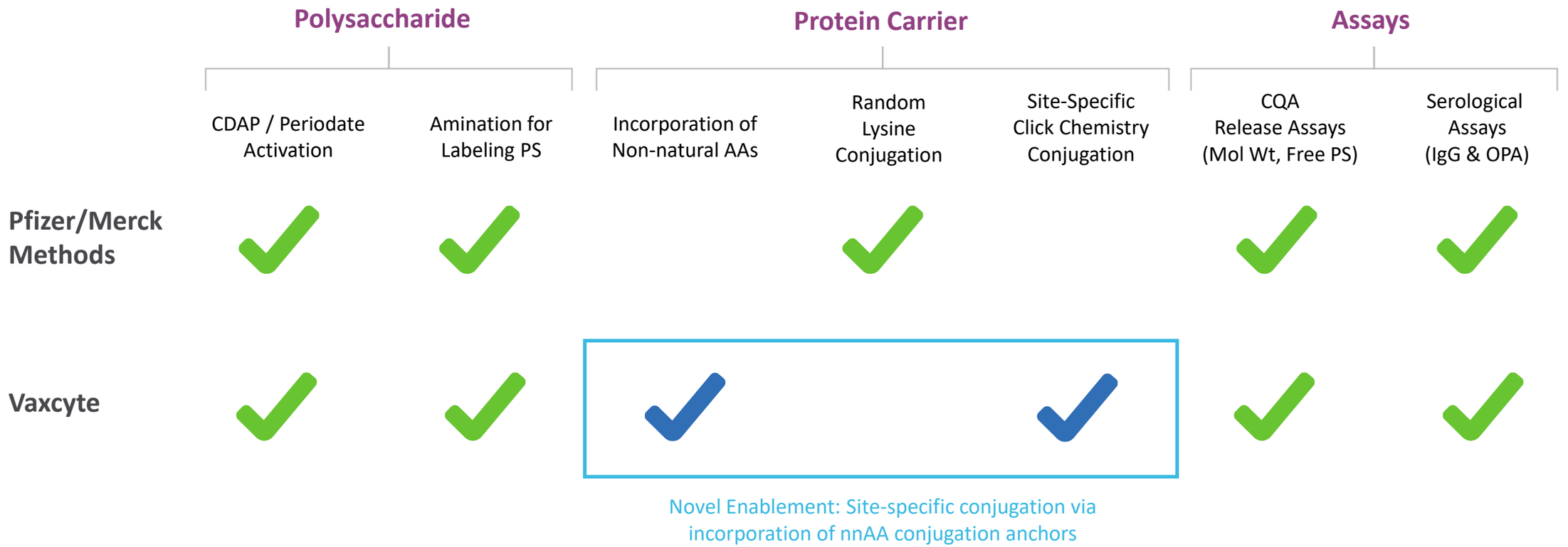


Carrier-Sparing Conjugates

- 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



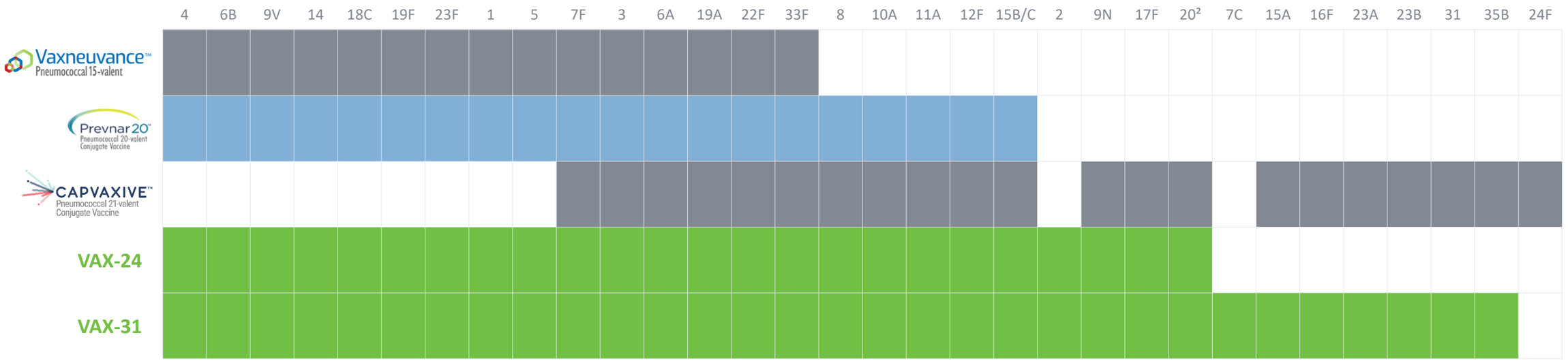
OPA = opsonophagocytic activity; IgG = immunoglobulin G.

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)

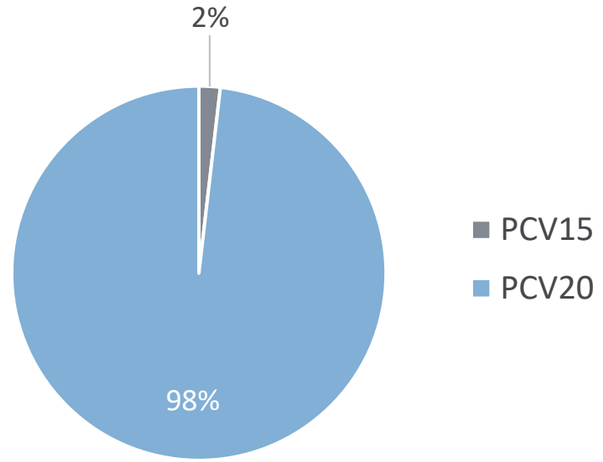
ATTRACTIVE MARGINS

- 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: $253 (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 October 2026).
(2) FDA safety assessment of PCV20 data presented at February 2024 ACIP meeting.

Pneumococcal Vaccine Market is Large, Durable and Poised for Significant Growth

Combined ~$8.5B Market Expected to Grow to ~$12B by 2030[1] Driven Primarily by Adult Market Expansion

Future Market

2030: ~$12B



Total Market

Today: ~$8.5B[4]

Pediatric market is large, well-established, and highly durable

ADULT SEGMENT GROWTH DRIVERS

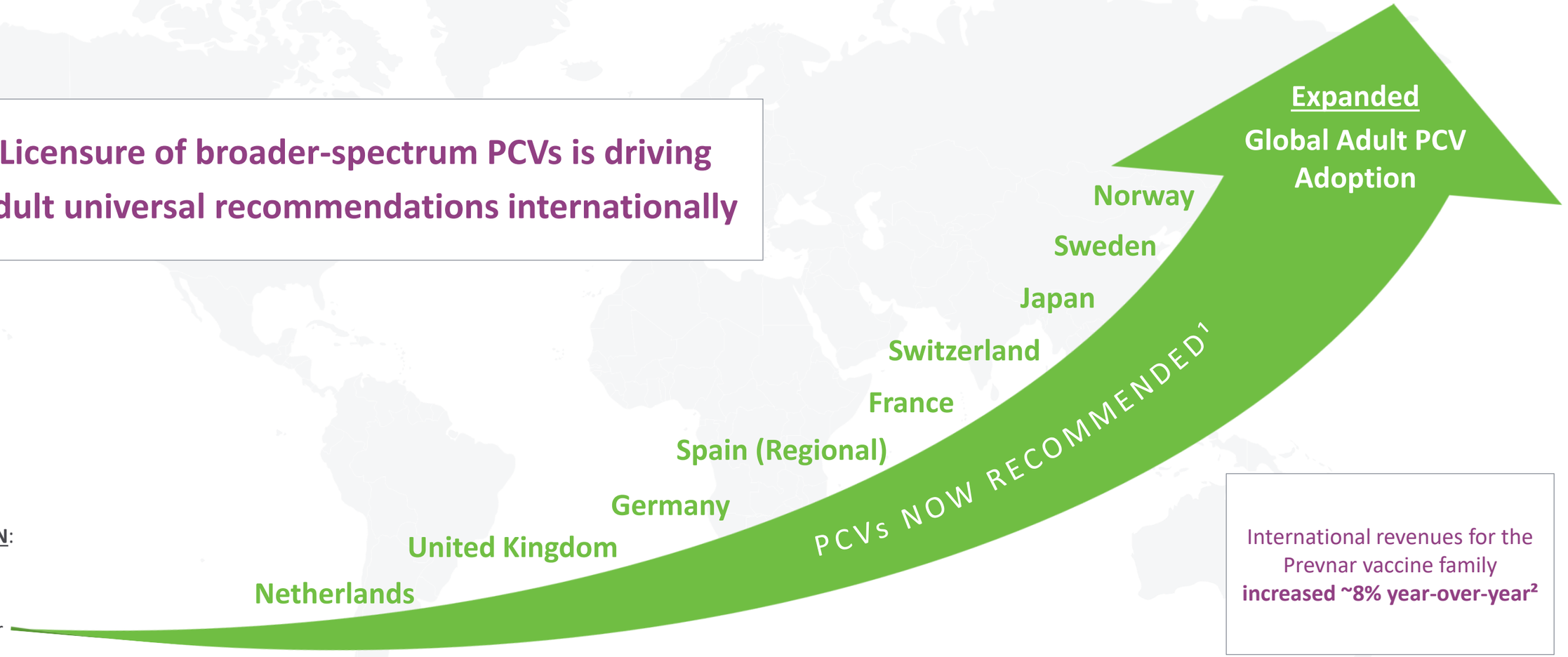
1. In 2024, universal recommendation expanded to U.S. adults ≥50 years (from ≥65 years)[2]
2. "Catch up" revaccination of individuals who received lower-valency pneumococcal vaccines[3]
3. Expanded adult PCV recommendations globally
4. Potential shift to two-dose schedule for U.S. adults (≥50 years and again at ≥65 years)
5. "At risk" adults aged 19-49 added to U.S. recommendation

(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).*
(4) *Combined 2025 annual pneumococcal vaccine sales reported by Merck, Pfizer and GSK.*

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



PRIOR ADULT RECOMMENDATION:

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

International revenues for the Prevnar vaccine family **increased ~8% year-over-year²**

PPSV23 = Pneumovax 23.

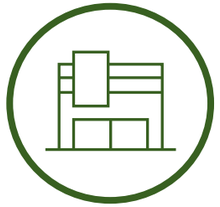
(1) Transition from PPSV23 to PCV-only or newly introduced PCV recommendation: France, Germany, Japan, Netherlands, Spain (regional, Galicia), Sweden, Norway, Switzerland, United Kingdom.

(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).

Commercial Strategy for U.S. Adult PCV Market

Initial Focus on Retail Pharmacies and Large Health Systems

~50% of U.S. Adult PCV Volume is Concentrated in 50-60 Accounts[1]



RETAIL PHARMACIES[1]

~45%

6 retail chains account for **~70-80%** of adult PCV volume in pharmacies



IDNs / HEALTH SYSTEMS[1]

~35%

~50 large health systems account for **~40-50%** of adult PCV volume in segment



PHYSICIAN OFFICES[1]

~20%

Physician offices represent an incremental growth opportunity for adult PCV volume

IDN = Integrated Delivery Network.
(1) Komodo claims data (March 2024- February 2026).

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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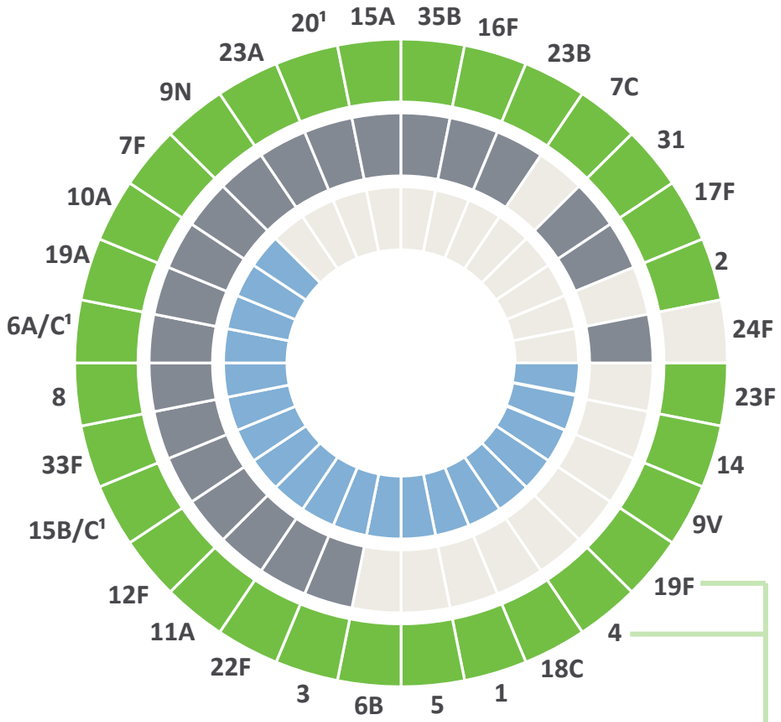
VAX-31 is Designed to Offer Comprehensive Coverage to Address Current Gaps

Broadening of Serotype and Disease Coverage Would Eliminate Tradeoffs Required by Current SoC

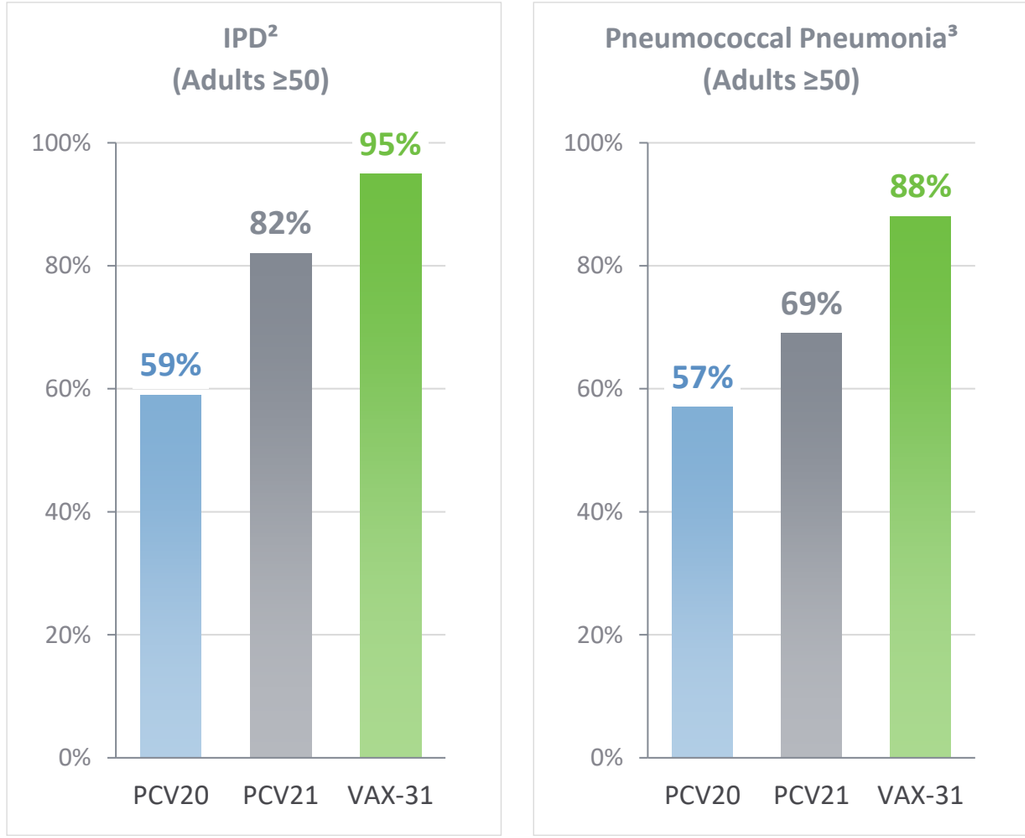
Spectrum of Serotype Coverage Drives Adoption in PCVs:



VAX-31
PCV21
PCV20

ST4 has been increasing in IPD prevalence post-2020, particularly in Western U.S. states,[4] and 19F continues to persist; neither ST included in PCV21.

