

# Corporate Presentation



May 8, 2024

**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, potentially best-in-class pneumococcal conjugate vaccines (PCV) 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 infant Phase 2 study and VAX-31 adult Phase 1/2 study; advancement of either VAX-24 or VAX-31 into a Phase 3 adult clinical program, and the timing of such studies and their data readouts; and the announcement of guidance for VAX-A1); 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 CARB-X and NIH; the growth and expansion of the pneumococcal vaccine market, and the potential for Vaxcyte's PCV franchise to have sustained leadership within such market; the potential conversion by the pneumococcal vaccine market to a prime-boost schedule; the market opportunity for Vaxcyte's vaccines; Vaxcyte's expectations regarding the potential benefits, spectrum coverage, clinical or regulatory pathways, adoption speed and immunogenicity of its vaccine candidates; VAX-31's advancement as a follow-on candidate to VAX-24; and other statements that are not historical fact. The words "anticipate," "believe," "continue," "could," "designed," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These forward-looking statements are based on Vaxcyte's current expectations and actual results and timing of events could differ materially from those anticipated in such forward-looking statements as a result of risks and uncertainties, including, without limitation, risks related to Vaxcyte's product development programs, including development timelines, success and timing of chemistry, manufacturing and controls and related manufacturing activities; potential delays or inability to obtain and maintain required regulatory approvals for its vaccine candidates; the risks and uncertainties inherent with preclinical and clinical development processes; the success, cost and timing of all development activities and clinical trials; and sufficiency of cash and other funding to support Vaxcyte's development programs and other operating expenses. These and other risks are described more fully in Vaxcyte's filings with the Securities and Exchange Commission (SEC), including its Quarterly Report on Form 10-Q filed with the SEC on May 8, 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 cells with textured, granular surfaces. Some cells are in focus, showing intricate internal structures, while others are blurred in the foreground and background, creating a sense of depth. The overall color palette is various shades of green.

## VAXCYTE MISSION STATEMENT

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

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

## VAX-24 Clinical Proof-of-Concept Obtained, Validating Carrier-Sparing Platform



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

- **Scalable platform** enabling broader-spectrum carrier-sparing PCVs
- **Lead candidate: VAX-24**
  - Potential best-in-class 24-valent PCV designed to replace SOC in adults/children
  - Phase 3-ready in adults following completion of clinical program with positive results from two Phase 2 studies and successful End-of-Phase 2 meeting with FDA
  - Breakthrough Therapy and Fast Track designations in adults
  - Enrollment complete in Phase 2 infant study
- **Next-generation candidate: VAX-31**
  - Broadest-spectrum PCV to enter clinic; designed to cover ~95% of IPD in U.S. adults
  - Enrollment complete in Phase 1/2 adult study



### HIGHLY ATTRACTIVE PCV MARKET

- **Well-defined ~\$8B** market segment **poised for substantial growth driven in the adult population**
- Leverages established surrogate immune endpoints as basis for full approval, **negating need for field efficacy studies**
- Spectrum of coverage is the **primary adoption driver**, yet incumbents **limited by carrier suppression**



### CELL-FREE PROTEIN SYNTHESIS 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-24 and VAX-31 key components
  - Building out capacity to satisfy global PCV demand for commercial markets
- **Seasoned management team, directors and advisors**
- **\$1.9 billion in cash, cash equivalents and investments** as of 3/31/24

*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**  
SVP Commercial Mfg & Supply Chain

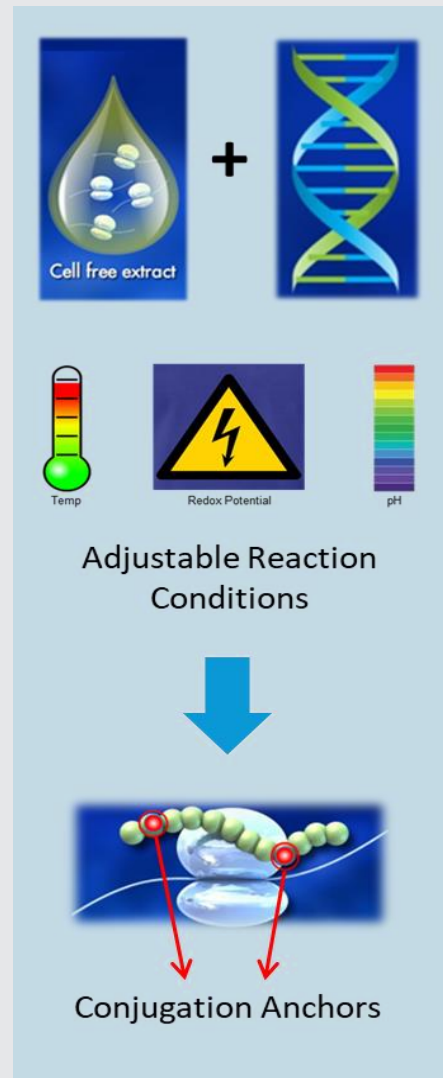


**Mark Wiggins, MBA**  
CBO



# 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



# Anticipated PCV Franchise Milestones<sup>1</sup>

Vaxcyte is Advancing Clinical Development of VAX-24 and VAX-31 with Several Key Upcoming Milestones

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## ADULT INDICATION

- Announce topline safety, tolerability and immunogenicity data from **VAX-31 adult Phase 1/2 study in 3Q:24**
- Advance either VAX-24 or VAX-31 to adult Phase 3 program
  - **If VAX-24:**
    - Initiate Phase 3 pivotal, non-inferiority study in adults aged 50 and older in **2H:24** and announce topline safety, tolerability and immunogenicity data in **2H:25**
    - Initiate balance of expected Phase 3 studies in **2025 and 2026**
  - **If VAX-31:**
    - Initiate full complement of expected Phase 3 studies in **2025 and 2026**

## INFANT INDICATION

- Announce topline safety, tolerability and immunogenicity data from **VAX-24 infant Phase 2 study in 2025**
  - **Primary three-dose immunization series by end of 1Q:25**, which will follow participants receiving all three doses in this series as well as the serology and data analysis
  - **Booster dose by end of 2025**

(1) Guidance as of May 8, 2024



# PCV Opportunity

# Global Impact of Pneumococcal Disease Remains Significant



## ABOUT STREPTOCOCCUS PNEUMONIAE

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

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



## CURRENT ~\$8 BILLION GLOBAL VACCINE CATEGORY

Vaccinations are recommended globally for infants and adults to prevent PD

Standard of Care schedule in the U.S.:

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



## GLOBAL INCIDENCE & IMPACT OF PD STILL SUBSTANTIAL

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

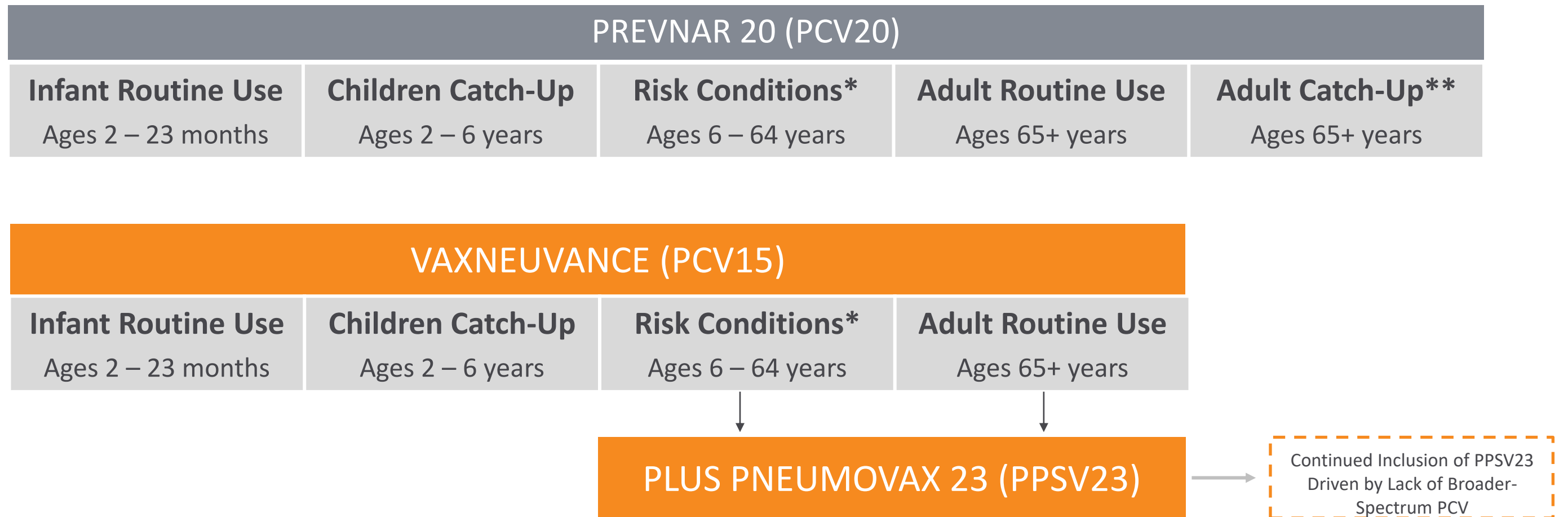
- In the U.S. alone, there are ~320K pneumococcal pneumonia cases per year resulting in ~150K hospitalizations
- IPD is a leading cause of invasive disease in children two years of age and under
- The bacteria associated with IPD is a major driver of deaths due to antimicrobial resistance

(1) <https://www.cdc.gov/pneumococcal/clinicians/clinical-features.html>

(2) <https://www.cdc.gov/vaccines/pubs/pinkbook/pneumo.html>

# ACIP Recommendations Reinforce Priority of Broader-Spectrum PCVs with PCV20 as Standard-of-Care

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



\*No prior vaccination with PCV13, PCV15 or PCV20.

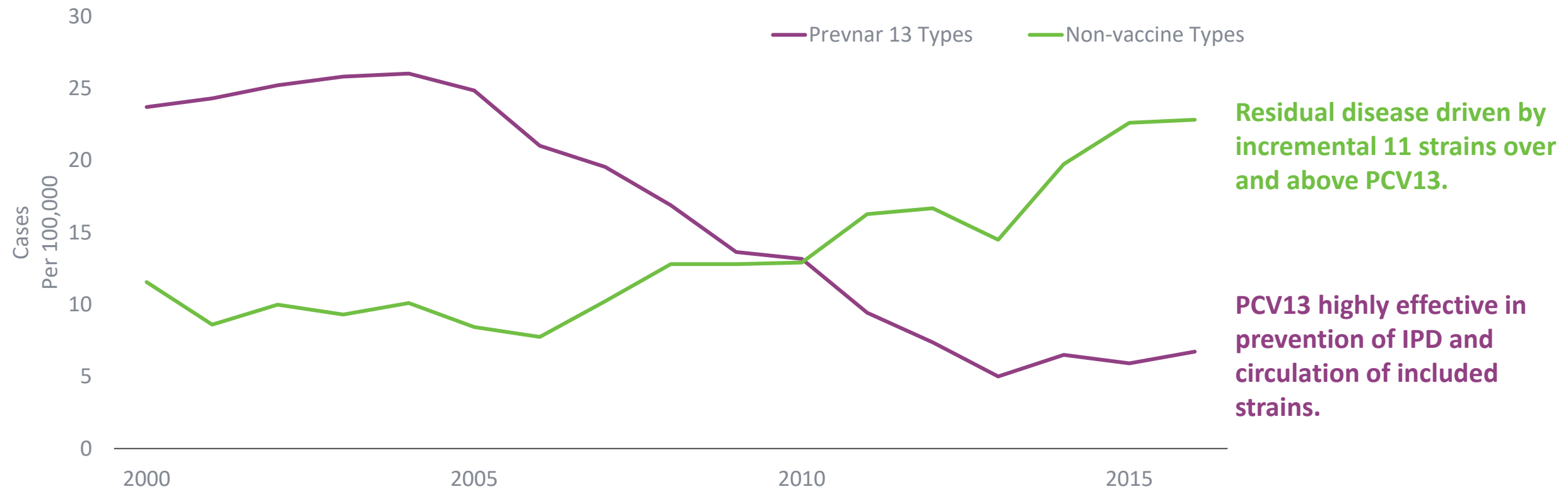
\*\*Shared clinical decision-making is recommended regarding use of a supplemental PCV20 dose for adults aged ≥65 years who have completed their recommended vaccine series with both PCV13 and PPSV23.

