

# Corporate Presentation



November 7, 2022

**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 a potentially best-in-class pneumococcal conjugate vaccine; demand for Vaxcyte's vaccine candidates; the timing of the initiation, progress and expected results of Vaxcyte's preclinical studies, clinical trials and research and development plans (including, the availability of data for the VAX-24 Phase 2 and Phase 3 studies and related regulatory interactions; the submission of a VAX-24 infant IND application and initiation of such study; the design of the VAX-XP clinical program, the submission of such IND and the availability of topline data; the announcement of guidance for VAX-A1; and the nomination of a final vaccine candidate for VAX-PG); the achievement of future funding milestones; the use and availability of funds from CARB-X; 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, regulatory pathway, adoption speed and immunogenicity of its vaccine candidates; VAX-XP'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; sufficiency of cash and other funding to support Vaxcyte's development programs and other operating expenses; and the ongoing COVID-19 pandemic, which could materially and adversely affect Vaxcyte's business and operations. 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 7, 2022 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, wrinkled surfaces. Some cells have darker, more complex internal structures. The cells are scattered across the frame, with some appearing in the foreground and others in the background, creating a sense of depth.

## VAXCYTE MISSION STATEMENT

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



# Key Corporate Highlights

Clinical-Stage Vaccine Innovation Company – Led by Pneumococcal Conjugate Vaccine (PCV) Franchise



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

- **Scalable platform** enabling broader-spectrum carrier-sparing PCVs
- **Lead candidate: VAX-24**
  - Reported positive topline Phase 1/2 data results in adults
  - Potential best-in-class 24-valent PCV designed to replace SOC in adults and children
  - Fast Track designation in adults; pursuing Breakthrough Therapy Designation
- **Follow-on candidate: VAX-XP**
  - 31-valent PCV designed to provide coverage for ~95% of PD circulating in the U.S. adult population



## CELL-FREE PROTEIN SYNTHESIS PLATFORM

- Leverages **site-specific** conjugation to expose on-target T- and B-cell antigens
- Enables **carrier-sparing** conjugates
- Permits production of **“tough-to-make”** antigens



## HIGHLY ATTRACTIVE PCV MARKET

- **Well-defined >\$7B** market segment **poised for substantial growth**
- Honors **well-understood PCV MOA**
- Leverages established **surrogate immune endpoints** and clinical pathways
- **Spectrum of coverage is primary adoption driver**



## ROBUST DEVELOPMENT PIPELINE

- Platform unlocks large market opportunities:
  - **VAX-A1:** Novel Group A Strep conjugate vaccine
  - **VAX-PG:** Novel periodontitis therapeutic vaccine



## ALIGNED CRITICAL RESOURCES

- **Strategic alignment** with Lonza (manufacturing)
- **Seasoned management team**, directors and advisors
- **~1.0B in cash, cash equivalents and investments** as of 9/30/22 pro forma for Oct. 2022 follow-on offering<sup>(1)</sup>

(1) Reflects cash, cash equivalents at September 30, 2022 of \$366.2M and net proceeds from October follow-on offering of ~\$650.7M.  
SOC = Standard-of-Care.  
PD = Pneumococcal Disease.



# Experienced Team with Track Record in Vaccines and Biopharma

## Management Team

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



**Andrew Guggenhime, MBA**  
*President & CFO*



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



**Mark Wiggins, MBA**  
*CBO*



**Jakub Simon, MD, MS**  
*CMO*



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



**Paul Sauer, MBA**  
*SVP PD & Manufacturing*

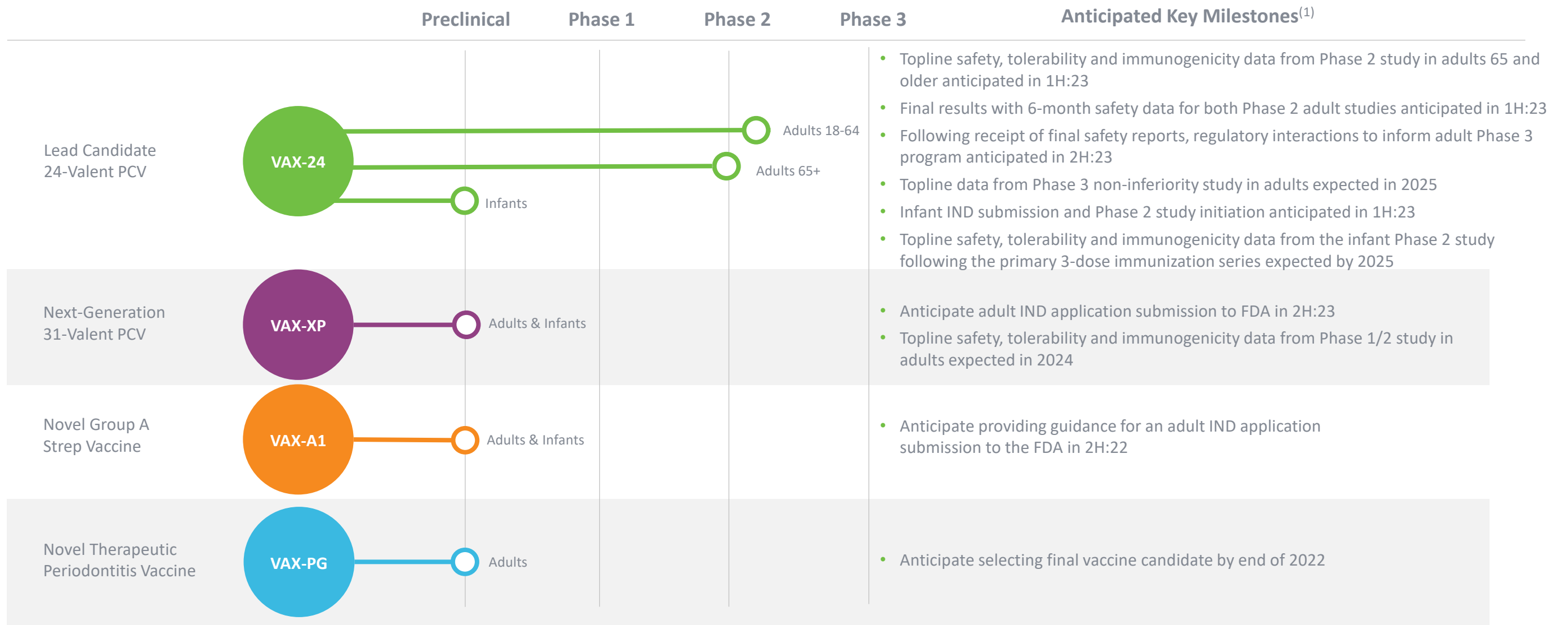


**Harp Dhaliwal, MBA**  
*SVP Commercial Mfg & Supply Chain*



# Pipeline of High-Fidelity Vaccines

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

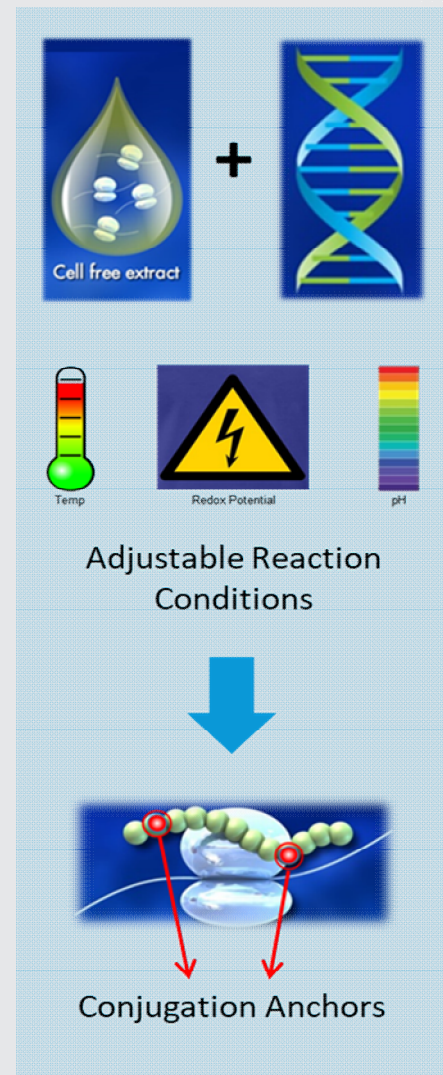


(1) Guidance provided as of November 7, 2022.



# 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

# 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 \$7 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 13<sup>®</sup> (PCV13) or Vaxneuvance<sup>™</sup> (PCV15) x 4 doses/each
- Adults: Prevnar 20<sup>™</sup> (PCV20) or PCV15 x 1 dose followed by Pneumovax<sup>®</sup> 23 (PPV23) x 1 dose, if PCV15



## 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 ~900K pneumococcal pneumonia cases per year resulting in ~150K hospitalizations
- Among children < age 5, PD is a leading cause of death globally

<sup>1</sup> Gierke 2015.

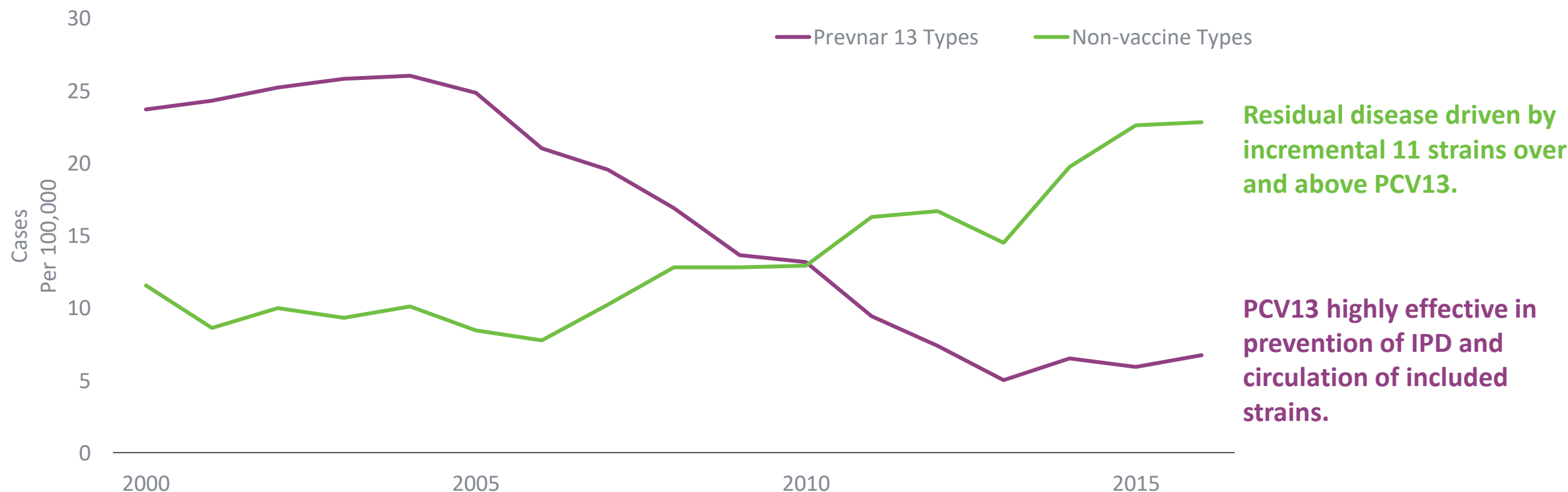
<sup>2</sup> <https://www.cdc.gov/abcs/reports-findings/survreports/spneu18.pdf> CDC 2018.