VAX-31 is Designed to Expand Protection with Broadest Disease Coverage in Adults



IPD = Invasive Pneumococcal Disease; SoC = standard of care; ST = serotype. (1) Immune responses elicited by 20C are expected to be highly cross-reactive with 20B. PCV21 includes 20A and VAX-31 includes 20C. Serotypes 6A/6C and 15B/15C are closely related subtypes for which cross-protection is assumed; PCV21, PCV20 and VAX-31 all include 6A, and PCV20 and VAX-31 include 15B. PCV21 includes 15C and showed cross-reactive responses against 15B, supporting an indication for IPD caused by both 15B and 15C. (2) % of IPD caused in individuals ≥50 yrs of age in the U.S. in 2022-2024 based on ABC surveillance data. (3) Non-bacteremic pneumonia; source: https://doi.org/10.1093/infdis/jiaf376. (4) Gierke R, et al. CDC/NCIRD. ISPPD-14, May 2026.

VAX-31 OPUS Phase 3 Program Serves as Cornerstone of Planned BLA Submission

TOPLINE REPORTED

OPUS-1 PIVOTAL TRIAL (N=4,047)

Topline results reported; complete data set to be published

ONGOING

OPUS-2: CONCOMITANT ADMINISTRATION WITH SEASONAL INFLUENZA VACCINE (N=1,390)

Enrollment complete; topline results anticipated 1H 2027

ONGOING

OPUS-3: ADULTS PREVIOUSLY VACCINATED WITH PNEUMOCOCCAL VACCINES (N=752)

Enrollment complete; topline results anticipated 1H 2027

PLANNED

MANUFACTURING CONSISTENCY STUDY (e.g. lot-to-lot) (N=TBD)

Planned: Data to be included in BLA submission

POTENTIAL VAX-31 REGULATORY APPROVAL

Planned post-licensure real-world effectiveness study following launch

(ST-Specific Community Acquired Pneumonia)

BLA = Biologics License Application.

VAX-31 OPUS-1 Pivotal Phase 3 Adult Trial: Topline Results

OPUS-1 Phase 3 Study:
Statistical Framework to Define Success

Co-Primary Immunogenicity Objectives (Adults ≥50):

CO-PRIMARY ENDPOINT GROUP 1 **11 serotypes shared by all 3 vaccines**	CO-PRIMARY ENDPOINT GROUP 2 **9 serotypes shared with PCV20 only**	CO-PRIMARY ENDPOINT GROUP 3 **8 serotypes shared with PCV21 only**	CO-PRIMARY ENDPOINT GROUP 4 **3 unique serotypes and cross-reactive 20B**
Noninferiority vs PCV20 and/or PCV21 **(OPA GMR: LBCI >0.667)[1]**	**Noninferiority vs PCV20** **(OPA GMR: LBCI >0.667)**	**Noninferiority vs PCV21** **(OPA GMR: LBCI >0.667)**	**Superiority vs PCV20 and/or PCV21** **(OPA GMR: LBCI >2.0)[1]**

Primary Immunobridging Objective (Adults 18-49):

If the above co-primary criteria are met: noninferiority of VAX-31 in adults aged 18-49 vs adults aged 50-64; all 32 comparisons[2] must meet OPA GMR NI at the LBCI >0.667.

Primary Safety Objective (Adults ≥18):

Evaluate **safety and tolerability of VAX-31** administered to adults aged 18-49 and ≥50.

Prespecified Individual Noninferiority Comparisons (Adults ≥50):

Evaluated **prespecified individual OPA GMR noninferiority comparisons of VAX-31 vs PCV20 or PCV21** in adults aged ≥50, among other immunogenicity evaluations, to provide additional data for regulators and recommending bodies.

(1) For groups 1 and 4: one-sided Hochberg-adjusted p-value <0.025 for at least one comparator.
(2) The 32 assessments include 31 vaccine serotypes and cross-reactive 20B.
OPA = opsonophagocytic activity; GMR = geometric mean ratio; LBCI = lower bound of the 2-sided 95% CI; NI = noninferiority.
Primary analyses use Month 1 OPA geometric mean ratios in the immunogenicity evaluable population.

OPUS-1 Phase 3 Topline Results:
VAX-31 Met All Primary Immunogenicity Endpoints and Safety Objectives

Co-Primary Immunogenicity Objectives (Adults ≥50):

OPUS-1 Inaugurates a More Stringent >0.667 Noninferiority Standard, Setting a New Bar for Adult PCV Clinical Studies

CO-PRIMARY ENDPOINT GROUP 1 11 serotypes shared by all 3 vaccines	CO-PRIMARY ENDPOINT GROUP 2 9 serotypes shared with PCV20 only	CO-PRIMARY ENDPOINT GROUP 3 8 serotypes shared with PCV21 only	CO-PRIMARY ENDPOINT GROUP 4 3 unique serotypes and cross-reactive 20B
11 of 11 met noninferiority (OPA GMR: LBCI >0.667)[1]	**9 of 9** met noninferiority (OPA GMR: LBCI >0.667)	**8 of 8** met noninferiority (OPA GMR: LBCI >0.667)	**4 of 4** met superiority (OPA GMR: LBCI >2.0)[1]

Primary Immunobridging Objective (Adults 18-49):

32 of 32 comparisons met noninferiority (OPA GMR LBCI >0.667)[2]

Primary Safety Objective (Adults ≥18):

VAX-31 was well tolerated, with a safety profile similar to PCV20 and PCV21 across all ages studied

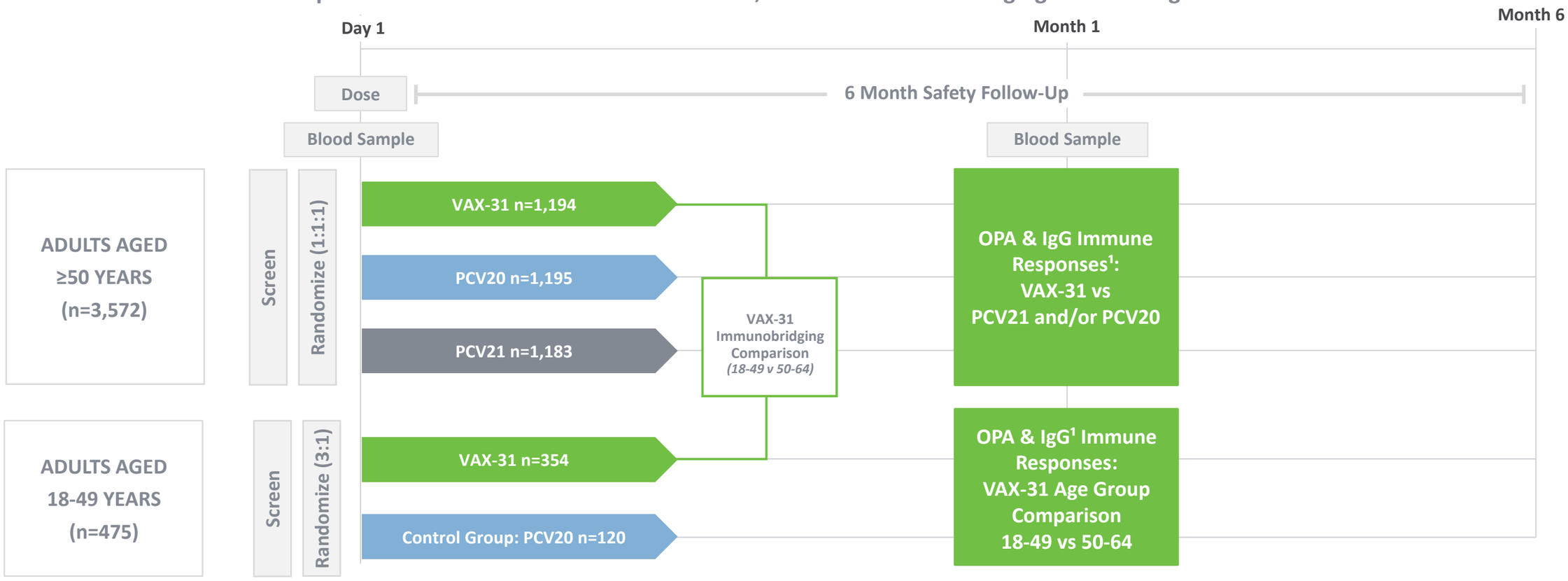
Prespecified Individual Noninferiority Comparisons (Adults ≥50):

VAX-31 vs PCV20	VAX-31 vs PCV21
20 of 20 shared serotypes met noninferiority criterion (OPA GMR LBCI >0.667)	**17 of 19** shared serotypes met noninferiority criterion (OPA GMR LBCI >0.667)

(1) Groups 1 and 4: one-sided Hochberg-adjusted p-value <0.025 against at least one comparator, as prespecified in the protocol.
(2) The 32 assessments include 31 vaccine serotypes and cross-reactive 20B.
OPA = opsonophagocytic activity; GMR = geometric mean ratio; NI = noninferiority; LBCI = lower bound of the 2-sided 95% CI. Evaluable Month 1 OPA geometric mean ratios.

OPUS-1 Phase 3 Pivotal, Randomized, Double-Blind, Active-Controlled Clinical Trial in Adults Aged 18 and Older (n=4,047*)

Designed to Establish New PCV Standard of Care for Adults Aged 50 and Older Through Head-to-Head Safety, Tolerability and Immunogenicity Comparisons of VAX-31 with PCV20 and PCV21; Evaluated Immunobridging to Adults Aged 18-49



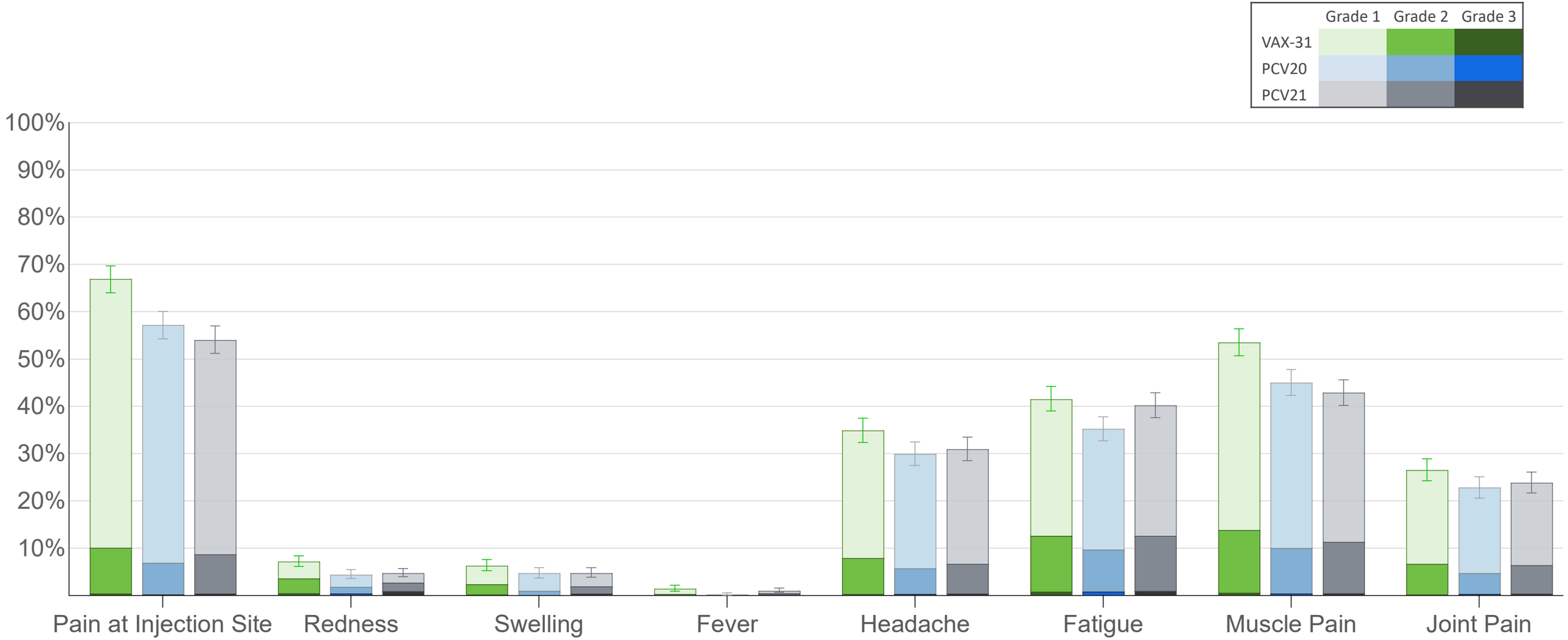
Safety and tolerability assessed through Month 6, including solicited local reactions and systemic events (Day 1-7), unsolicited AEs (Day 1-Month 1), and SAEs, NOCIs and MAAEs (Day 1-Month 6)

OPA = opsonophagocytic activity; IgG = immunoglobulin G; AEs = adverse events; SAEs = serious adverse events; NOCIs = new onset of chronic illnesses; MAAEs = medically attended adverse events.
(*) 1 participant in the 18-49 age group received PCV21.
(1) IgG comparisons of VAX-31 versus PCV21 and/or PCV20 are secondary endpoints.

Tolerability and Safety Data

Local and Systemic Solicited AEs in Adults Aged 50 Years and Older

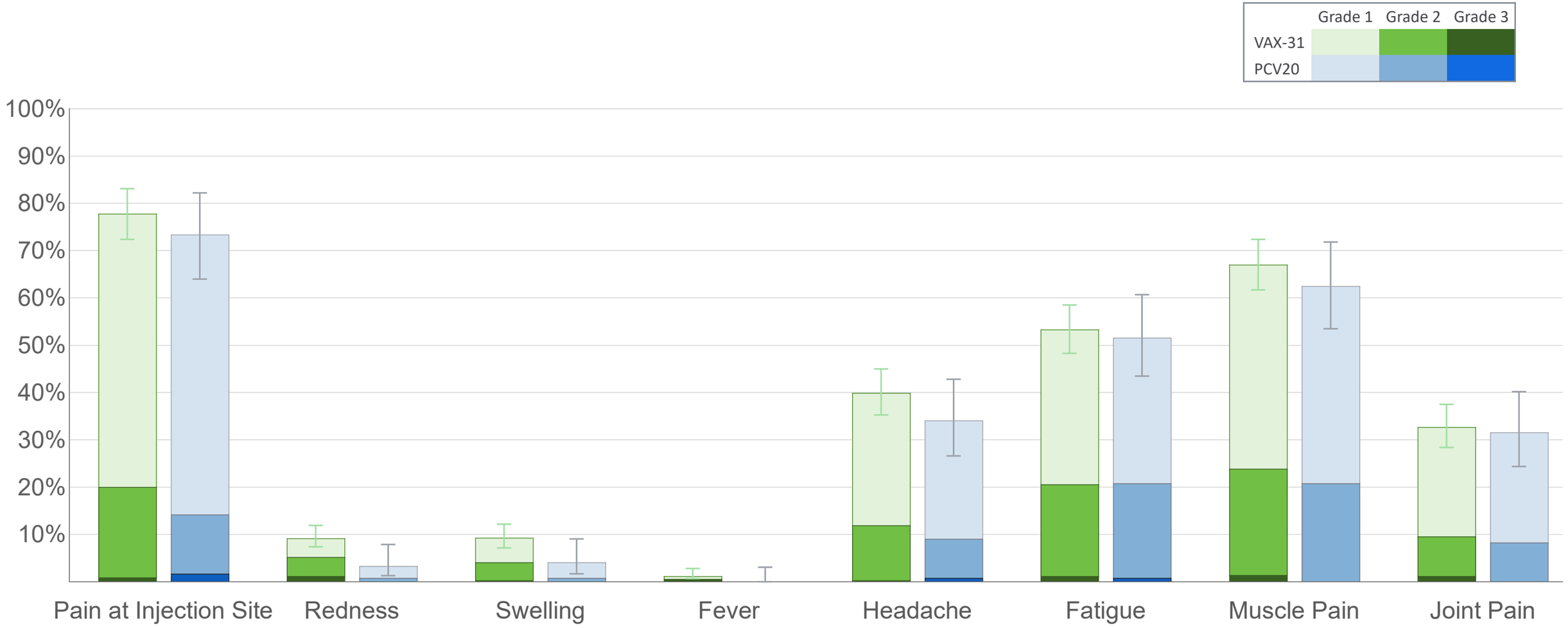
VAX-31 was Well-Tolerated and Consistent with PCV20 and PCV21, Majority of AEs Resolved Within 48 Hours



AEs = adverse events.

