

# Corporate Presentation



January 2025

**VAXCYTE**  
*protect humankind™*

# Forward-Looking Statements

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This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements related to the potential benefits of Vaxcyte's vaccine candidates, including breadth of coverage and the ability to deliver potentially better immune responses, a potentially best-in-class pneumococcal conjugate vaccine (PCV) franchise and the improvement upon the standard-of-care; demand for Vaxcyte's vaccine candidates; the design, timing of initiation, progress and expected results of Vaxcyte's preclinical studies, clinical trials and research and development plans (including, but not limited to, the design, timing and availability of data for the VAX-24 and VAX-31 infant Phase 2 studies; the timing and availability of data for the VAX-31 adult Phase 3 studies; and the announcement of guidance for VAX-A1); 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; Vaxcyte's ability to establish global commercial manufacturing capacity for its PCV candidates; the ability of Vaxcyte to commercialize VAX-24 and VAX-31 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 potential conversion by the pneumococcal vaccine market to a prime-boost schedule; the market opportunity for Vaxcyte's vaccines; Vaxcyte's expectations regarding the potential benefits, spectrum coverage, clinical or regulatory pathways, adoption speed and immunogenicity of its vaccine candidates 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 5, 2024 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.

The background of the slide is a green-tinted microscopic image showing several large, spherical bacteria with a textured, wrinkled surface. There are also smaller, similar-looking spheres scattered throughout the field of view.

## 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

## Positive Phase 1/2 Adult Data for VAX-31 and VAX-24 Validate Potential of Site-Specific, Carrier-Sparing Platform



### POTENTIAL BEST-IN-CLASS PCV FRANCHISE

- **Scalable, site-specific platform** enabling broader-spectrum carrier-sparing PCVs
- **Adult Indication**
  - **VAX-31:** Advancing to Phase 3 program based on the positive Phase 1/2 data; received FDA Breakthrough Therapy designation
  - Broadest-spectrum PCV in clinic; designed to cover >95% of IPD, including currently circulating and historically prevalent strains, in U.S. adults aged 50 and older
- **Pediatric Indication: VAX-24 and VAX-31 advancing in parallel**
  - **VAX-24:** Enrollment complete in Phase 2 infant study
  - **VAX-31:** Enrolling subjects in Phase 2 study



### HIGHLY ATTRACTIVE PCV MARKET

- **Well-defined ~\$8B market segment poised for substantial growth**
  - **Age range in US expanded to include adults ≥ 50 years of age;** and
  - As more developed countries adopt or expand **universal vaccination of adults**
- Leverages established surrogate immune endpoints as basis for full approval, **negating need for field efficacy studies**
- Serotype and disease spectrum of coverage is the **primary adoption driver**, yet incumbents **limited by carrier suppression**



### EXCLUSIVE CELL-FREE PLATFORM

- **Vaxcyte PCV Franchise**
  - Leverages **site-specific conjugation** to expose protective T- and B-cell antigens
  - Enables **carrier-sparing** conjugates that honor well-understood PCV MOA
- Permits production of **“tough-to-make” antigens**
- **Platform unlocks large market opportunities**
  - **VAX-A1:** Novel Group A Strep vaccine
  - **VAX-PG:** Novel periodontitis vaccine
  - **VAX-GI:** Novel Shigella vaccine



### ALIGNED CRITICAL RESOURCES

- **Strategic alignment with Lonza**
  - Global commercial manufacturing agreement to produce VAX-31 and VAX-24 key components
  - Building out capacity to satisfy global PCV demand for commercial markets
- **Seasoned management team, directors and advisors**
- **\$3.3 billion in cash, cash equivalents and investments** as of 9/30/24

SOC = Standard-of-Care, IPD = Invasive Pneumococcal Disease, MOA = Mechanism of Action.

# Experienced Team with Track Record in Vaccines and Biopharma

## Management Team

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



**Andrew Guggenime, MBA**  
President & CFO



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



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



**Sally Bolmer**  
SVP Regulatory Affairs



**Harp Dhaliwal, MBA**  
CTO

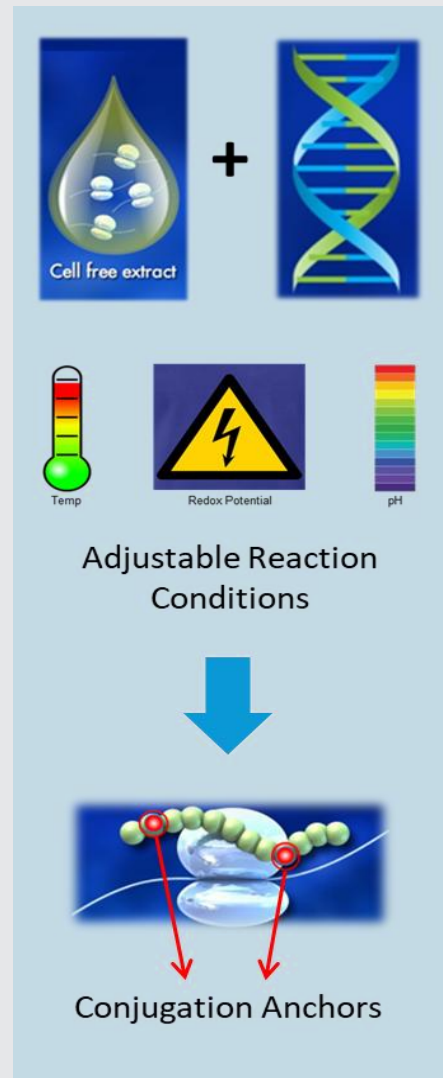


**Mark Wiggins, MBA**  
CBO



# Cell-Free Protein Synthesis Platform Unlocks Multiple Vaccine Applications

Design and Produce Proteins Beyond Reach of Conventional Methods



## CELL-FREE PROTEIN SYNTHESIS

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

## SPEED, FLEXIBILITY, SCALABILITY

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

## SUPERIOR CONJUGATE VACCINES

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

## NOVEL PROTEIN VACCINES

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



# Pipeline of High-Fidelity Vaccines

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



# Clinical Development Next Steps and Anticipated Milestones

## Potential Best-in-Class PCV Franchise for Adult and Infant Segments

Population	Investigational PCV	Key Anticipated Milestones
 <b>Adults</b>	<b>VAX-31</b> <b>31-valent PCV candidate</b>	<ul style="list-style-type: none"><li>• Following FDA End-of-Phase 2 meeting, initiate Phase 3 pivotal, non-inferiority study by mid-2025 and announce topline safety, tolerability and immunogenicity data in 2026<sup>(1)</sup>.</li><li>• Initiate remaining Phase 3 studies in 2025 and 2026<sup>(1)</sup>.</li></ul>
 <b>Infants</b>	<b>VAX-24</b> <b>24-valent PCV candidate</b>	<ul style="list-style-type: none"><li>• Announce topline safety, tolerability and immunogenicity data from primary three-dose immunization series of Phase 2 study, which is fully enrolled with 802 healthy infants, by end of 1Q:2025<sup>(2)</sup>, followed by topline data from booster dose by end of 2025<sup>(1)</sup>.</li></ul>
	<b>VAX-31</b> <b>31-valent PCV candidate</b>	<ul style="list-style-type: none"><li>• Announce topline safety, tolerability and immunogenicity data from primary three-dose immunization series of Phase 2 study, which is enrolling subjects, in mid-2026, followed by topline data from booster dose approximately nine months later<sup>(2)</sup>.</li></ul>

1. Guidance as of November 12, 2024.  
2. Guidance as of December 3, 2024.



# PCV Opportunity

# Global Health Impact of Pneumococcal Disease Remains Significant



## ABOUT STREPTOCOCCUS PNEUMONIAE

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

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



## CURRENT ~\$8 BILLION GLOBAL VACCINE CATEGORY

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

Routine SOC schedule in the U.S.:

- Infants :
  - Prevnar 20<sup>®</sup> (PCV20) x 4 doses; or
  - Vaxneuvance<sup>®</sup> (PCV15) x 4 doses
- Adults aged 50 and older (single dose):
  - PCV20 or Capvaxive<sup>™</sup> (PCV21); or
  - PCV15 & Pneumovax<sup>®</sup> 23 (PPV23)



## GLOBAL INCIDENCE & IMPACT OF PD STILL SUBSTANTIAL

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

- In the U.S. alone, over 150K hospitalizations occur annually<sup>3</sup>
- *Streptococcus pneumoniae* is the leading cause of vaccine preventable deaths globally in children under five<sup>4</sup>
- ~300k children under five years old die annually worldwide due to *Streptococcus pneumoniae*<sup>5</sup>

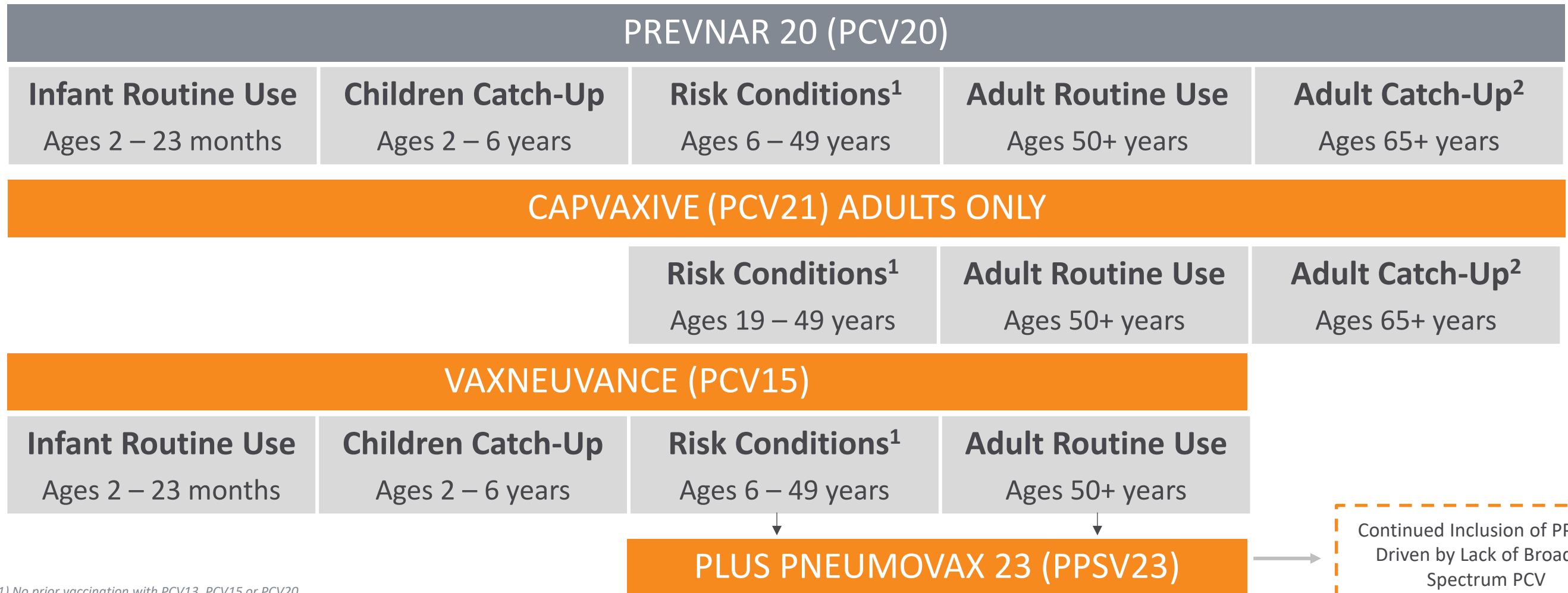
(1) <https://www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/>, (2) <https://www.cdc.gov/pinkbook/hcp/table-of-contents/chapter-17-pneumococcal-disease.html>.

(3) GBD 2019 Diseases and Injuries Collaborators. *Lancet* 2020; 396: 1204-22. Supplementary Appendix 2.

(4) <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8677503/table/T2/>, <https://www.cdc.gov/pneumococcal/php/surveillance/index.html#:~:text=Global%20trends,deaths%20occur%20in%20developing%20countries>.

# ACIP Recommendations Reinforce Need for Broader-Spectrum PCVs

## Advisory Committee on Immunization Practices (ACIP) Pneumococcal Vaccine Recommendations



(1) No prior vaccination with PCV13, PCV15 or PCV20.

(2) Shared clinical decision-making is recommended regarding use of a supplemental PCV21 or PCV20 dose for adults aged ≥65 years who have completed their recommended vaccine series with both PCV13 and PPSV23.