<sup>3</sup> <https://www.cdc.gov/pneumococcal/clinicians/clinical-features.html>.

# 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>

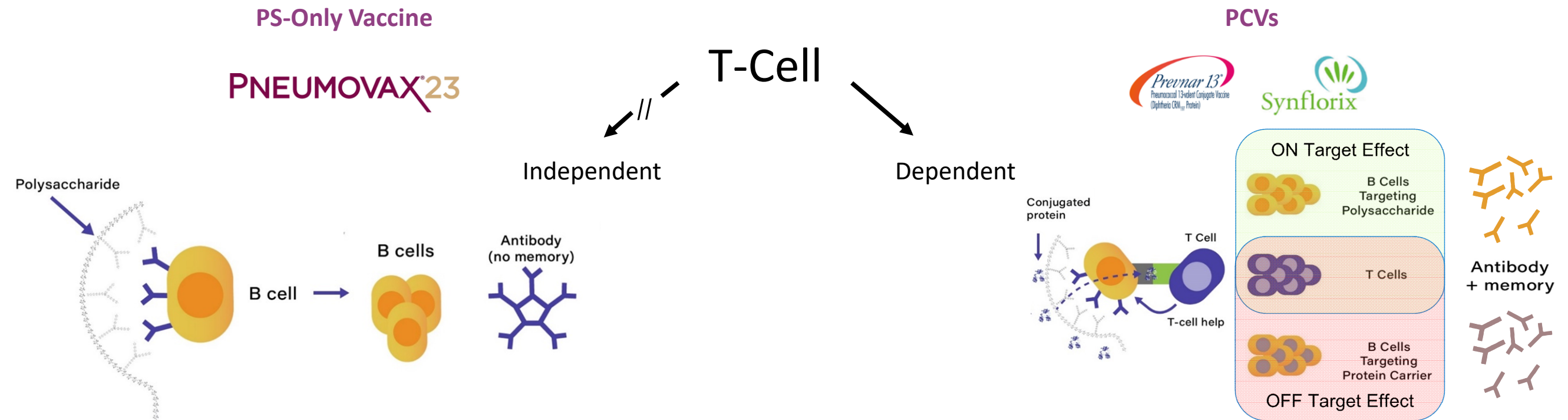


(1) Ladhani et al, Lancet Infect Dis 2018 Apr;18(4):441-45 inclusive of unpublished raw data.



# 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 Strugnelli et al, Understanding Modern Vaccines, Vol 1, Issue 1, 61-88.

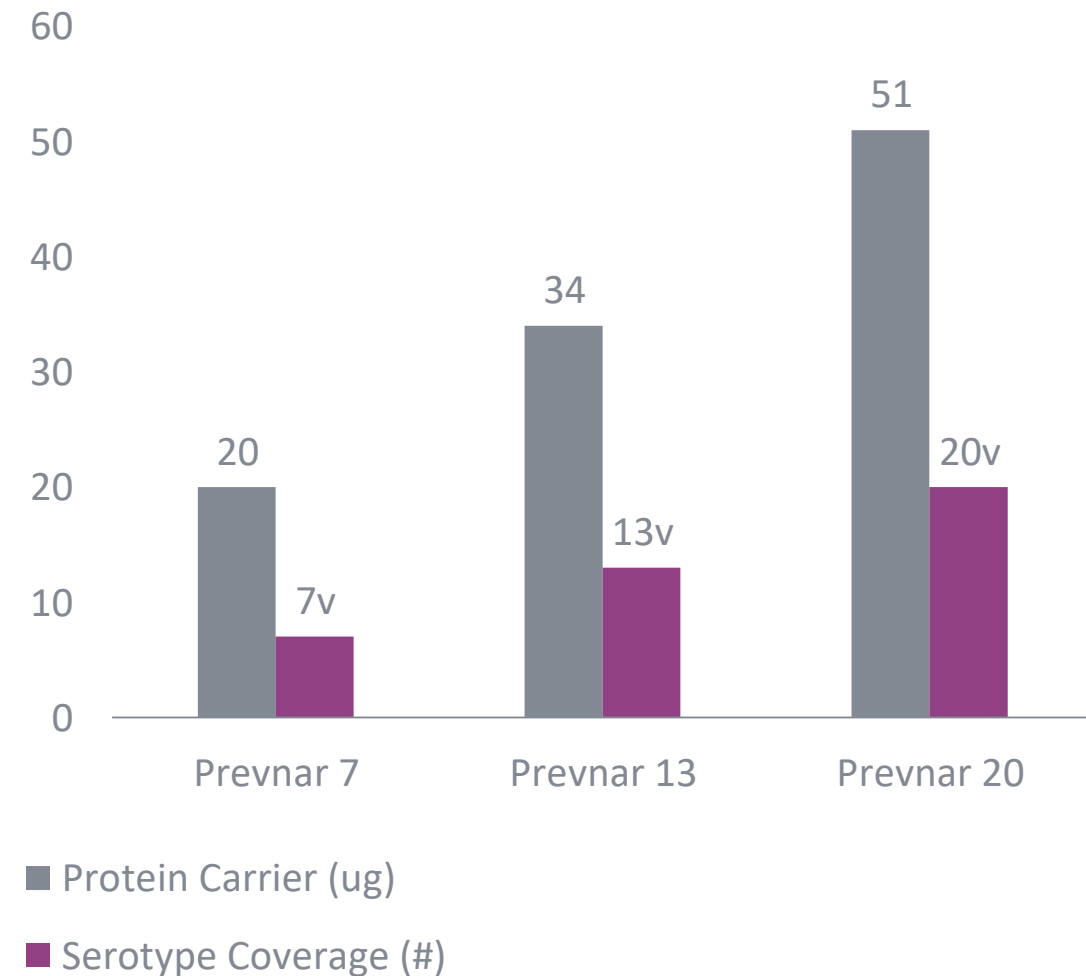
(1) Protein carrier in Pevnar 13 is a modified form of diphtheria toxin (CRM<sub>197</sub>).

# Limitations of Current PCVs

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

## LIMITATIONS OF CONVENTIONAL CHEMISTRY

- Random conjugation
- Higher ratio of protein carrier to polysaccharide, due to reaction conditions required for conjugation
- Further exacerbates carrier suppression, due to competition for CD4+ help between disease-specific polysaccharides and non-disease specific protein carrier



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



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

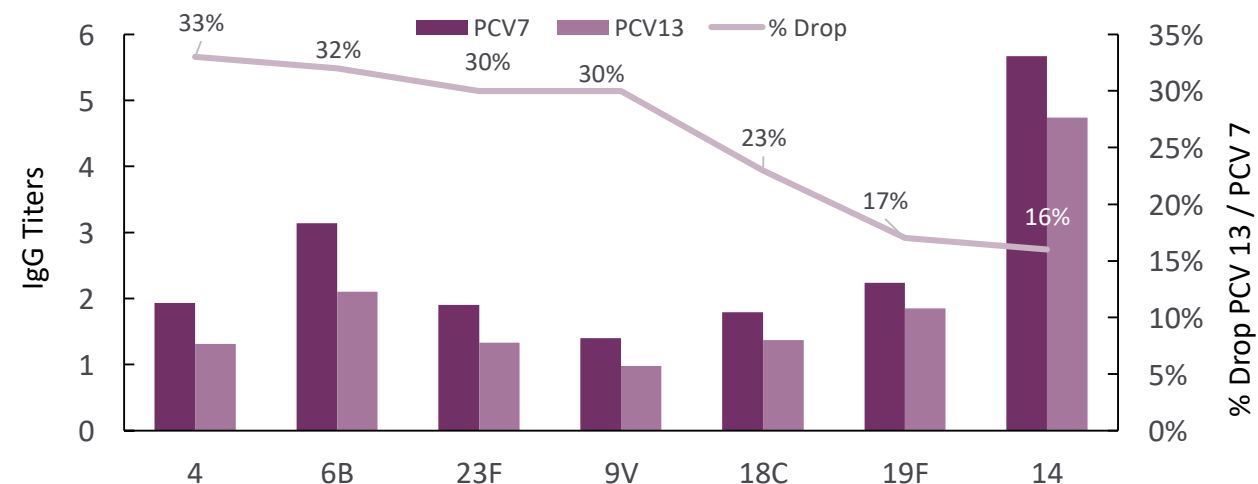
## Coverage Expansion Using Conventional Chemistry Has Led to Carrier-Induced Immune Suppression

### CARRIER SUPPRESSION

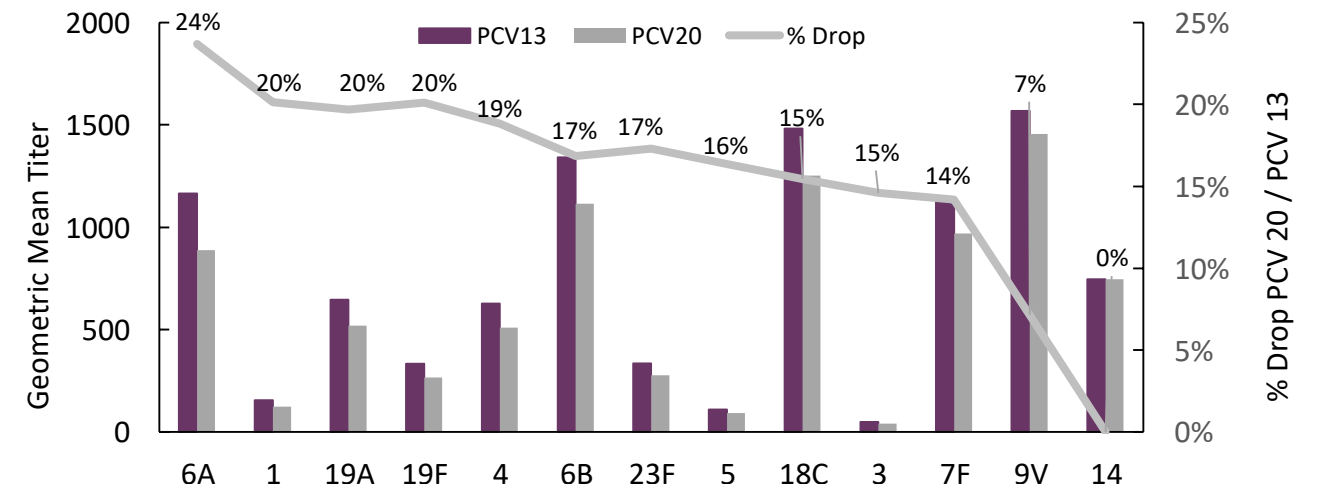
Diminished immune response to target polysaccharides due to cumulative amount of protein carrier

- 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):  
PREVNAR 7 VS PREVNAR 13<sup>(1)</sup>



ADULT IMMUNE RESPONSES (OPA):  
PREVNAR 13 VS PREVNAR 20<sup>(2)</sup>



(1) Yeh et al, Pediatrics. 126: e493 (2010).