Local and Systemic Solicited AEs Similar to PCV20 in Adults Aged 18-49

VAX-31 was Well-Tolerated and Consistent with PCV20, Majority of AEs Resolved Within 48 Hours



AEs = adverse events.

Overall Safety Profile Similar to PCV20 and PCV21

	50 YEARS AND OLDER SAFETY POPULATION			18-49 YEARS SAFETY POPULATION	
	VAX-31	PCV20	PCV21	VAX-31	PCV20
Number of Subjects	1194	1195	1183	354	120
Unsolicited AE (1-Month), n (%)	75 (6.3)	99 (8.3)	96 (8.1)	37 (10.5)	11 (9.2)
Related, n (%)	19 (1.6)	24 (2.0)	28 (2.4)	9 (2.5)	3 (2.5)
MAAE, n (%)	71 (5.9)	104 (8.7)	90 (7.6)	26 (7.3)	10 (8.3)
Related, n (%)	2 (0.2)	5 (0.4)	3 (0.3)	0	0
NOCI, n (%)	7 (0.6)	9 (0.8)	12 (1.0)	2 (0.6)	3 (2.5)
Related, n (%)	0	0	0	0	0
SAE, n (%)	14 (1.2)	13 (1.1)	13 (1.1)	2 (0.6)	0
Related, n (%)	0	0	0	0	0
Death[1], n (%)	2 (0.2)	0	2 (0.2)	0	0
Related, n (%)	0	0	0	0	0
Discontinuation, n (%)	0	0	0	0	0
Related, n (%)	0	0	0	0	0

AEs = adverse events; MAAE = medically attended adverse event; NOCI = new onset of chronic illness; SAE = serious adverse event; Discontinuation = subject discontinued from the study due to an AE.
(1) All four deaths were assessed as unrelated to study vaccination. Two deaths were classified in the injury and poisons category (overdose), with one in the VAX-31 arm and one in the PCV21 arm. The remaining deaths were cardiac arrest in a participant with established cardiovascular risk factors 104 days after vaccination, and sepsis secondary to a pre-existing Group B Streptococcus-infected wound with bacteremia 11 days after vaccination.

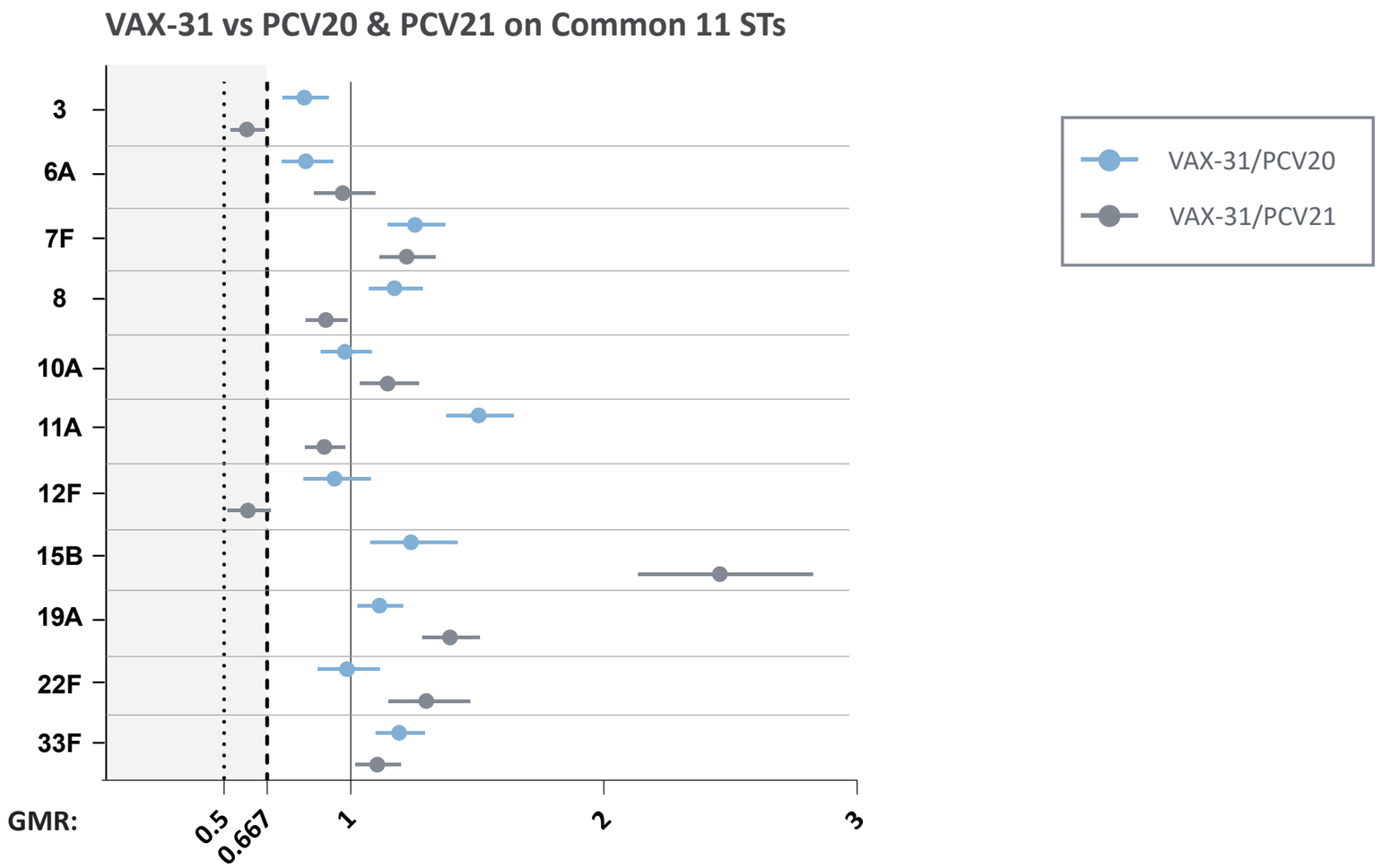
Immunogenicity Data

In Adults Aged ≥50 Years and 18-49 Years

11 STs in Common With PCV20 and PCV21

Met 11 of 11 ST OPA GMR Comparisons Per Prespecified NI Criterion[1] (LBCI >0.667) vs PCV20 and/or PCV21

CO-PRIMARY ENDPOINT GROUP 1



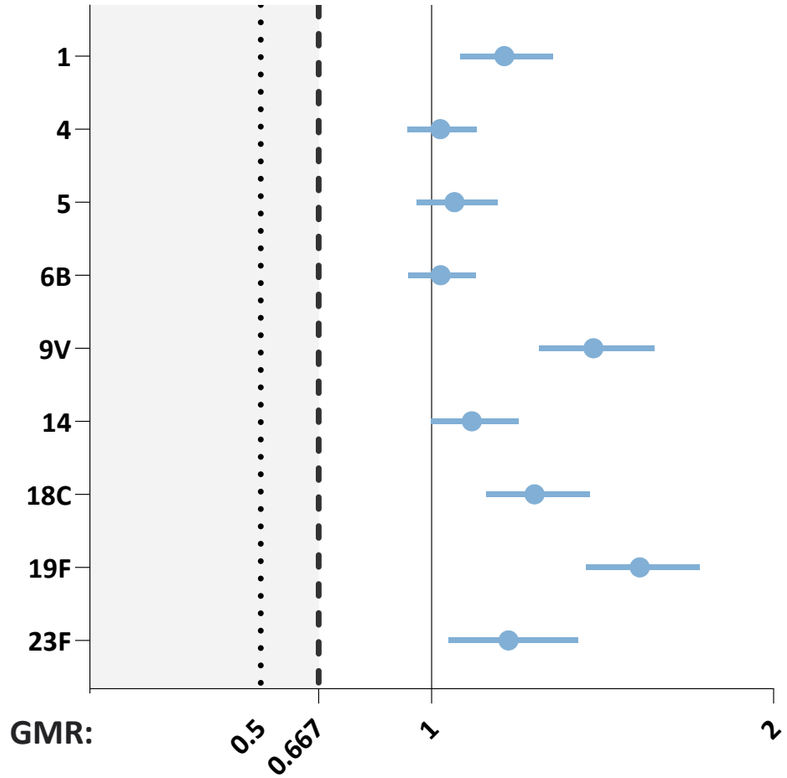
ST = serotype; OPA = opsonophagocytic activity; GMR = geometric mean ratio; LBCI = lower bound of the 2-sided 95% CI.
(1) SAP criterion: lower bound of the 95% CI of the OPA GMR >0.667, Hochberg-adjusted.

9 STs in Common With Only PCV20 and 8 STs Common With Only PCV21

Met 9 of 9 ST OPA GMR Comparisons vs PCV20 and 8 of 8 vs PCV21 Per Prespecified NI Criterion (LBCI >0.667)

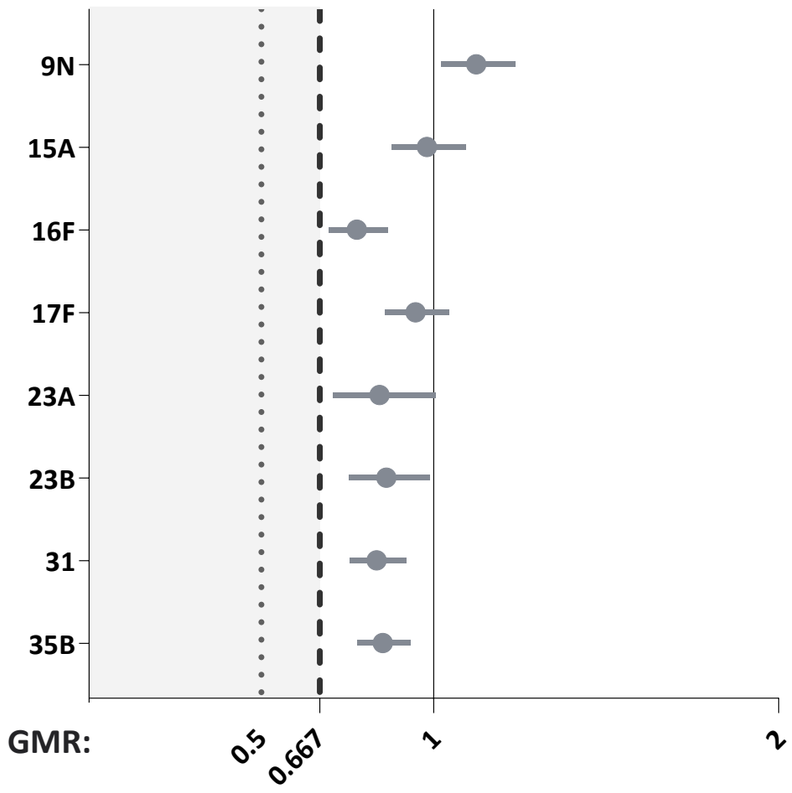
CO-PRIMARY ENDPOINT GROUP 2

VAX-31 vs PCV20: Shared 9 STs



CO-PRIMARY ENDPOINT GROUP 3

VAX-31 vs PCV21: Shared 8 STs

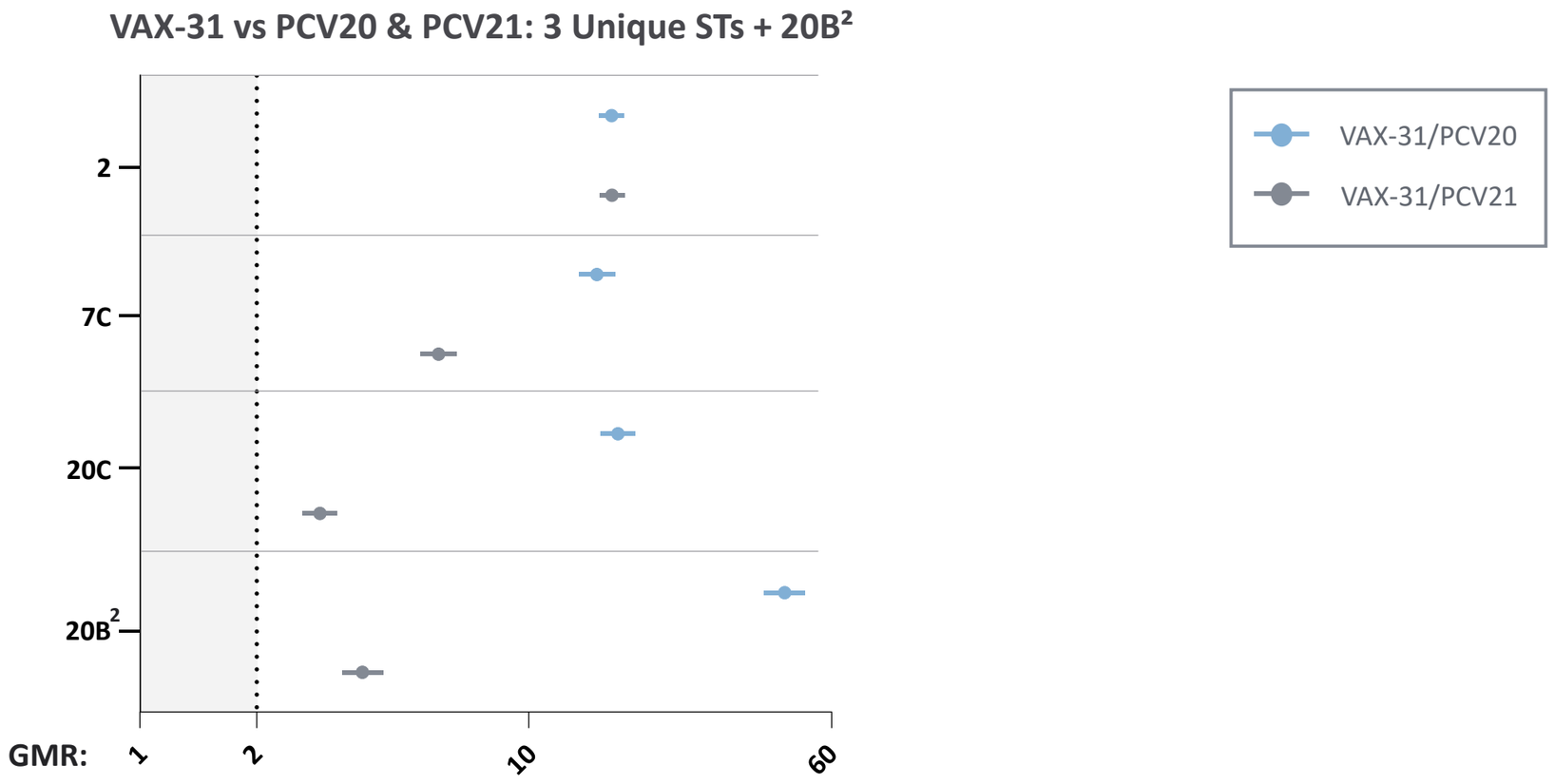


ST = serotype; OPA = opsonophagocytic activity; GMR = geometric mean ratio; LBCI = lower bound of the 2-sided 95% CI.