Source: Centers for Disease Control and Prevention Morbidity and Mortality Weekly Report, Volume 73 No. 3, September 8, 2023

# 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**

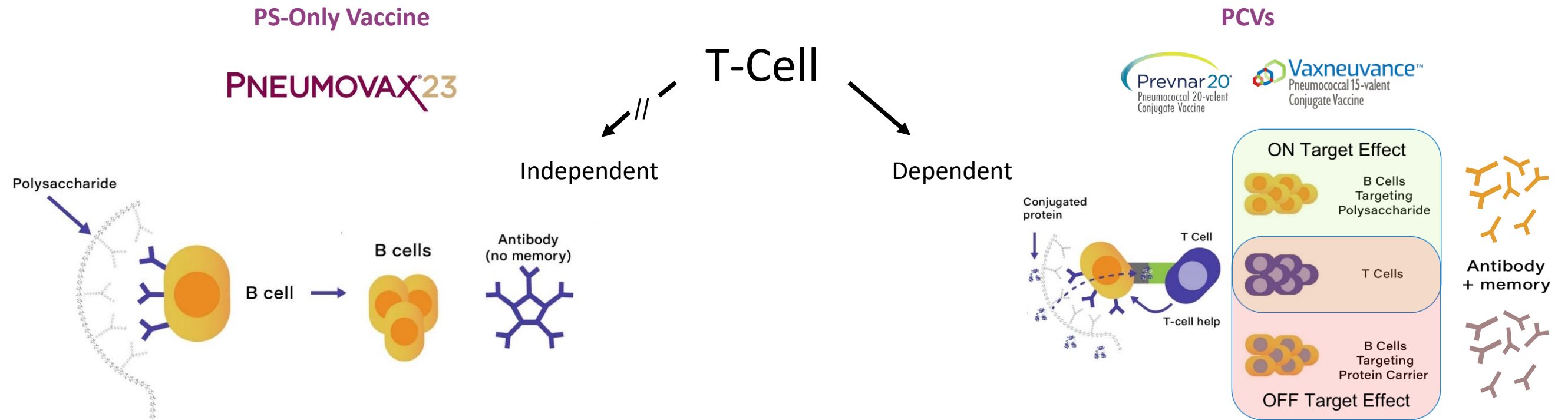
UK IPD CASES IN ADULTS  $\geq 65$ <sup>1</sup>



(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.

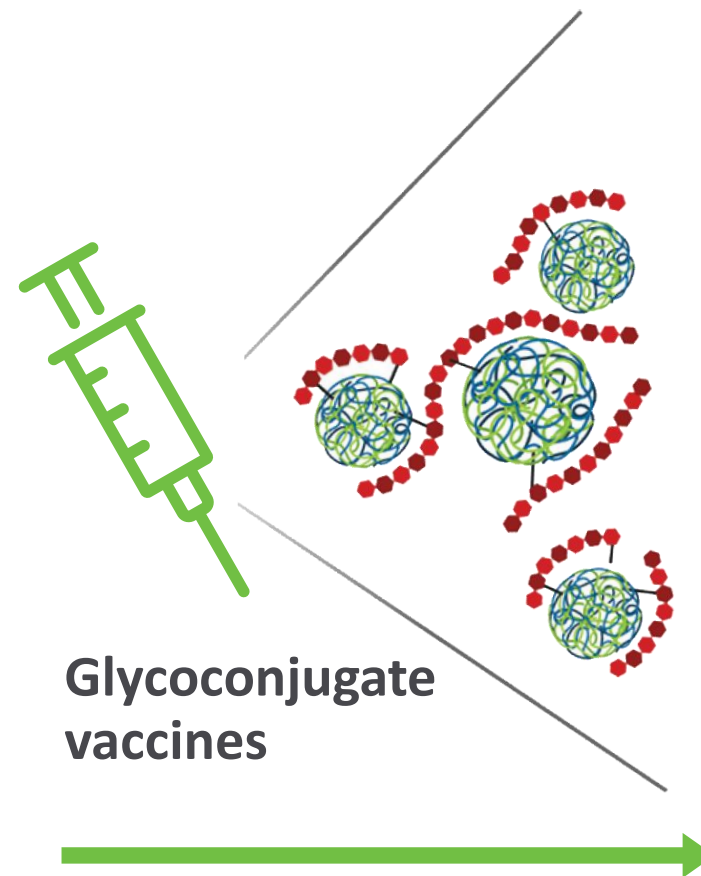
(1) Protein carrier in Pevnar 20 is a modified form of diphtheria toxin (CRM<sub>197</sub>).

# Limitations of Current PCVs

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

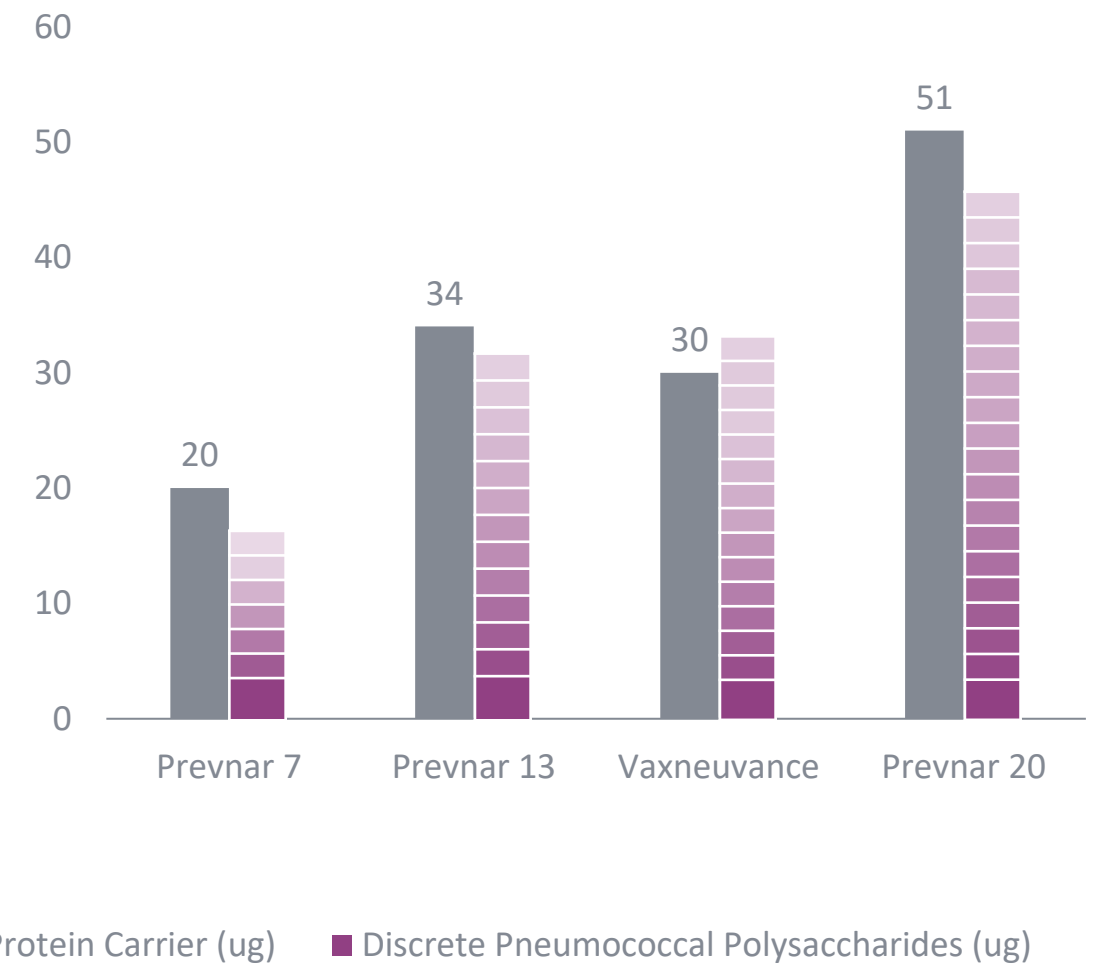
## LIMITATIONS OF CONVENTIONAL CHEMISTRY

- 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



**Glycoconjugate vaccines**

## PROTEIN CARRIER DIVERTS IMMUNE RESPONSE



Sources: Prevnar 20 BLA Clinical Review Memorandum. STN: 125731/0 June 8, 2021, Prevnar 7, Prevnar 13 and Vaxneuvance product inserts.

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

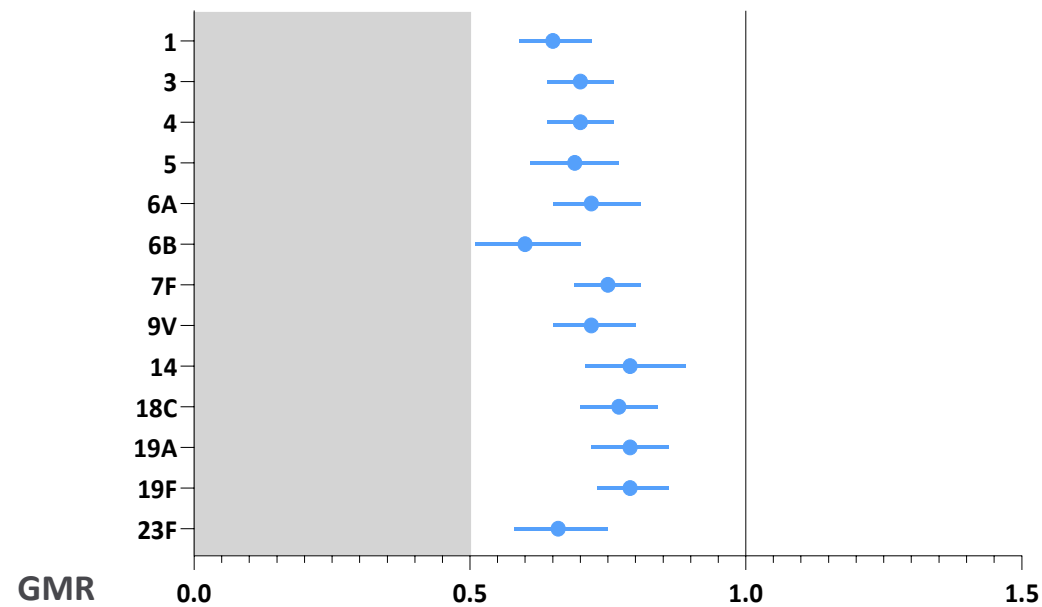
## Coverage Expansion Using Conventional Chemistry Has Led to Carrier-Induced Immune Suppression

### CARRIER SUPPRESSION

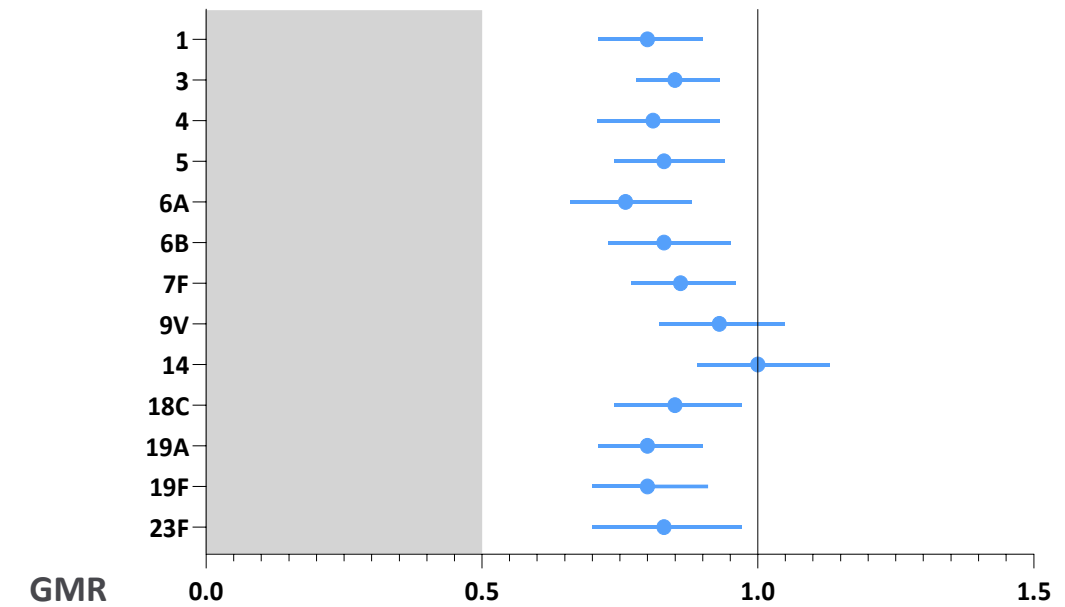
Diminished immune response to target polysaccharides due to cumulative amount of protein carrier

- 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.