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

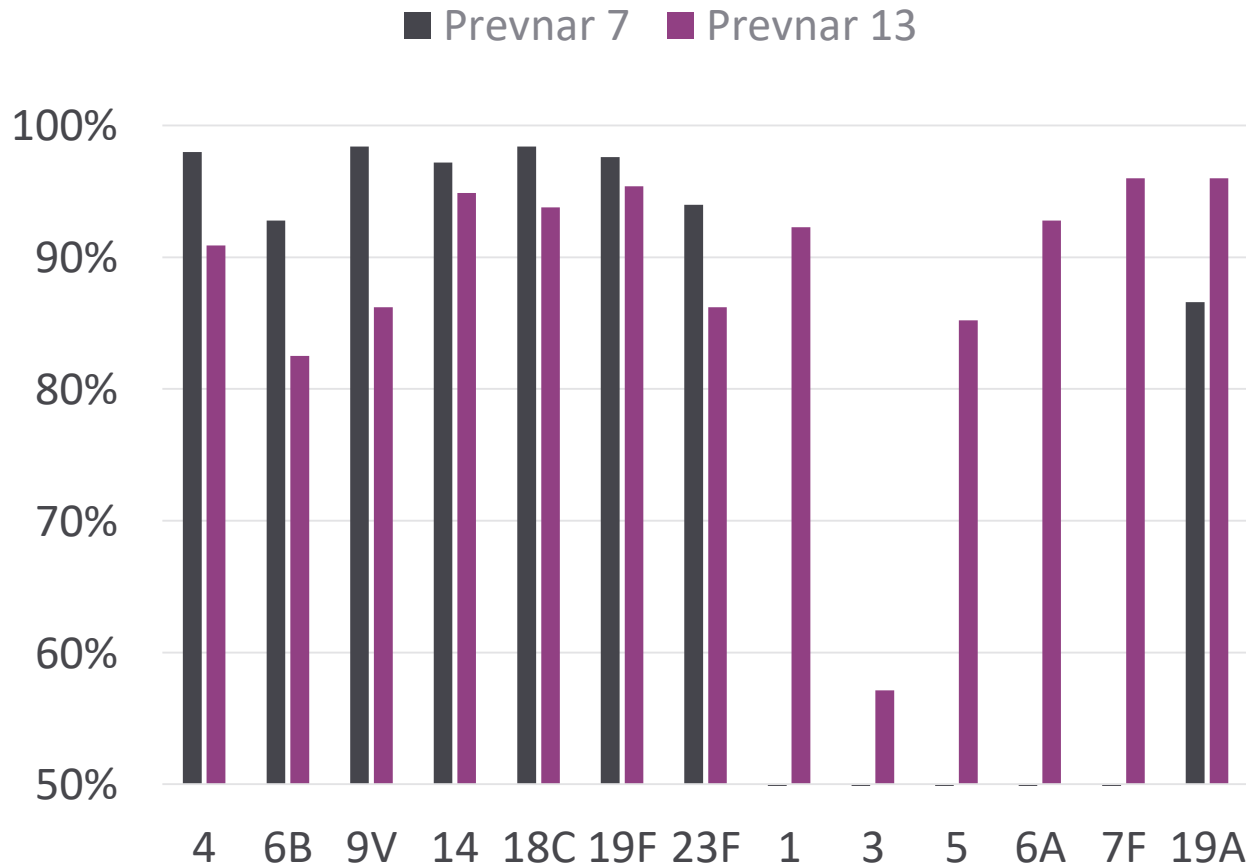
OPA = Opsonophagocytic assay.

IgG - Immunoglobulin G

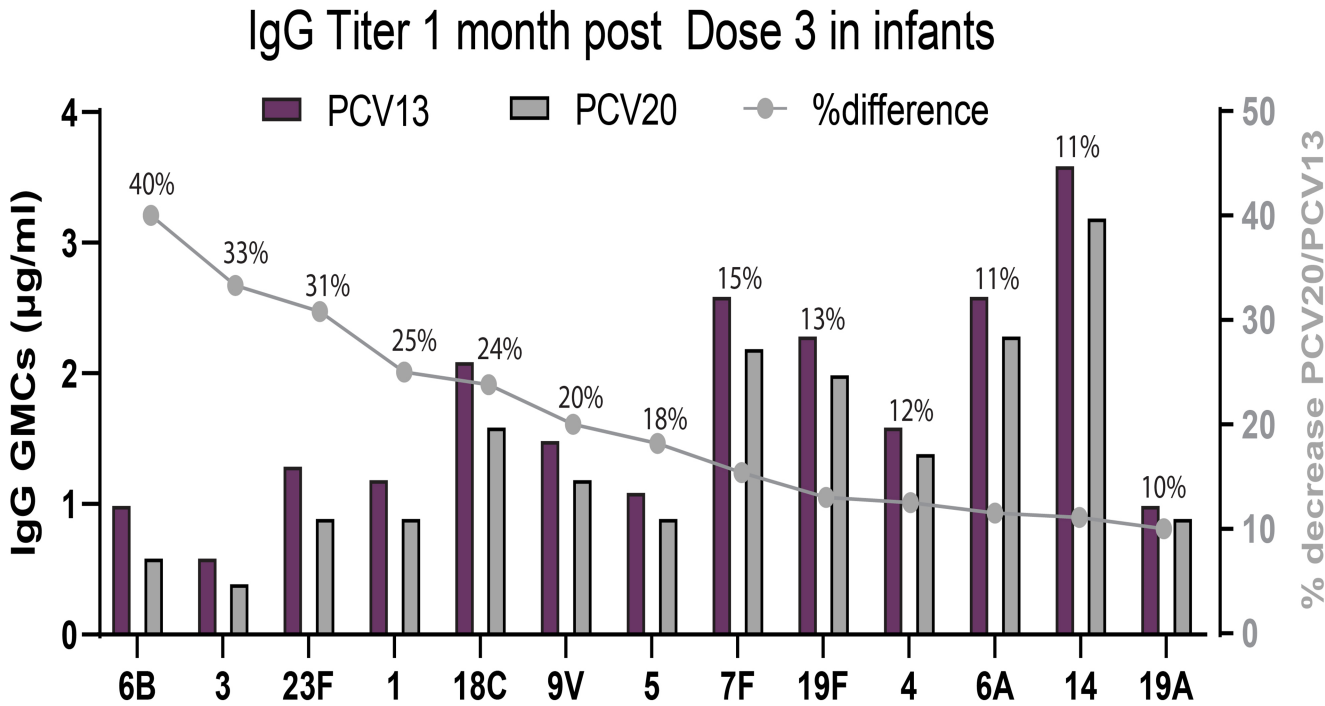
# Limitations of Current PCVs: Adding Conjugates Results in Lower Seroprotective Levels<sup>1,2</sup>

CURRENT REGULATORY GUIDANCE: MUST BE WITHIN 10%<sup>3</sup> TO BE NON-INFERIOR POST-DOSE 3

PH 3 INFANT DATA % SEROPROTECTED  
PREVNAR 7 VS PREVNAR 13<sup>(1,2)</sup>



PH 2 INFANT DATA IMMUNE TITERS  
PREVNAR 13 VS PREVNAR 20<sup>(4)</sup>

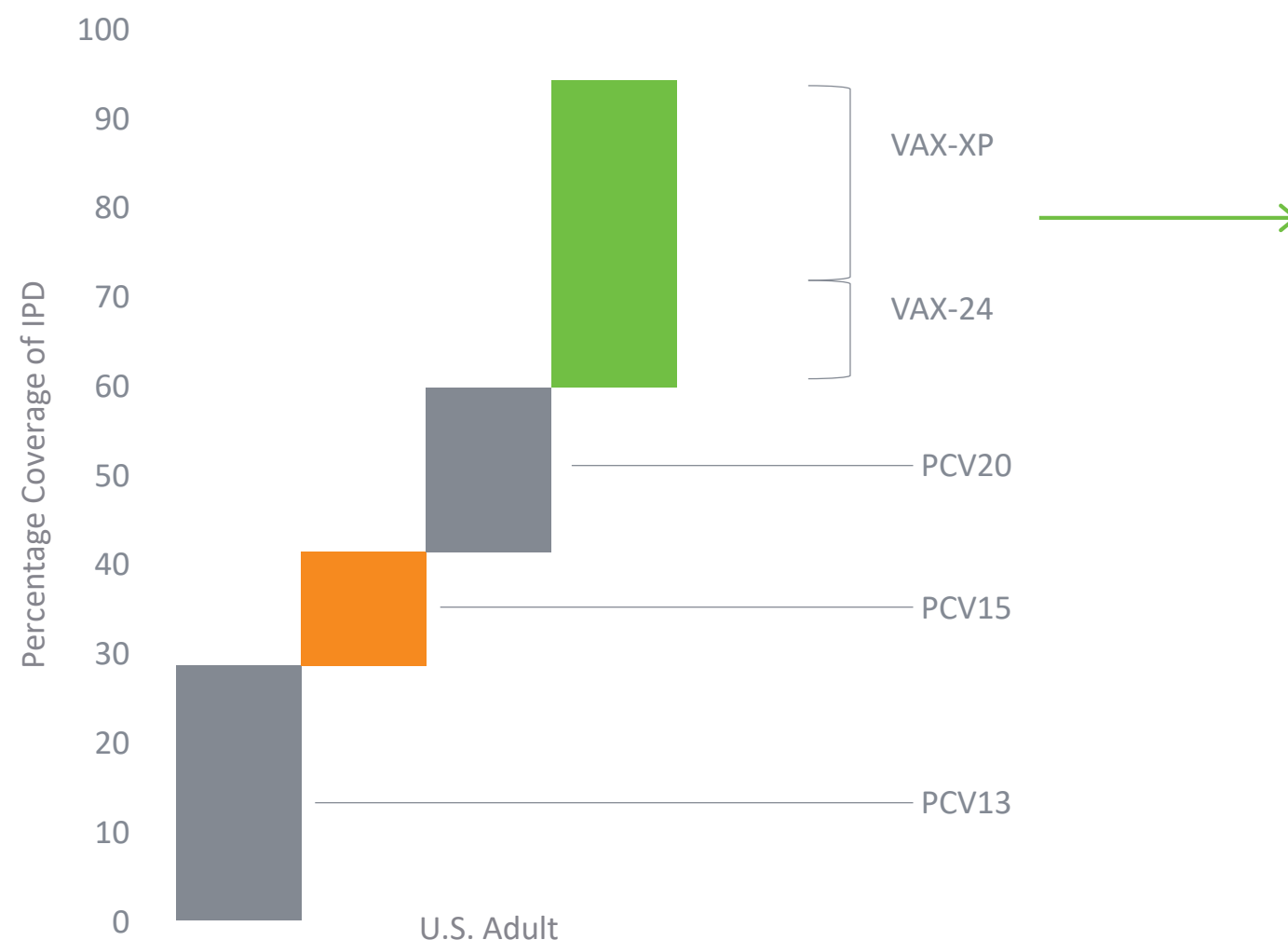


(1) Prevnar 13 BLA Clinical Review Memorandum by FDA. February 17, 2010.  
(2) Seroprotection is defined as a serotype-specific IgG antibody level of  $\geq 0.35\text{mcg/mL}$ .  
(3) Non-inferiority comparison is LL of 95% CI of the comparator to the mean % responders of the SoC.  
(4) Clintrials.gov NCT03512288 Phase 2 study (N=460).