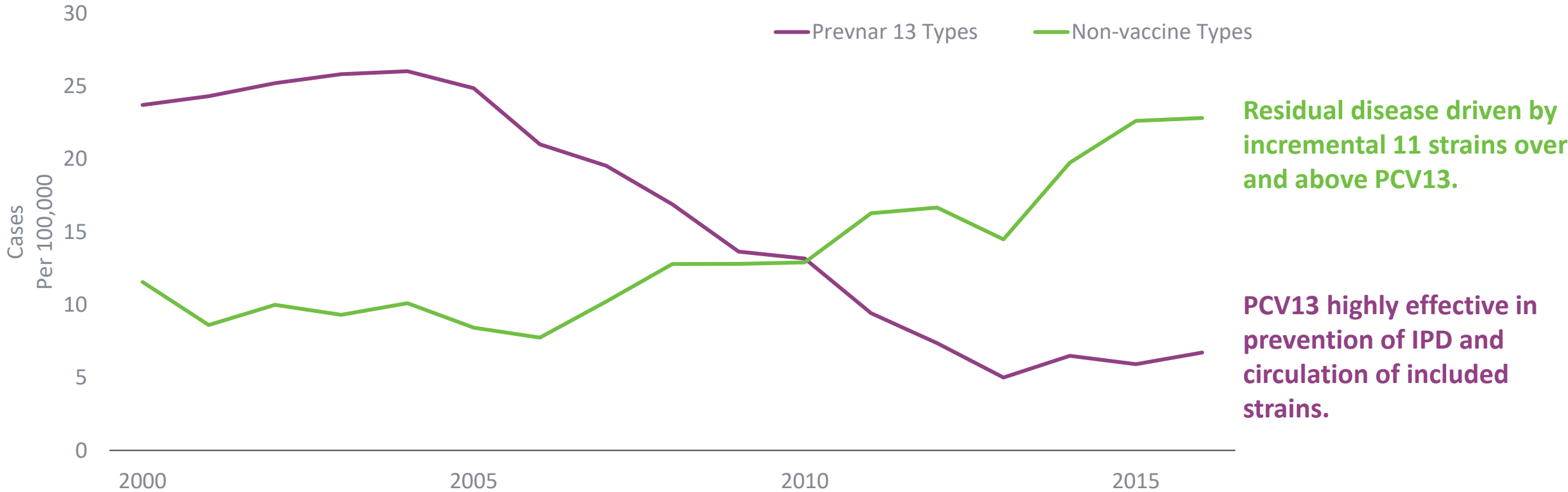
Sources: 1. <https://stacks.cdc.gov/view/cdc/133252>, 2. [https://www.cdc.gov/pneumococcal/hcp/vaccinerecommendations/index.html?CDC\\_AA\\_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fvpd%2Fpneumo%2Fhcp%2Frecommendations.htm](https://www.cdc.gov/pneumococcal/hcp/vaccinerecommendations/index.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fvpd%2Fpneumo%2Fhcp%2Frecommendations.htm),

(3) <https://www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/>, 4. <https://www.cdc.gov/mmwr/volumes/72/rr/rr7203a1.htm>.

# Serotype Replacement Drives Need for Broader-Spectrum Vaccines

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

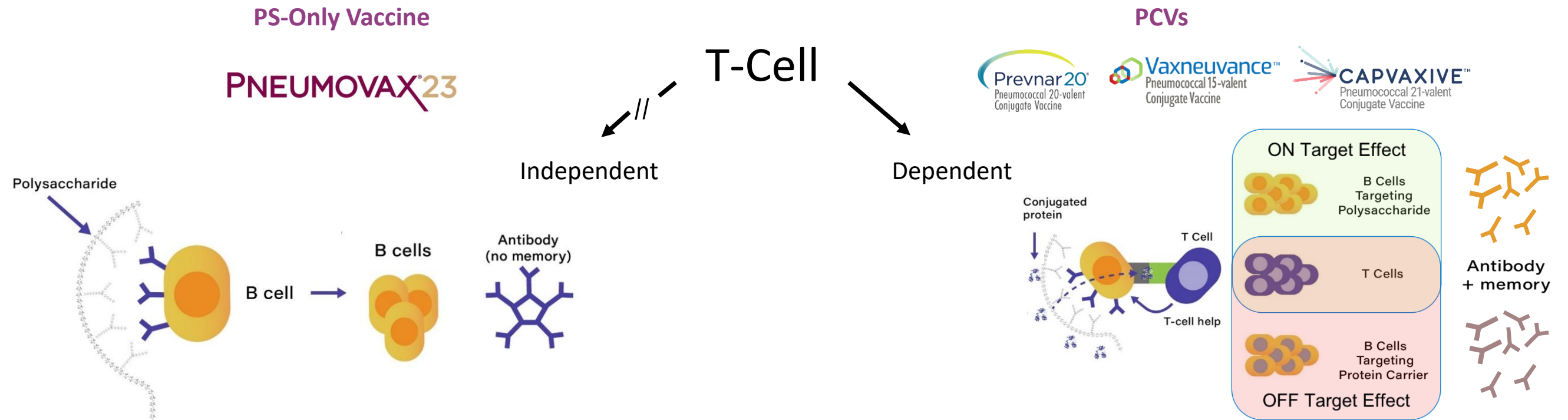
UK IPD CASES IN ADULTS  $\geq 65$ <sup>1</sup>



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

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

PCV Efficacy Driven by T-Cell Epitopes on Diphtheria Toxin Protein Carrier – CRM<sub>197</sub><sup>1</sup>



## Broad Coverage But Limited Protection in Adults - Not Boostable

Pneumococcal capsular polysaccharides (PS) antigens lead to:

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

## Narrow Coverage But Highly Effective in Adults & Infants - Boostable

Conjugation of PS to protein carrier leads to:

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

Note: Graphics adapted from Strugnell et al, Understanding Modern Vaccines, Vol 1, Issue 1, 61-88.

(1) Protein carrier in Pevnar 20 is a modified form of diphtheria toxin (CRM<sub>197</sub>).

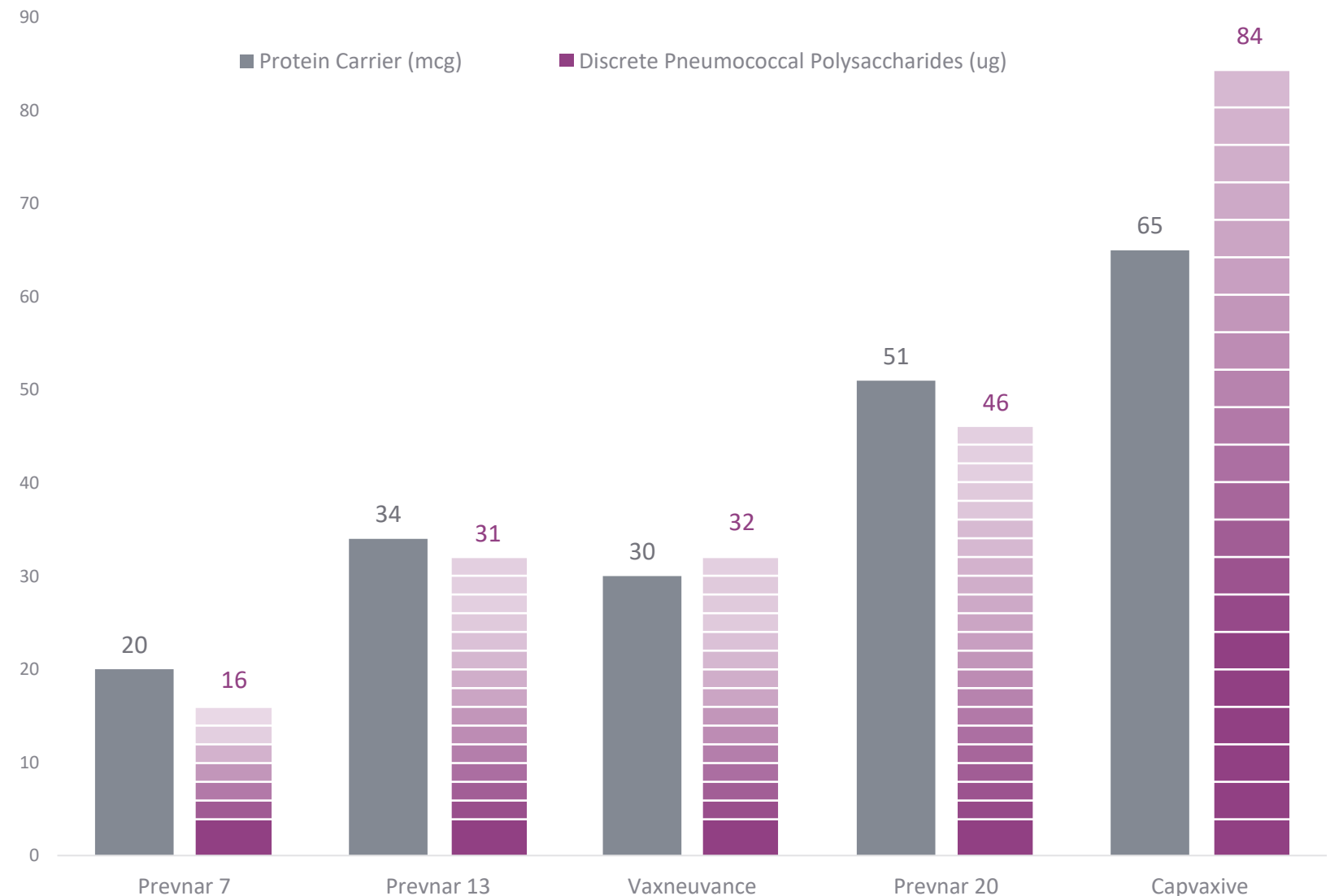
# Limitations of Current PCVs

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

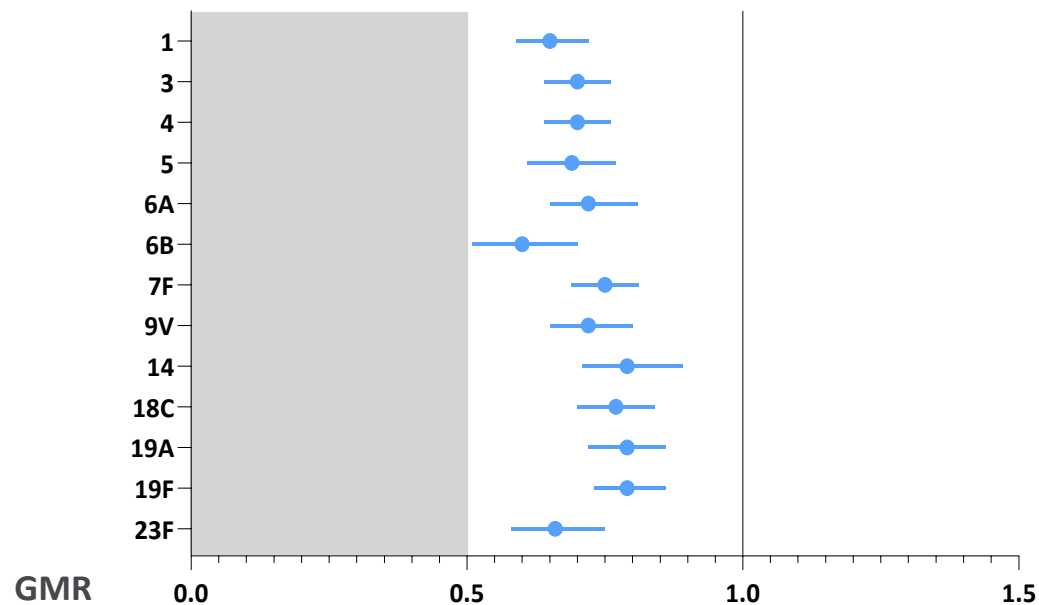
## Coverage Expansion Using Conventional Chemistry Has Led to Carrier-Induced Immune Suppression

### CARRIER SUPPRESSION

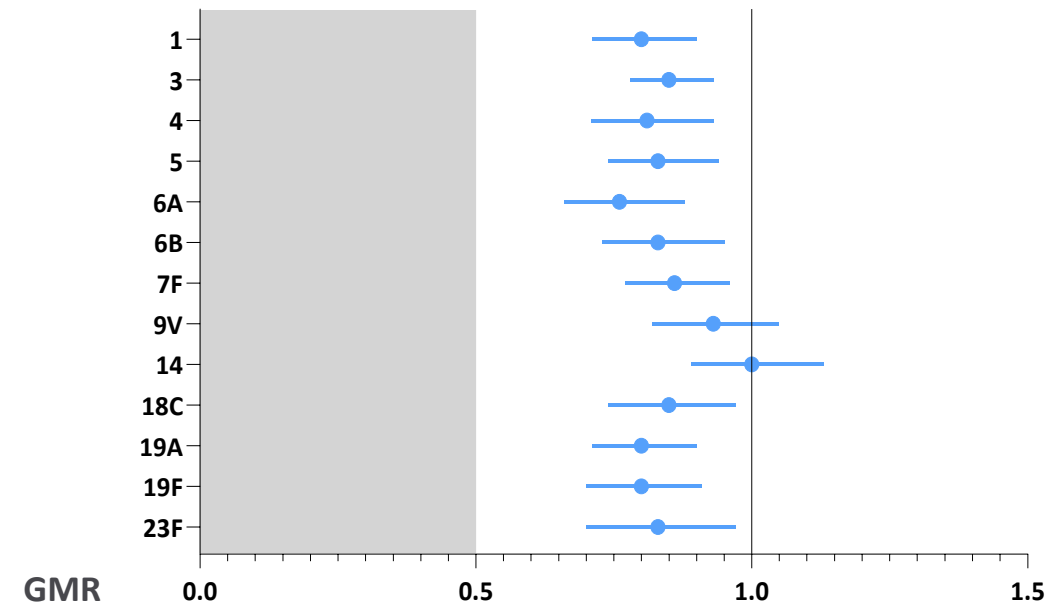
Diminished immune response to target polysaccharides due to cumulative amount of protein carrier

- 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<sup>1</sup>



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



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

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

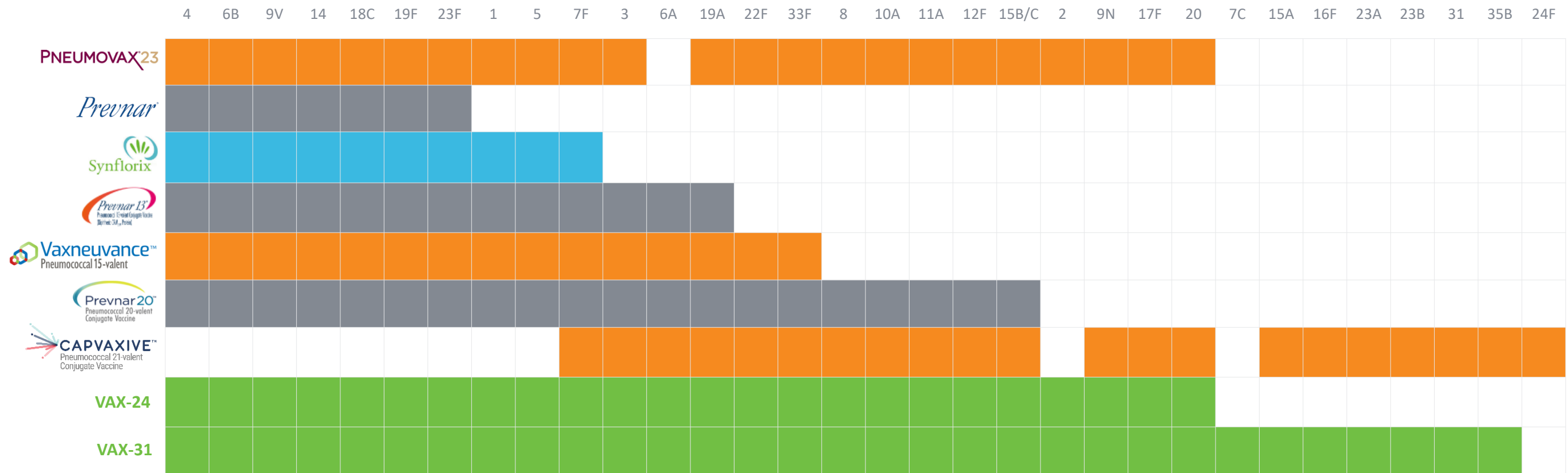
OPA = Opsonophagocytic assay.