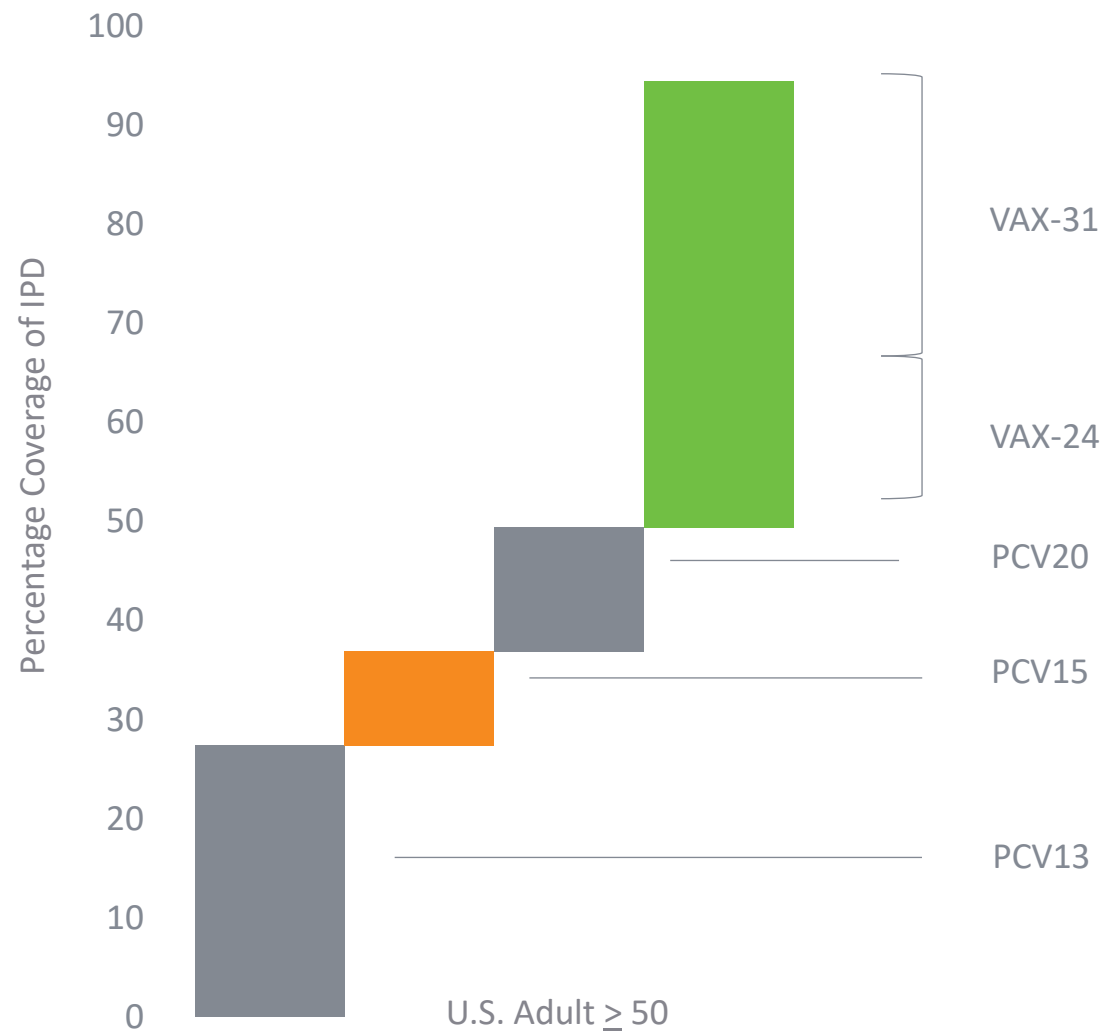
OPA = Opsonophagocytic assay.

GMR = Geometric Mean Ratio

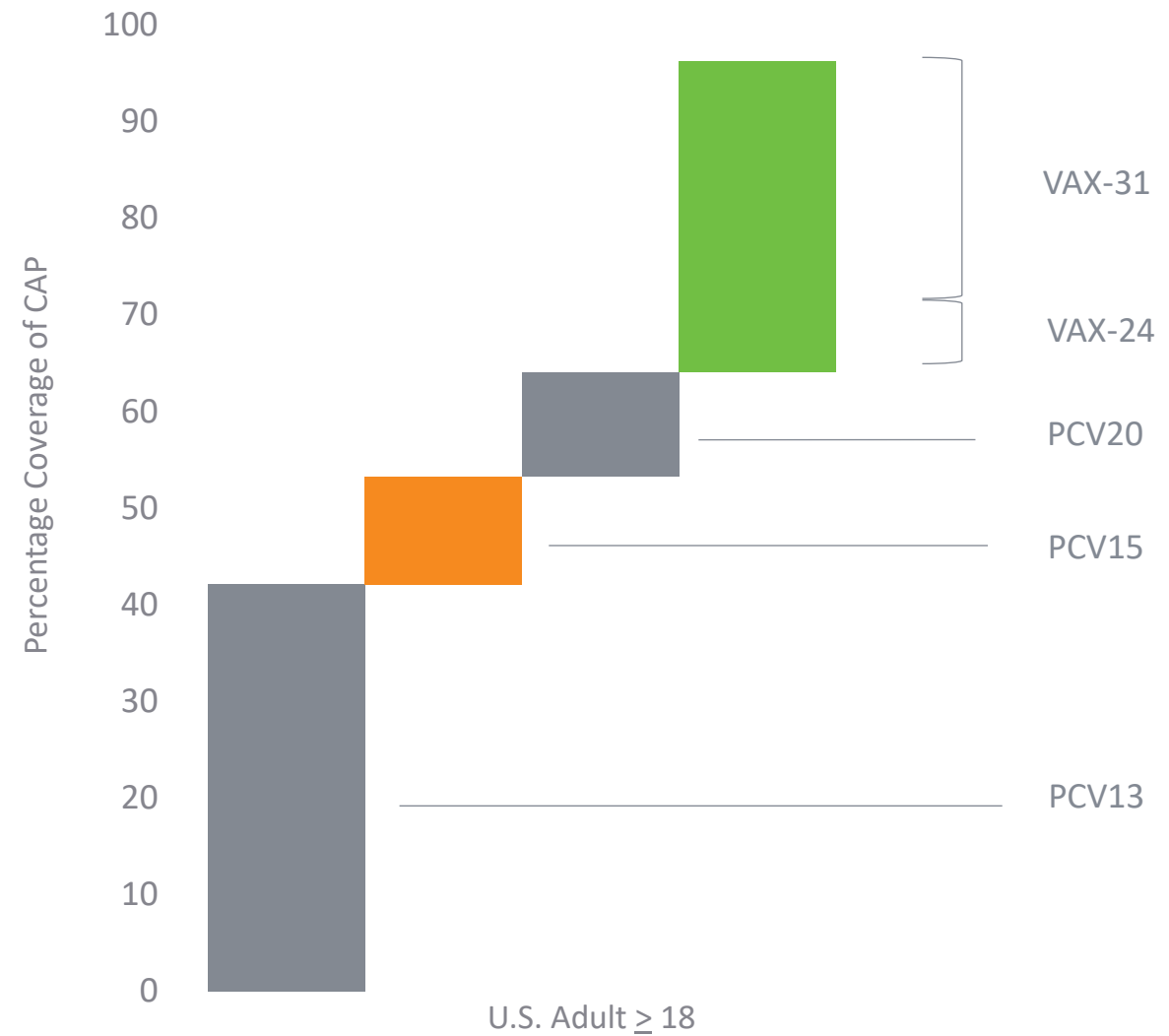
# Spectrum of Coverage Drives Adoption in PCV Segment

## Significant Unmet Needs Remain Despite Available Vaccines

ESTIMATED COVERAGE OF PCVs BASED ON CIRCULATING INVASIVE PNEUMOCOCCAL SEROTYPES<sup>1,2</sup>



ESTIMATED COVERAGE OF PCVs BASED ON CIRCULATING COMMUNITY-ACQUIRED PNEUMONIA (CAP) IN STUDY POPULATION WITH S. PNEUMONIAE DETECTED<sup>3</sup>

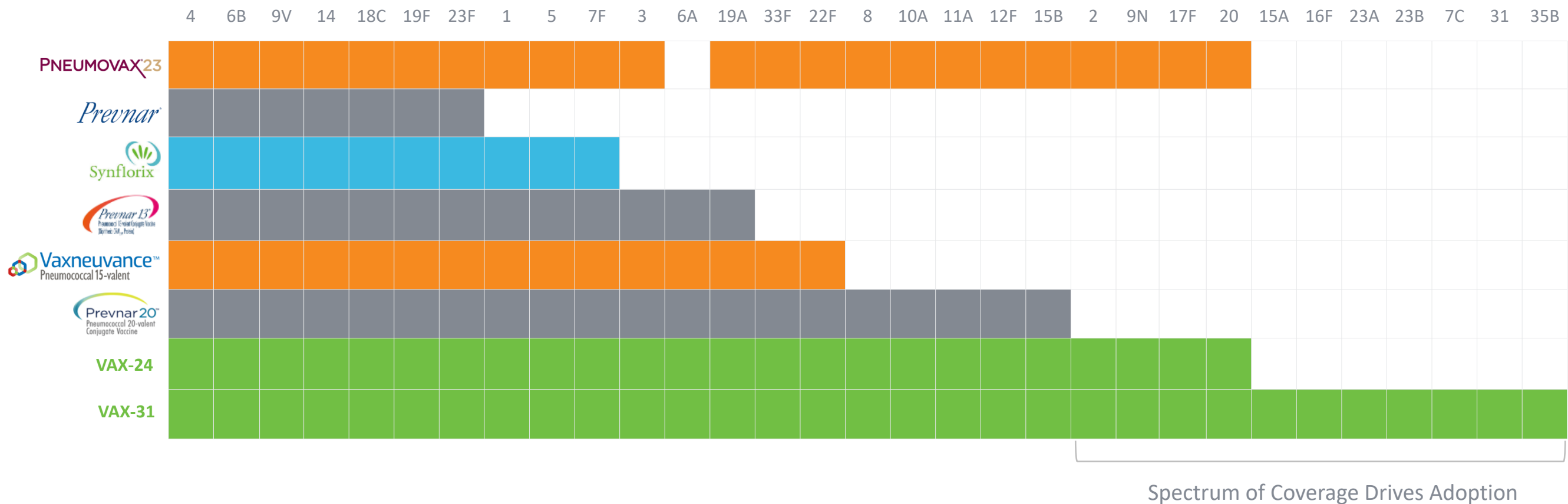




# Vaxcyte Carrier-Sparing PCV Franchise has Potential for Sustained Leadership in Growing ~\$8B Pneumococcal Vaccine Market

**VAX-31:** Next-generation 31-valent PCV, the broadest-spectrum PCV in the clinic, showcases franchise approach and scalability of carrier-sparing conjugates

**VAX-24:** Phase 3-ready, category-leading 24-valent PCV incorporating carrier-sparing conjugates



Spectrum of Coverage Drives Adoption

Source: Prescribing information for Prevnar, Prevnar 13, Prevnar20, Synflorix, Vaxneuvance, and Prevnar 20. Company filings for Vaxcyte.

# Pneumococcal Vaccine Market is Highly Attractive

## VAX-24 and VAX-31 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

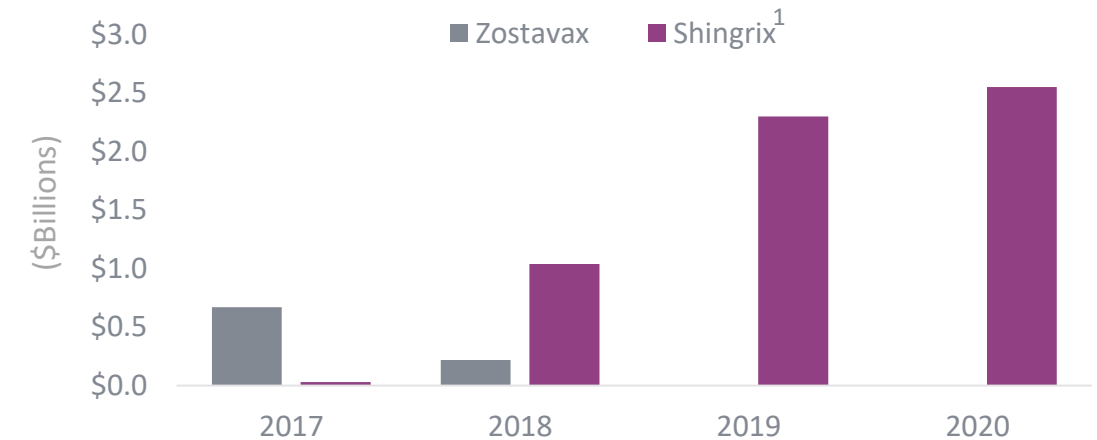
- Prevnar Family (PCV7/PCV13/PCV20) & PPSV23 have generated >\$100B in revenues; PCV13 and PCV20 had combined annual sales of ~\$6.4B in 2023