3 Unique VAX-31 STs and 20B

Met 4 of 4 ST OPA GMR Comparisons Per Prespecified Superiority Criterion (LBCI >2.0) vs PCV20 and/or PCV21[1]

CO-PRIMARY ENDPOINT GROUP 4

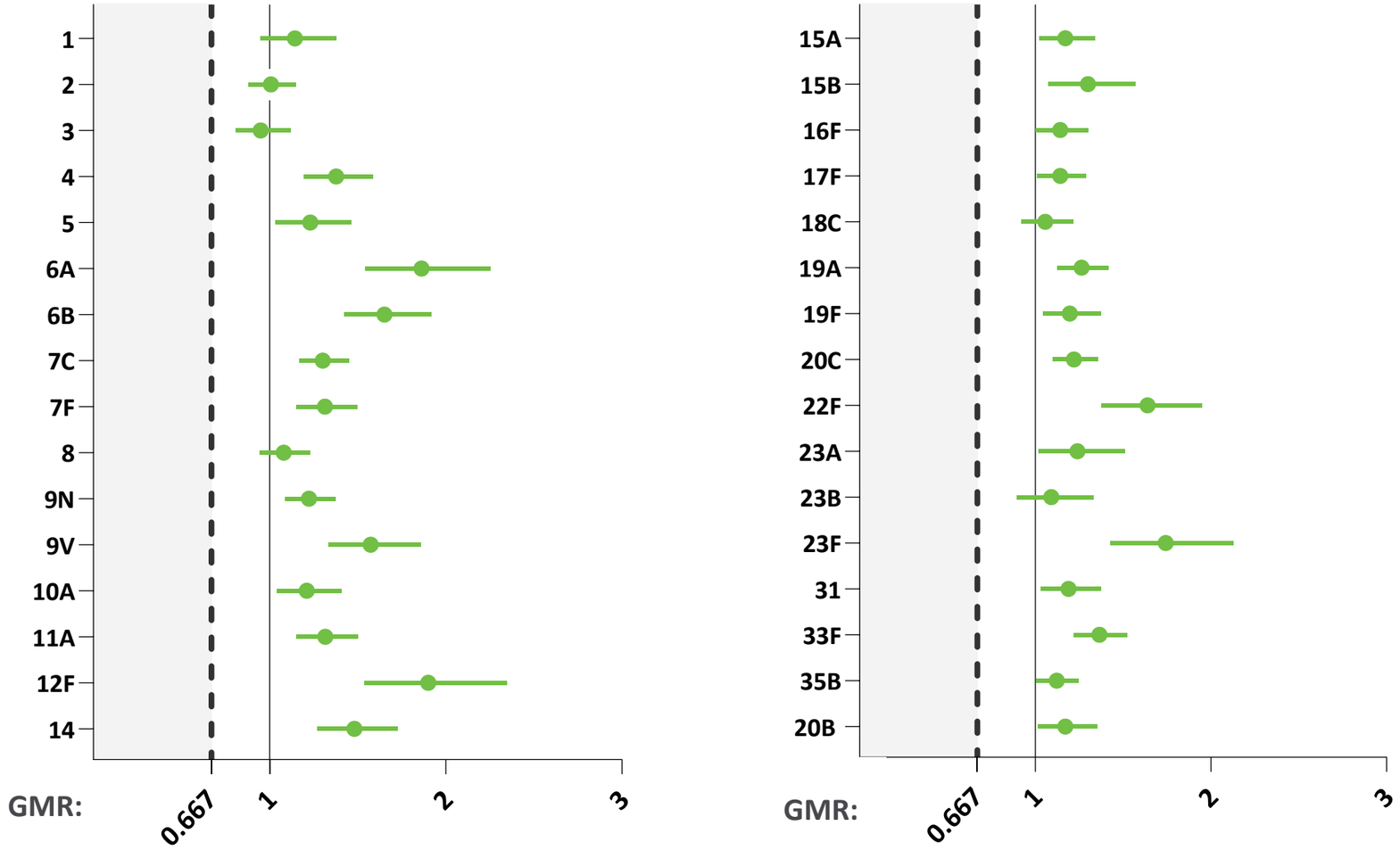


ST = serotype; OPA = opsonophagocytic activity; GMR = geometric mean ratio; LBCI = lower bound of the 2-sided 95% CI.
(1) With Hochberg multiplicity analysis per protocol.
(2) VAX-31 includes serotype 20C; 20B is being evaluated in clinical studies to demonstrate cross-protection. For further detail on serogroup 20, see footnote 2 on slide 15.

Immunobridging Comparison in 18-49-Year-Olds vs 50-64-Year-Olds

Met Prespecified Primary Endpoint Across All 32 STs[1] (OPA GMR With LBCI >0.667)

VAX-31 Immunobridging OPA GMR Comparison (18-49 vs 50-64)



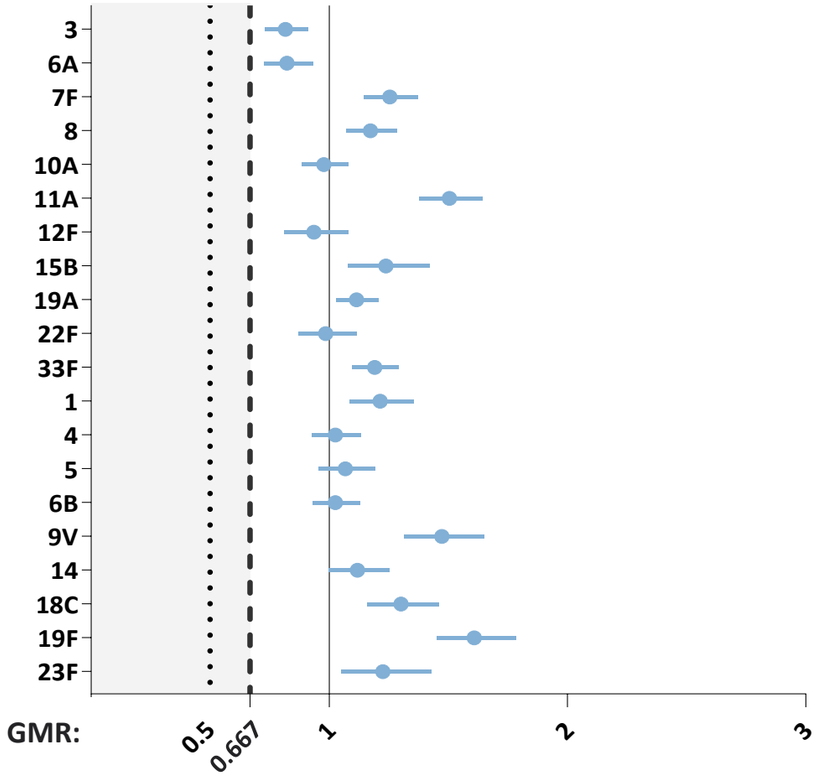
ST = serotype; OPA = opsonophagocytic activity; GMR = geometric mean ratio; LBCI = lower bound of the 2-sided 95% CI.
(1) The 32 assessments include 31 vaccine serotypes and cross-reactive 20B.

Comparator-Specific Assessments: VAX-31 Immune Responses vs PCV20 and PCV21

VAX-31 Met Noninferiority Criterion for 20/20 STs vs PCV20 and 17/19 STs vs PCV21

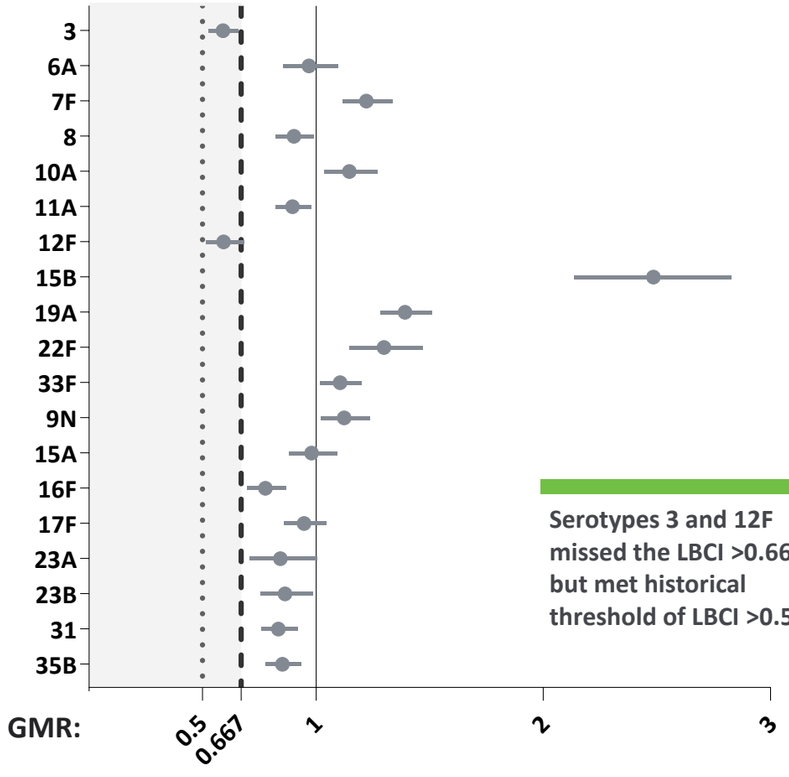
VAX-31 vs PCV20: Common 20 STs

OPA GMRs met prespecified NI criterion (LBCI >0.667) for 20 of 20 common STs



VAX-31 vs PCV21: Common 19 STs

OPA GMRs met prespecified NI criterion (LBCI >0.667) for 17 of 19 common STs



Serotypes 3 and 12F missed the LBCI >0.667 but met historical threshold of LBCI >0.5.

In the U.S., as PCV21 serotypes account for a larger share of adult disease coverage, U.S. regulators may focus more on the individual PCV21 comparison to VAX-31 in review of BLA submission.

ST = serotype; OPA = opsonophagocytic activity; GMR = geometric mean ratio; LBCI = lower bound of the 2-sided 95% CI.

VAX-31 Data Support Potential Best-in-Class Adult PCV Profile with Broadest Coverage Relative to SoC; Advancing Toward BLA Submission

Broad and robust immune responses observed across all 31 STs + 20B for all ages evaluated.
Met all prespecified co-primary and immunobridging endpoints.

VAX-31 was well-tolerated with a safety profile similar to PCV20 and PCV21.

VAX-31 has the potential to offer significantly broader ST and disease coverage vs SoC vaccines.
Represents incremental 13-36% of IPD coverage[1] and incremental 19-31% of pneumococcal pneumonia coverage[2].

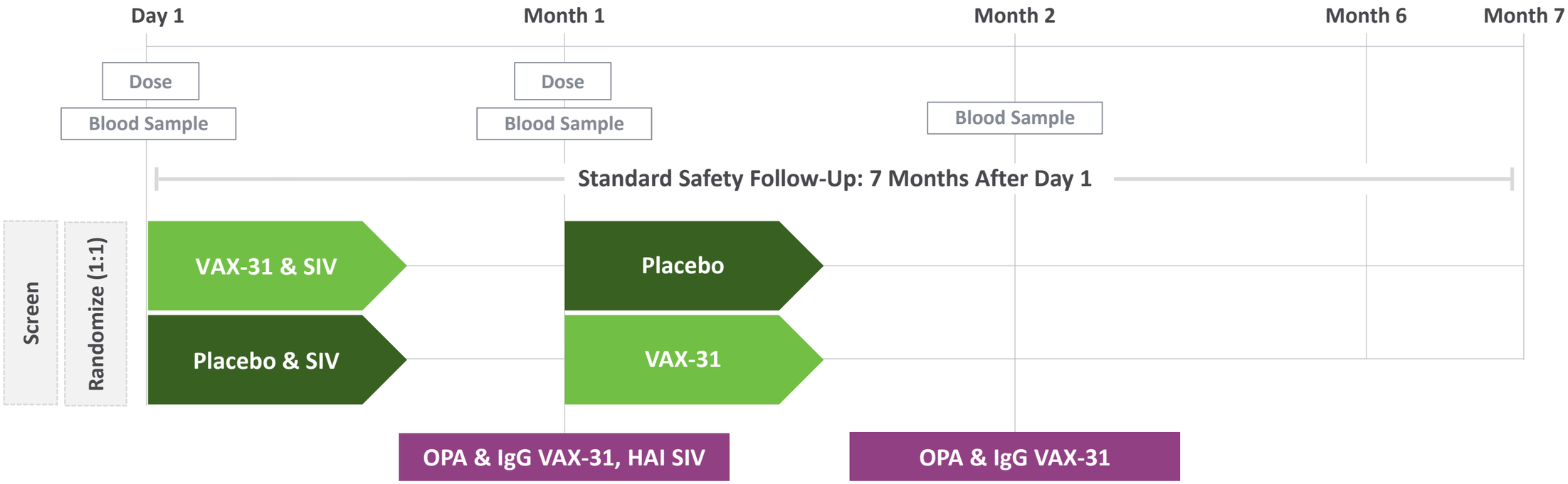
The OPUS-1 results support VAX-31's potential best-in-class profile, serving as cornerstone of the planned BLA, and further validate Vaxcyte's cell-free platform technology.

SoC = standard of care; BLA = Biologics License Application; ST = serotype.
(1) % of IPD caused in individuals ≥50 yrs of age in the U.S. in 2022-2024 based on ABC surveillance data.
(2) Non-bacteremic pneumonia; source: https://doi.org/10.1093/infdis/jiaf376.

OPUS-2 and OPUS-3 Adult Phase 3 Trials

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

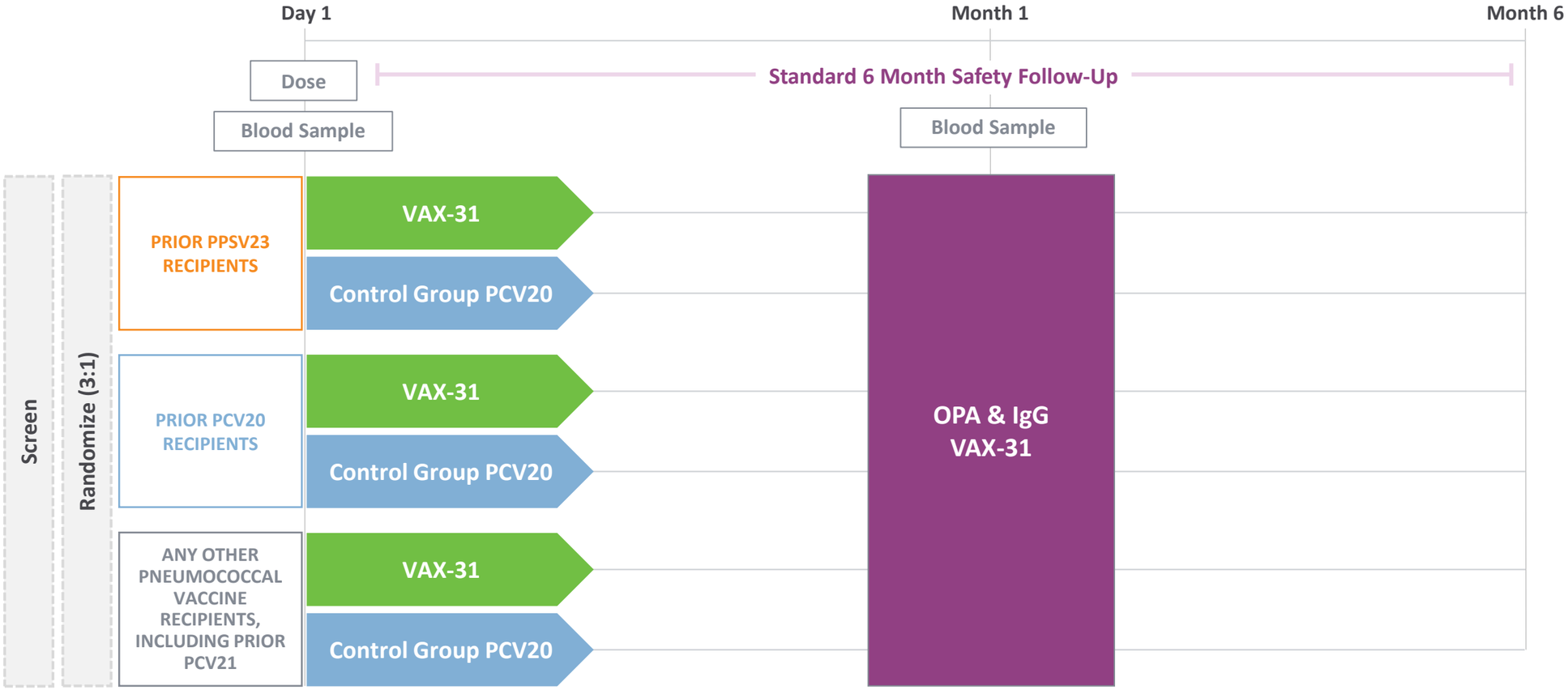


OPA = opsonophagocytic activity, IgG = immunoglobulin G, HAI = hemagglutination inhibition, SIV = seasonal influenza vaccine.

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



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

(1) 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 IMMUNOGENICITY 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 IMMUNOGENICITY 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.