# 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



## VAX-24 & VAX-XP PROFILE

Vaxcyte's carrier-sparing PCV franchise designed to provide broadest coverage of any PCVs:

- VAX-24 has the potential to provide an incremental 10-15% coverage of IPD in U.S. adults vs. the SOC today, which would eclipse the coverage of Pneumovax 23
- VAX-XP, a 31-valent follow-on PCV, is designed to provide coverage for ~95% of the IPD currently circulating in the U.S. adult population

(1) Data in the US is for 2017, inclusive of those > 5 yrs of age.

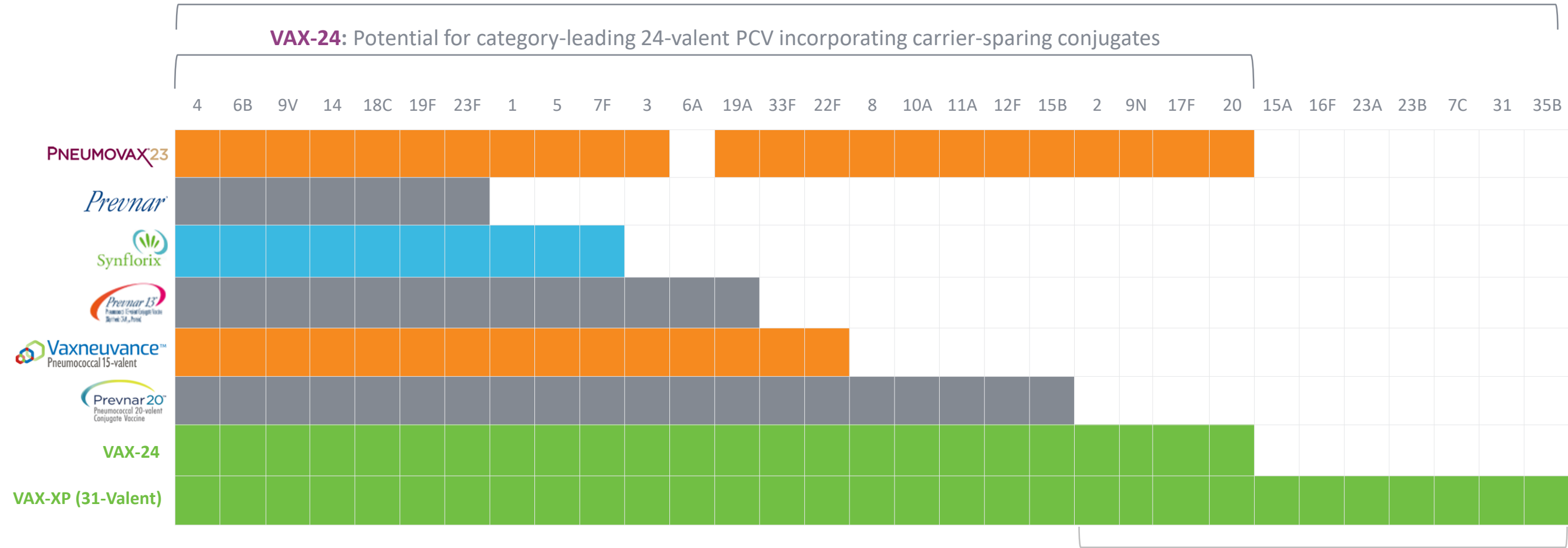
(2) Varghese et al. Clin Micro and Infect (2020) 26(4): 512.e1-512.e10.  
SOC = standard of care.



# Vaxcyte Carrier-Sparing PCV Franchise has Potential for Sustained Leadership in Growing >\$7B Pneumococcal Vaccine Market

**VAX-XP:** Next-generation 31-valent PCV showcases franchise approach and scalability of carrier-sparing conjugates

**VAX-24:** Potential for 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 has the Potential to Become the Most Broad-Spectrum PCV

### PNEUMOCOCCAL VACCINE MARKET DYNAMICS

#### SPECTRUM OF COVERAGE DRIVES ADOPTION

- Potential for rapid adoption, with ACIP recommendation driving uptake
- Examples: PCV13 vs Prevnar 7 (PCV7) and Shingrix® vs Zostavax®

#### ATTRACTIVE MARGINS

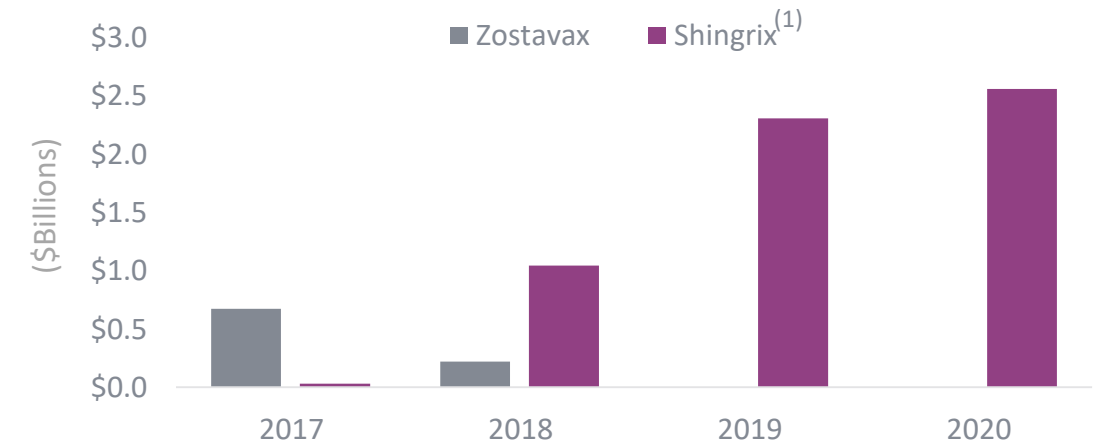
- Pneumococcal vaccines are premium priced in the U.S., delivering highly attractive margins
- Broader-spectrum PCVs maintain premium price

#### PCVs ARE BEST-IN-CLASS

- Well-understood T-cell dependent MOA tied to co-presentation of disease-specific polysaccharide antigens with mapped T-cell epitopes on protein carrier
- Well-defined clinical development path: Non-inferiority to SOC using validated surrogate immune endpoints adequate for full approval for follow-on PCVs

#### DURABLE REVENUE STREAM

- PCV13 & PPV23 have generated >\$100B in revenues with annual sales of ~\$6B to the Prevnar franchise and ~\$1B to PPV23



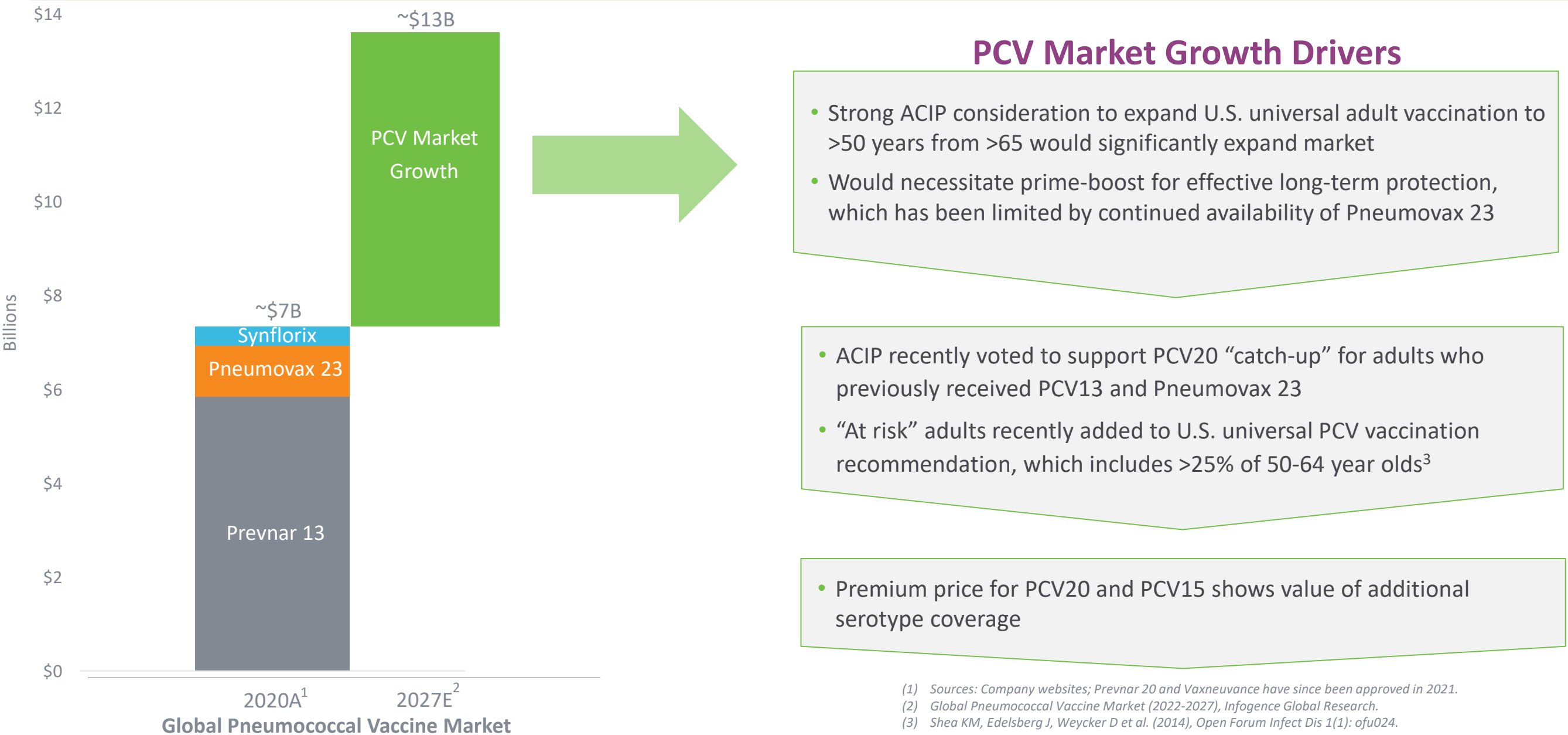
- FDA approved in 4Q:2017 to prevent shingles in adults
- ACIP granted “preferred recommendation”
- Replaced the incumbent (Zostavax from Merck)