#### ATTRACTIVE MARGINS

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

#### 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



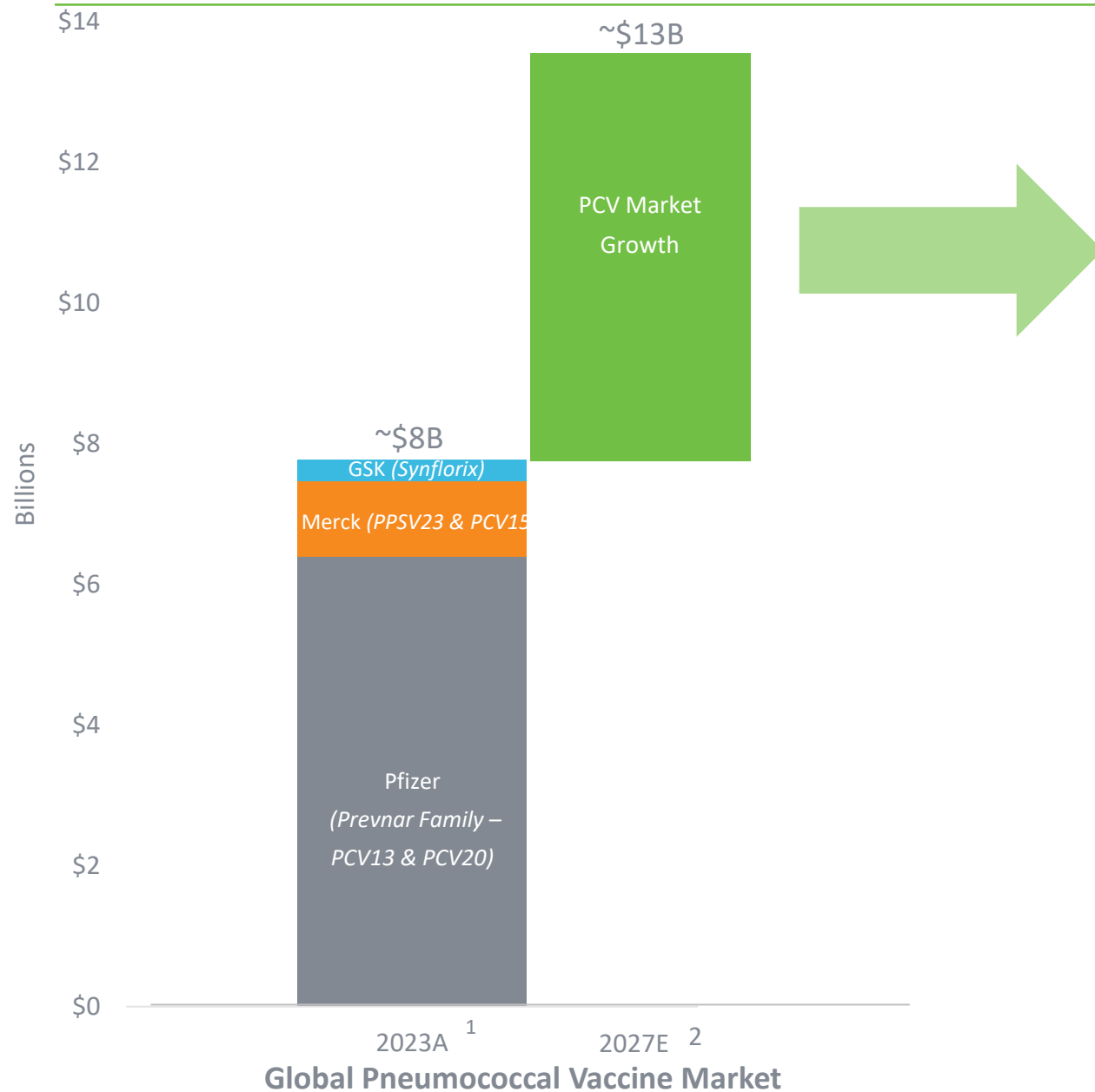
- FDA approved in 4Q:2017 to prevent shingles in adults
- ACIP granted “preferred recommendation”
- Replaced the incumbent (Zostavax from Merck)

MOA = mechanism of action; SOC = standard of care; ACIP = US CDC Advisory Committee on Immunization Practices.

(1) Revenues reported in GSK (Shingrix) and Merck (Zostavax) financial filings.

# Pneumococcal Vaccine Market Poised for Significant Growth

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



## PCV Market Growth Drivers

- Strong ACIP consideration to expand U.S. universal adult vaccination to ≥50 years from ≥65 would significantly expand market
  - Would necessitate prime-boost for effective long-term protection, which has been limited by continued availability of Pneumovax 23
  - Serotype epidemiology and availability of broader-valency PCVs may lead to adult recommendations outside the U.S.
- ACIP voted to support PCV20 “catch-up” for adults who previously received PCV13 and Pneumovax 23
  - “At risk” adults added to U.S. universal PCV vaccination recommendation, which includes >25% of 50-64 year olds<sup>3</sup>
- Premium price for PCV20 and PCV15 shows value of additional serotype coverage

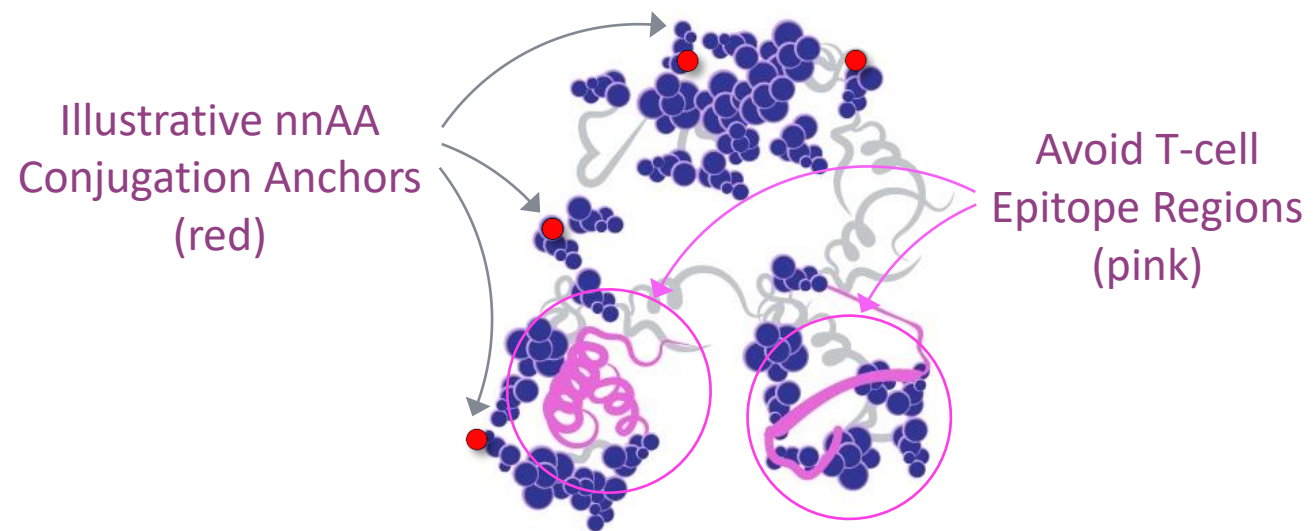
(1) Sources: Company websites.  
 (2) Global Pneumococcal Vaccine Market (2022-2027), Infogence Global Research.  
 (3) Shea KM, Edelsberg J, Weycker D et al. (2014), Open Forum Infect Dis 1(1): ofu024.

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

# Vaxcyte's PCV Franchise Employs Carrier-Sparing Conjugates

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

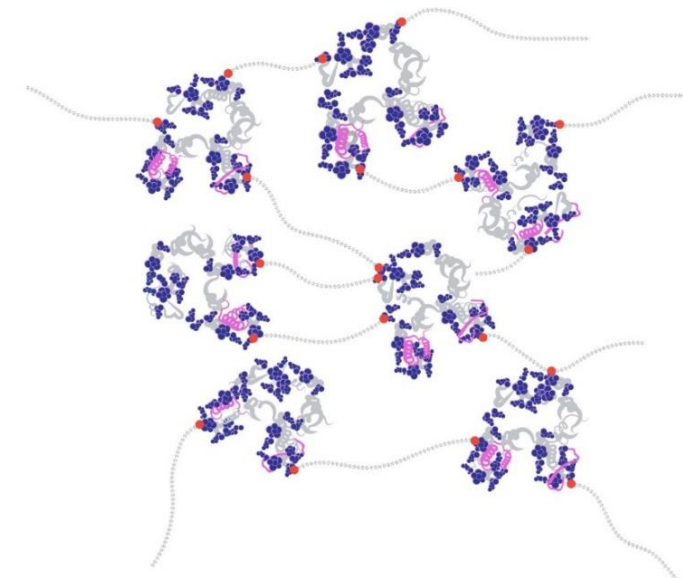
PRECISE, SITE-SPECIFIC CONJUGATION SITES ON PROPRIETARY eCRM<sup>®</sup> PROTEIN CARRIER



### 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-24 & VAX-31 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-24 and VAX-31 conjugates form standard PCV interstrand crosslinked matrices
  - Perceived as foreign by the host
  - Allows use of standard critical quality attributes and serological assays

# Vaxcyte PCV Franchise Design Leverages Many Standard PCV Conventions

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

	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-24 and VAX-31
- Vaxcyte has leveraged the same animal models utilized in the development of both approved PCVs (Prevnar and Synflorix)

# PCV Franchise Adult Indication

# VAX-24 Adult Clinical Program



# VAX-24 Phase 2 Adult Program Data Key Take-Aways (n=1,041)

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**SAFETY:** Full six-month safety data demonstrated VAX-24 has a safety and tolerability profile similar to PCV20 for all doses in both adult Phase 1/2 and Phase 2 studies



**IMMUNOGENICITY:** VAX-24 showed robust immune responses across all 24 serotypes in both Phase 2 studies for the conventional 2.2mcg dose, demonstrating the potential of VAX-24 to **expand coverage and improve immunogenicity over the current standard-of-care**

- Optimal VAX-24 2.2mcg dose to potentially be advanced to Phase 3:
  - In Phase 2 study in adults aged 50-64, met the standard Opsonophagocytic Activity (OPA) response non-inferiority criteria for all 20 serotypes common with PCV20, of which 16 achieved higher immune responses
  - In Phase 2 study in adults aged 65 and older, met the standard OPA response non-inferiority criteria for 18/20 serotypes common with PCV20
  - In both Phase 2 studies, met the standard superiority criteria for all 4 additional serotypes unique to VAX-24

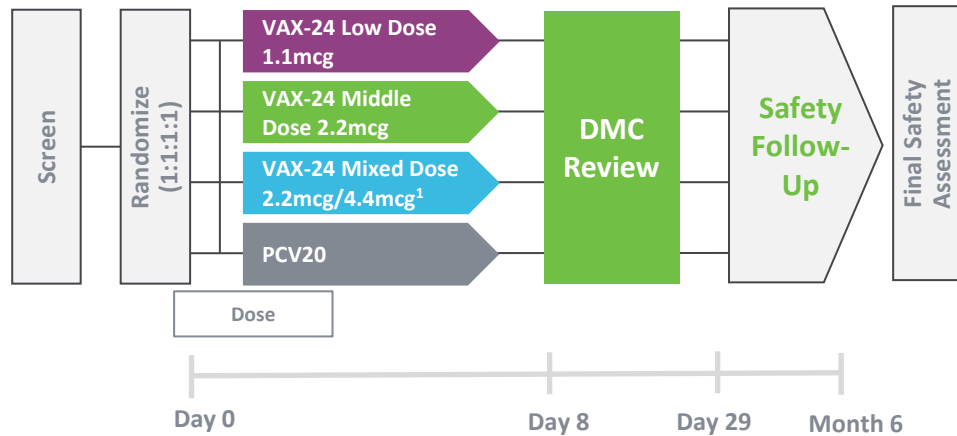


**VAX-24 IS PHASE 3-READY WITH BEST-IN-CLASS POTENTIAL**

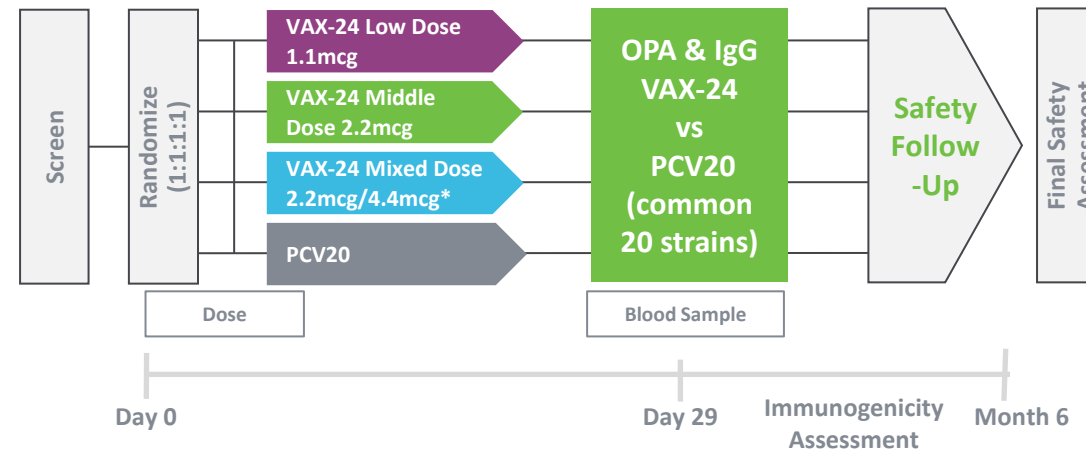
- Successful End-of-Phase 2 meeting with FDA provided alignment on key elements of the potential Phase 3 program (e.g., approximate number of overall subjects) and confirmation that a field efficacy study is not required