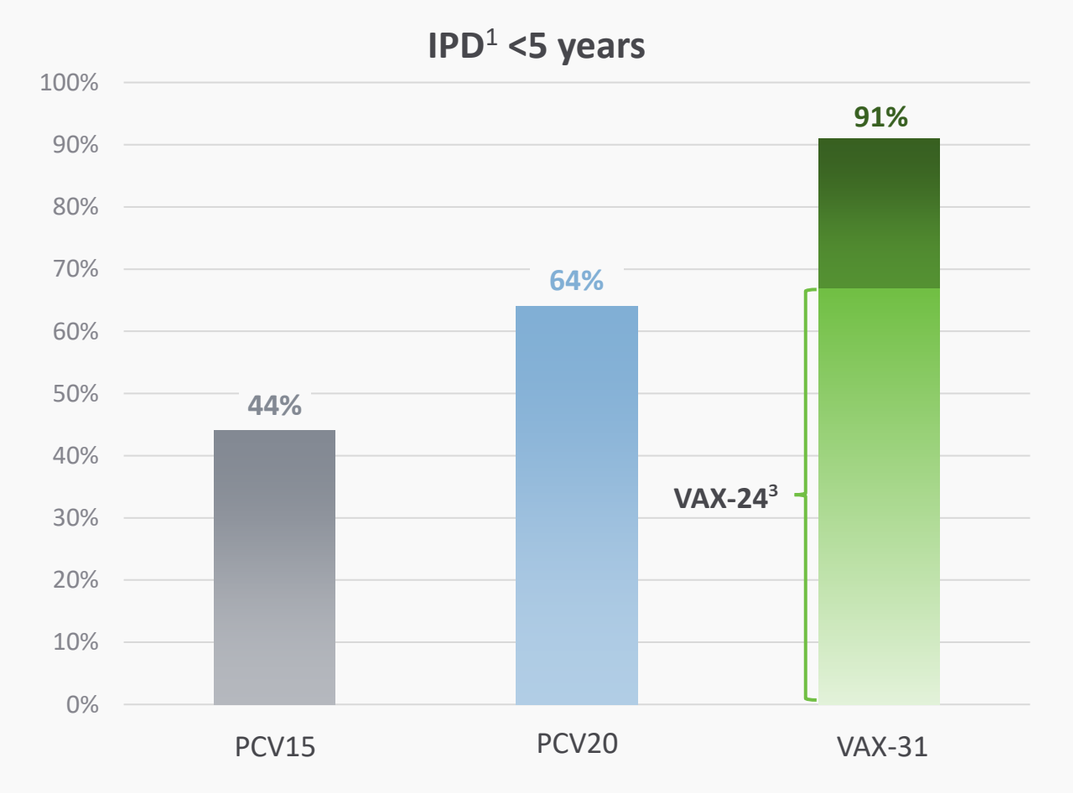
PCV Infant Clinical Program

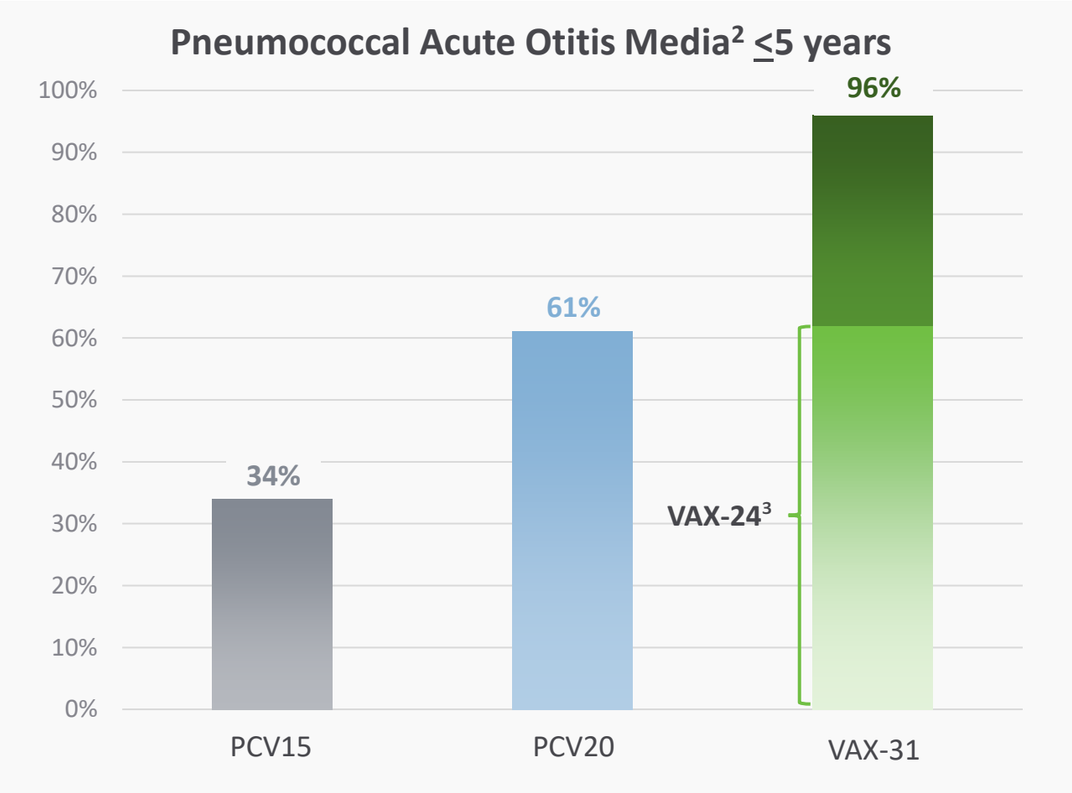
VAXCYTE
protect humankind™



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

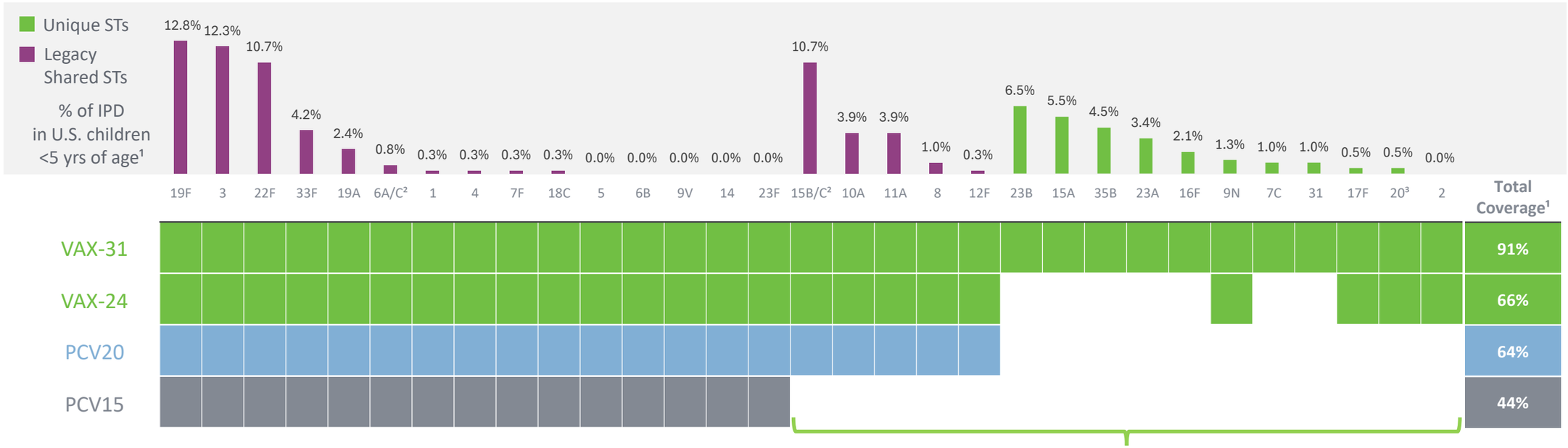




All estimates assume cross-protection between serotypes 6A and 6C and between 15B and 15C.
(1) CDC 2022-2024 Active Bacterial Core (ABC) Surveillance data; IPD cases with missing serotype data were excluded, non-typeable cases were included in the denominator.
(2) In U.S. children five years of age or 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 66% 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 ~91% 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 27-47% MORE IPD COVERAGE COMPARED TO CURRENT STANDARD-OF-CARE INFANT PCVs

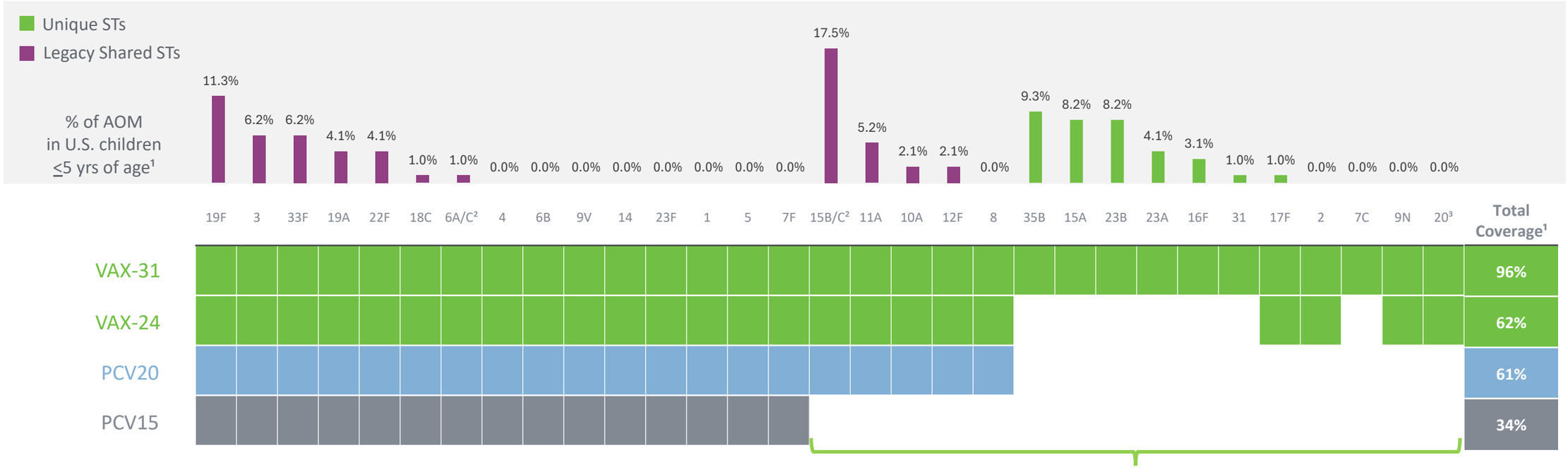
LEGACY SHARED 20 STs: In the infant study, VAX-24 had higher responses on the highest circulating STs (3 & 19F) and while there were some lower relative responses compared to PCV20, they were restricted to a small subset of shared STs with limited residual disease.

(1) % of IPD caused in individuals <5 yrs of age in the U.S. in 2022-2024 based on ABC surveillance 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 0.8% 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-31 Infant Clinical Program



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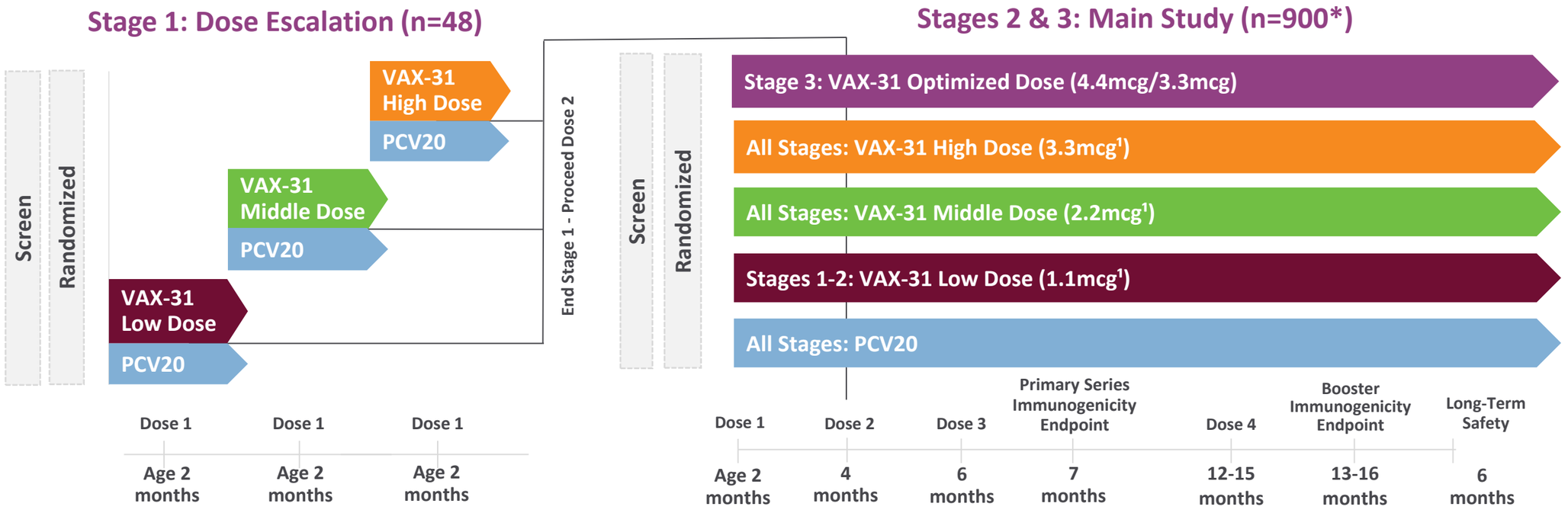
Enrollment Completed in VAX-31 Infant Phase 2 Study

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	

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

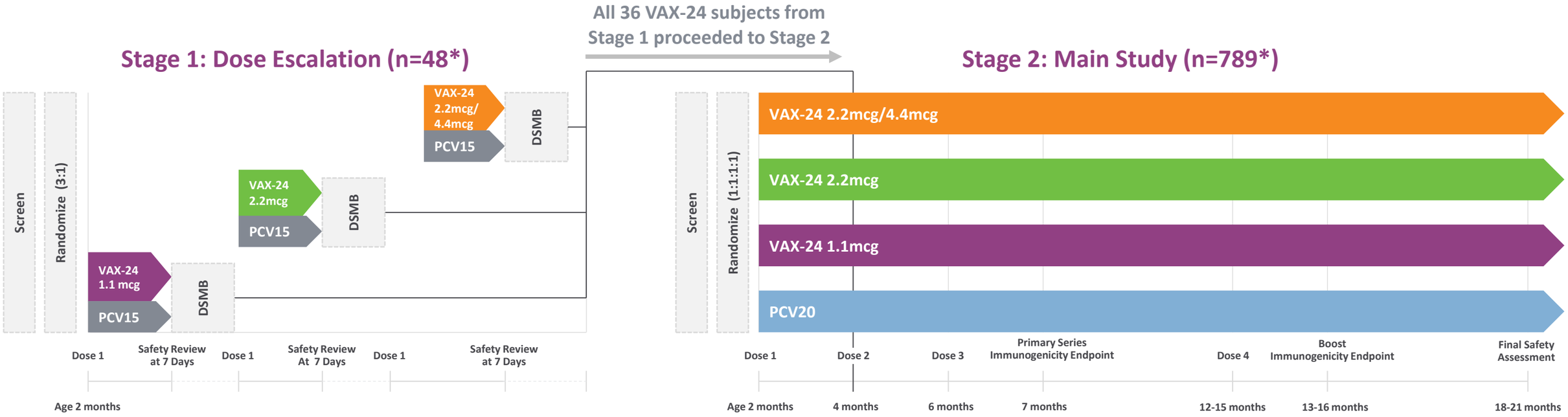
Final VAX-24 Phase 2 Infant Study Results and Platform Demonstrate Potential to Achieve Broadest Coverage of Any Infant PCV On-Market

- **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)