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



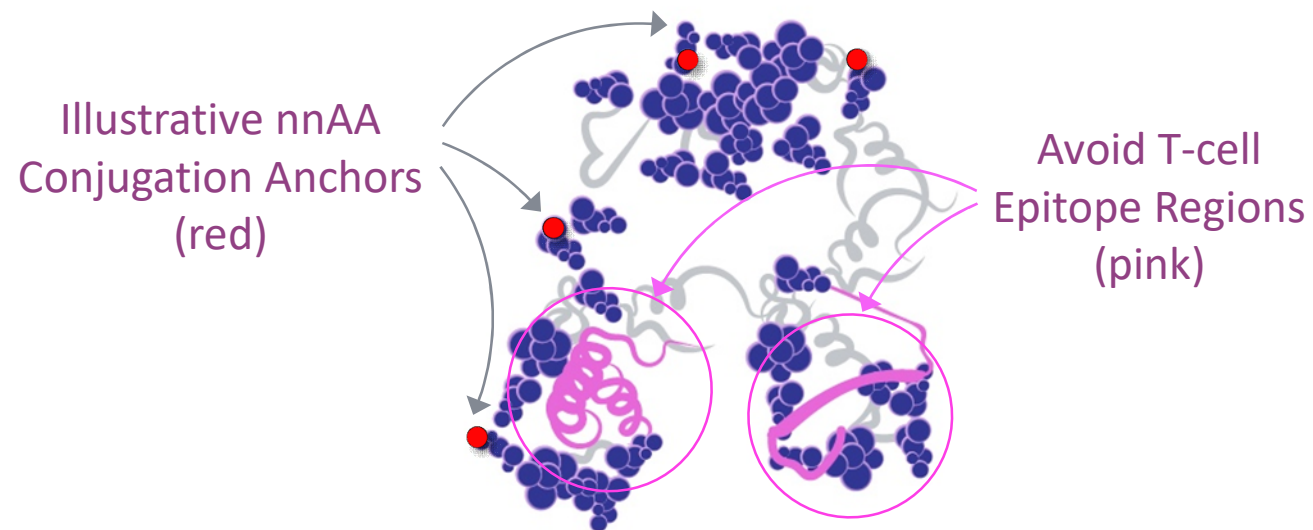


# Differentiated PCV Franchise Led by VAX-24

# VAX-24 Employs Carrier-Sparing Conjugates

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

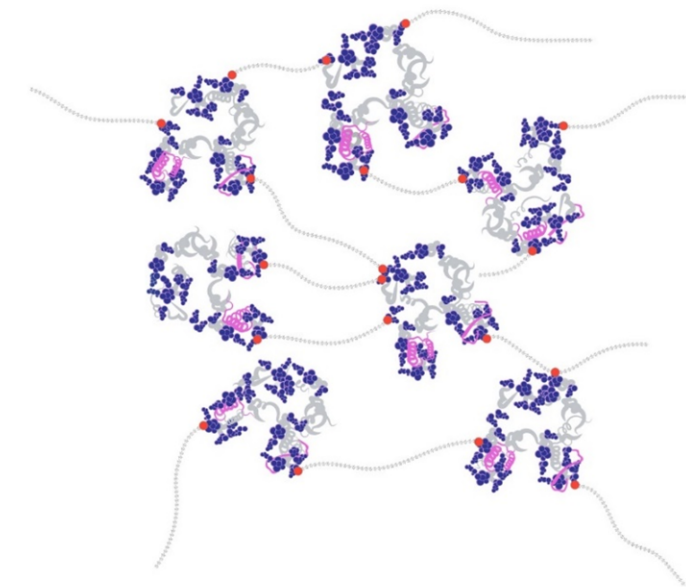
PRECISE, SITE-SPECIFIC CONJUGATION SITES ON PROPRIETARY  
eCRM<sup>®</sup> PROTEIN CARRIER



## 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 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-XP 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 nnAA 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-XP
- Vaxcyte has leveraged the same animal models utilized in the development of both approved PCVs (Prevnar and Synflorix)



# VAX-24 Phase 1/2 Study Topline Results

# VAX-24 Phase 1/2 Study Topline Data Key Take-Aways

Unprecedented Results Support Best-in-Class Potential for VAX-24 and Identify Optimal Dose for Advancement

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**SAFETY: VAX-24 demonstrated a safety and tolerability profile similar to Prevnar 20™ (PCV20) for all doses**



**IMMUNOGENICITY: Met or exceeded regulatory standard for all 24 serotypes (STs) for VAX-24 conventional 2.2mcg dose without the need to push dose higher**

- Optimal 2.2mcg dose being advanced to Phase 3:
  - Met the standard OPA response non-inferiority criteria for all 20 STs common with PCV20, of which 16 achieved higher immune responses
  - Met the standard superiority criteria for all 4 additional STs unique to VAX-24
- All VAX-24 doses (1.1mcg, 2.2mcg, and 2.2mcg/4.4mcg) eligible to advance



**PLATFORM: VAX-24 data validate Vaxcyte's carrier-sparing PCV franchise to increase spectrum of coverage AND maintain robust immune responses to serotypes in current standard-of-care PCVs**

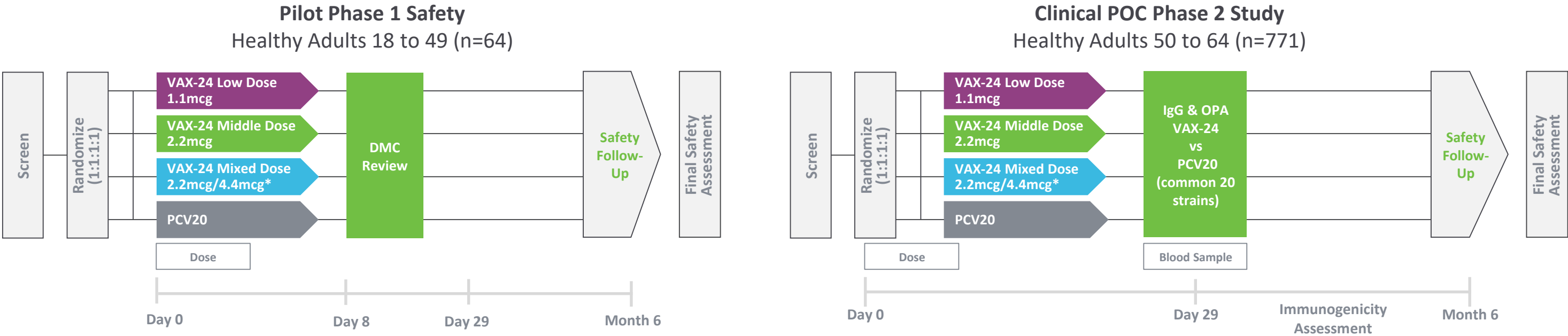


**PCV FRANCHISE: VAX-XP, a 31-valent PCV candidate, advancing as follow-on to VAX-24**

- Learnings from Phase 1/2 study to inform optimal design for VAX-XP clinical program given ability to add STs without sacrificing overall immune responses

# VAX-24 Phase 1/2 Clinical Proof-of-Concept Study Design

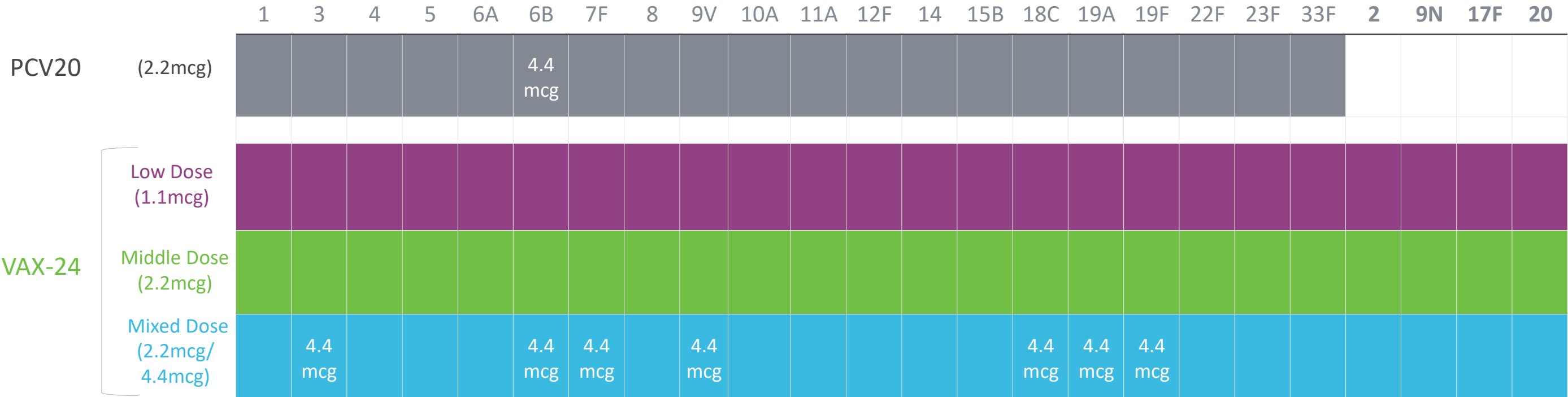
**Design:** Randomized, Observer-Blind, Dose-Finding, Controlled Study to Evaluate Safety, Tolerability & Immunogenicity of VAX-24 vs SOC in Adults Aged 18-64



\* 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.