# Robust VAX-24 Phase 2 Clinical Program in Adults Evaluated Safety, Tolerability and Immunogenicity

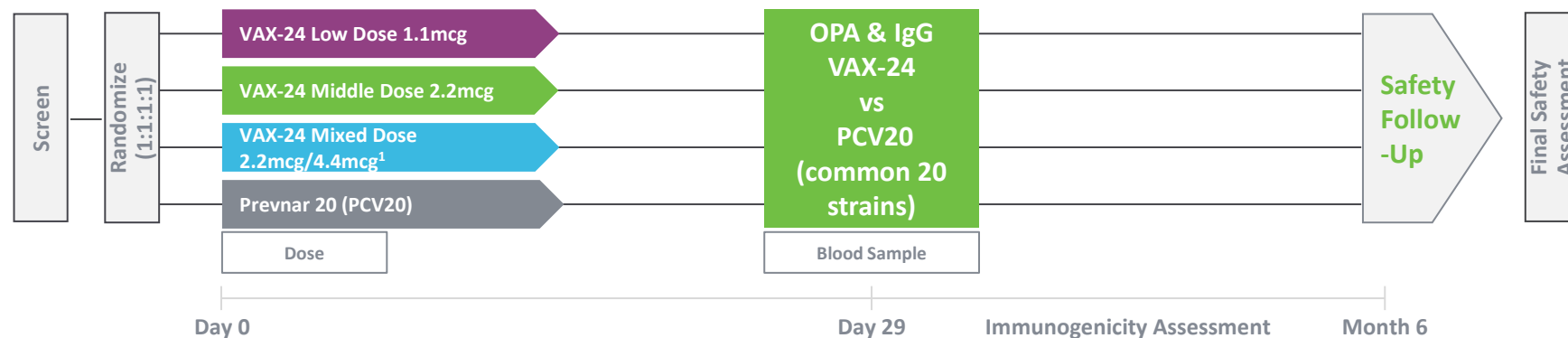
**Pilot Phase 1 Safety**  
Healthy Adults 18 to 49 (n=64)



**Clinical Proof-of-Concept Phase 2 Study**  
Healthy Adults 50 to 64 (n=771)



**Phase 2 Study**  
Adults Aged 65 and Older (n=207)



## OVERVIEW OF VAX-24 ADULT PHASE 2 PROGRAM

- Two randomized, observer-blind, dose-finding, controlled clinical studies that evaluated the safety, tolerability and immunogenicity of VAX-24 delivered positive results:
  - Phase 1/2 proof-of-concept study in adults aged 18 to 48 (Phase 1: n=64) and aged 50 to 64 (Phase 2: n=771)
  - Phase 2 study in adults aged 65 and older (n=207)
- 1,042 healthy adults enrolled across both studies

(1) For the VAX-24 Mixed Dose, a 4.4mcg dose is used for serotypes 3, 6B, 7F, 9V, 18C, 19A and 19F; a 2.2 mcg dose is used for the remaining serotypes.

# Combined Six-Month Safety Data from Both Adult VAX-24 Studies

## Safety Results Similar to PCV20 and Across Cohorts

	VAX-24 – Low Dose (1.1mcg)	VAX-24 – Middle Dose (2.2mcg)	VAX-24 – Mixed Dose (2.2mcg/4.4mcg)	PCV20
Number of Subjects with	261	258	260	262
Unsolicited TEAE, n (%)	38 (14.6)	28 (10.9)	29 (11.2)	42 (16.0)
Related Unsolicited TEAE, n (%)	4 (1.5)	9 (3.5)	5 (1.9)	8 (3.1)
MAAE, n (%)	32 (12.3)	29 (11.2)	26 (10.0)	37 (14.1)
Related MAAE, n (%)	0	0	0	0
NOCI, n (%)	4 (1.5)	4 (1.6)	7 (2.7)	5 (1.9)
Related NOCI, n (%)	0	0	0	0
SAE, n (%)	3 (1.1)	4 (1.6)	2 (0.8)	4 (1.5)
Related SAE, n (%)	0	0	0	0
Death, n (%)	0	1 (0.4) <sup>1</sup>	0	0
Related Death, n (%)	0	0	0	0

(1) 66-year-old white, obese male (BMI:47.4) with hypertension. No solicited AEs were reported after vaccination. Participant suffered sudden cardiac death six months post-vaccination determined by Principal Investigator to be not related to study product due to participant's history of hypertensive cardiovascular disease.

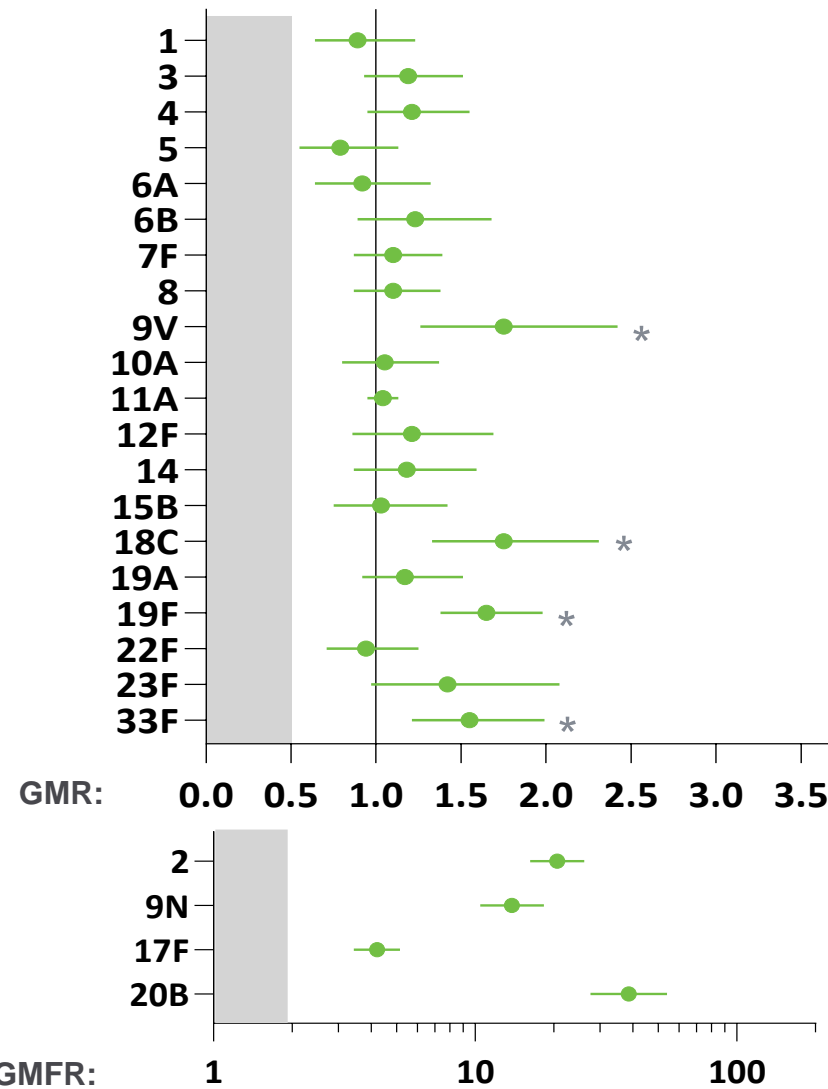
TEAE = Treatment emergent adverse events

Excludes Solicited AEs

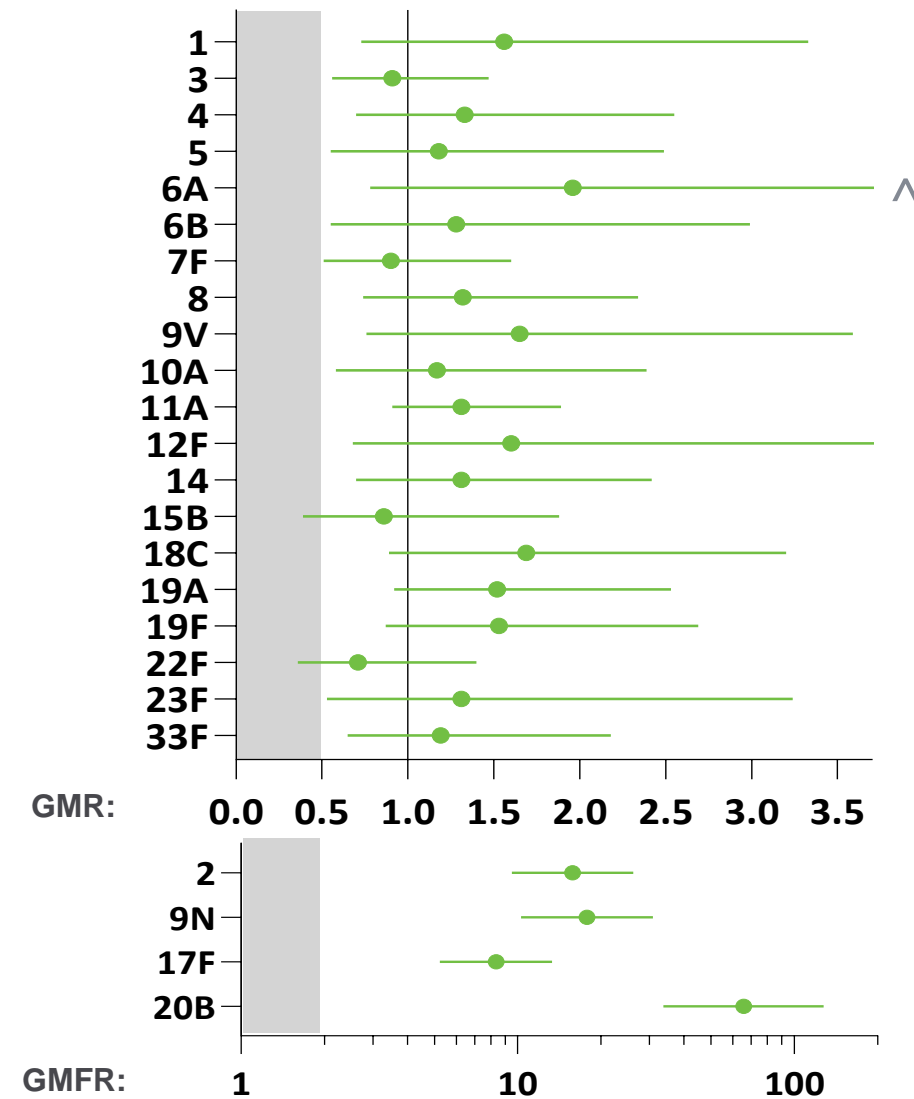
Data final as of June 21, 2023

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

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)



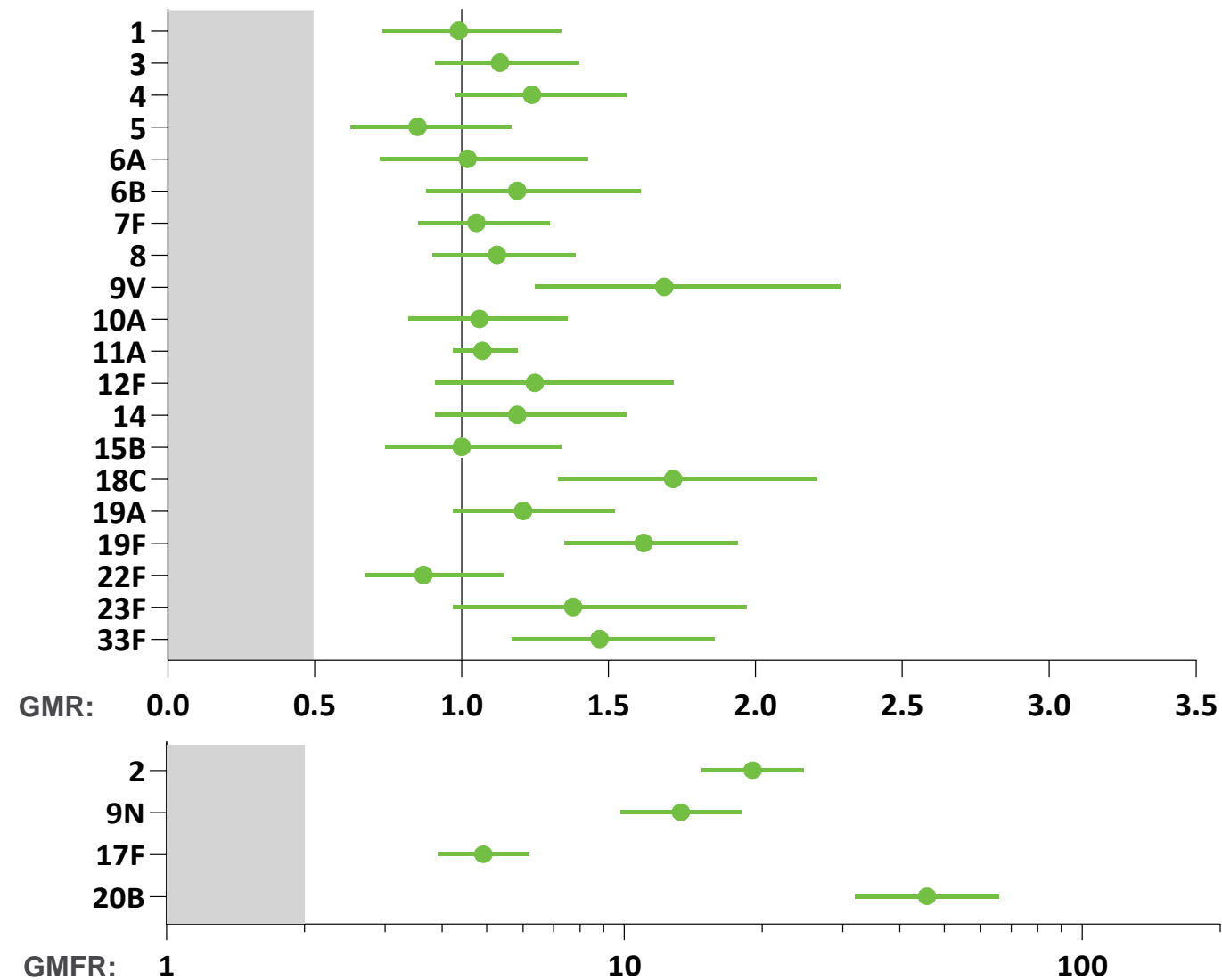
(1) Sample size of n~180 calculated as median between immunogenicity evaluable VAX-24 n=179 and PCV20 n=181 rounded to nearest 10.