GMR = Geometric Mean Ratio.

# Vaxcyte's Carrier-Sparing PCV Franchise has Potential to Address Need for Broader-Spectrum of Coverage in Growing ~\$8B Pneumococcal Market

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

**VAX-24:** Potential best-in-class infant PCV candidate, covering more serotypes than any pneumococcal infant vaccine on-market today



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.



# Pneumococcal Vaccine Market is Highly Attractive

## VAX-31 and VAX-24 Have the Potential to Become the Broadest-Spectrum PCVs

### PNEUMOCOCCAL VACCINE MARKET DYNAMICS

#### PCVs ARE BEST-IN-CLASS

- Well-understood T-cell dependent MOA tied to co-presentation of disease-specific polysaccharide antigens with T-cell epitopes on protein carrier to drive durable and boostable immune responses
- Well-defined clinical development path with surrogate immune endpoints as basis for full approval, negating need for field efficacy trials

#### DURABLE REVENUE STREAM

- Prevnar Family (PCV7/PCV13/PCV20) & PPSV23 have generated >\$100B in revenues
- PCV13 and PCV20 had combined annual sales of ~\$6.4B in 2023

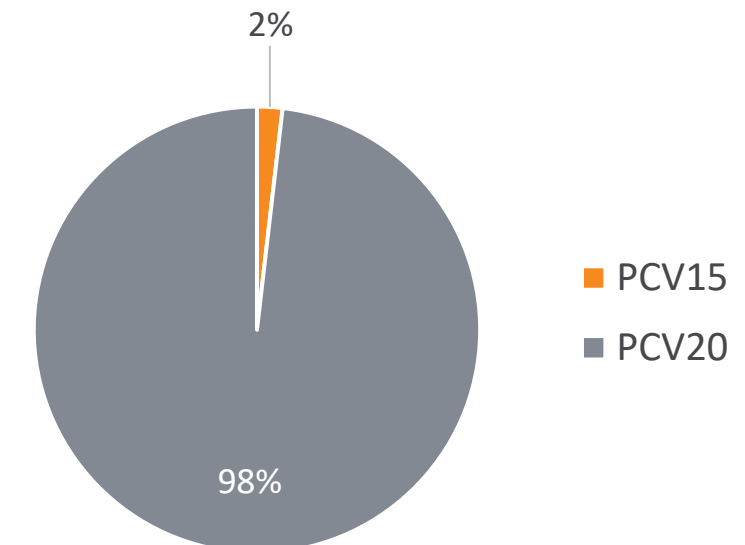
#### ATTRACTIVE MARGINS

- Pneumococcal vaccines are premium priced in the U.S., delivering highly attractive margins
- Broader-spectrum PCVs extend premium price<sup>1</sup>
  - PCV21: \$288
  - PCV20: \$262
  - PCV15: \$229

#### 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 PCV MARKET ADOPTION

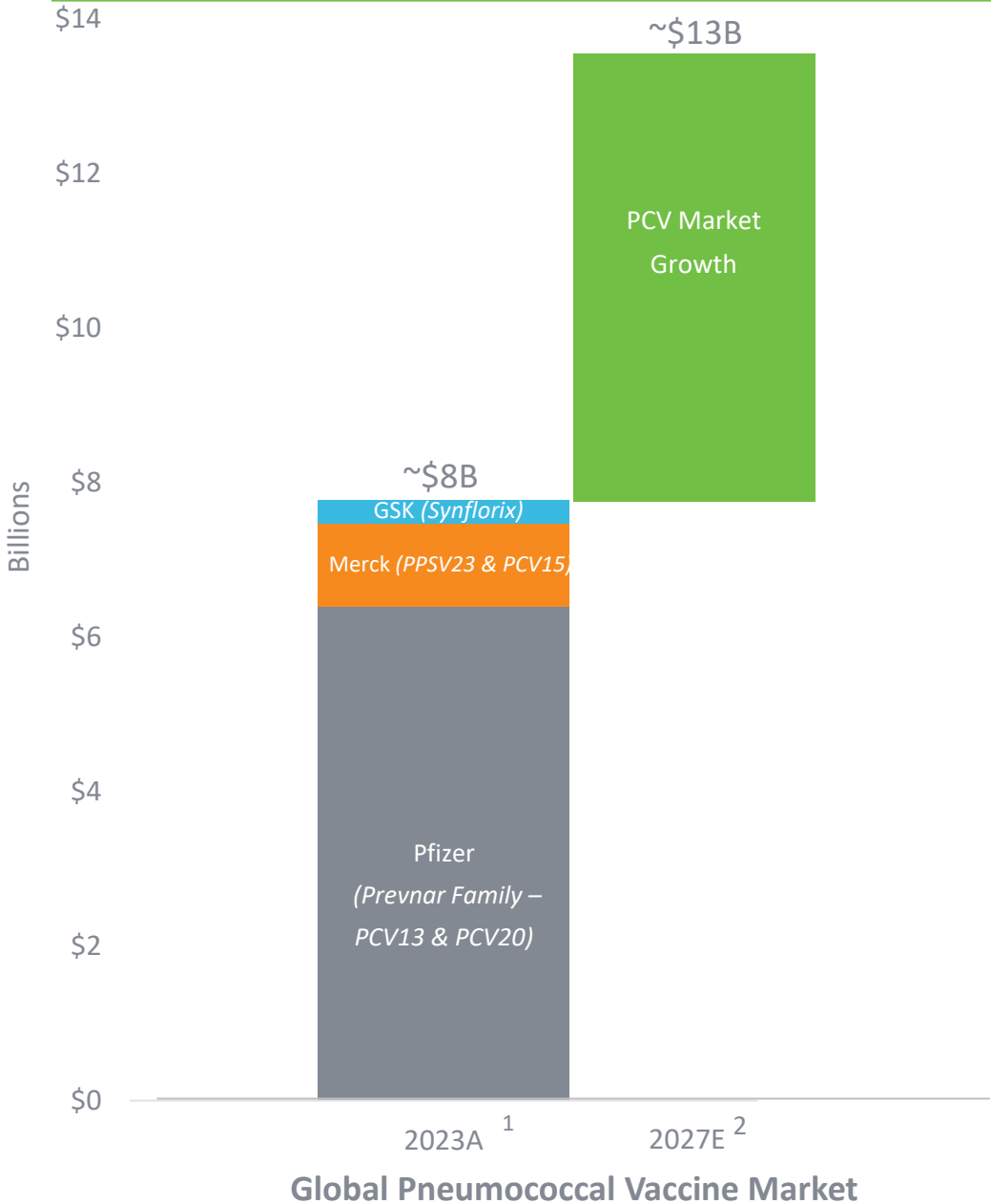


PCV VACCINATION IN ADULTS AGED ≥ 65  
JULY 2021 - NOVEMBER 2023<sup>2</sup>

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

# Pneumococcal Vaccine Market Poised for Significant Growth

Expected to Reach ~\$13B by 2027 Driven Primarily by Growth in Adult Market



## PCV MARKET – KEY GROWTH DRIVERS

- ACIP recently expanded U.S. universal adult vaccination by lowering the age to ≥50 years from ≥65, which significantly expands market
- ACIP indicated strong consideration for a potential future shift to a prime-boost schedule to support effective long-term protection in adults
- Serotype epidemiology and availability of broader-valency PCVs may lead to additional adult recommendations outside the U.S.
- “At risk” adults aged 19-49 years included in U.S. universal PCV vaccination recommendation

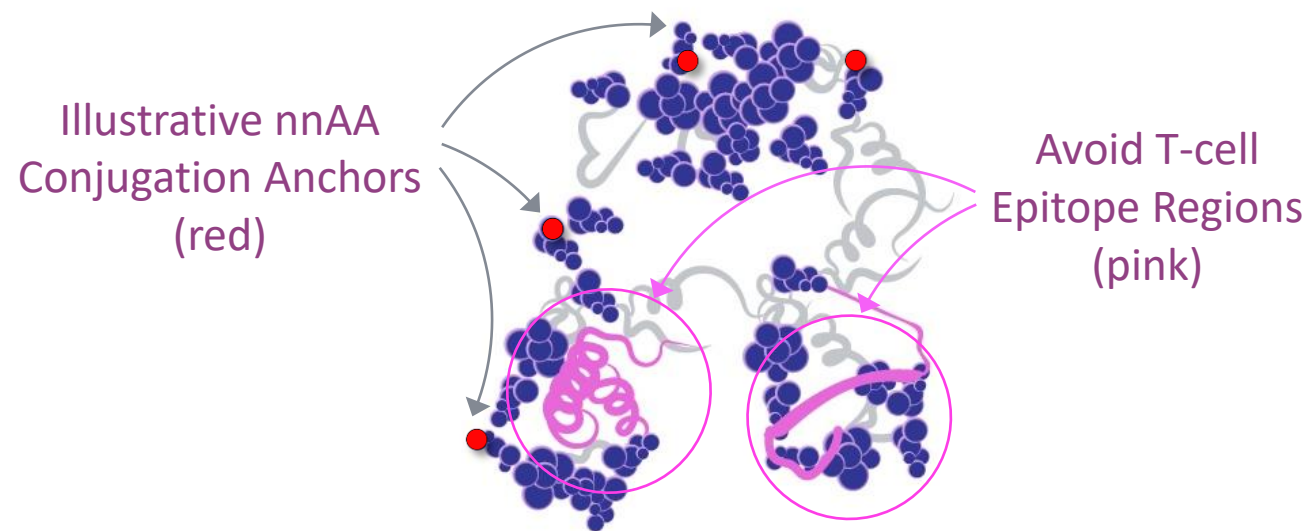
(1) Sources: Company websites.  
 (2) Global Pneumococcal Vaccine Market (2022-2027), Infogence Global Research.  
 (3) <https://www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/>.

# Differentiated PCV Franchise: VAX-31 and VAX-24

# Vaxcyte's PCV Franchise Employs Carrier-Sparing Conjugates

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

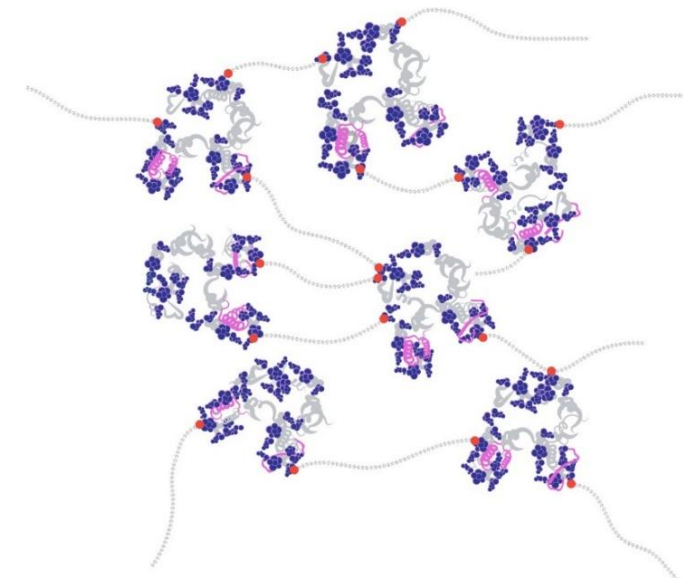
PRECISE, SITE-SPECIFIC CONJUGATION SITES ON PROPRIETARY eCRM<sup>®</sup> PROTEIN CARRIER



## eCRM: Enhanced Potency Potential

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

FINAL VAX-31 & VAX-24 CONJUGATES IN CUSTOMARY MATRIX FORM



## Carrier-Sparing Conjugates

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

# Vaxcyte PCV Franchise Design Leverages Many Standard PCV Conventions

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

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

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

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

# VAX-31 Adult Clinical Program

# Summary of VAX-31 Adult 50+ Phase 1/2 Study Topline Data Findings

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

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**SAFETY AND TOLERABILITY:** At all doses studied, VAX-31 was well tolerated and demonstrated a safety profile similar to Prevnar 20® (PCV20) for all doses