# Study Evaluated Three VAX-24 Doses



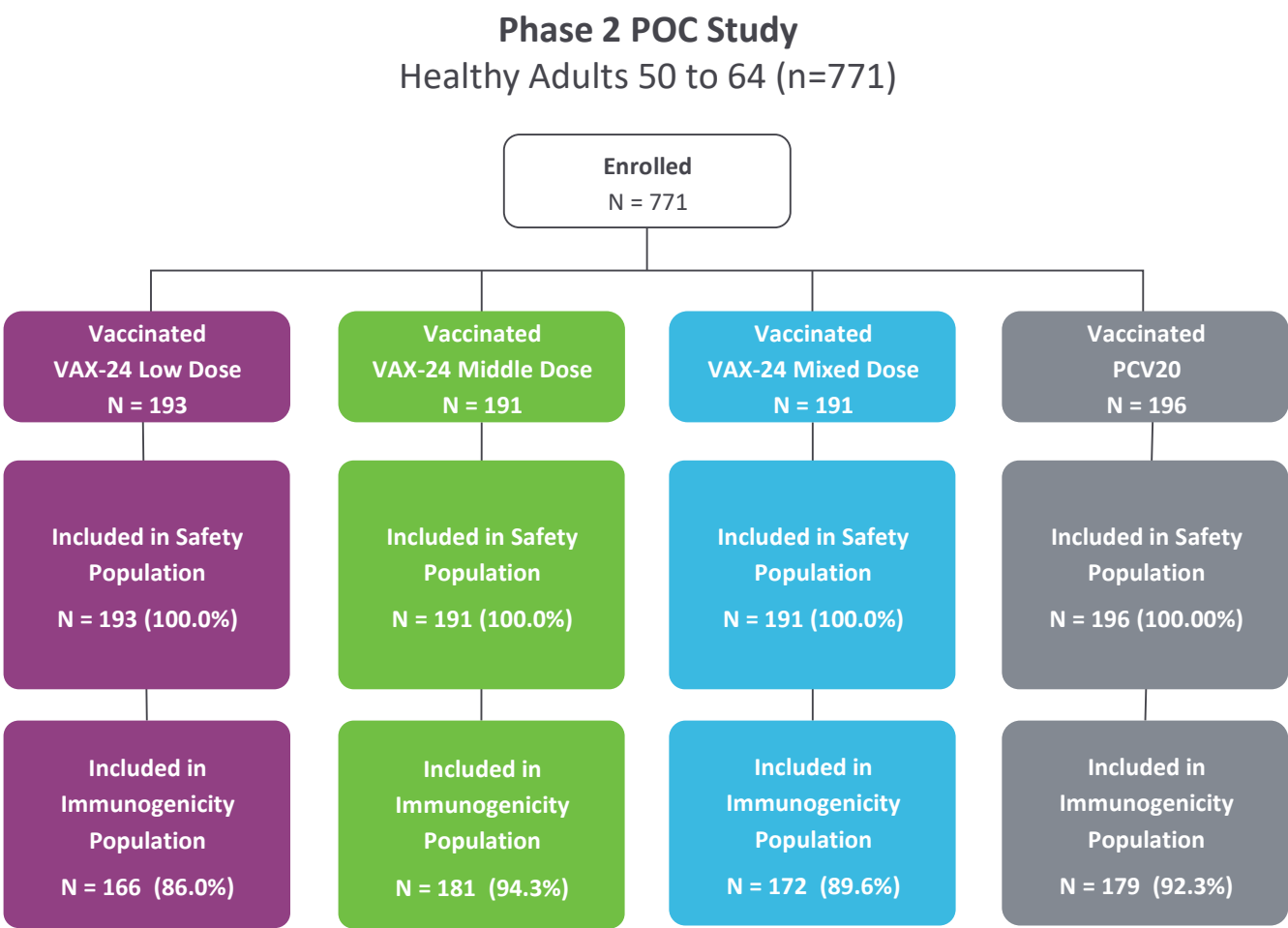
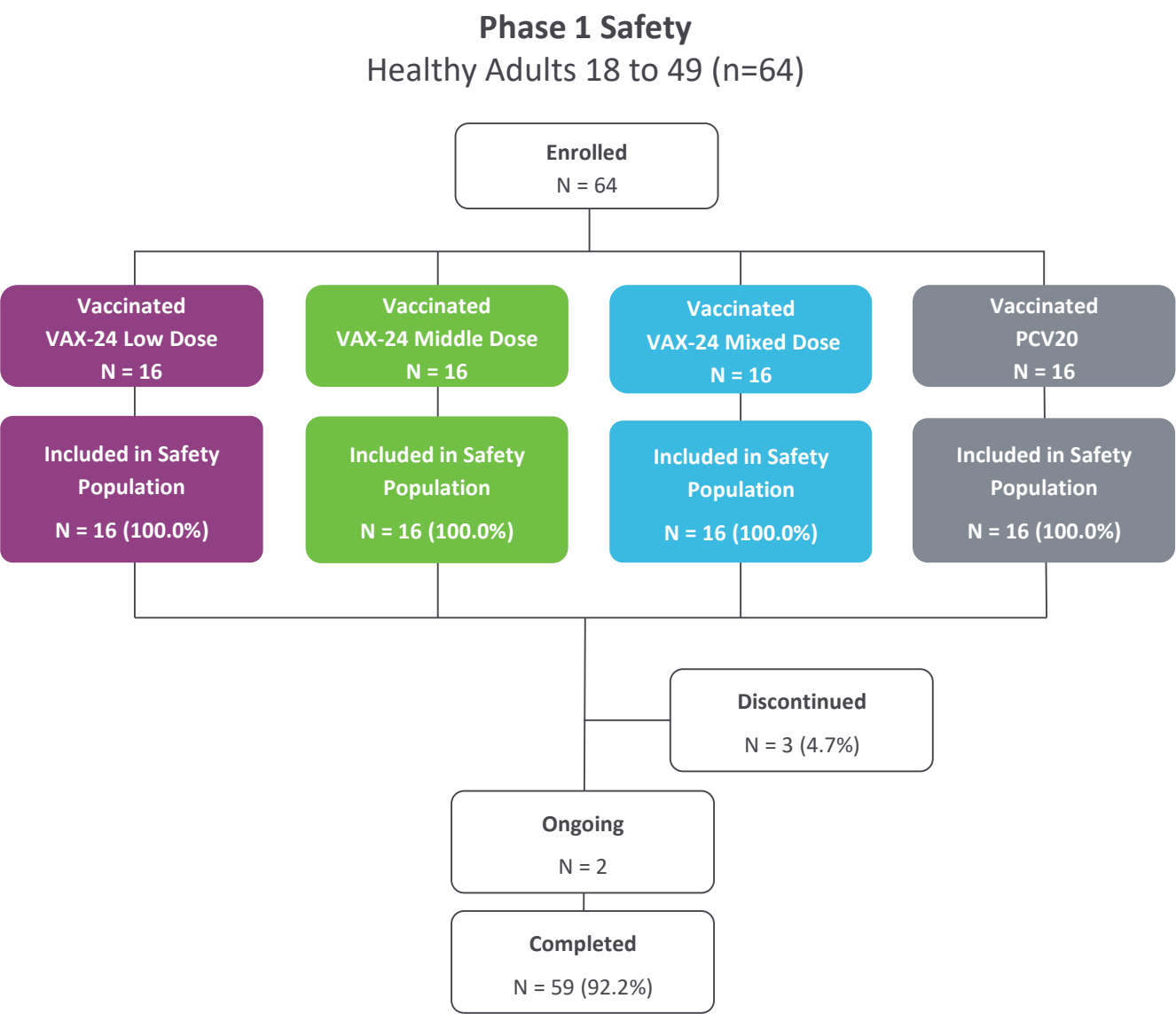
- Mixed Dose includes seven serotypes at 4.4mcg strategically chosen based on epidemiological relevance or prior evidence of dose-dependent immune responses to increase the probability of generating non-inferior immune responses for those serotypes.

# Study Safety, Tolerability and Immunogenicity Outcome Measures

	DAY 7	DAY 29	DAY 180
<b>SAFETY AND TOLERABILITY OUTCOME MEASURES</b> (PHASE 1 AND 2 PORTIONS OF THE STUDY)	<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 (AEs)</li><li>Serious adverse events (SAEs)</li></ul>	<ul style="list-style-type: none"><li>SAEs and new onset of chronic illnesses (NOCI) medically attended adverse events</li></ul>
<b>IMMUNOGENICITY OUTCOME MEASURES</b> (PHASE 2 PORTION OF THE STUDY ONLY)		<ul style="list-style-type: none"><li>Opsonophagocytic assay (OPA) geometric mean titer (GMTs)</li><li>IgG geometric mean concentration (GMCs)</li><li>% of subjects achieving a 4-fold rise in OPA</li><li>Geometric Mean Ratios (GMR) in serotype-specific OPA</li></ul>	

# Phase 1/2 Study Disposition

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



9 subjects were lost to follow-up in Phase 2

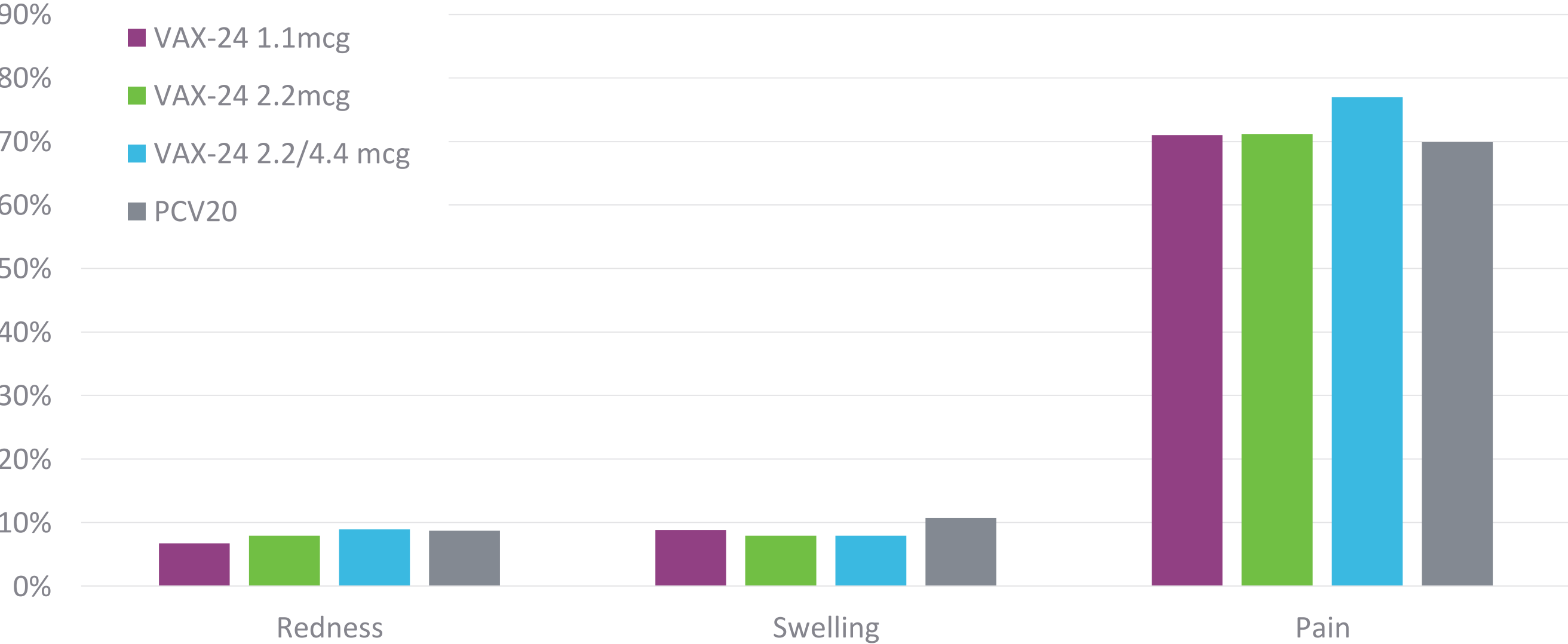
# Phase 2 Demographic Population

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

	VAX-24 – Low Dose (1.1mcg)		VAX-24 – Middle Dose (2.2mcg)		VAX-24 – Mixed Dose (2.2mcg/4.4mcg)		PCV20	
	Safety	Immunogenicity	Safety	Immunogenicity	Safety	Immunogenicity	Safety	Immunogenicity
<b>Number of Subjects</b>	193	166	191	181	191	172	196	179
<b>Median age, years (range)</b>	57.0 (50-64)	57.0 (50-64)	57.0 (50-64)	57.0 (50-64)	57.0 (50-64)	57.0 (50-64)	57.0 (50-64)	57.0 (50-64)
<b>Sex, n (%)</b>								
Female	110 (57.0)	96 (57.8)	119 (62.3)	113 (62.4)	134 (70.2)	125 (72.7)	129 (65.8)	118 (65.9)
Male	83 (43.0)	70 (42.2)	72 (37.7)	68 (37.6)	57 (29.8)	47 (27.3)	67 (34.2)	61 (34.1)
<b>Race, n (%)</b>								
White	145 (75.1)	127 (76.5)	157 (82.2)	149 (82.3)	155 (81.2)	140 (81.4)	155 (79.1)	139 (77.7)
Black	40 (20.7)	32 (19.3)	31 (16.2)	29 (16.0)	29 (15.2)	27 (15.7)	30 (15.3)	29 (16.2)
Asian	1 (0.5)	1 (0.6)	0 (0.0)	0 (0.0)	2 (1.0)	2 (1.2)	3 (1.5)	3 (1.7)
Native Hawaiian	blinded	blinded	blinded	blinded	blinded	blinded	blinded	blinded
American Indian or Native Alaskan	blinded	blinded	blinded	blinded	blinded	blinded	blinded	blinded
Other	3 (1.6)	2 (1.2)	2 (1.0)	2 (1.1)	1 (0.5)	1 (0.6)	2 (1.0)	2 (1.1)
<b>Median Height, cm (range)</b>	168.3 (150-200)	168.4 (150-200)	167.6 (145-193)	167.6 (145-193)	167.6 (145-193)	167.6 (145-193)	167.6 (142-196)	167.6 (142-196)
<b>Median weight, kg (range)</b>	87.82 (49.2-159.2)	86.87 (49.8-159.2)	86.80 (51.4-155.1)	86.80 (51.4-155.1)	83.01 (47.9-205.5)	83.10 (48.9-205.5)	82.83 (45.3-189.9)	82.70 (45.3-185.5)
<b>Median BMI, kg/m<sup>2</sup> (range)</b>	29.87 (18.0-55.0)	29.39 (18.8-55.0)	30.54 (18.7-52.6)	30.44 (18.7-52.6)	29.42 (18.0-57.3)	29.48 (18.0-57.3)	29.06 (17.4-72.7)	29.11 (17.4-72.7)