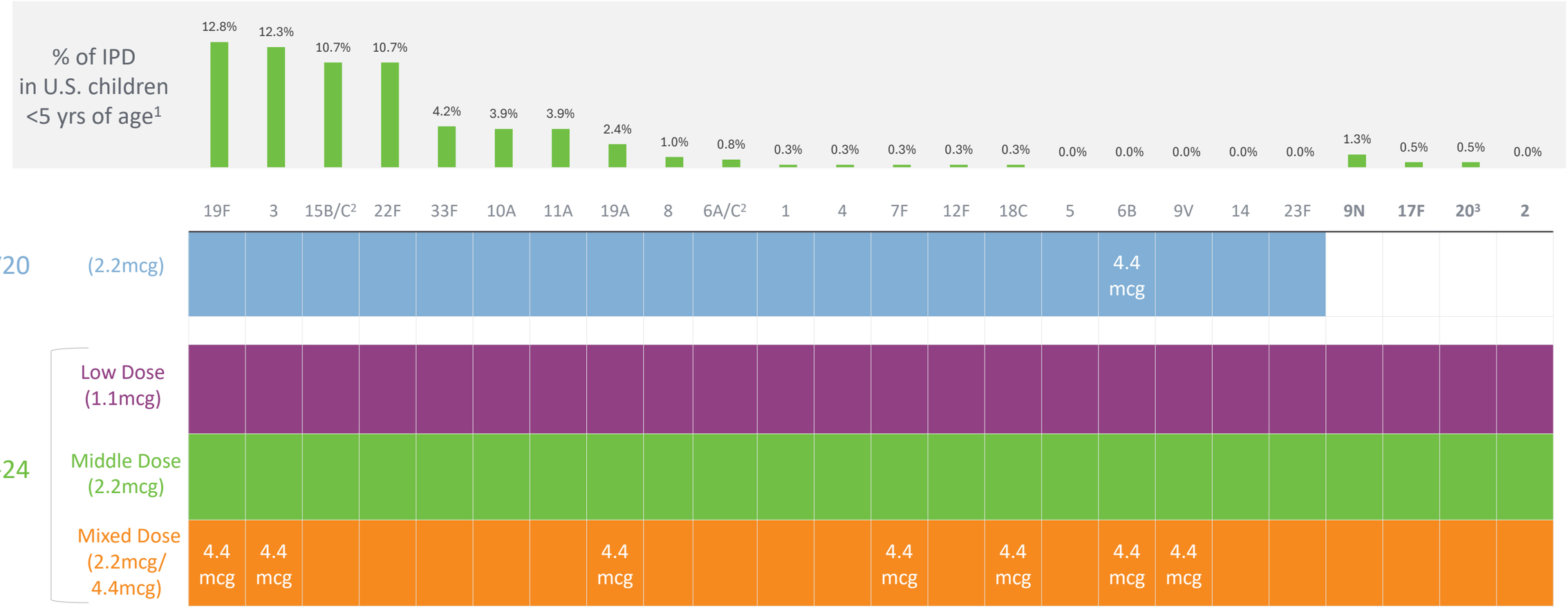
Randomized, Observer-Blind, Active-Controlled, Dose-Finding, Clinical Study to Evaluate Safety, Tolerability and Immunogenicity of VAX-24 vs. Standard-of-Care (PCV20) in 803 Healthy Infants



(*) 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 2022-2024 based on ABC surveillance 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

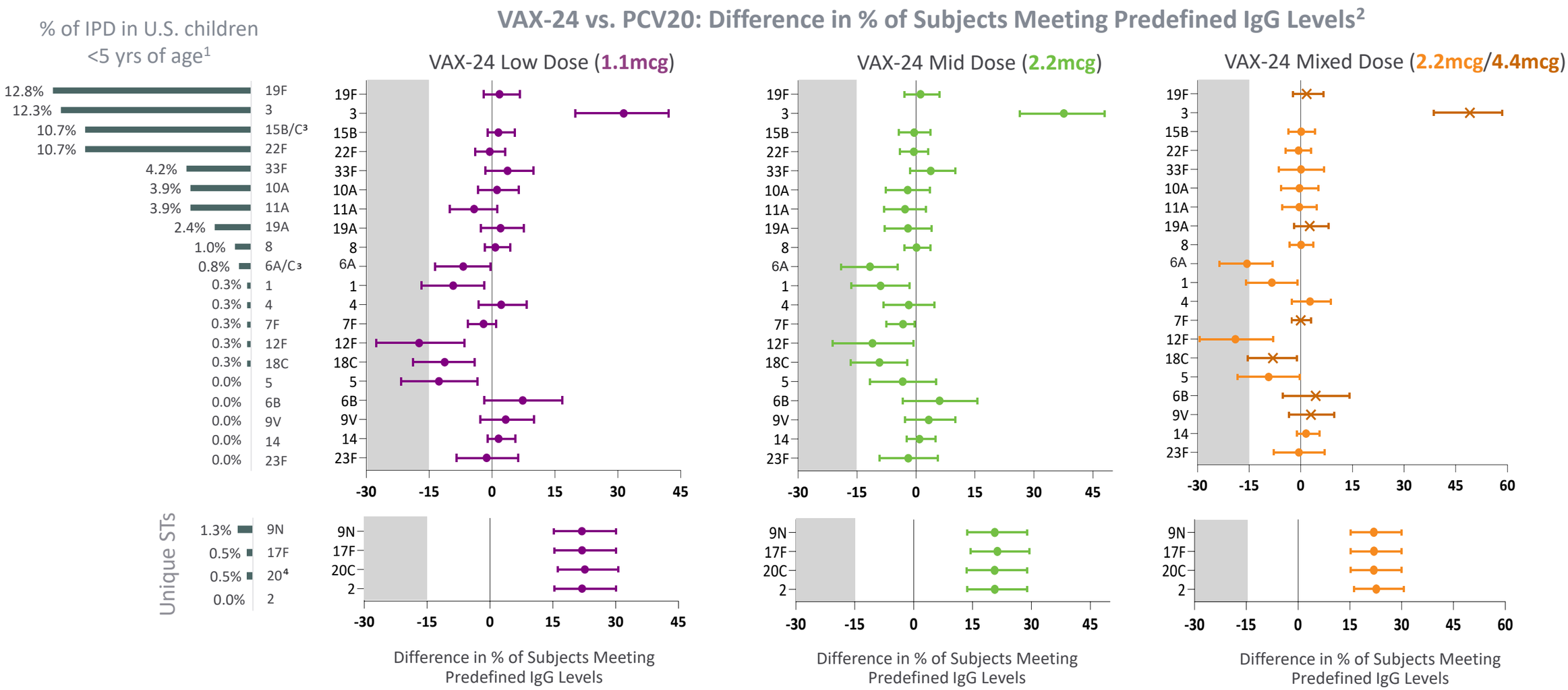
	VAX-24 Low Dose	VAX-24 Mid Dose	VAX-24 Mixed Dose	PCV20
NUMBER OF SUBJECTS	195	186	191	185
Unsolicited TEAE, n (%)	167 (85.6)	161 (86.6)	163 (85.3)	169 (91.4)
Related Unsolicited TEAE, n (%)	6 (3.1)	13 (7.0)	13 (6.8)	6 (3.2)
MAAE, n (%)	172 (88.2)	155 (83.3)	167 (87.4)	161 (87.0)
Related MAAE, n (%)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



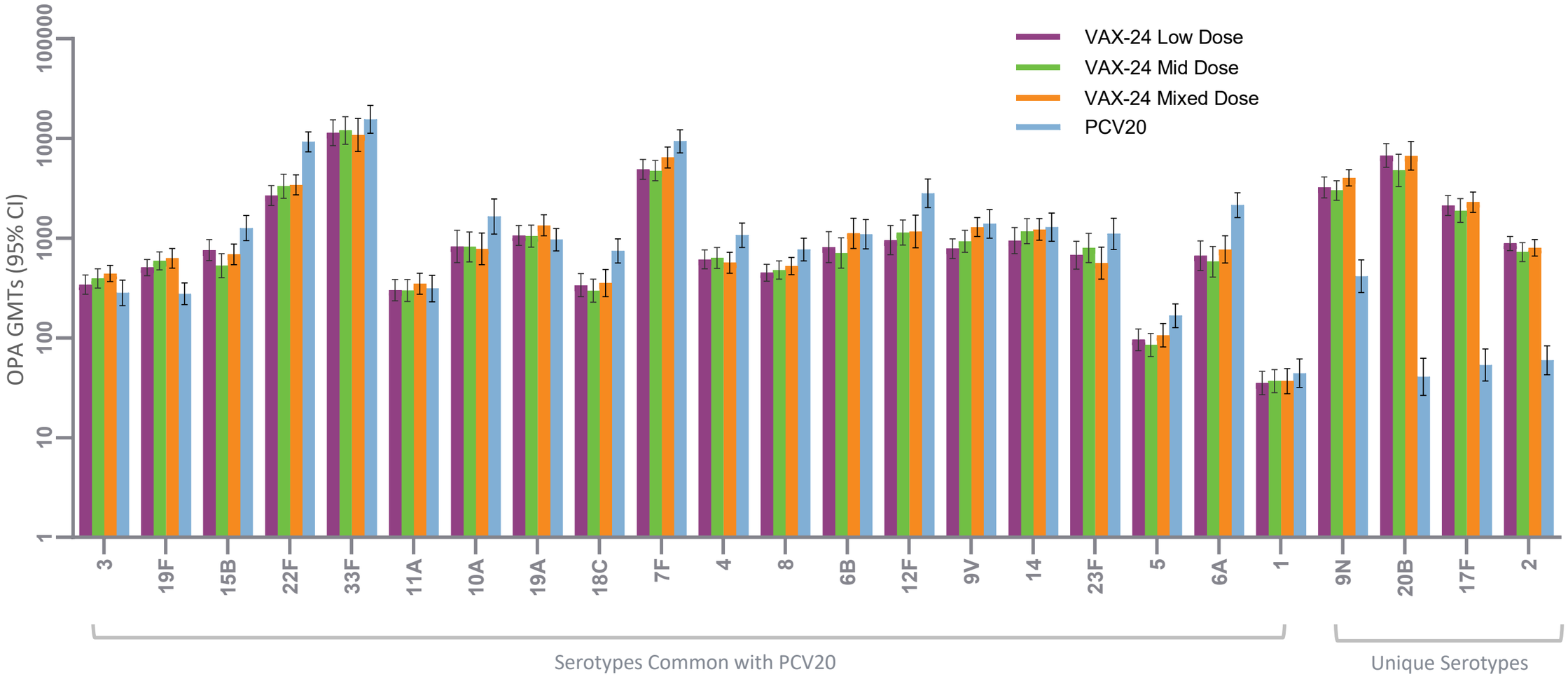
NI = noninferiority; ST = serotype; IgG = immunoglobulin G.

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

(1) % of IPD caused in individuals <5 yrs of age in the U.S. in 2022-2024 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



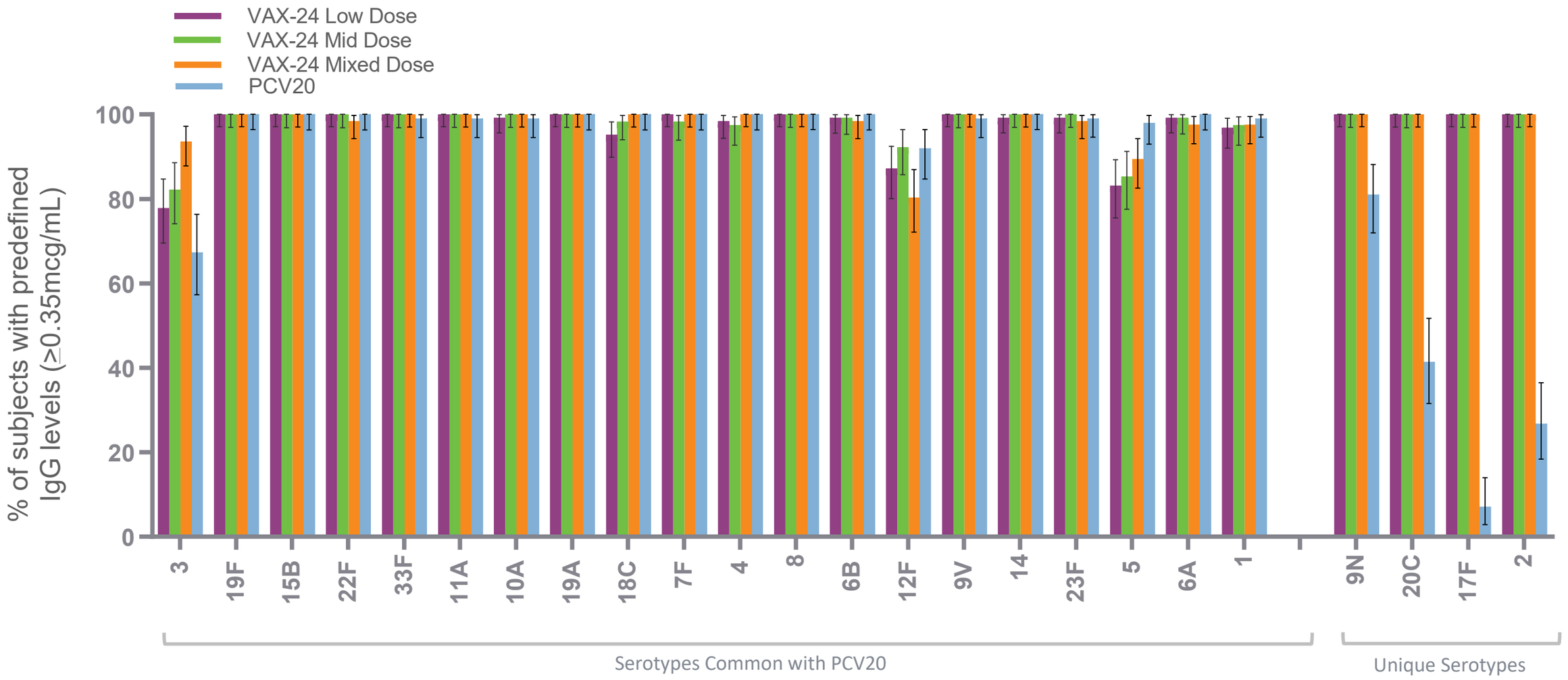
OPA = opsonophagocytic activity; GMT = geometric mean titer; IgG = immunoglobulin G.

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.

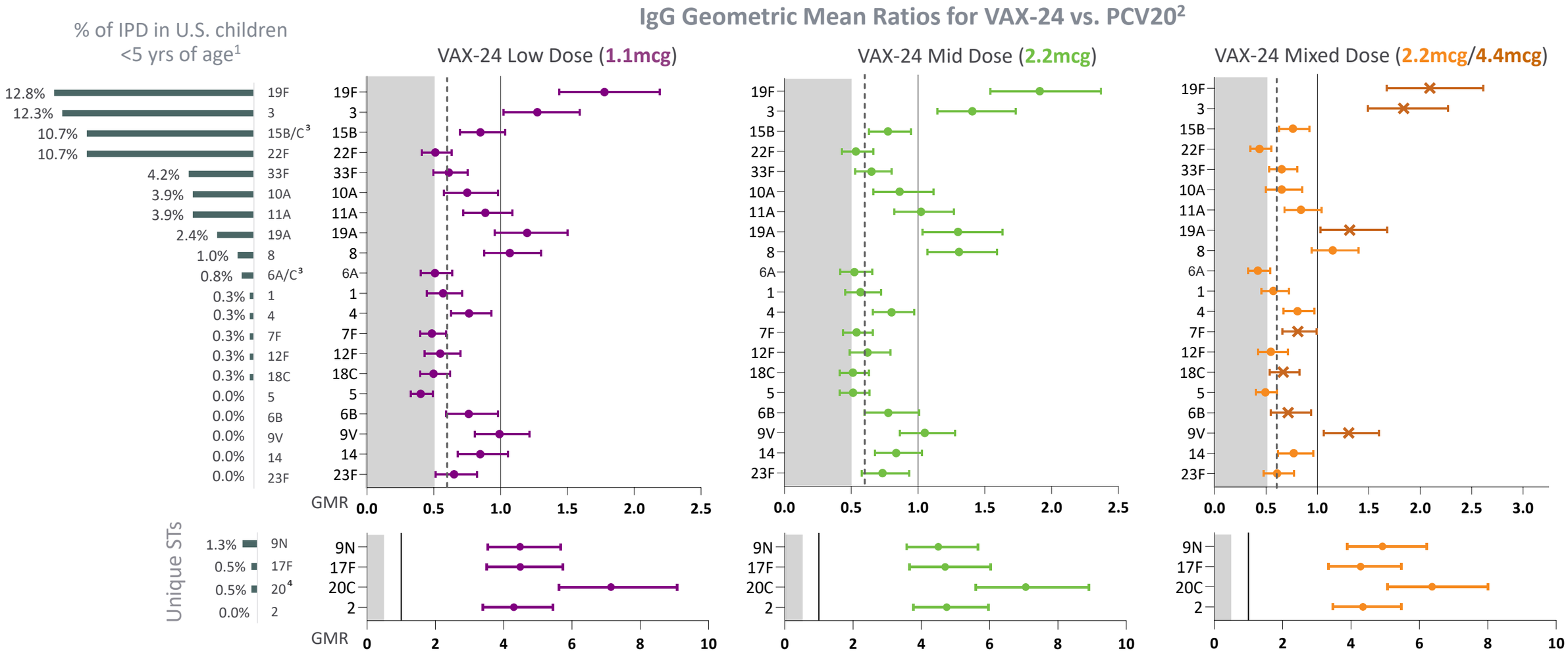
VAX-24 Demonstrated High Overall Seroconversion Rates Across All Doses PD4



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.