**IMMUNOGENICITY:** At all doses studied, VAX-31 demonstrated robust OPA immune responses for all 31 serotypes (STs) -- all three doses advanceable to Phase 3

- High and Middle doses met or exceeded OPA regulatory immunogenicity criteria for all 31 STs, Low dose for 29 of 31 STs
- For the 20 STs common with PCV20: High dose, 18 had GMR greater than 1.0 and 7 achieved statistically higher immune responses; Middle dose, 13 had GMR greater than 1.0 and 5 achieved statistically higher immune responses; Low dose, 8 had GMR greater than 1.0 and 3 achieved statistically higher immune responses
- For the 11 additional STs unique to VAX-31: All 11 met the superiority criteria at all doses



**PLATFORM:** The VAX-31 data further validate the potential of Vaxcyte's carrier-sparing platform to deliver the broadest-spectrum PCVs that provide protection against both currently circulating and historically prevalent STs



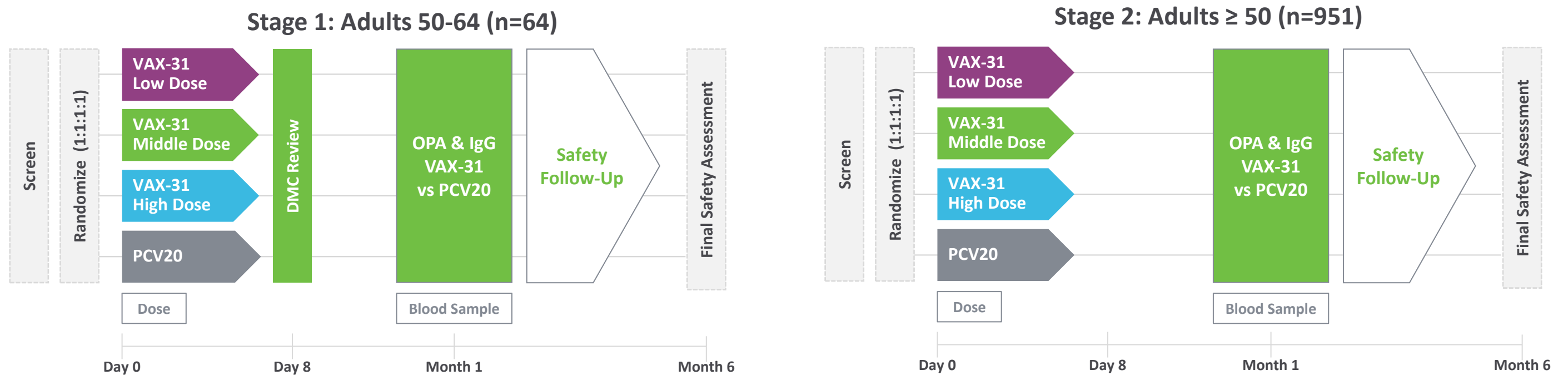
**PCV Franchise Strategy:**

- Adults: VAX-31 selected to advance to Phase 3, dose to be chosen prior to study initiation
- Pediatrics: Advance both VAX-24 and VAX-31

GMR = geometric mean ratio; OPA = Opsonophagocytic activity.

# Overview of VAX-31 Phase 1/2 Clinical Study Design (N=1,015)

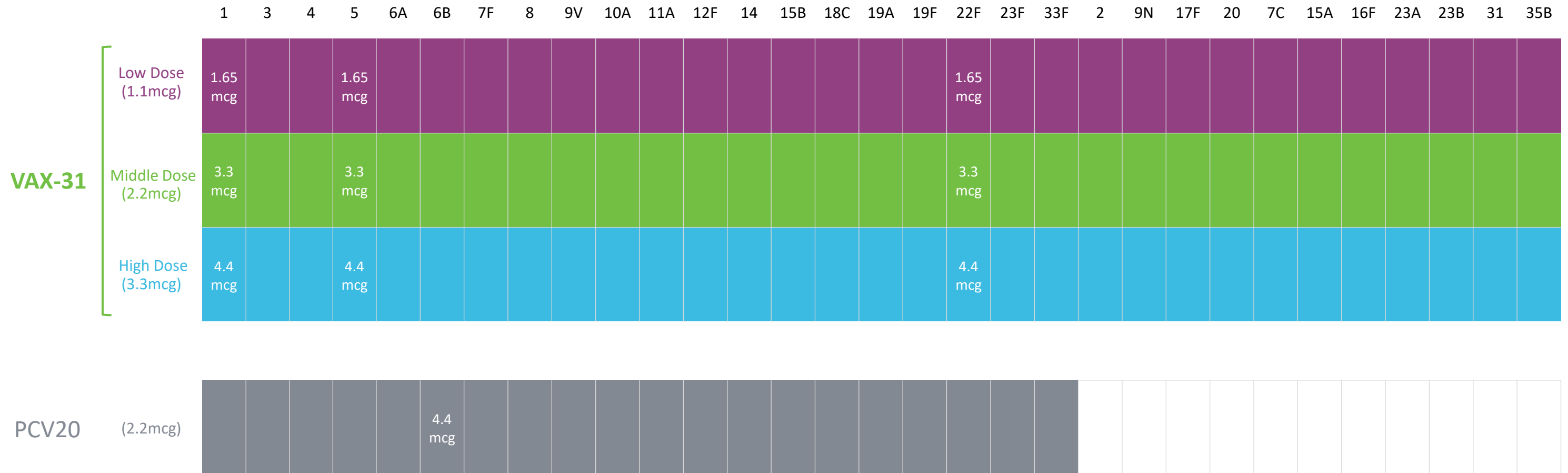
Randomized, Observer-Blind, Dose-Finding, Controlled Study to Evaluate Safety, Tolerability and Immunogenicity of VAX-31 vs Standard-of-Care (PCV20) in 1,015 Healthy Adults  $\geq 50$  Years



DMC: Data Monitoring Committee, IgG: Immunoglobulin G.

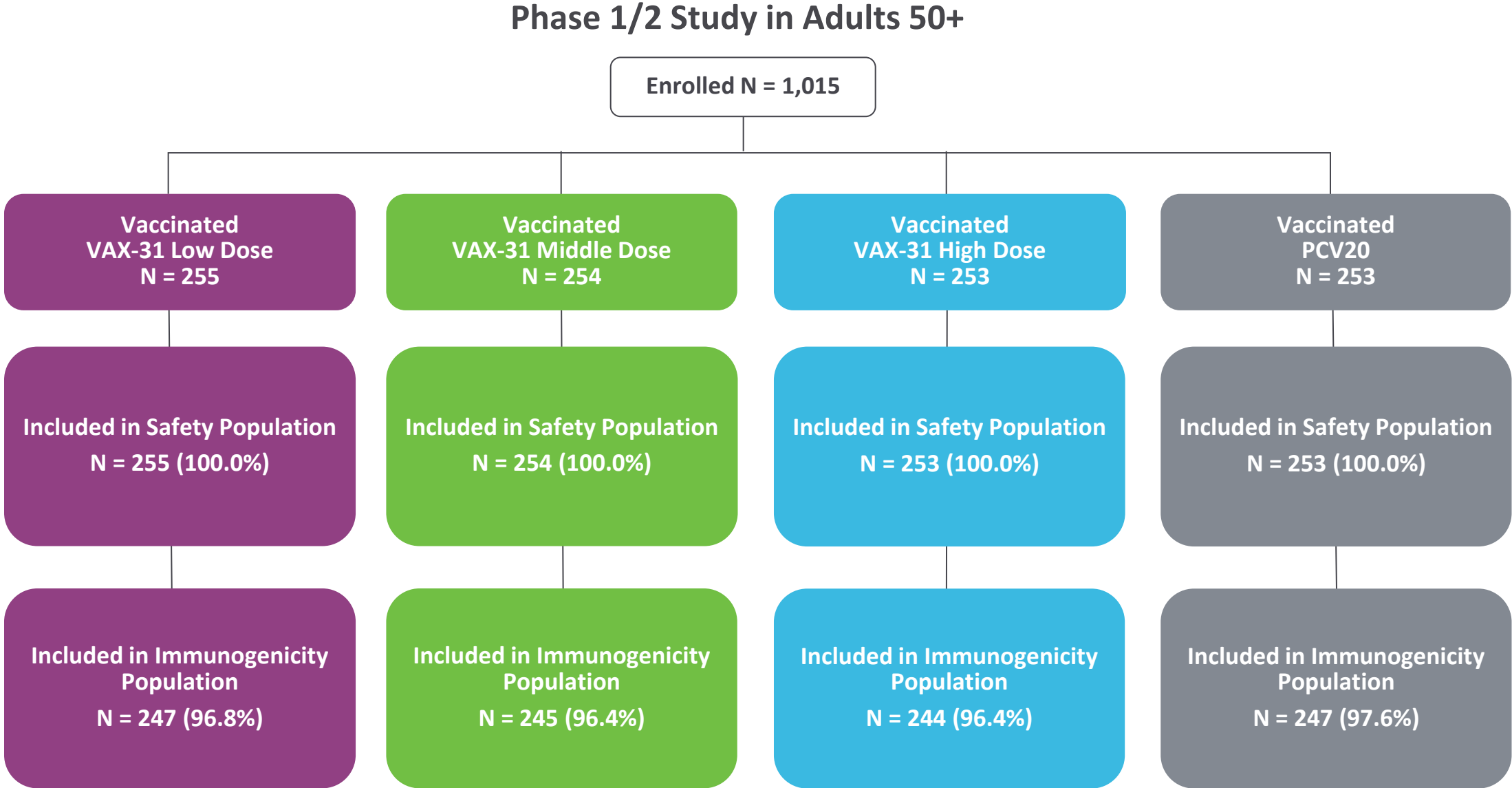


# Study Evaluated Three VAX-31 Doses



# Study Disposition

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



24 subjects (2.4%) discontinued and did not complete the full Month 6 safety follow-up (lost to follow-up (13), withdrawal by subject (11)).