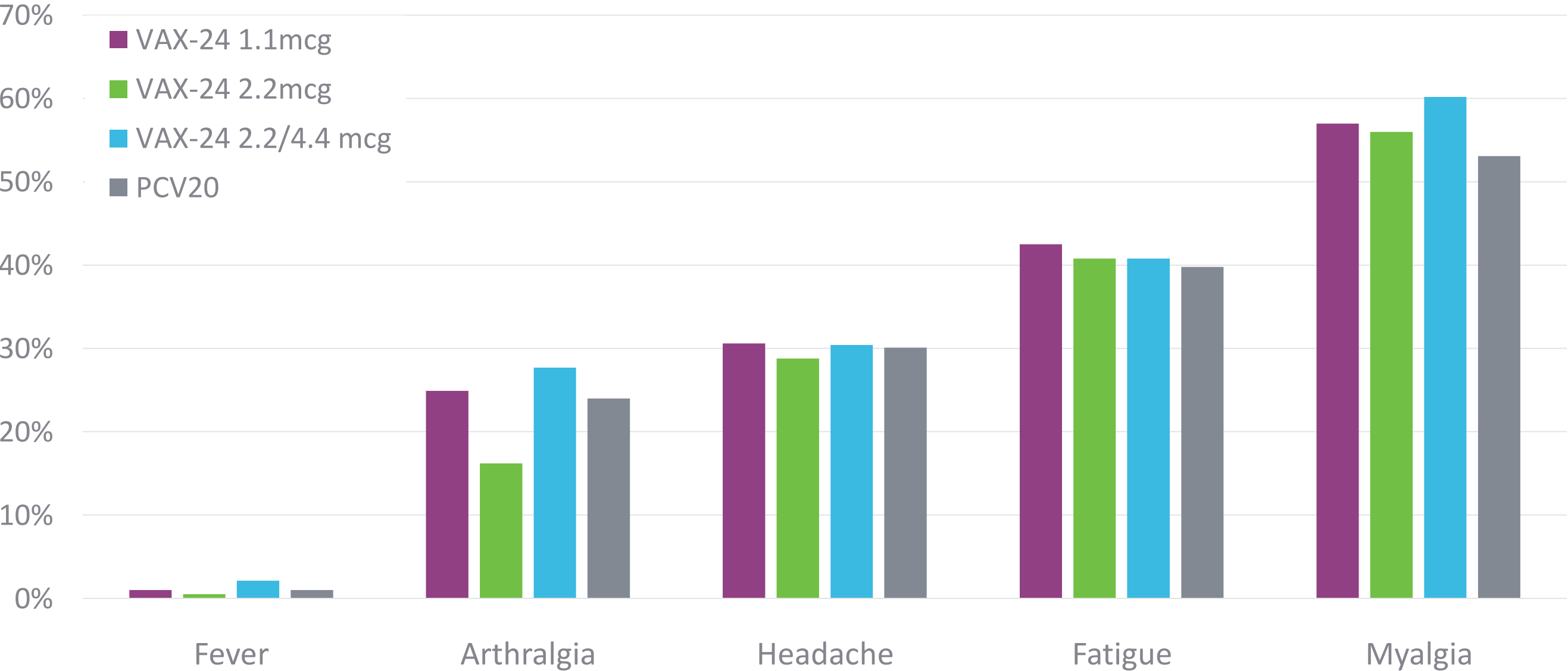


# Local Solicited AEs Similar to PCV20 and Across Cohorts Through Day 7



*Represents data for the 50-64 year age group; as of August 31, 2022.*

# Systemic Solicited AEs Similar to PCV20 and Across Cohorts Through Day 7



Represents data for the 50-64 year age group; as of August 31, 2022.

# VAX-24 Safety Profile 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	193	191	191	196
Subjects with TEAE, n (%)	29 (15.0)	21 (11.0)	22 (11.5)	31 (15.8)
Subjects with SAE or NOCI, n (%)	2 (1.0)	3 (1.6)	5 (2.6)	4 (2.0)
Subjects with related SAE, n (%)	0	0	0	0
Subjects with related NOCI, n (%)	0	0	0	0
Deaths, n (%)	0	0	0	0

*Represents data for the 50-64 year age group; as of August 31, 2022.*

# Standard Regulatory Criteria for Evaluating PCV Immunogenicity Results

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## CRITERIA FOR 20 SEROTYPES COMMON TO VAX-24 AND PCV20:

### Non-inferiority Standard:

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

### Superiority Standard:

- Lower bound of 2-sided 95% CI of the OPA GMT ratio 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 4 INCREMENTAL SEROTYPES IN VAX-24:

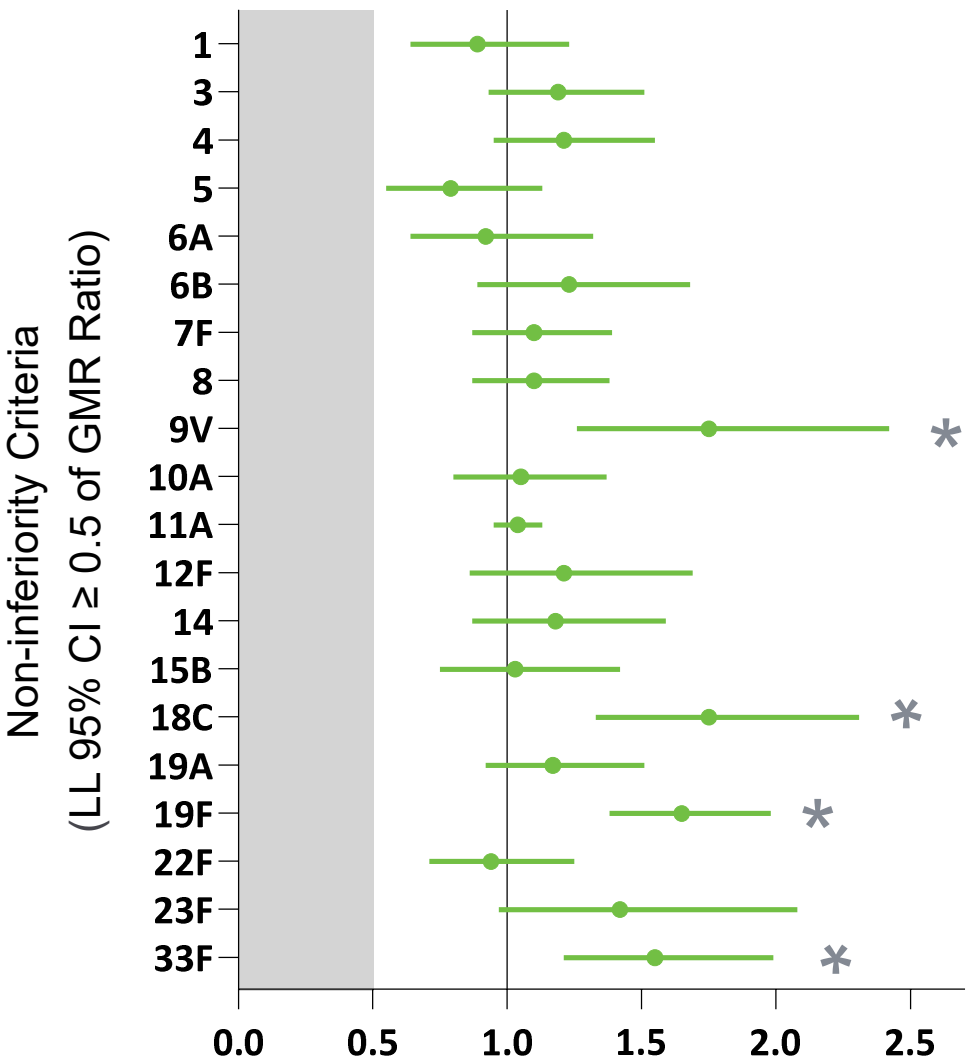
### Superiority Standard:

- 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%
- Lower bound of the 2-sided 95% CI of the OPA GMT ratio is greater than 2.0