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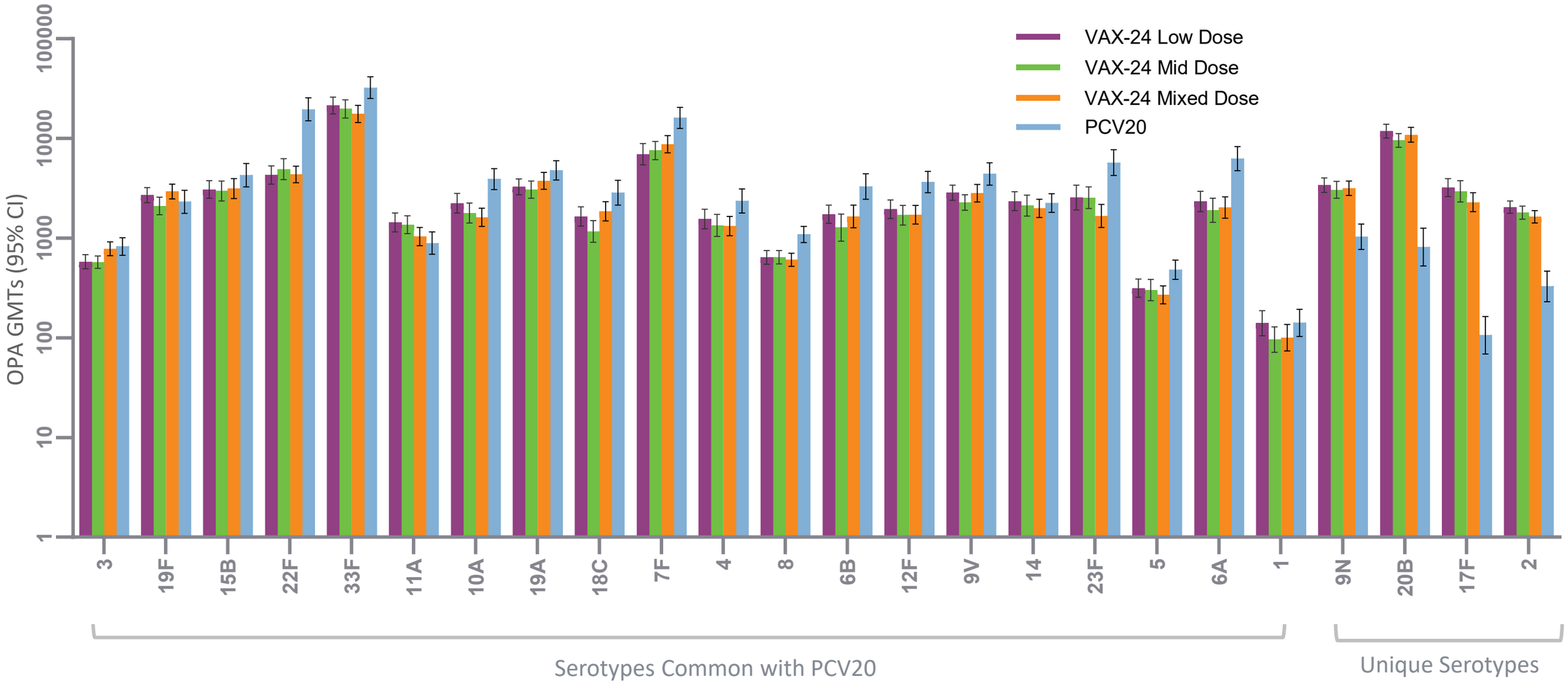
(1) % of IPD caused in individuals <5 yrs of age in the U.S. in 2022-2024 based on ABC surveillance data.
(2) GMRs for unique STs were calculated compared to ST 12F, which is the ST in PCV20 with the lowest GMC Post-Dose 3 (excluding ST 3 or lower responding STs).
(3) Serotypes 6A/6C and 15B/15C are 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 G.

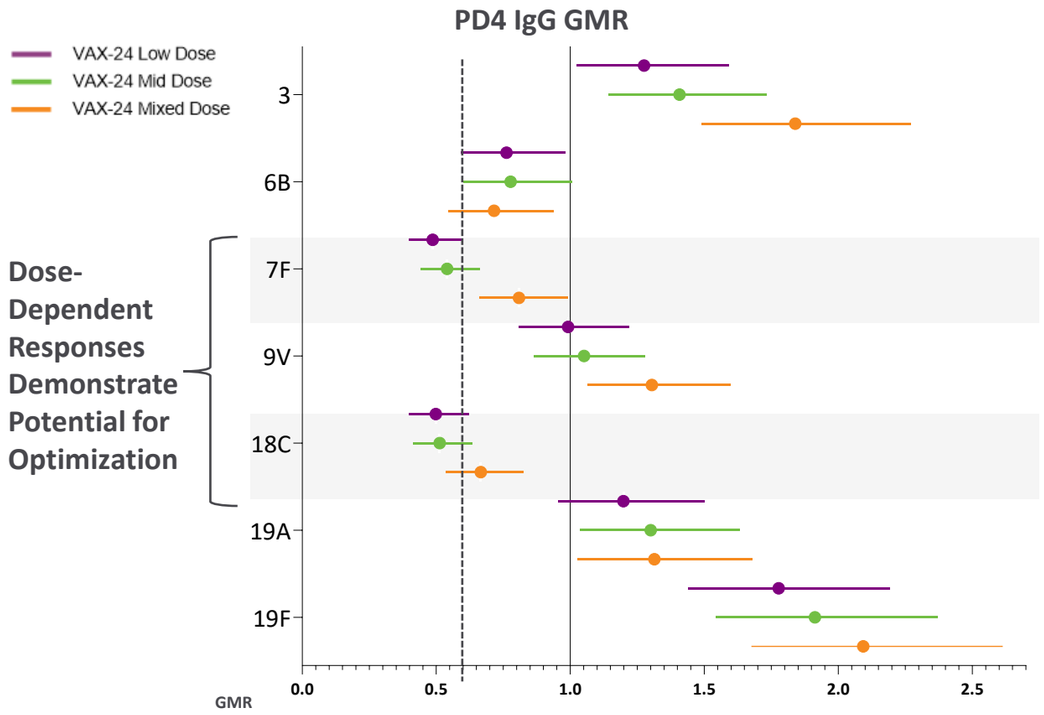
Serotypes 6A/6C and 15B/15C are closely related subtypes for which cross-protection is assumed.
The serogroup 20 antigen contained in VAX-24 and VAX-31, formerly known as a 20B variant, has been officially reclassified as 20C. For additional details on serogroup 20, please see footnote 2 on slide 15. Serotype 20B was studied in this OPA analysis.

Expanded Analysis of Dose-Dependent Immune Responses

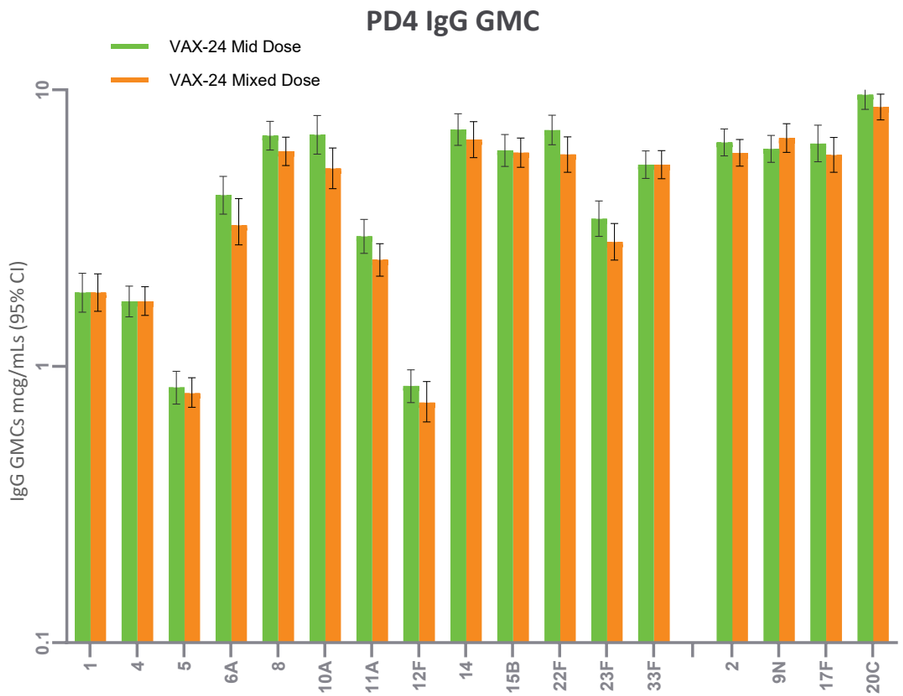
Dose Response Evidenced PD4 Across Most Serotypes

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 G.

(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.

Group A Strep Opportunity & VAX-A1 Clinical Program

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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 RESPONSIBLE 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]



Antibiotic resistance to Group A Strep has increased over the past decade[3], leading the CDC to categorize the disease as a concerning threat[4]

(1) https://academic.oup.com/cid/article/77/6/917/7180116.
(2) https://academic.oup.com/cid/article/74/6/983/6311854?login=false.
(3) https://jamanetwork.com/journals/jama/fullarticle/2832277.
(4) https://arpsp.cdc.gov/artr/antimicrobial-resistance-threats.

Group A Strep Infection Rates Have Increased Substantially

HIGH GROUP A STREP CASE COUNTS AND RISING ANTIBIOTIC RESISTANCE

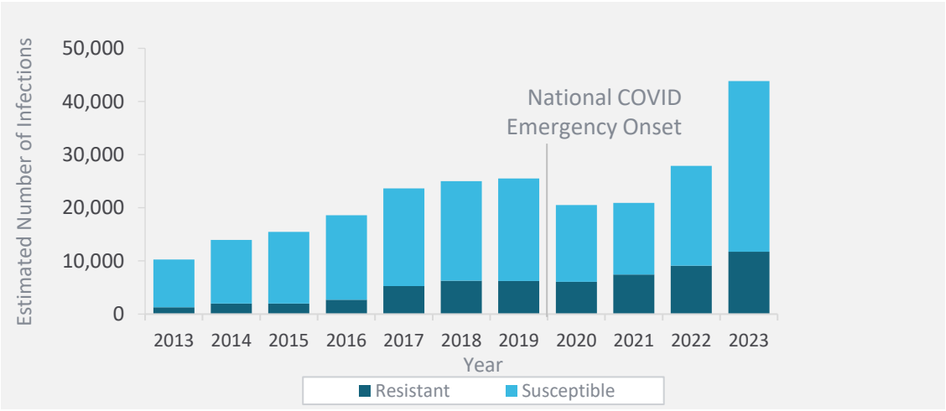
BETWEEN 2013 AND 2023, THE ESTIMATED NUMBER OF GROUP A STREP:

Invasive infections increased **~4×**

Drug-resistant invasive infections increased **~10×**

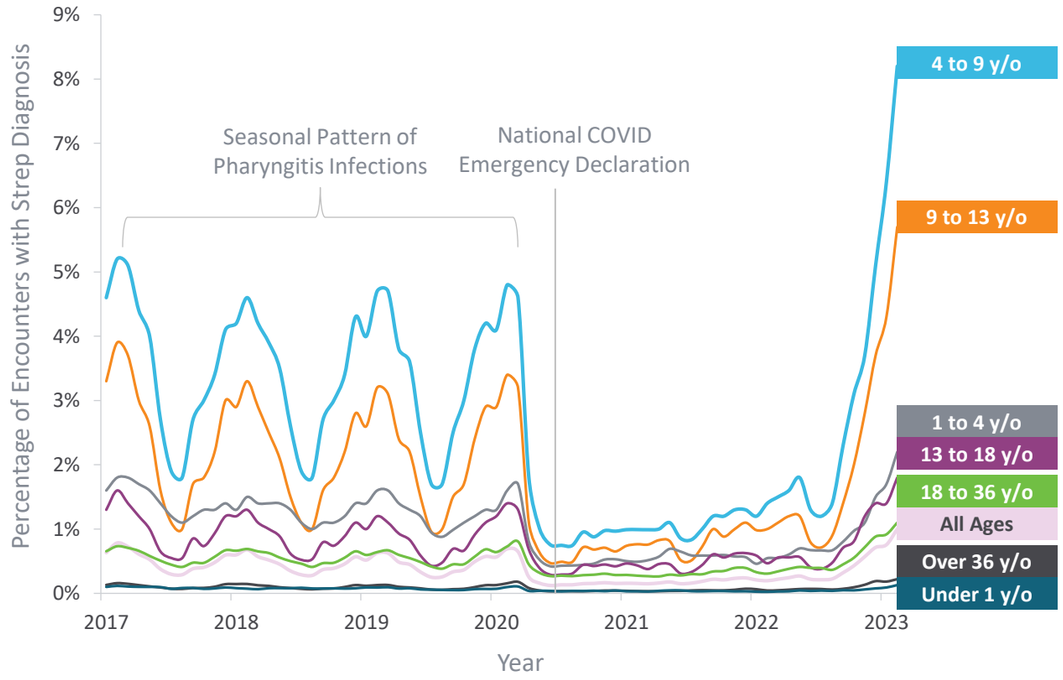
2023 saw the highest count reported to date; 2024 and 2025 CDC case rates elevated, yet showing signs of post-COVID emergency stabilization[2]

Invasive Group A Strep Infections by Resistance in the U.S.[3]



SIGNIFICANT INCREASE IN PHARYNGITIS RATES POST-COVID PANDEMIC IN THE U.S.[1]

Percentage of Encounters for Pharyngitis by Age in the U.S.[1]



(1) 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.
(2) https://pmc.ncbi.nlm.nih.gov/articles/PMC12388776/.
(3) https://arpsp.cdc.gov/artr/GAS.