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

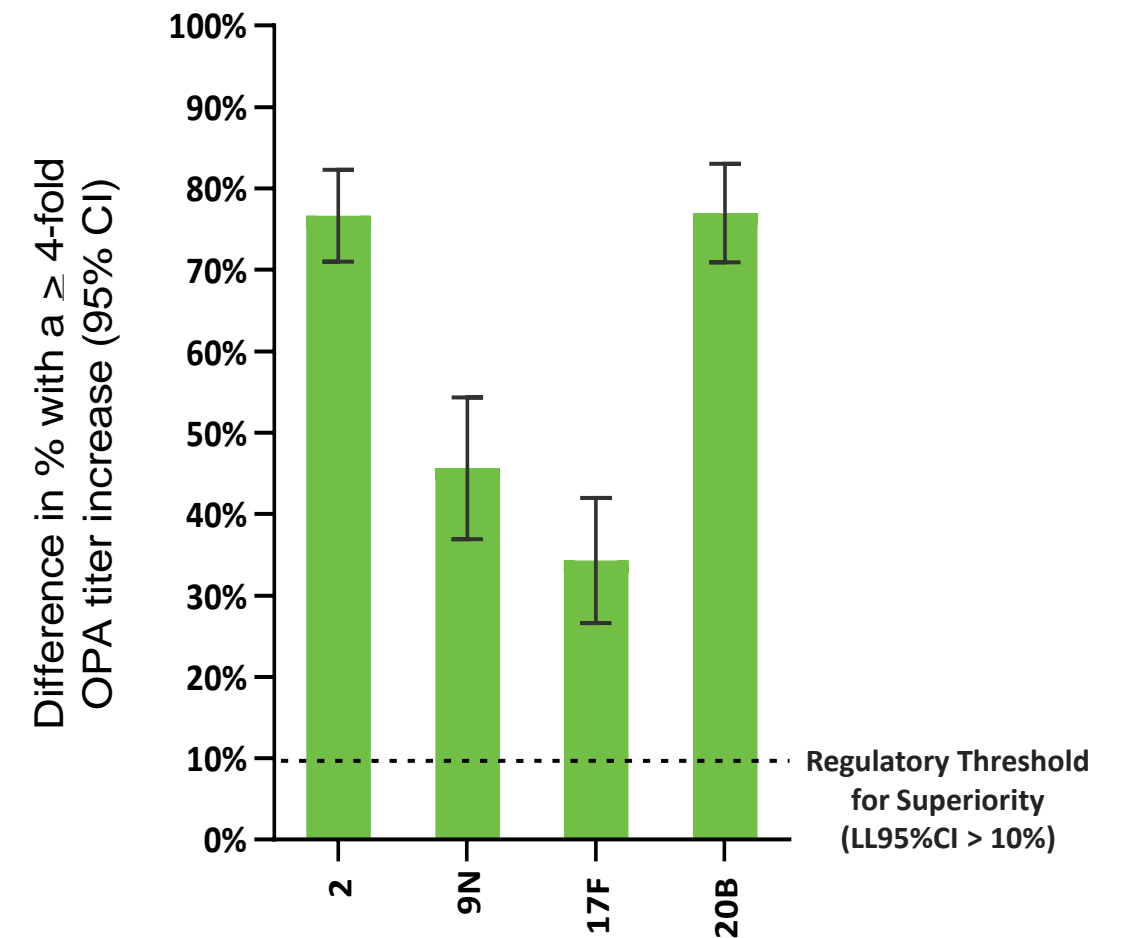
# Pooled Analyses Support Advancement of VAX-24 to Phase 3

Met Standard OPA Response Non-Inferiority Criteria for All 20 Common STs

Prespecified Pooled Data From VAX-24 2.2mcg Phase 2 Studies in Adults Aged 50+ (n~225<sup>1</sup>)



Pooled Data From VAX-24 2.2mcg Phase 2 Studies in Adults Aged 50+ (n~205<sup>2</sup>)



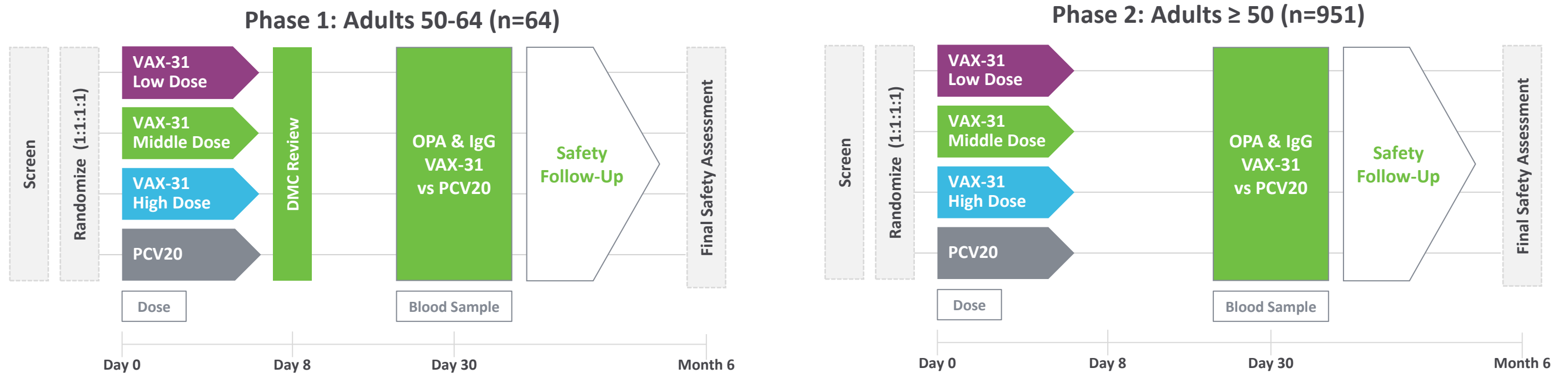
(1) Sample size of ~225 calculated as median between immunogenicity evaluable VAX-24 n=228 and PCV20 n=224 rounded to nearest 5.

(2) Sample size of ~205 calculated as median between pre and post results for serotypes presented VAX-24 n=212 and PCV20 n=201 rounded to nearest 5.

# VAX-31 Adult Clinical Program

# Enrollment Complete in VAX-31 Phase 1/2 Clinical Study in Adults Aged 50+

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



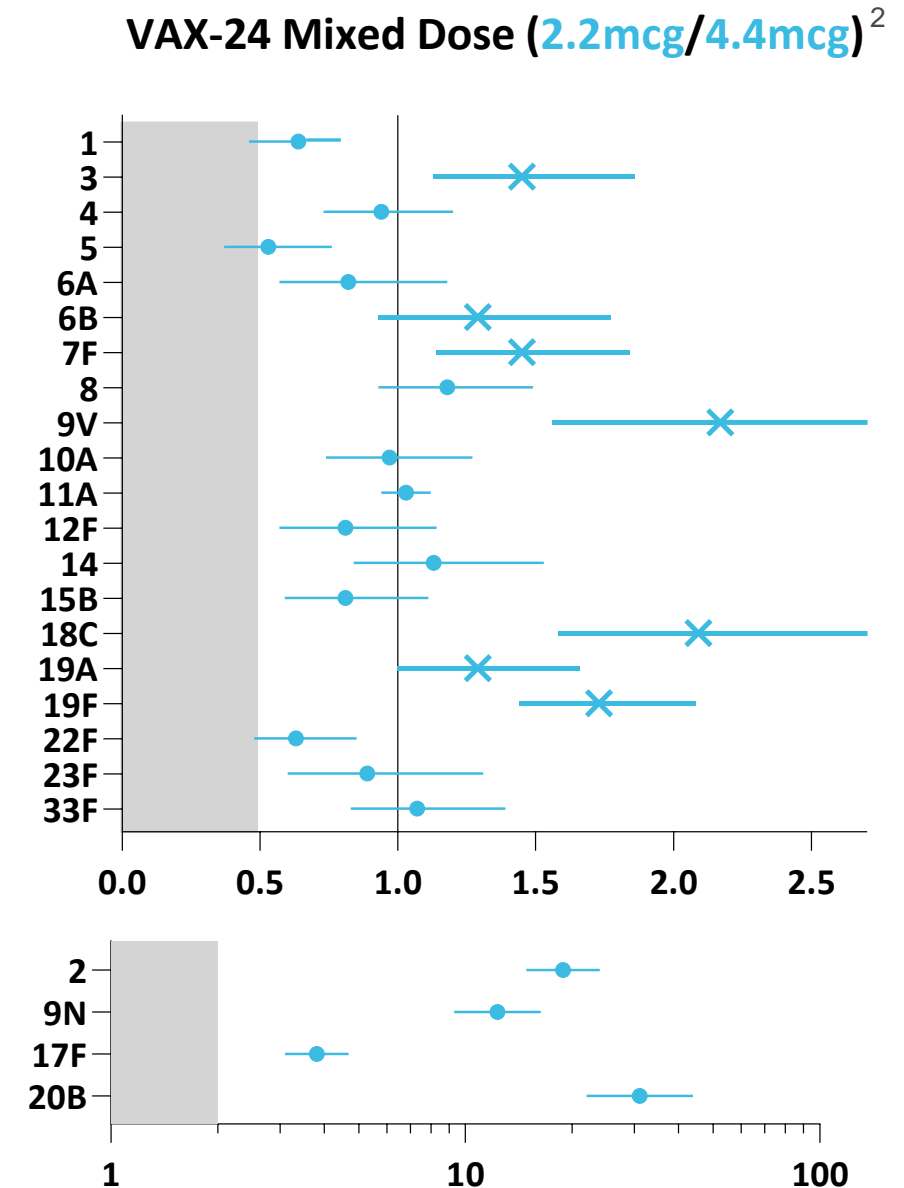
## STUDY OVERVIEW

- Phase 1 evaluated the safety and tolerability of a single injection of VAX-31 at three doses (low, middle, high) and compared to PCV20 in 64 healthy adults aged 50-64. Following the satisfactory independent Data Monitoring Committee (DMC) review of Phase 1 safety and tolerability data, the study proceeded to Phase 2.
- Phase 2 portion of the study is evaluating the safety, tolerability and immunogenicity of a single injection of VAX-31 at the same three dose levels and compared to PCV20 in 951 healthy adults 50 years of age and older.
- Serology samples will be collected to assess immunogenicity for all participants in the study. The immunogenicity objectives include an assessment of the induction of antibody responses, using opsonophagocytic activity (OPA) and immunoglobulin G (IgG), at each VAX-31 dose and compared to PCV20. Participants will be evaluated for safety through six months after vaccination.

# VAX-31 Designed to Significantly Broaden Disease Protection While Maintaining Coverage of Previously Circulating Strains

## REPRESENTS MAJOR POTENTIAL ADVANCEMENT IN SEROTYPE AND DISEASE COVERAGE

- VAX-31 is the broadest-spectrum PCV to enter the clinic and is built on foundation established with VAX-24
- Designed to cover ~95% of IPD circulating in U.S. adults
- Enrollment completed in adult Phase 1/2 dose-ranging study with 1,015 adults aged 50 and older with topline data expected in Q3:24<sup>1</sup>



(1) Guidance as of May 8, 2024.

(2) Data from mixed dose cohort of VAX-24 Phase 2 study in adults aged 50-64.