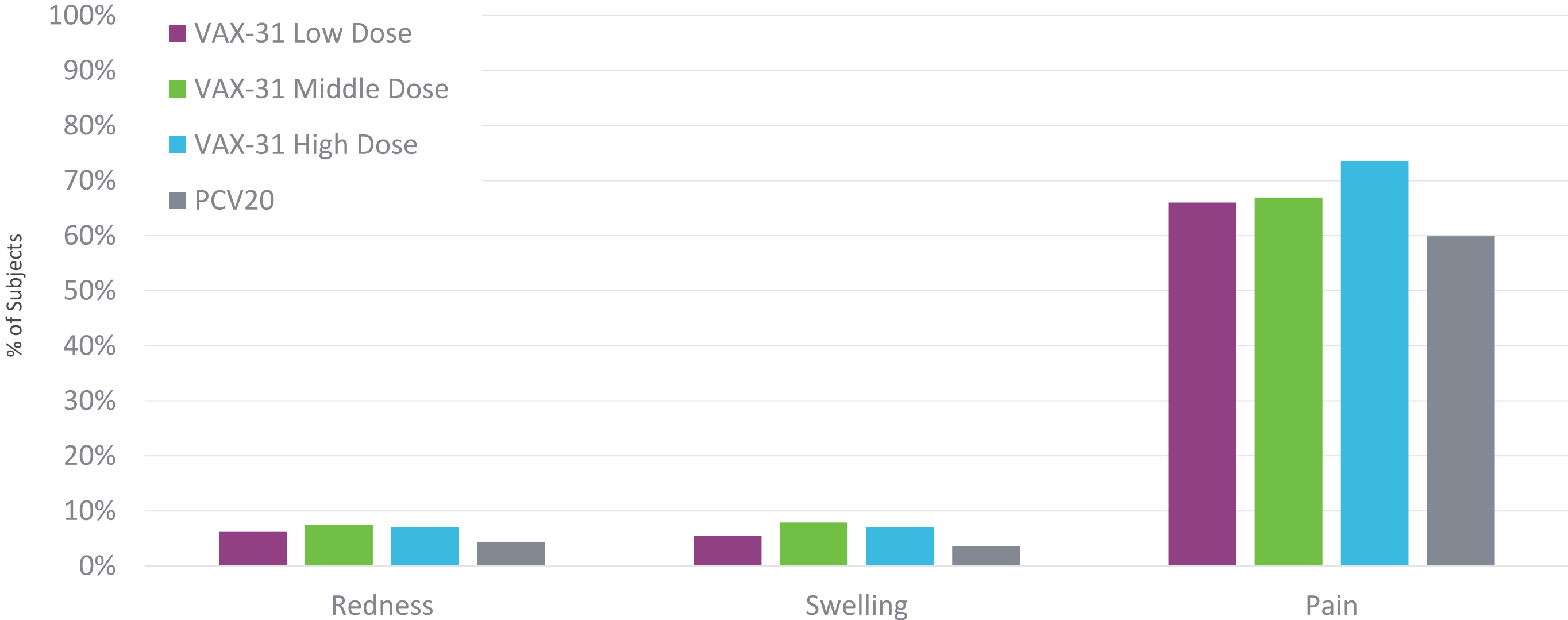
# Population Demographics

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

	VAX-31 Low Dose		VAX-31 Middle Dose		VAX-31 High Dose		PCV20	
	Safety	Immunogenicity	Safety	Immunogenicity	Safety	Immunogenicity	Safety	Immunogenicity
<b>Number of Subjects</b>	255	247	254	245	253	244	253	247
<b>Median Age, Years (range)</b>	58.0 (50-84)	58.0 (50-84)	58.0 (50-86)	58.0 (50-86)	59.0 (50-79)	59.0 (50-79)	60.0 (50-82)	60.0 (50-82)
<b>Sex, n (%)</b>								
Female	151 (59.2)	147 (59.5)	160 (63.0)	154 (62.9)	150 (59.3)	145 (59.4)	148 (58.5)	146 (59.1)
Male	104 (40.8)	100 (40.5)	94 (37.0)	91 (37.1)	103 (40.7)	99 (40.6)	105 (41.5)	101 (40.9)
<b>Race, n (%)</b>								
White	189 (74.1)	183 (74.1)	190 (74.8)	184 (75.1)	196 (77.5)	190 (77.9)	185 (73.1)	180 (72.9)
Black	59 (23.1)	57 (23.1)	56 (22.0)	55 (22.4)	51 (20.2)	49 (20.1)	60 (23.7)	59 (23.9)
Asian	3 (1.2)	3 (1.2)	5 (2.0)	3 (1.2)	4 (1.6)	3 (1.2)	3 (1.2)	3 (1.2)
Native Hawaiian	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
American Indian or Native Alaskan	2 (0.8)	2 (0.8)	3 (1.2)	3 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	2 (0.8)	2 (0.8)	0 (0.0)	0 (0.0)	2 (0.8)	2 (0.8)	3 (1.2)	3 (1.2)
Multiracial	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Median Height, cm (range)</b>	167.6 (146-196)	167.6 (146-196)	169.1 (142-188)	169.1 (142-188)	168.0 (145-196)	168.0 (145-196)	167.6 (147-190)	167.6 (147-190)
<b>Median Weight, kg (range)</b>	82.56 (44.5-176.6)	82.2 (44.5-176.6)	85.80 (43.7-167.0)	85.9 (43.7-167.0)	84.00 (49.9-152.8)	84.01 (49.9-152.8)	83.64 (43.9-170.6)	83.9 (43.9-170.6)
<b>Median BMI, kg/m<sup>2</sup> (range)</b>	28.90 (16.9-53.5)	28.86 (16.9-53.5)	30.42 (18.2-58.3)	30.37 (18.2-58.3)	28.82 (18.2-53.6)	28.85 (18.2-53.6)	29.11 (16.6-57.6)	29.23 (16.6-57.6)

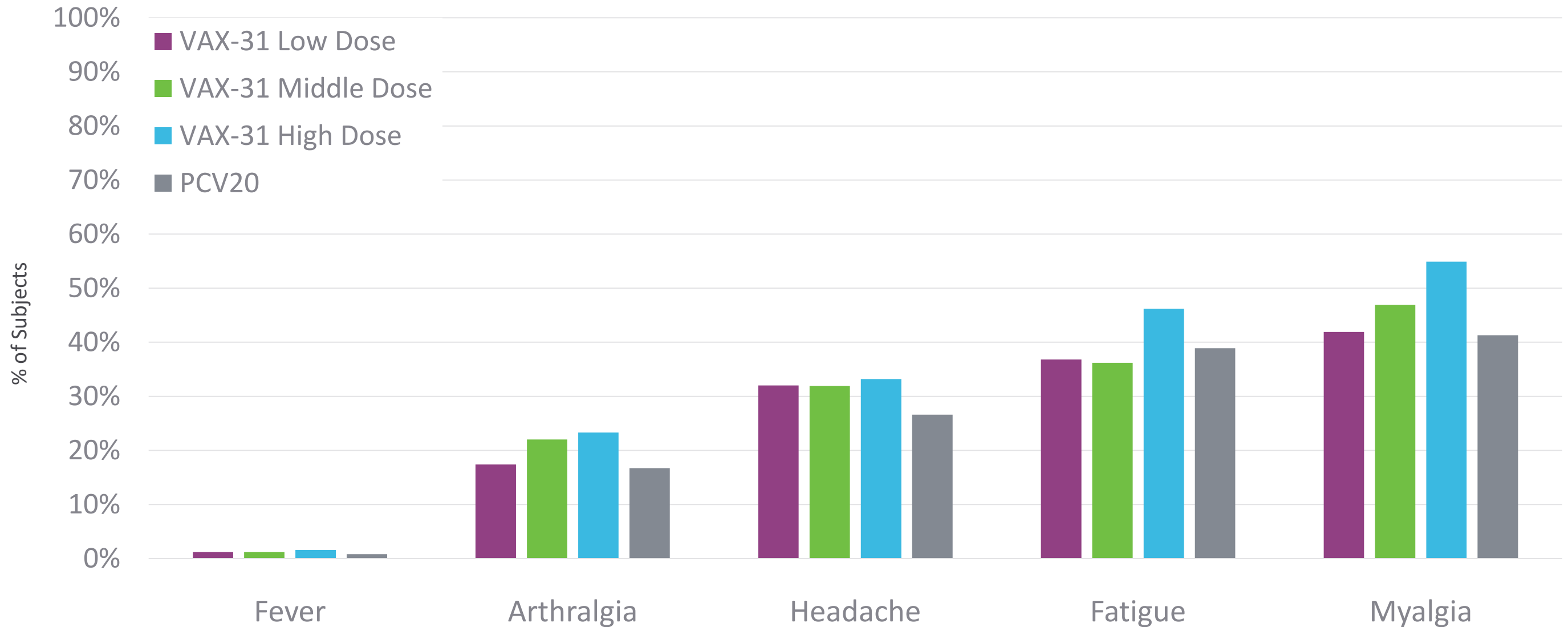
# All VAX-31 Doses Well Tolerated and Consistent with PCV20 Across Cohorts

## Local Solicited AEs Through 7 Days



# All VAX-31 Doses Well Tolerated and Consistent with PCV20 Across Cohorts

## Systemic Solicited AEs Through 7 Days



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

*TEAE = Treatment emergent adverse events; MAAE = Medically attended adverse events; NOCI = New onset of chronic illnesses; SAE = Serious adverse events.  
Excludes Solicited AEs.*

# Precedent Immunogenicity Regulatory Criteria for Adult Phase 2/3 PCV Studies

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## CRITERIA FOR 20 SEROTYPES COMMON TO VAX-31 AND PCV20:

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### Non-inferiority:

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

## CRITERIA FOR 11 INCREMENTAL SEROTYPES IN VAX-31:

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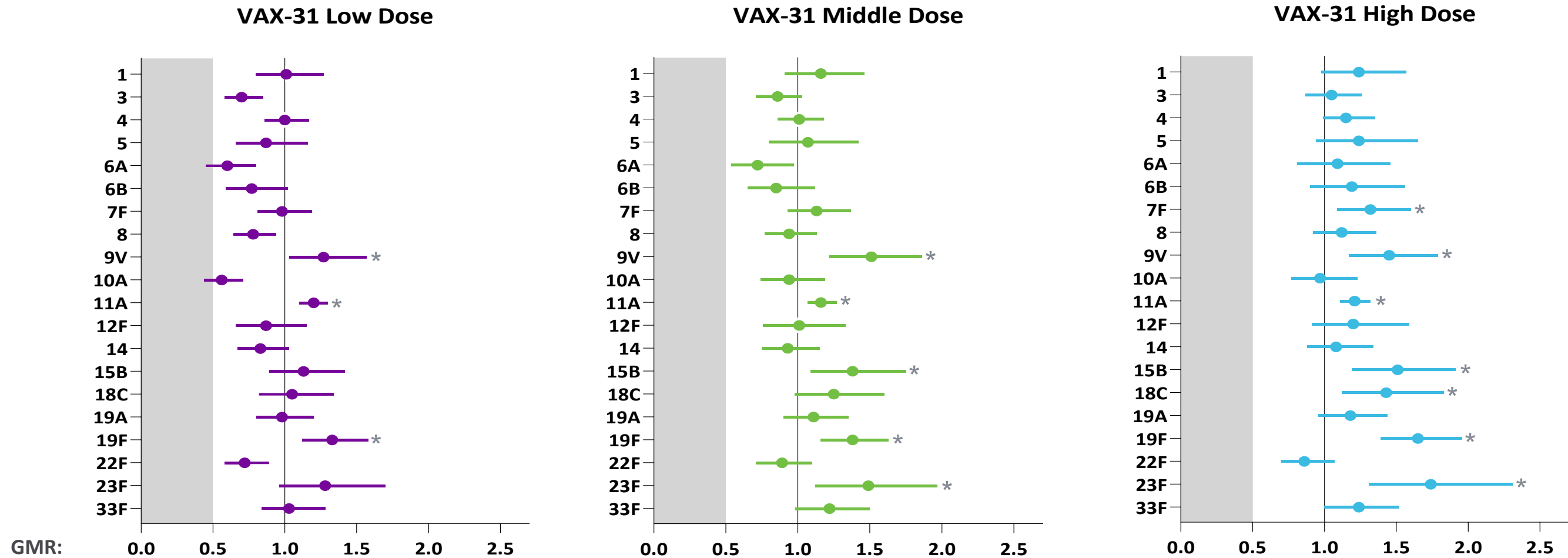
### Superiority:

- Lower bound of the 2-sided 95% CI of the difference in the proportions of participants with a  $\geq 4$ -fold increase from Day 1 to Month 1 is greater than 10%
- Lower bound of the 2-sided 95% CI of the OPA GMR is greater than 2.0

*CI = confidence interval.*

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

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



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

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

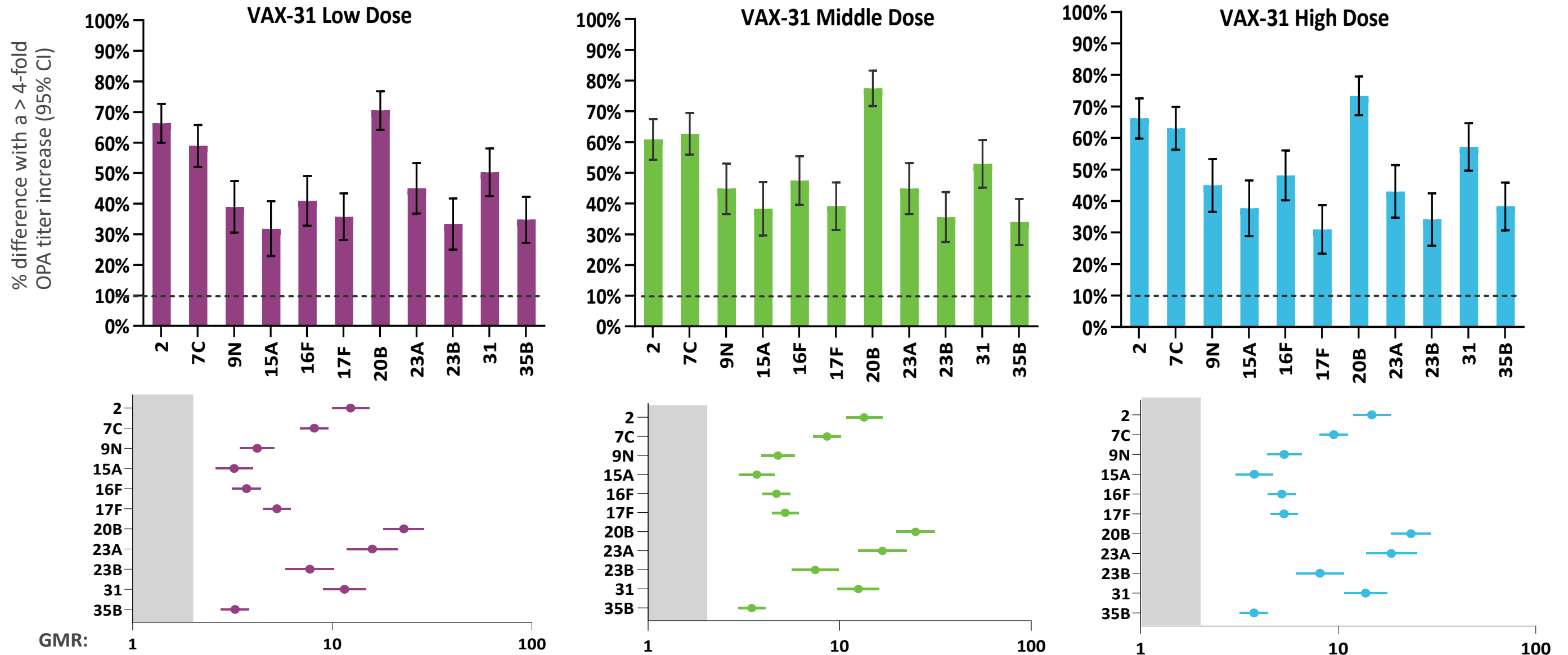
**High dose:** 18 of 20 STs had a GMR greater than 1.0 and 7 STs achieved statistically higher immune responses

\* Reached statistical significance for superiority.