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

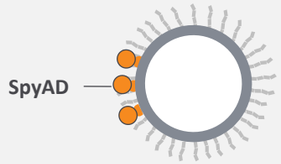
VAX-A1 IS DESIGNED TO:

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					

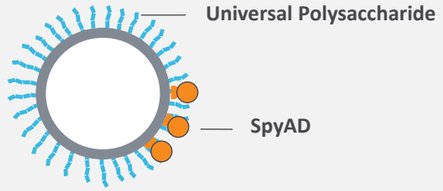
(1) https://www.nature.com/articles/s41541-023-00690-2.pdf.
(2) *SpyAD = S. pyogenes adhesion and division protein; GAC^{PR} = modified Group A carbohydrate.*

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

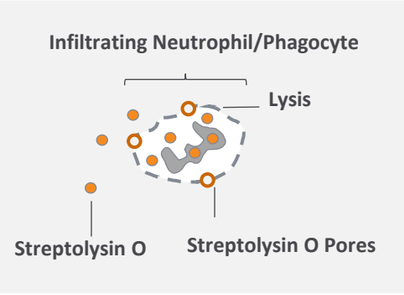


GAC^{PR} is comprised of a Polyrhamnose (PR) backbone, which has been designed to remove potentially cross-reactive epitopes associated with autoimmune complications

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)

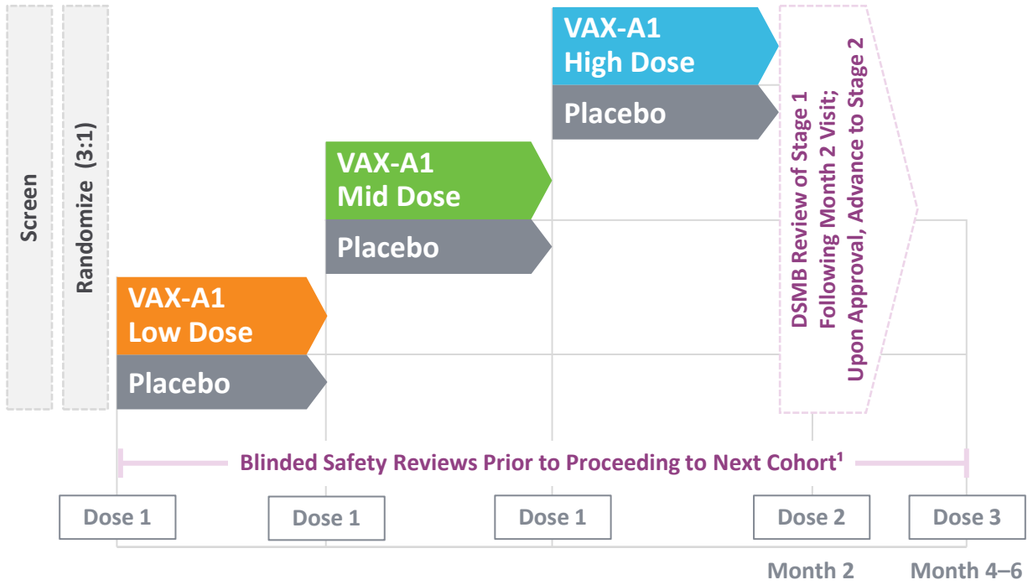
Surface-expressed antigen that cleaves human C5a complement protein, which delays recruitment of phagocytes to the site of infection and alters clearance and trafficking of Group A Strep



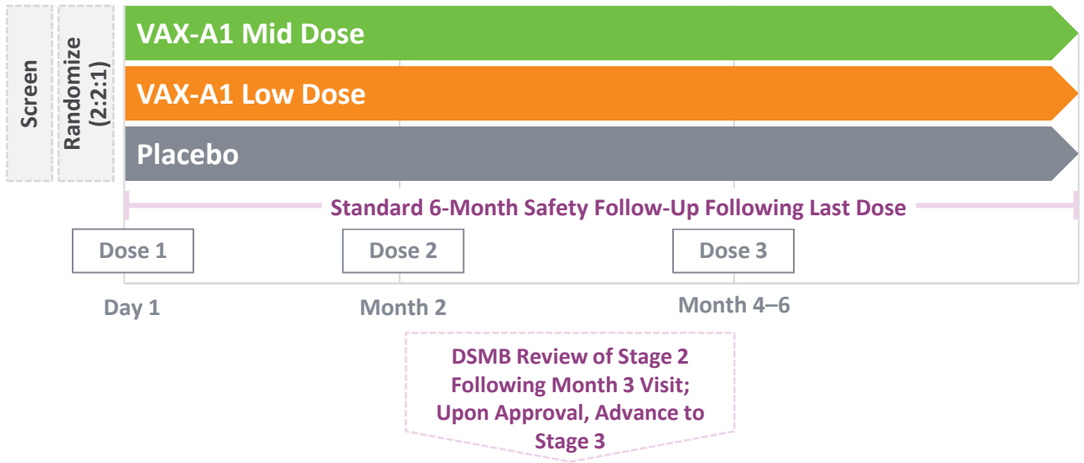
(1) SpyAD = S. pyogenes adhesion and division protein; GAC^{PR} = modified Group A carbohydrate.

Phase 1, 3-Stage, Dose-Escalation Study Evaluating VAX-A1 in Adults Aged 18-40 (n~80) Advancing to Stage 2

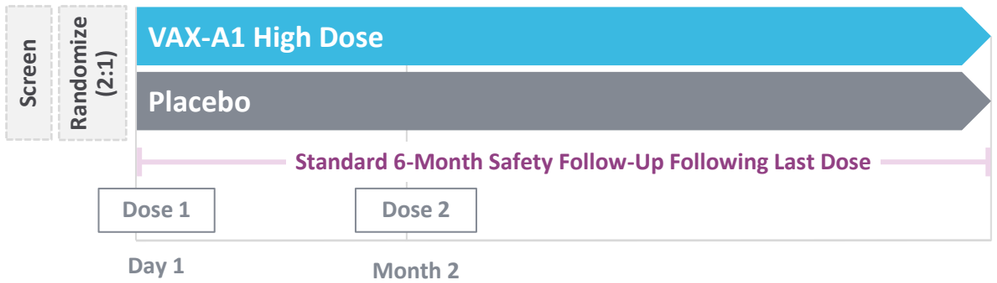
Stage 1: Dose Escalation



Stage 2: Low and Mid Dose Expansion



Stage 3: High Dose Expansion



Primary Objectives: safety and tolerability assessed through end of study participation, including solicited local and systemic AEs and laboratory abnormalities (7 days after each dose), unsolicited AEs (30 days after each dose), and SAEs, MAAEs, NOCIs, AESIs[2] and AEs leading to discontinuation (through end of study)

Secondary Objectives: antigen-specific immune responses assessed for each VAX-A1 antigen[3] and dose level at baseline, 1 month after each dose, and 6 months after last dose, including serum IgG GMT, GMFR from baseline, percentage of participants with ≥2-fold increase from baseline, and percentage of participants with serum IgG ≥ LLOQ

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

SAEs = serious adverse events; MAAEs = medically attended adverse events; NOCIs = new onset chronic illnesses; AEs = adverse events; AESIs = adverse events of special interest; GMT = geometric mean titer; GMFR = geometric mean fold rise; LLOQ = lower limit of quantification.
(1) 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.
(2) Includes acute rheumatic fever, acute carditis and acute glomerulonephritis. (3) VAX-A1 antigens include SLO, ScpA, SpyAD and GAC^{PR}.

Shigella: VAX-GI Preclinical Program

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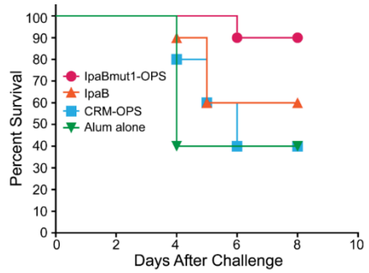
VAX-GI: Shigella Vaccine Program

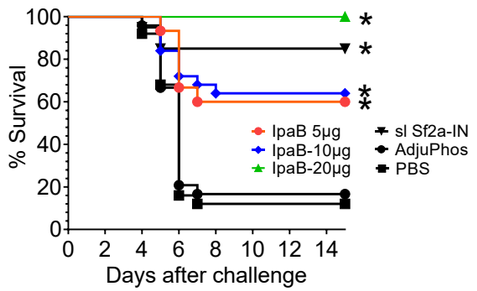
Novel Shigella Vaccine to Prevent Widespread Global Morbidity & Mortality, Particularly in Children

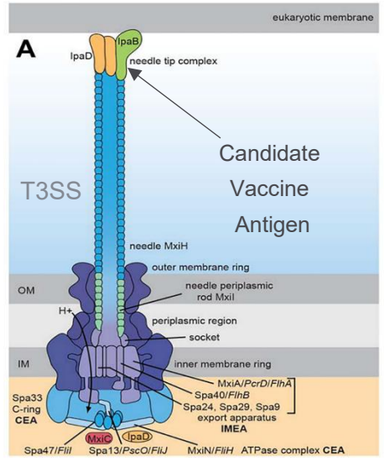
UNMET NEED	• Shigella is a bacterial illness with no available preventative treatment • Estimated to cause 80-165 million cases of disease and 600,000 deaths annually, and most cases and deaths are among children[1] • With the aim of reducing morbidity and mortality due to the disease, the World Health 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

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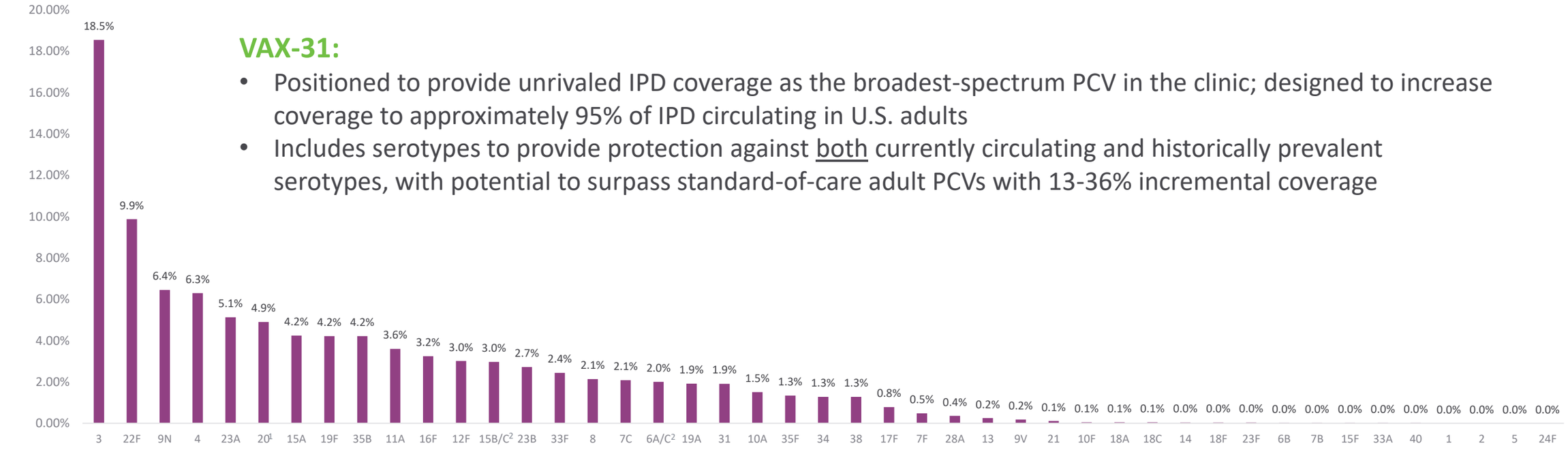
- Large Market Opportunity for Broadest-Spectrum PCV in the Clinic
- Cell-Free Protein Synthesis Enabled Pipeline
- Aligned Critical Commercial Manufacturing and Supply Chain Resources
- Robust Pipeline with Multiple Novel Vaccines

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 in the clinic; 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 13-36% incremental coverage



Total IPD Coverage (U.S. %)[3]
69%
34%
46%
59%
82%
95%

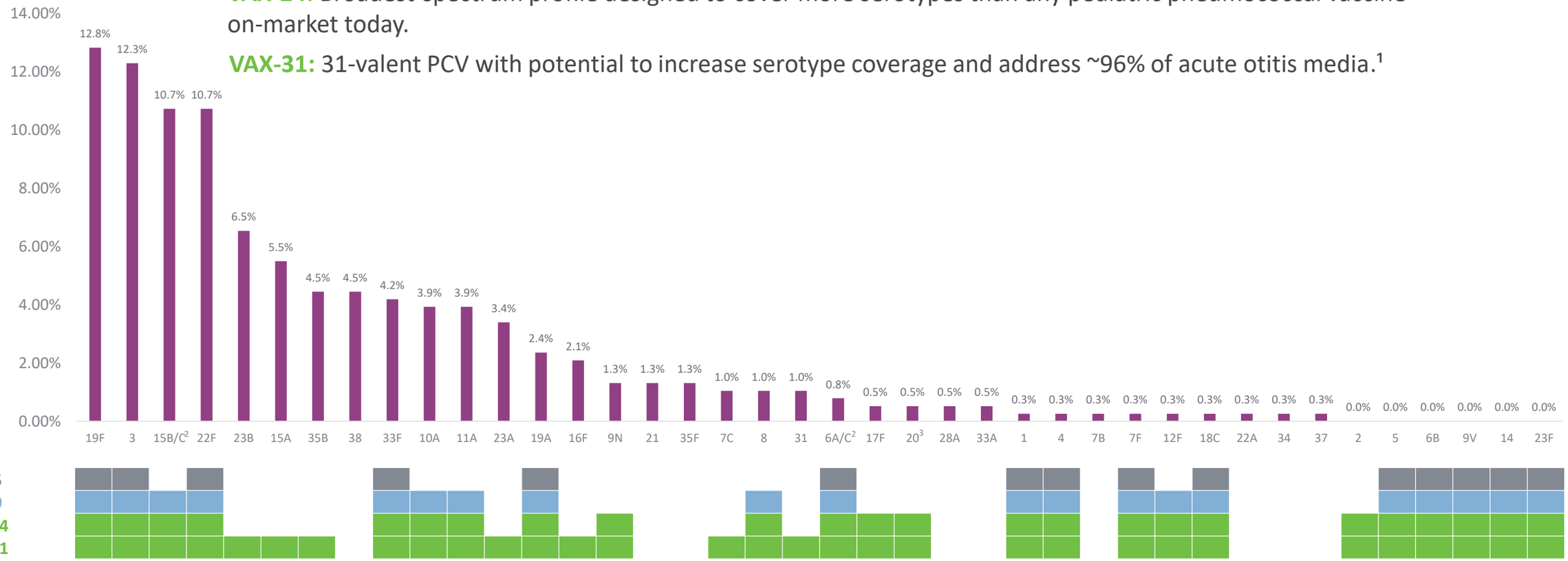
(1) The serogroup 20 antigen contained in VAX-24 and VAX-31, formerly known as a 20B variant, has been officially reclassified as 20C. For additional details on serogroup 20, please see footnote 2 on slide 15.
(2) 15C coverage due to cross-reaction against 15B. 6C coverage due to cross-protection by 6A.
(3) % of IPD caused in individuals ≥50 yrs of age in the U.S. in 2022-2024 based on ABC surveillance data.

Spectrum of Coverage Drives Adoption in Vital Pediatric Population

Pediatric Segment Represents Majority of ~$8.5B 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]

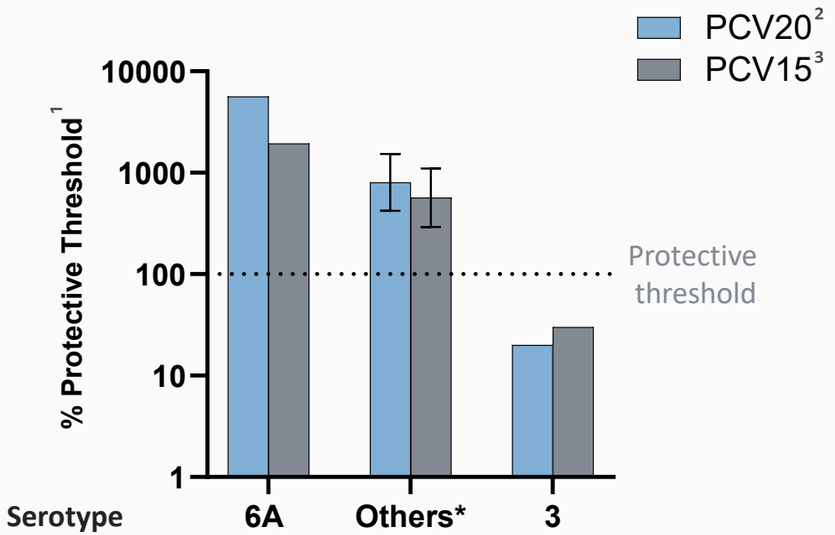


Total IPD Coverage (U.S. %)[4]
44%
64%
66%
91%

(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 0.8% 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 2022-2024 based on ABC surveillance data.

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

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

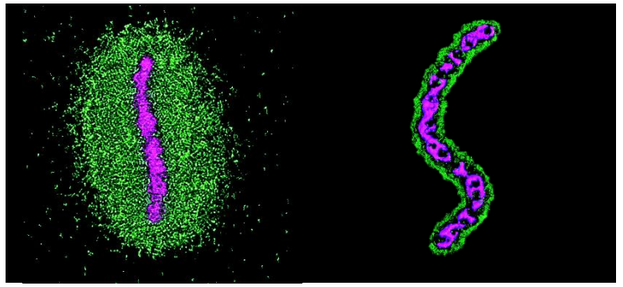


ST3 REMAINS AN OUTLIER AS CIRCULATION HAS NOT BEEN EFFECTIVELY CONTROLLED BY VACCINATION

KEY FACTORS DETERMINE WHY ST3 REQUIRES HIGHER LEVEL OF PROTECTIVE ANTIBODY

- **Thick Polysaccharide Capsule:** serotype 3 forms a robust physical barrier that impairs opsonization and phagocytosis, requiring higher antibody levels for effective coating
- **Capsule Shedding & Antibody Neutralization:** serotype 3 releases free polysaccharides that bind and neutralize antibodies before they reach the bacterial surface

Serotype 3 Typical *S. pneumoniae*



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

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(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.*

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