# Precedent PCVs Have Well-Defined, Validated Surrogate Immune Endpoints

PCV15 and PCV20 Leveraged These Endpoints in Phase 2 and 3 Studies as Basis for Full Approvals

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## CRITERIA FOR COMMON SEROTYPES:

### Non-inferiority:

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

### Superiority:

- Lower bound of 2-sided 95% CI of the OPA GMR is greater than 1.2
- Lower bound of the 2-sided 95% CI of the difference in proportions of participants with a  $\geq 4$ -fold increase from Day 1 to Day 29 is greater than 0

## CRITERIA FOR INCREMENTAL SEROTYPES:

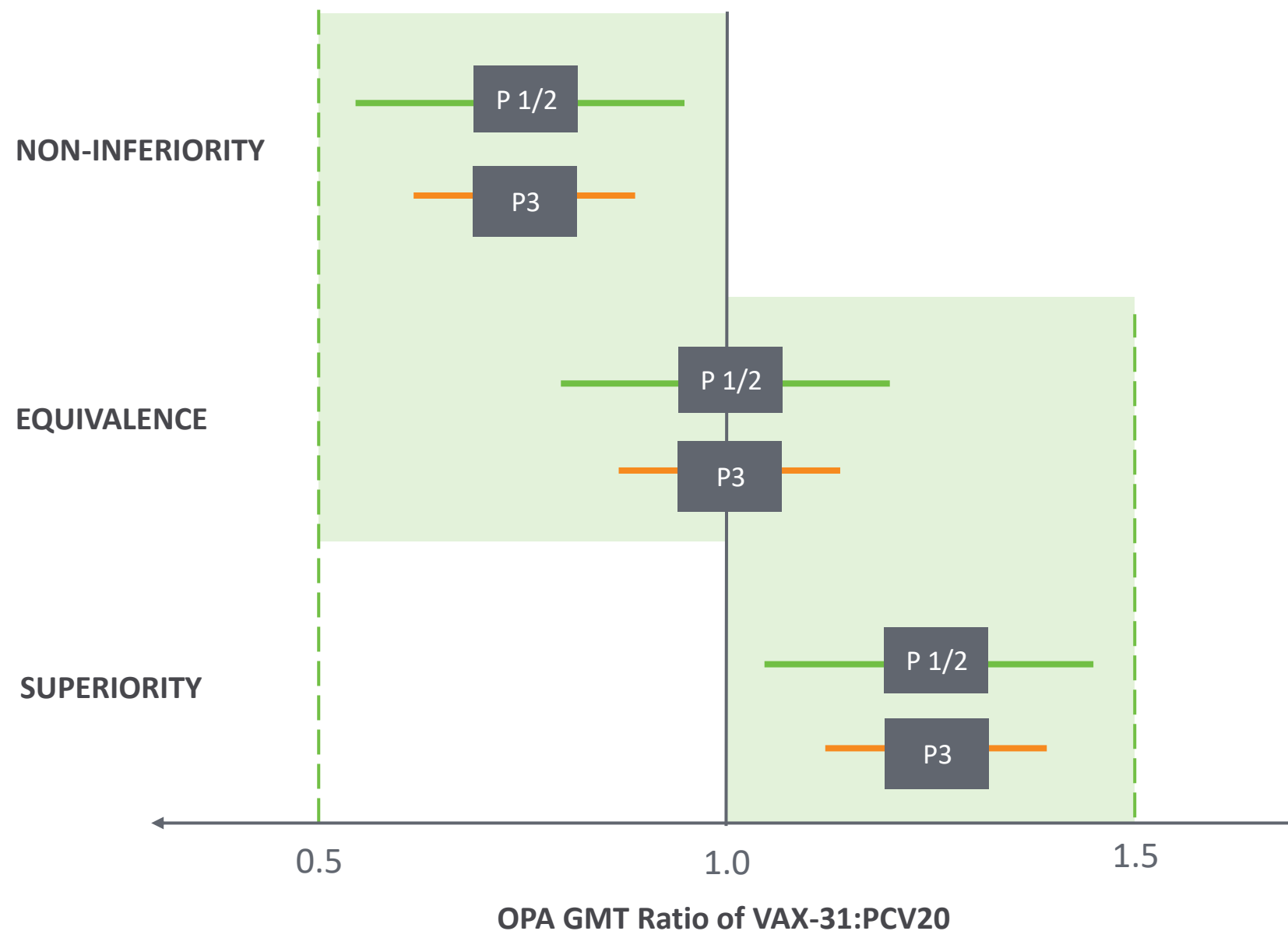
### Superiority:

- 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 Day 29 is greater than 10% of subjects
- Lower bound of the 2-sided 95% CI of the OPA GMR is greater than 2.0

CI = confidence interval, OPA = opsonophagocytic activity, GMR = geometric mean ratio.

# VAX-31 Phase 2 Key Objective: Determine Treatment Effect (Immunogenicity) to Power for Minimum Hurdle of Non-Inferiority in Phase 3 Pivotal Study

- Key focus of VAX-31 Phase 1/2 study is on OPA GMR point estimates, not lower limit of 95th CI
- Due to the smaller size of this Phase 1/2 study vs a Phase 3 study, CI anticipated to be wider
- If the GMRs are 0.6 or higher for each serotype, prior Phase 3 PCV studies have shown that these ratios are adequate to achieve the non-inferiority threshold
- Study designed to inform powering of planned Phase 3 study; not designed or powered to demonstrate non-inferiority
  - CI expected to contract for larger Phase 3 study (n~1000/cohort)

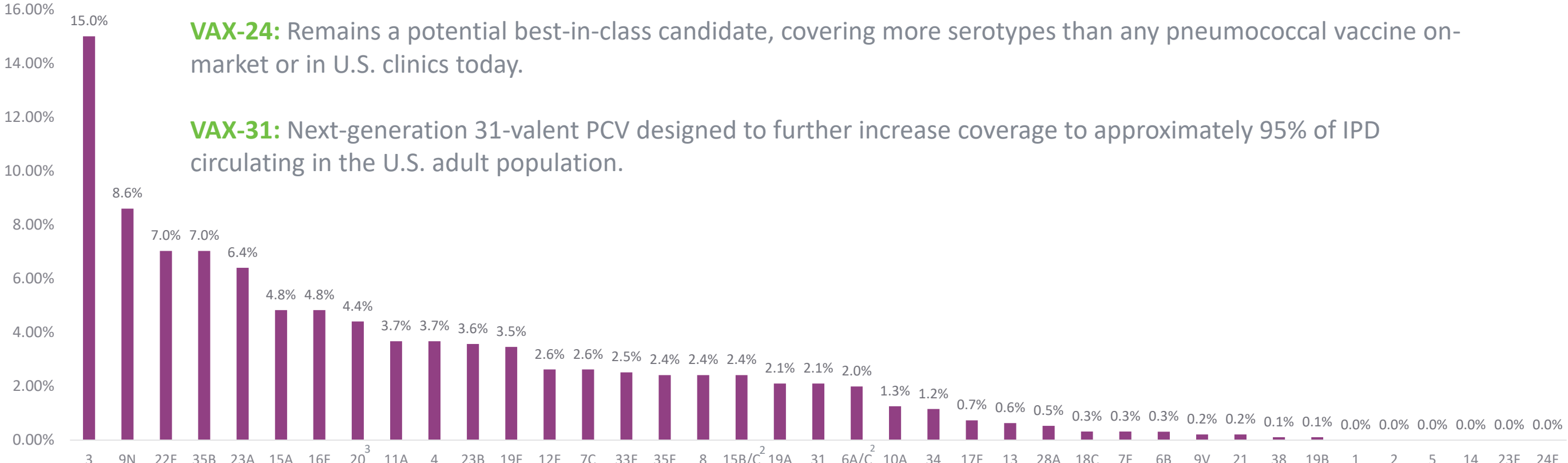


(1) For illustrative purposes only; not depicting a specific vaccine result.

# Adult PCV Franchise Designed to Offer Broader Protection While Covering Previously Circulating Strains Currently Contained via Ongoing Vaccination

**VAX-24:** Remains a potential best-in-class candidate, covering more serotypes than any pneumococcal vaccine on-market or in U.S. clinics today.

**VAX-31:** Next-generation 31-valent PCV designed to further increase coverage to approximately 95% of IPD circulating in the U.S. adult population.

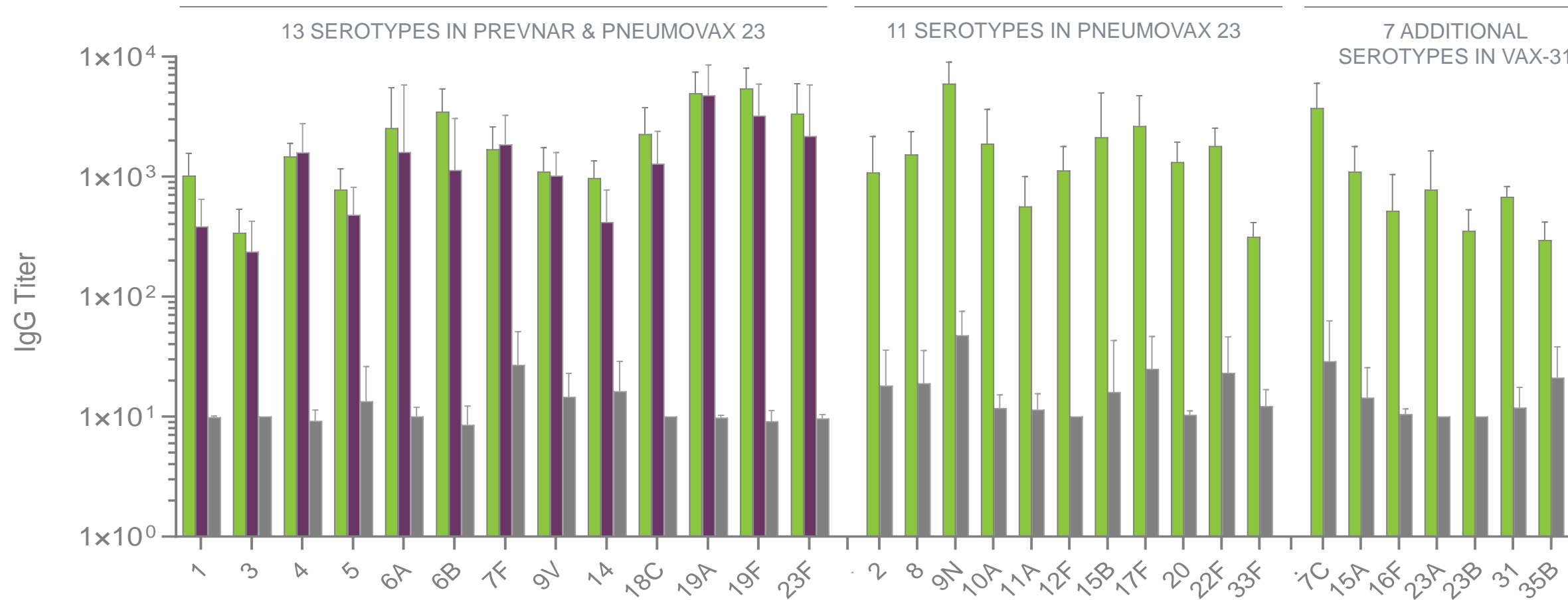


(1) % US coverage is the percentage of IPD caused in individuals <2 yrs of age in the United States in the 2021 based on ABC surveillance data. Reference: CDC. 2016-2021 Serotype Data for IPD Cases by Age Group from ABC surveillance. <https://data.cdc.gov/Public-Health-Surveillance/2016-2021-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p>. Accessed October 19, 2023.  
 (2) 15C coverage due to cross-reaction against 15B. 6C coverage due to cross-protection by 6A.  
 (3) Coverage for ST20 for VAX-24 and VAX-31 is based on Serotype 20B.  
 (4) V116 is not currently FDA approved.

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

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

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

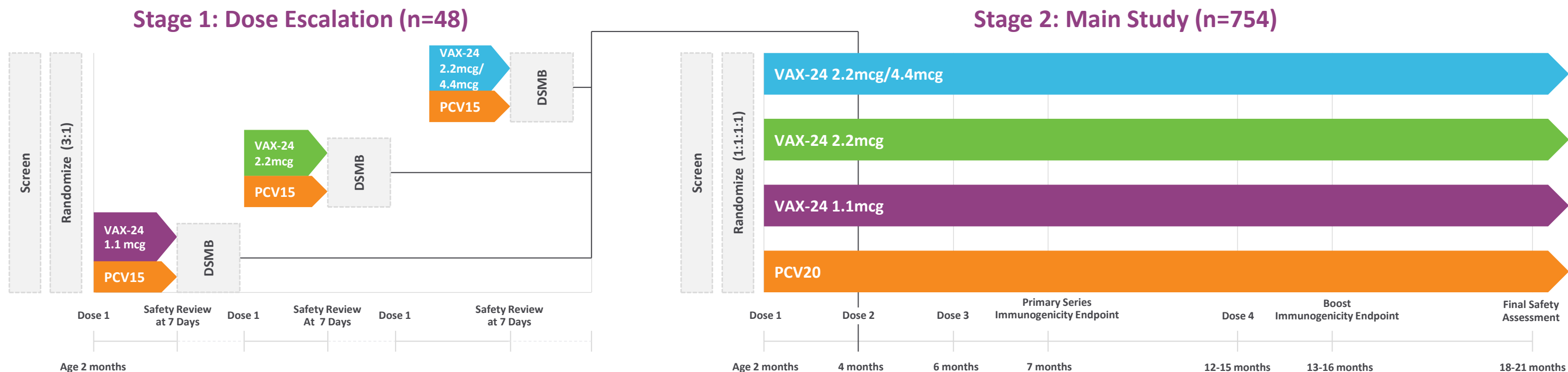


Note: +/- 95% confidential interval.