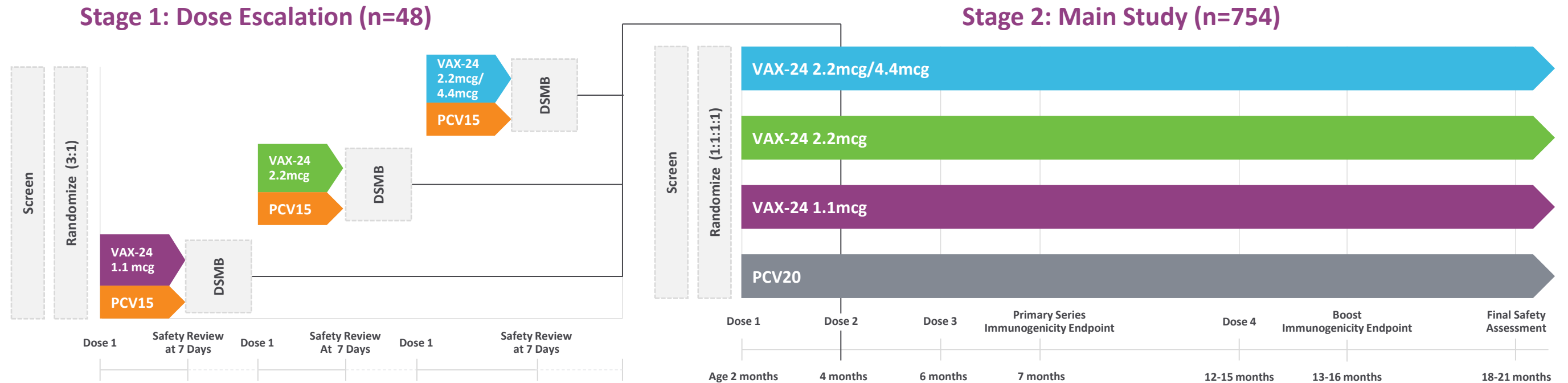
# VAX-31 Induced Robust Immune Responses for All 11 Incremental STs

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



# VAX-24 Infant Clinical Program

# Enrollment Complete in VAX-24 Infant Phase 2 Clinical Study



## STUDY OVERVIEW

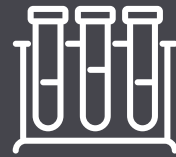
- Randomized, Observer-Blind, Active-Controlled, Dose-Finding, Clinical Study to Evaluate Safety, Tolerability and Immunogenicity of VAX-24 vs SOC in Healthy Infants
- **Stage 1** evaluated the safety and tolerability of a single injection of VAX-24 at three dose-escalating levels and compared to PCV15, which was the broadest-spectrum PCV at the time of study initiation, in 48 healthy infants. Infants were enrolled and dosed at two months of age and evaluated seven days post-dose. Following satisfactory Data Safety Monitoring Board review of safety and tolerability data, the study proceeded to Stage 2.
- **Stage 2** is evaluating the safety, tolerability and immunogenicity of VAX-24 at three dose levels and compared to PCV20 in 754 healthy infants. Participants who received VAX-24 in Stage 1 continued the standard dosing regimen as part of Stage 2 and will be included in the safety, tolerability and immunogenicity analysis of the study. Per ACIP guideline, the primary immunization series includes three doses given at two months, four months and six months of age, followed by a booster dose at 12-15 months of age. The study protocol for Stage 2 was amended and the study comparator changed to PCV20, which is currently the broadest-spectrum PCV recommended by the ACIP.

# Study Safety, Tolerability and Immunogenicity Key Outcome Measures

	DAY 7 AFTER EACH DOSE	1 MONTH POST-DOSE 1-4; ONGOING DURING PRIMARY SERIES	1 MONTH POST-DOSE 3 (PD3)*	1 MONTH POST-DOSE 4 (PD4)*	6 MONTHS PD4
SAFETY AND TOLERABILITY OUTCOME MEASURES	<ul style="list-style-type: none"> <li>Solicited local reactions</li> <li>Solicited systemic events</li> </ul>	<ul style="list-style-type: none"> <li>Unsolicited adverse events (AE)</li> </ul>	<ul style="list-style-type: none"> <li>Serious adverse events (SAE), new onset of chronic illnesses (NOCI) and medically attended adverse events (MAAE)</li> </ul>	<ul style="list-style-type: none"> <li>SAE, NOCI and MAAE</li> </ul>	<ul style="list-style-type: none"> <li>Unsolicited AE</li> <li>SAE, NOCI and MAAE</li> </ul>
IMMUNOGENICITY OUTCOME MEASURES			<ul style="list-style-type: none"> <li>% of subjects achieving Immunoglobulin G (IgG) antibody concentration <math>\geq 0.35</math> mcg/mL</li> <li>IgG Geometric Mean Concentration (GMC)</li> <li>Opsonophagocytic activity (OPA) Geometric Mean Titer (GMT)</li> </ul>	<ul style="list-style-type: none"> <li>% of subjects achieving IgG antibody concentration <math>\geq 0.35</math> mcg/mL</li> <li>IgG GMC</li> <li>OPA GMT</li> <li>IgG and OPA Geometric Mean Fold Rise (GMFR) from pre-Dose 4 to 1-month PD4</li> <li>% of subjects achieving a 4-fold rise in IgG and OPA from pre-Dose 4 to 1-month PD4</li> <li>% of subjects achieving IgG concentration <math>\geq 1.0</math> mcg/mL</li> </ul>	

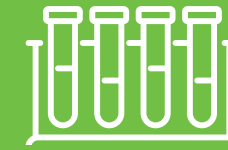
\*Effect on immunogenicity of concomitant vaccination will be evaluated on a subset of subjects PD3 and PD4 based on serum availability.

# Precedent Regulatory Criteria for Infant Phase 2/3 PCV Studies: Co-Primary Immunogenicity Endpoints (Post-Prime and Post-Boost)



## PRIMARY SERIES NON-INFERIORITY POST-DOSE 3 “PRIME”

- **For the 20 STs common with PCV20:** Lower bound of the 95% CI for the difference between the proportion of participants achieving the pre-defined IgG concentration ( $\geq 0.35$  mcg/mL) is  $> -10\%$  for each ST
- **For the 4 STs unique to VAX-24:** Achieving the IgG concentration  $> -10\%$  differential compared to the ST with the lowest response rate in PCV20, excluding ST3



## BOOSTER DOSE NON-INFERIORITY POST-DOSE 4 “BOOST”

- **For the 20 STs common with PCV20:** Lower bound of the 95% CI for IgG GMC ratio is  $> 0.5$  for each ST
- **For the 4 STs unique to VAX-24:** Meeting the  $> 0.5$  IgG GMC ratio threshold compared to the ST with lowest IgG CMC in PCV20, excluding ST3

CI = confidence interval; ST = serotype; PD = Post Dose.

# PCV20 Granted U.S. Licensure Based on Phase 3 Results vs. PCV13

## Missed Non-Inferiority for 5 of 13 Common and 1 of 7 Unique Serotypes for Co-Primary Endpoint

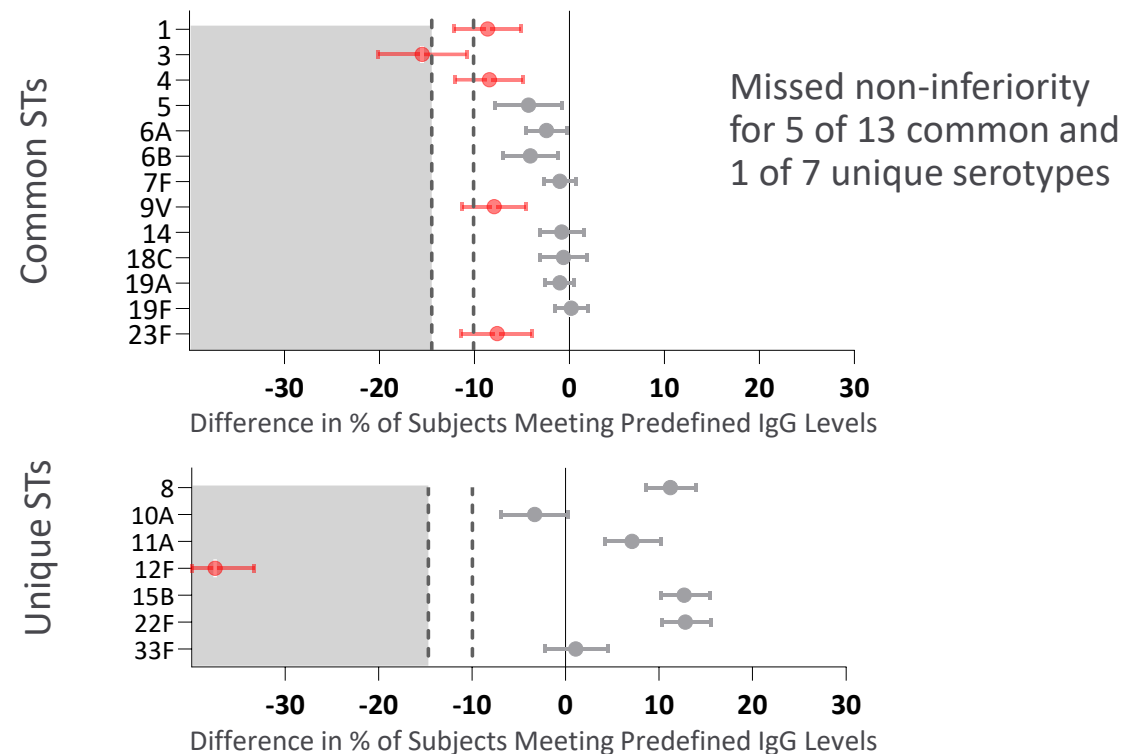
### PRIMARY SERIES NON-INFERIORITY CRITERIA POST-DOSE 3

- For STs in common with SoC, lower bound of the 95% CI for the difference between the proportion of participants achieving the pre-defined IgG concentration ( $\geq 0.35$  mcg/mL) is  $> -10\%$  for each ST
- For the STs unique to broader spectrum PCV, achieving the IgG concentration  $> -10\%$  differential compared to the ST with lowest response rate in SoC PCV, excluding ST3

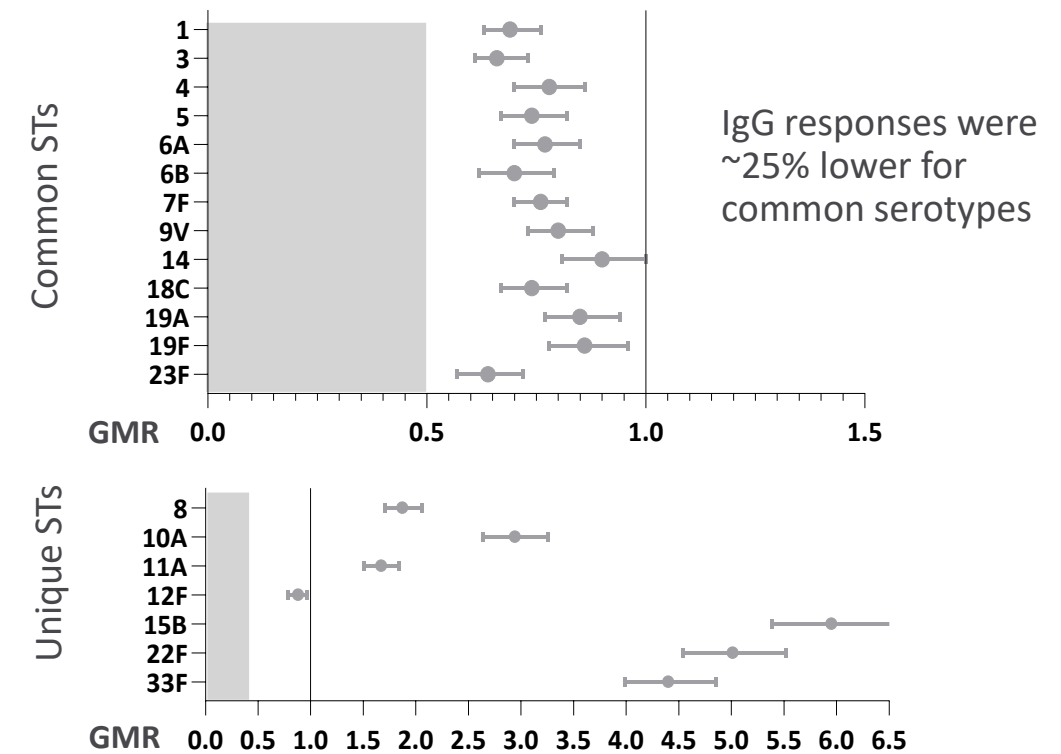
### BOOSTER DOSE NON-INFERIORITY CRITERIA POST-DOSE 4

- For STs in common with SoC, lower bound of the 95% CI for IgG GMC ratio is  $> 0.5$  for each ST
- The STs unique to broader spectrum PCV, meeting the  $> 0.5$  IgG GMC ratio threshold compared to the ST with lowest IgG CMC in SoC, excluding ST3

PCV20 vs. PCV13: Difference in % of Subjects Meeting Predefined IgG Levels<sup>1</sup>

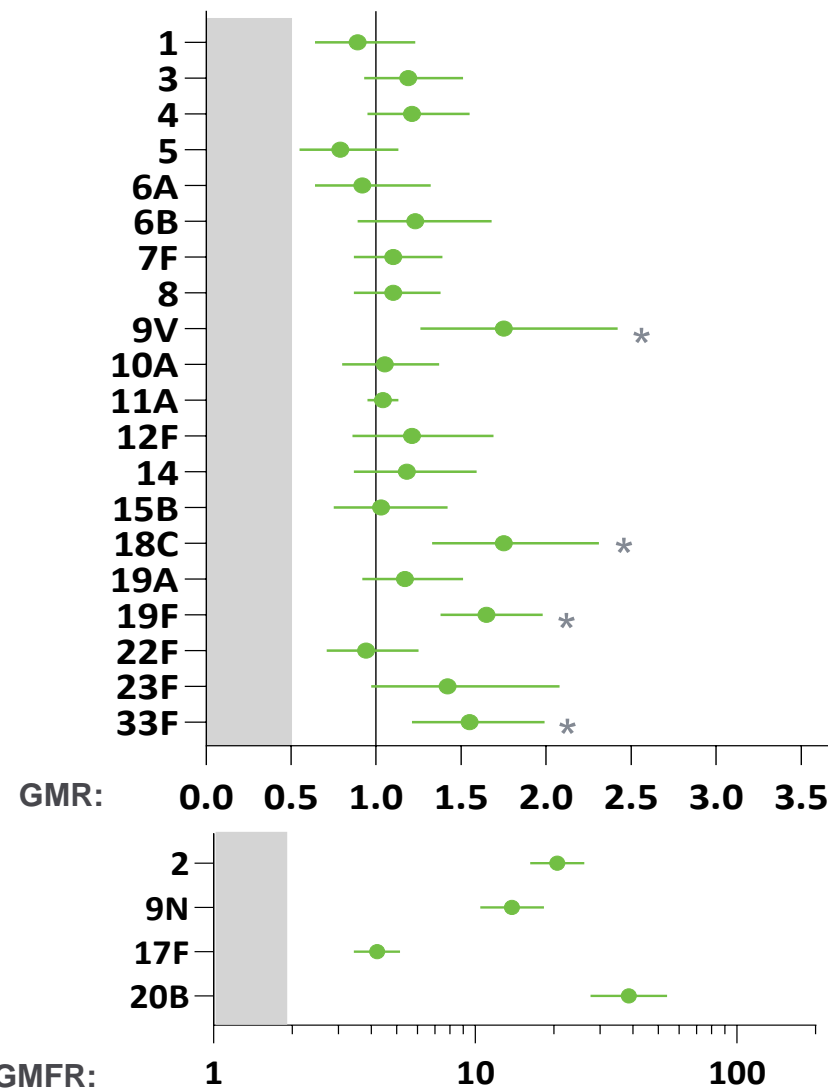


PCV20 vs. PCV13: IgG GMR Post-Boost<sup>2</sup>

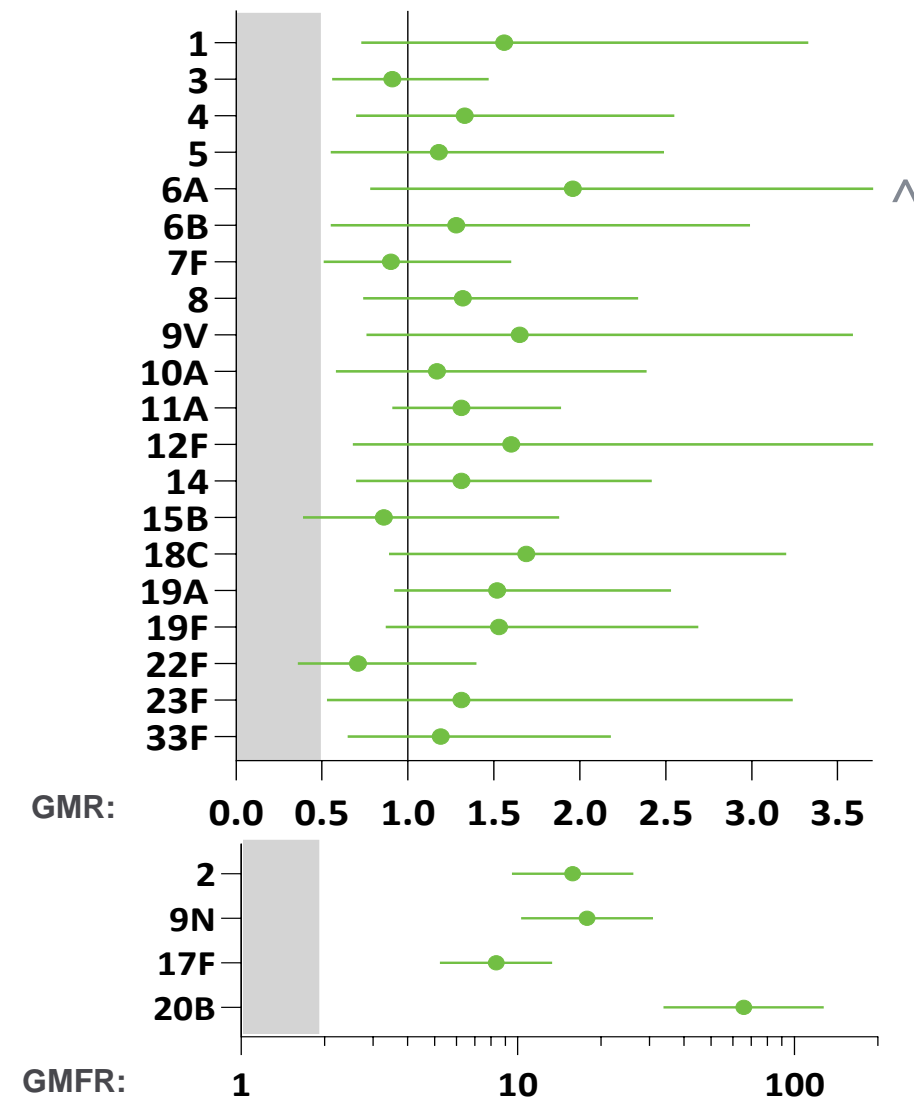


# Strength of Adult Phase 2 Study Results Show Potential of VAX-24

**VAX-24 Phase 2 Study in Adults Aged 50-64  
2.2mcg (n~180)<sup>1</sup>**



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



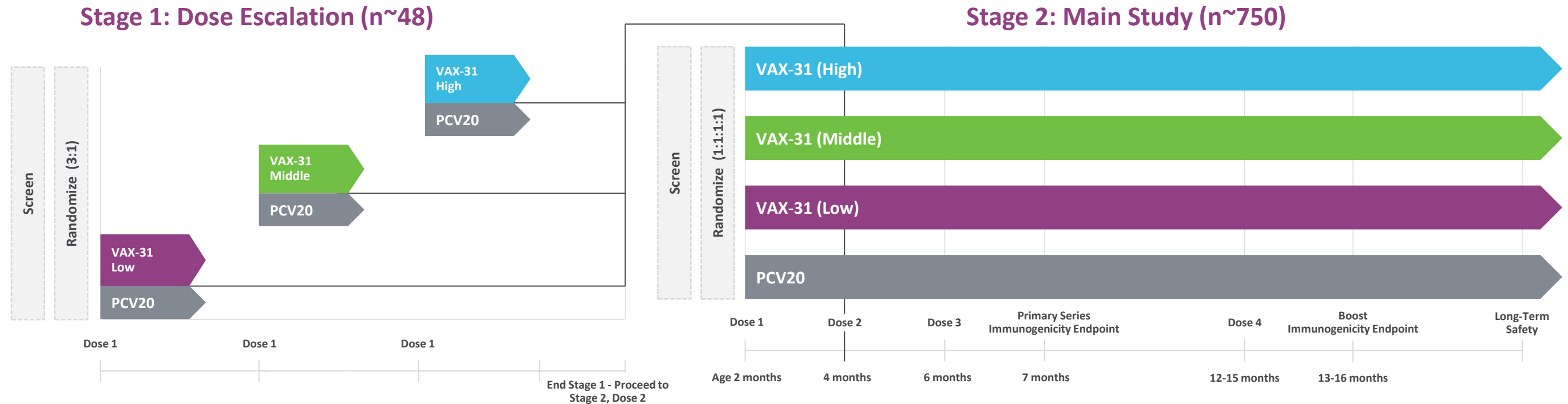
(1) Sample size of n~180 calculated as median between immunogenicity evaluable VAX-24 n=179 and PCV20 n=181 rounded to nearest 10.

\* Reached statistical significance for superiority. ^ Upper Limit = 4.93.

# VAX-31 Infant Clinical Program



# Enrolling Subjects in Stage 1 of VAX-31 Infant Phase 2 Clinical Study



## STUDY OVERVIEW

- This is a randomized, double-blind, active controlled, dose-finding, two-stage clinical study evaluating the safety, tolerability and immunogenicity of VAX-31 compared to PCV20 in healthy infants.
- **Stage 1** is evaluating the safety and tolerability of VAX-31 at three dose levels compared to PCV20 in approximately 48 infants in a dose-escalation approach. In the low, middle and high doses, all serotypes were dosed at 1.1mcg, 2.2mcg and 3.3mcg, respectively, except serotypes 1, 5 and 22F, which were dosed at 1.65mcg, 3.3mcg, and 4.4mcg, respectively. Participants who receive VAX-31 in Stage 1 will continue the standard dosing regimen as part of Stage 2 and will be included in the safety, tolerability and immunogenicity analysis of the study.
- **Stage 2** will evaluate safety, tolerability and immunogenicity of VAX-31 at the same three dose levels and compared to PCV20 in ~750 healthy infants. Per ACIP guideline, the primary immunization series includes three doses given at two months, four months and six months of age, followed by a booster dose at 12-15 months of age.
- **The key prespecified immunogenicity study endpoints** include an assessment of immune responses for each of the VAX-31 dose levels in comparison with PCV20 for the 20 common and the 11 unique serotypes in VAX-31. Post-primary series (post-dose 3 or PD3) immune responses will be assessed based on serotype-specific immunoglobulin G (IgG) seroresponse rates (proportion of participants achieving the accepted IgG threshold value of  $\geq 0.35$ mcg/mL) at 30 days PD3. IgG geometric mean titers will be assessed at 30 days PD3 and post-dose 4, along with other key immunogenicity endpoints.
- All participants will be evaluated for safety six months following the booster dose at 12-15 months of age.

# Non-PCV Pipeline

# VAX-A1: Group A Strep Conjugate Vaccine Program

## Novel Conjugate Vaccine Designed to Provide Universal Protection Against a High Priority Pathogen

### UNMET NEED

- Group A Strep results in an estimated 800M cases of illness annually worldwide, including pharyngitis, or strep throat, and certain severe invasive infections and sequelae<sup>1</sup>
- Upgraded CDC threat given significant source of antibiotic Rxs driving resistance which has nearly tripled in past decade
- Responsible for post-infectious immune-mediated rheumatic heart disease leading to over 300K deaths in 2015
- Highly prevalent in children and rate of invasive disease in adults > 65 has more than doubled (exceeding IPD rate in adults)

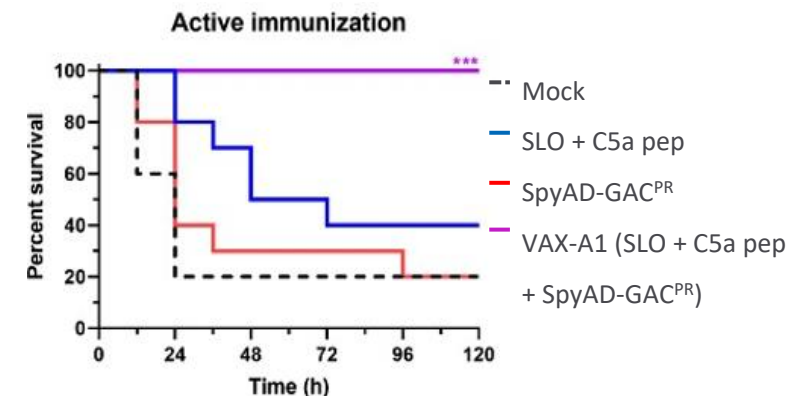
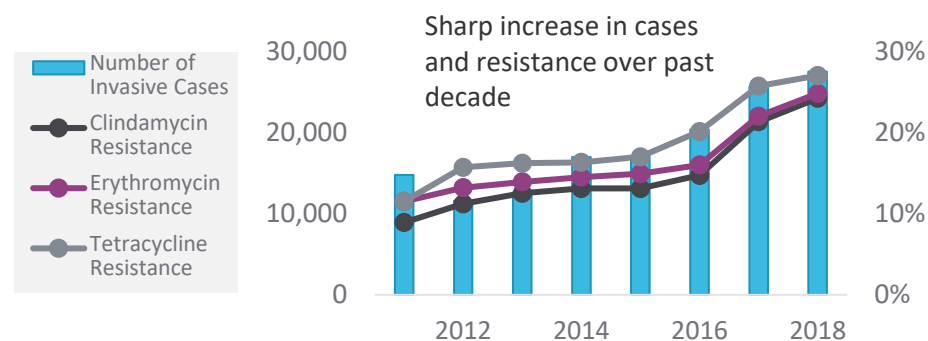
### VAX-A1: BROAD-SPECTRUM, MONOVALENT CONJUGATE VX

- Designed to confer robust, boostable and durable protection against a broad-spectrum of subtypes of Group A Strep
- Leverages site-specific conjugation to disease-specific carrier to expose mapped T- and B-cell epitopes
- Proprietary conserved antigen – Polyrihamnose – conjugated to an immunogenic disease-specific carrier along with two conserved virulence factors

### PROGRAM STATUS

- Partially funded by grant from CARB-X (consortium of BMGF, Wellcome Trust, U.S. Biodefense Agency (BARDA)). The grant provided total funding of \$11.7 million upon the achievement of development milestones, the last of which was successfully achieved in 2Q:24.
- Initiated IND-enabling activities in 2H:21
- Development of VAX-A1 continues to advance and further information about the anticipated timing of an IND application will be provided as the program progresses

### KEY DATA



CDC. Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: US Department of Health and Human Services, CDC; 2019.

BMGF = Bill & Melinda Gates Foundation.

(1) <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7152370/>.