# PCV Franchise Infant Indication

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

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



## STUDY OVERVIEW

- 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 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. 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. The key prespecified immunogenicity study endpoints include an assessment of the induction of immunoglobulin G (IgG) antibody responses 30 days post-dose three (proportion of participants achieving accepted IgG threshold of  $\geq 0.35\mu\text{g}/\text{mL}$ ) and IgG geometric mean titer ratios 30 days post-dose 4 on a serotype-by-serotype basis for all three VAX-24 dose levels and compared to PCV20.
- All participants will be evaluated for safety six months following the booster dose at 12-15 months of age.

*SOC = standard-of-care.*

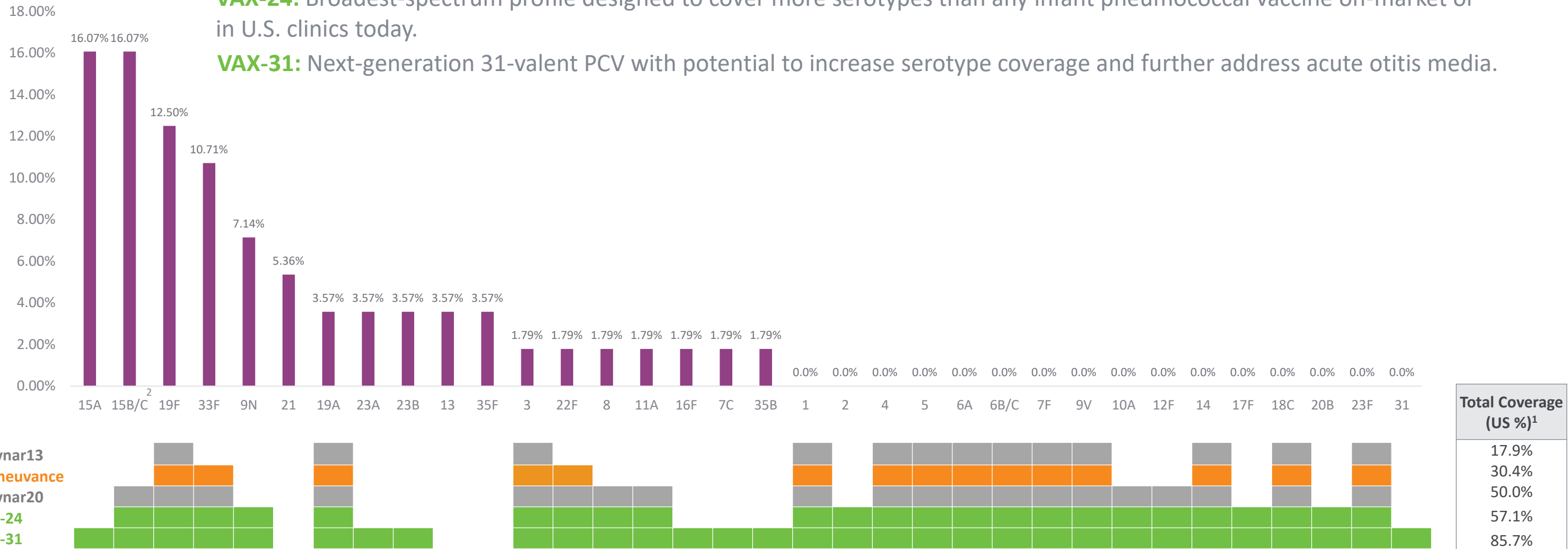
*ACIP = Advisory Committee on Immunization Practices.*

# Spectrum of Coverage Drives Adoption in Vital Infant Population

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

**VAX-24:** Broadest-spectrum profile designed to cover more serotypes than any infant pneumococcal vaccine on-market or in U.S. clinics today.

**VAX-31:** Next-generation 31-valent PCV with potential to increase serotype coverage and further address acute otitis media.



(1) % US coverage is the percentage of IPD caused in individuals <2 yrs of age in the United States in the 2021 based on ABC surveillance data. Reference: CDC. 2016-2021 Serotype Data for IPD Cases by Age Group from ABC surveillance. <https://data.cdc.gov/Public-Health-Surveillance/2016-2021-Serotype-Data-for-Invasive-Pneumococcal-/qvzb-qs6p>. Accessed October 19, 2023.

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

# Non-PCV Pipeline



# VAX-A1: Group A Strep Conjugate Vaccine Program

## Novel Conjugate Vaccine Designed to Provide Universal Protection

### UNMET NEED

- Group A Strep results in an estimated 800M cases of illness annually worldwide, including pharyngitis, or strep throat, and certain severe invasive infections and sequelae
- 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)

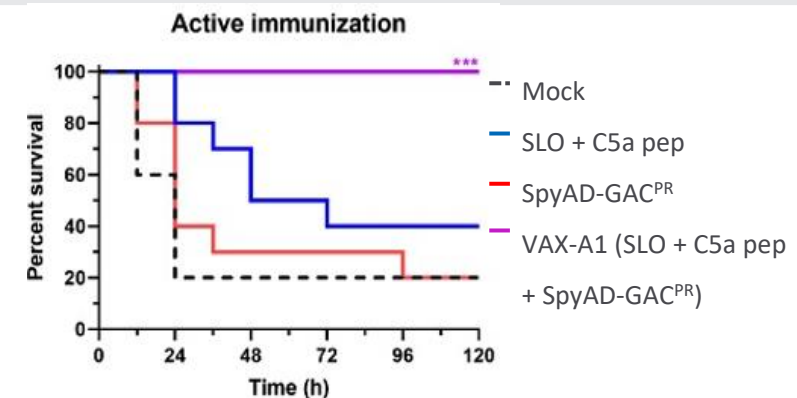
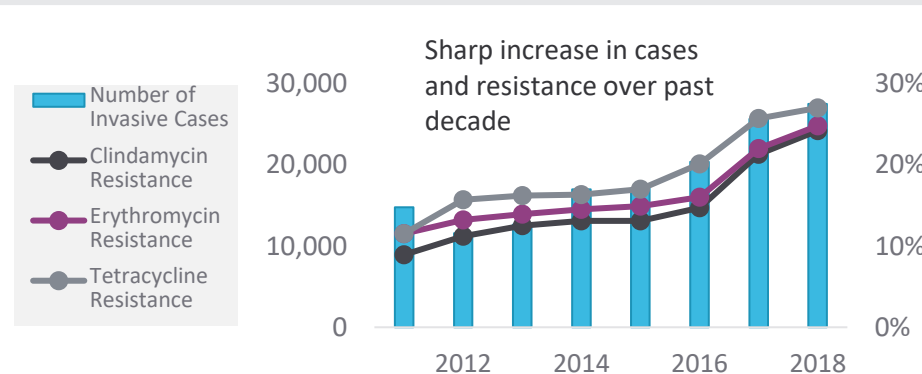
### VAX-A1: BROAD-SPECTRUM, MONOVALENT CONJUGATE VX

- 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 – Polyrrhamnose – 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)); received \$11.7M to date, with total potential funding of up to \$14.6M inclusive of grants to date
- 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.

# VAX-PG: Periodontitis Vaccine Program

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

### UNMET NEED

- Periodontal disease is a chronic oral inflammatory disease leading to destruction of soft and hard tissues supporting the teeth
- Highly prevalent: estimated 65M U.S. adults afflicted
- 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
- Associated with increased risk of heart attack, stroke, cardiovascular disease and Alzheimer’s Disease

### VAX-PG: MULTIVALENT THERAPEUTIC VACCINE

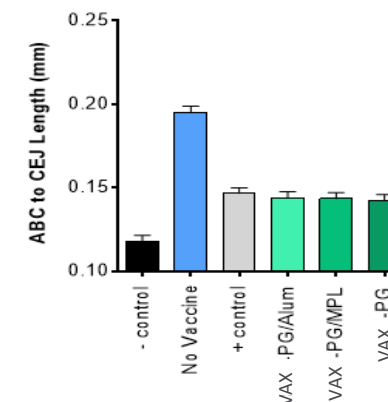
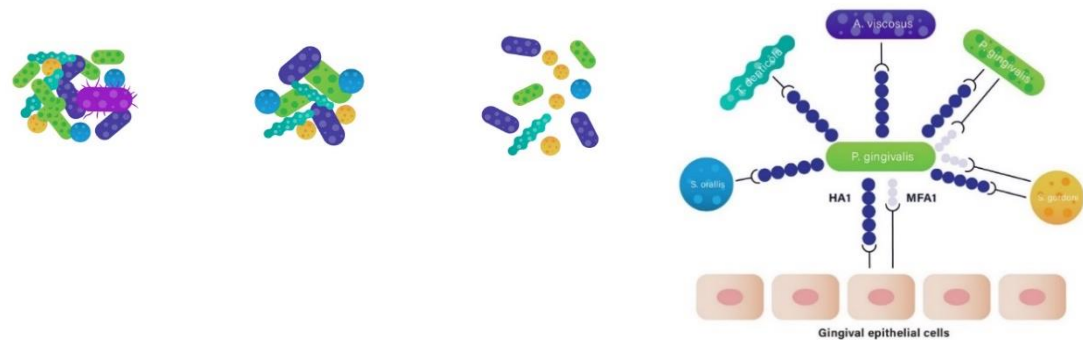
- Incorporates proprietary combination of known virulence factors of keystone pathogen
- Preclinical model demonstrated protein-specific IgG response following immunization and protected mice from *P. gingivalis*-elicited oral bone loss
- Initial goal to develop therapeutic vaccine that slows or stops disease progression

### PROGRAM STATUS

- Preclinical proof-of-concept published in Journal of Clinical Periodontology
- A final vaccine candidate for VAX-PG was nominated in Q4 2022 and the program continues to advance

### MOA & KEY DATA

- Restoration of balanced microbiota by interrupting underlying inflammatory condition



**Challenge Study Results**

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

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

# VAX-GI: Shigella Vaccine Program

## Novel Shigella Vaccine

### UNMET NEED

- Shigella is a bacterial illness with no available preventative treatment
- Affects an estimated 188M people worldwide each year and results in approximately 164,000 deaths annually, mostly among children under five years of age in low-income and middle-income settings<sup>1</sup>
- 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
- Will pursue conjugate and protein-only approaches simultaneously
- Conjugate approach: IpaB-LPS/IpaH/VirG; Protein-only approach: IpaB/IpaH/VirG

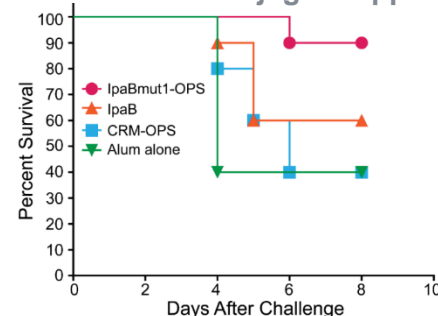
### PROGRAM STATUS

- 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

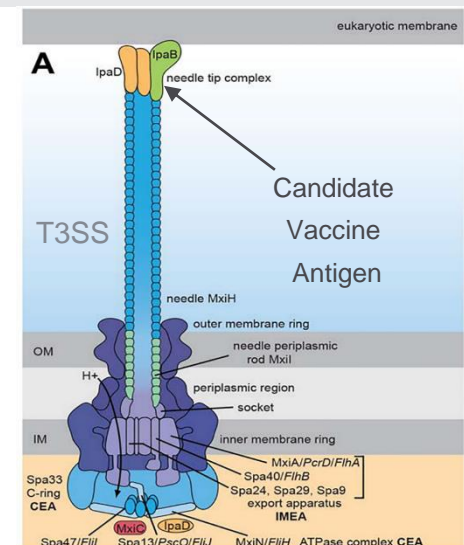
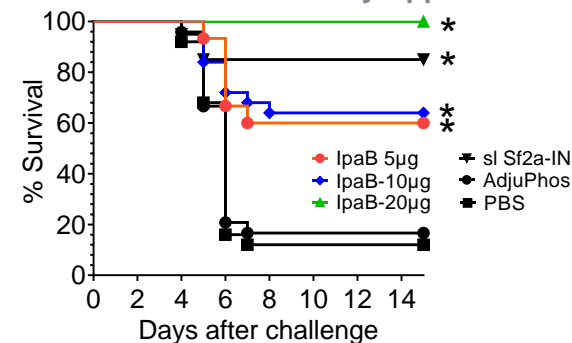
### MOA & KEY DATA

- 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