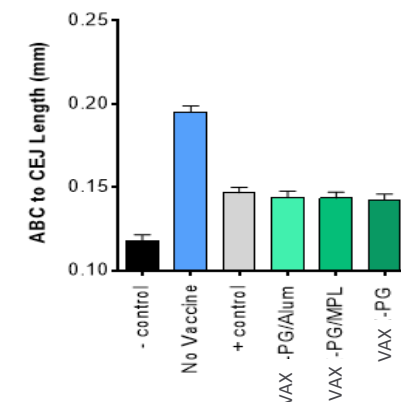
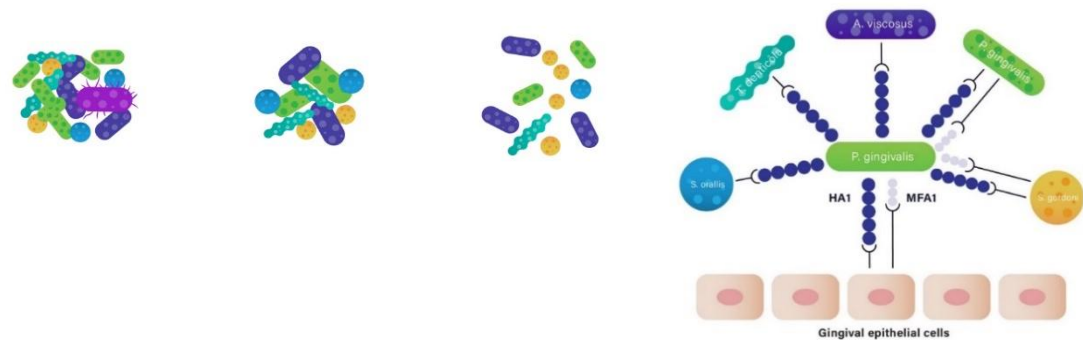
# VAX-PG: Periodontitis Vaccine Program

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

<p><b>UNMET NEED</b></p>	<ul style="list-style-type: none"> <li>Periodontal disease is a chronic oral inflammatory disease leading to destruction of soft and hard tissues supporting the teeth</li> <li>Highly prevalent: estimated 65M U.S. adults afflicted<sup>1</sup></li> <li>Periodontal disease caused an estimated loss of approximately \$330 billion in the U.S. and Europe in 2018, with the direct costs alone exceeding \$6B<sup>2</sup></li> <li>Associated with increased risk of heart attack, stroke, cardiovascular disease and Alzheimer’s Disease</li> </ul>
<p><b>VAX-PG: MULTIVALENT THERAPEUTIC VACCINE</b></p>	<ul style="list-style-type: none"> <li>Incorporates proprietary combination of known virulence factors of keystone pathogen</li> <li>Preclinical model demonstrated protein-specific IgG response following immunization and protected mice from <i>P. gingivalis</i>-elicited oral bone loss</li> <li>Initial goal to develop therapeutic vaccine that slows or stops disease progression</li> </ul>
<p><b>PROGRAM STATUS</b></p>	<ul style="list-style-type: none"> <li>Preclinical proof-of-concept published in Journal of Clinical Periodontology</li> <li>A final vaccine candidate for VAX-PG was nominated in Q4 2022 and the program continues to advance</li> </ul>

**MOA & KEY DATA**

- Restoration of balanced microbiota by interrupting underlying inflammatory condition



**Challenge Study Results**

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

(1) <https://www.cdc.gov/mmwr/preview/mmwrhtml/su6203a21.htm>.

(2) <https://pubmed.ncbi.nlm.nih.gov/34053082/#:~:text=Indirect%20costs%2C%20those%20related%20to,%E2%82%AC2.52B%20in%20Europe.>

# 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.
- With the aim of reducing morbidity and mortality due to the disease, the World Health Organization lists Shigella vaccine development as a priority goal<sup>2</sup>

### 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

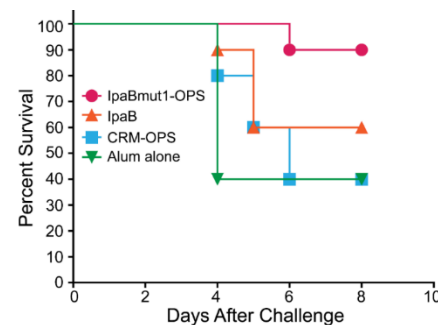
### PROGRAM STATUS

- New program added to preclinical pipeline
- Decision on final candidate to be determined by a human challenge study conducted at the University of Maryland, Baltimore
- Currently optimizing process for scale-up and production

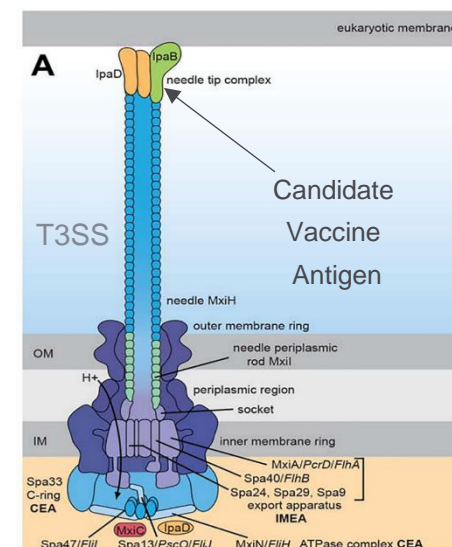
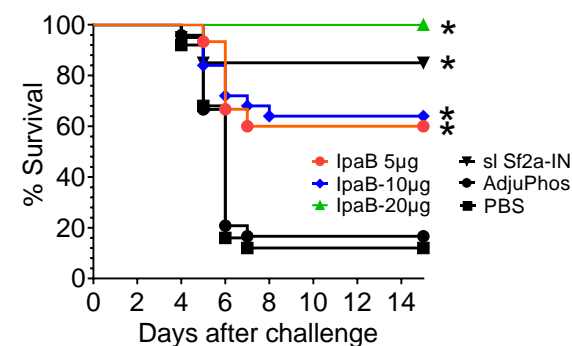
### MOA & KEY DATA

- 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) Lancet. 2018 Feb 24;391(10122):801-812.

(2) <https://www.who.int/publications/i/item/9789240036741>.

# Key Corporate Highlights

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Large Market Opportunity for Lead PCV Franchise

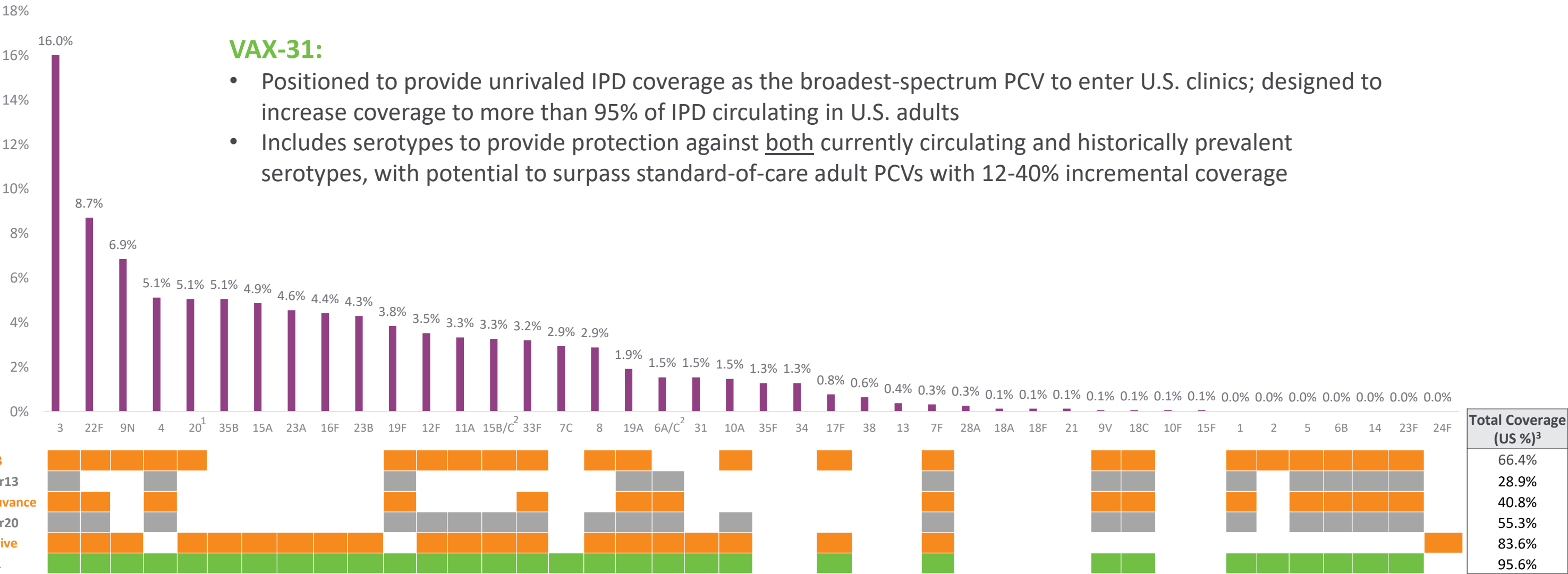
Cell-Free Protein Synthesis Enabled Pipeline

Robust Pipeline with Multiple Novel Vaccines

Aligned Critical Resources

# Appendix

# Spectrum of Coverage Drives Adoption in PCV Segment: VAX-31 Designed to Increase Coverage to >95% of IPD Circulating in U.S. Adults



(1) Coverage for ST20 for VAX-31 is based on Serotype 20B.  
 (2) 15C coverage due to cross-reaction against 15B. 6C coverage due to cross-protection by 6A.  
 (3) % US coverage is the percentage of IPD caused in individuals >50yrs of age in the United States in the 2022 based on ABC surveillance data. Reference: [https://data.cdc.gov/Public-Health-Surveillance/1998-2022-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p/about\\_data](https://data.cdc.gov/Public-Health-Surveillance/1998-2022-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p/about_data).

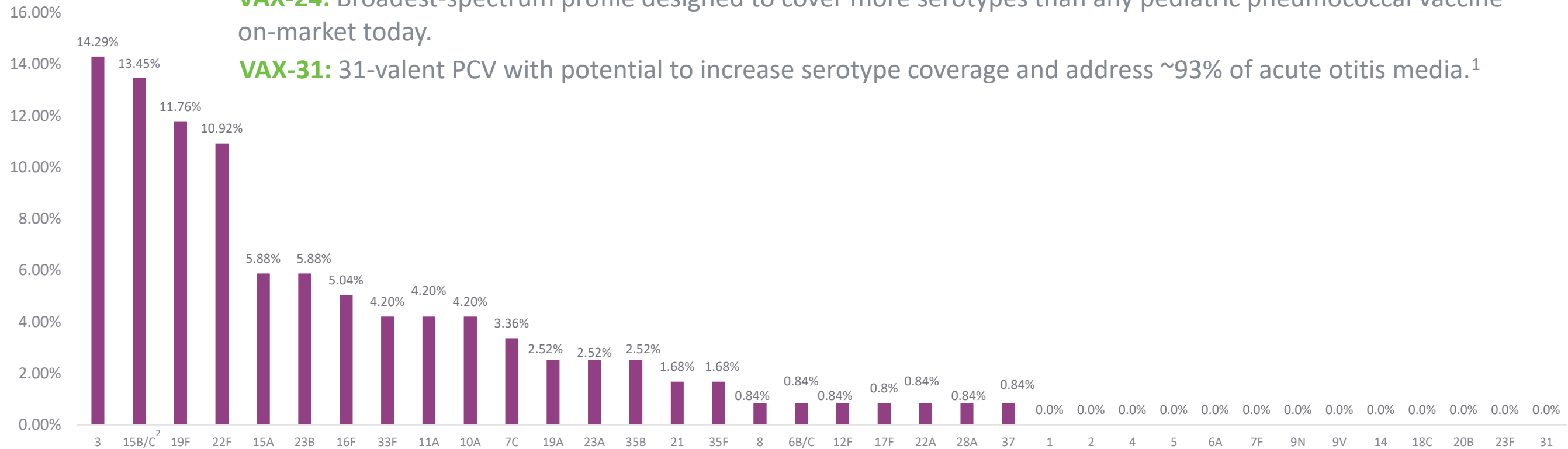


# Spectrum of Coverage Drives Adoption in Vital Pediatric Population

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

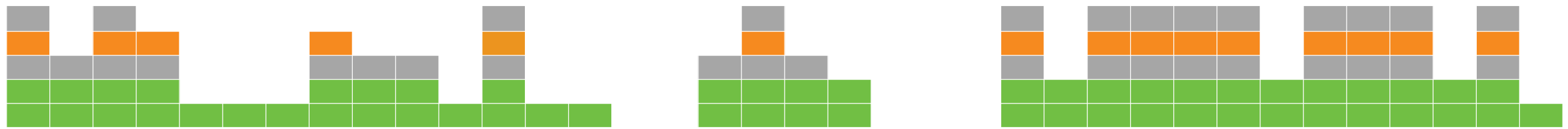
**VAX-24:** Broadest-spectrum profile designed to cover more serotypes than any pediatric pneumococcal vaccine on-market today.

**VAX-31:** 31-valent PCV with potential to increase serotype coverage and address ~93% of acute otitis media.<sup>1</sup>



Total Coverage (US %) <sup>3</sup>
24.9%
44.5%
68.1%
68.9%
94.1%

**Pevnar13**  
**Vaxneuvance**  
**Pevnar20**  
**VAX-24**  
**VAX-31**



(1) Kaur et al, Characterization of Streptococcus pneumoniae isolates obtained from the middle ear fluid of US children, 2011–2021.

(2) 15C coverage due to cross protection against 15B. Co

(3) % US coverage is the percentage of IPD caused in individuals <5 yrs of age in the United States in 2022 based on ABC surveillance data. Reference: CDC. 2022 Serotype Data for IPD Cases by Age Group from ABC surveillance. [https://data.cdc.gov/Public-Health-Surveillance/1998-2022-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p/about\\_data](https://data.cdc.gov/Public-Health-Surveillance/1998-2022-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p/about_data). Accessed August 28, 2024