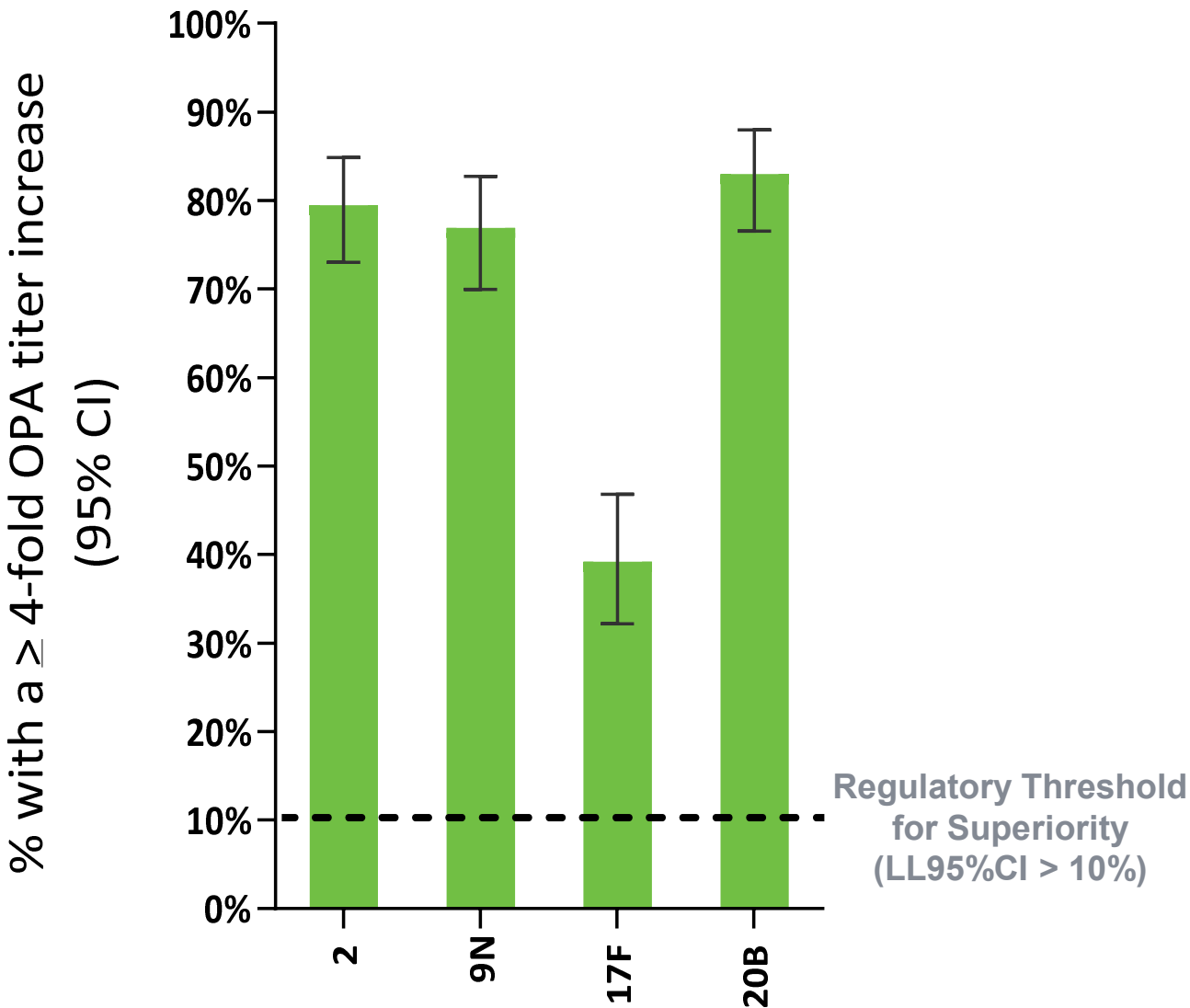


# VAX-24 2.2mcg Dose Met Regulatory Criteria for All 24 Serotypes

Met non-inferiority standard for all 20 common serotypes for the OPA GMR of VAX-24 : PCV20



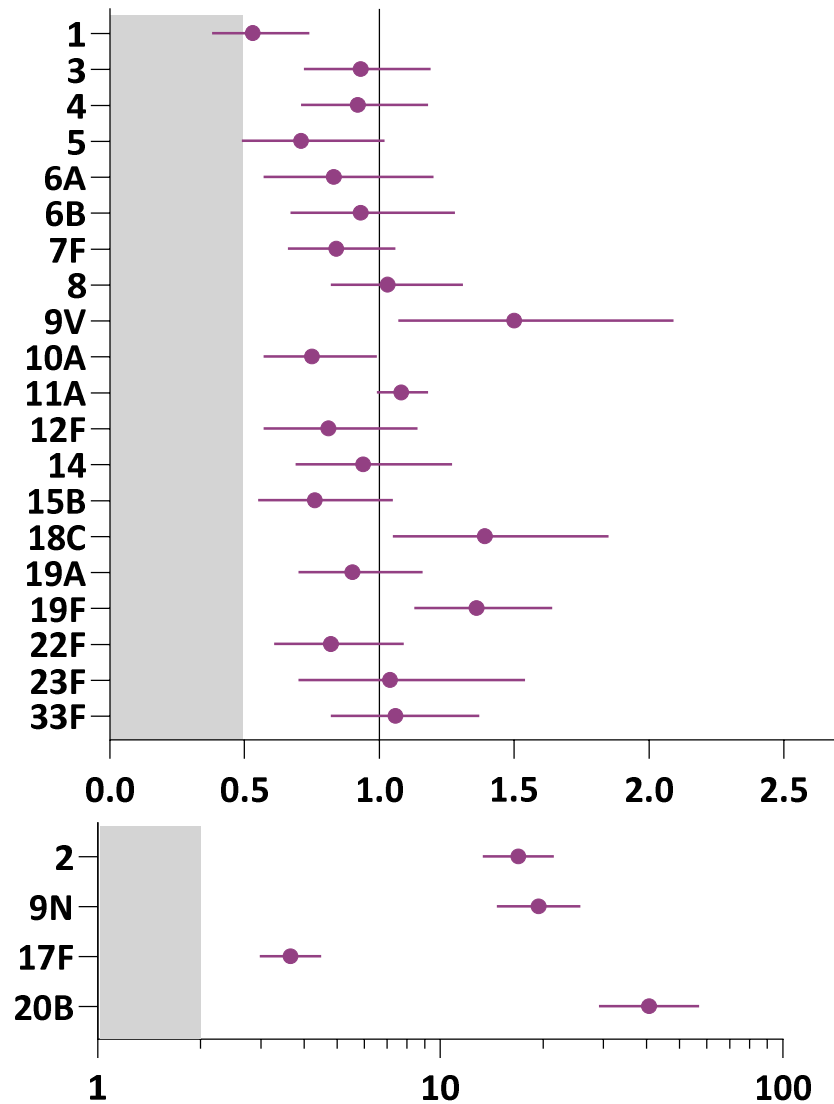
Met superiority standard for all 4 incremental serotypes in VAX-24 based on 4-fold rise



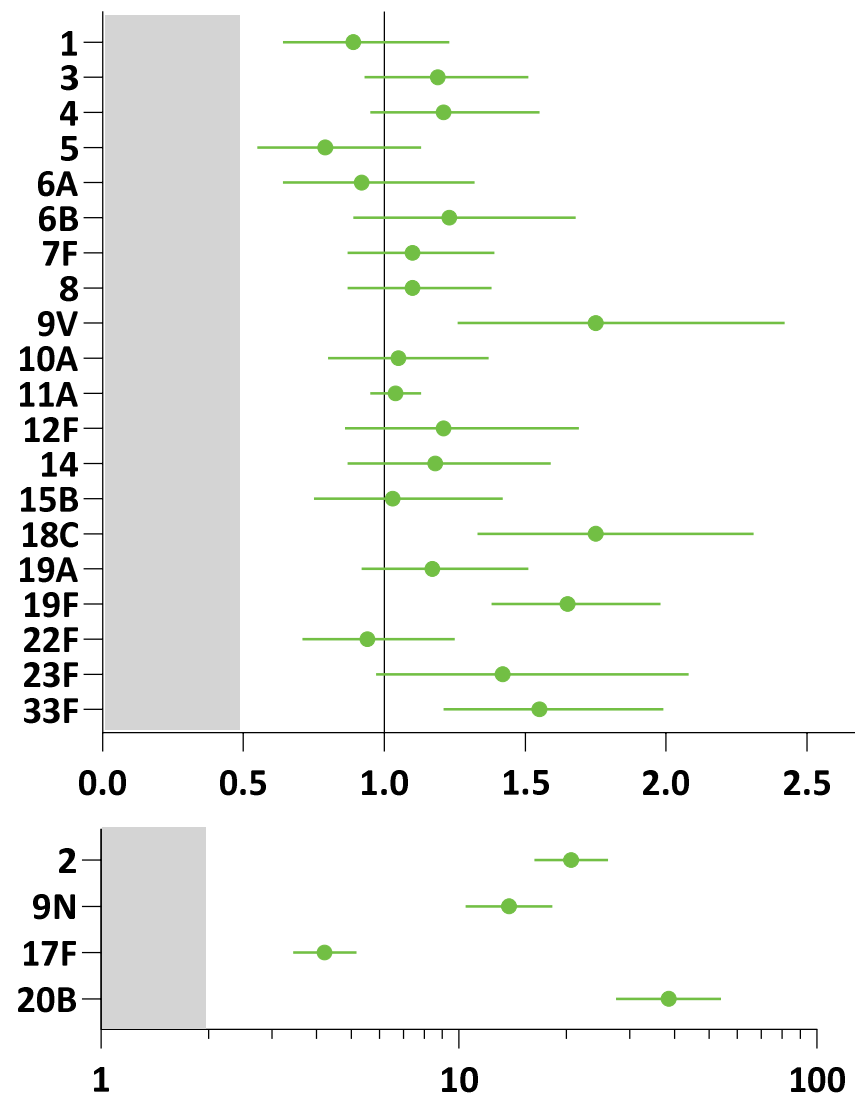
# All 3 Doses Induced Immune Responses Sufficient to Move to Phase 3

2.2mcg Dose Demonstrated Higher OPA GMRs for 16 of the 20 Shared Serotypes and Will be Advanced

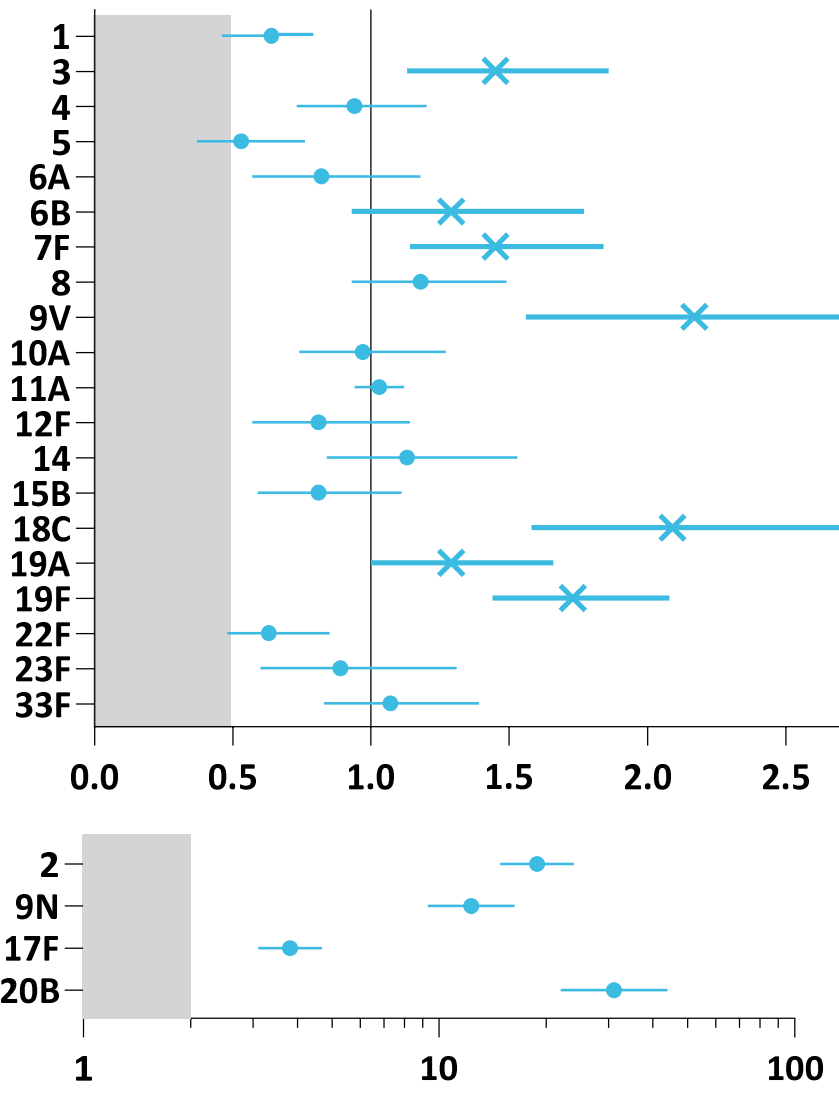
VAX-24 Low Dose (1.1mcg)



VAX-24 Middle Dose (2.2mcg)

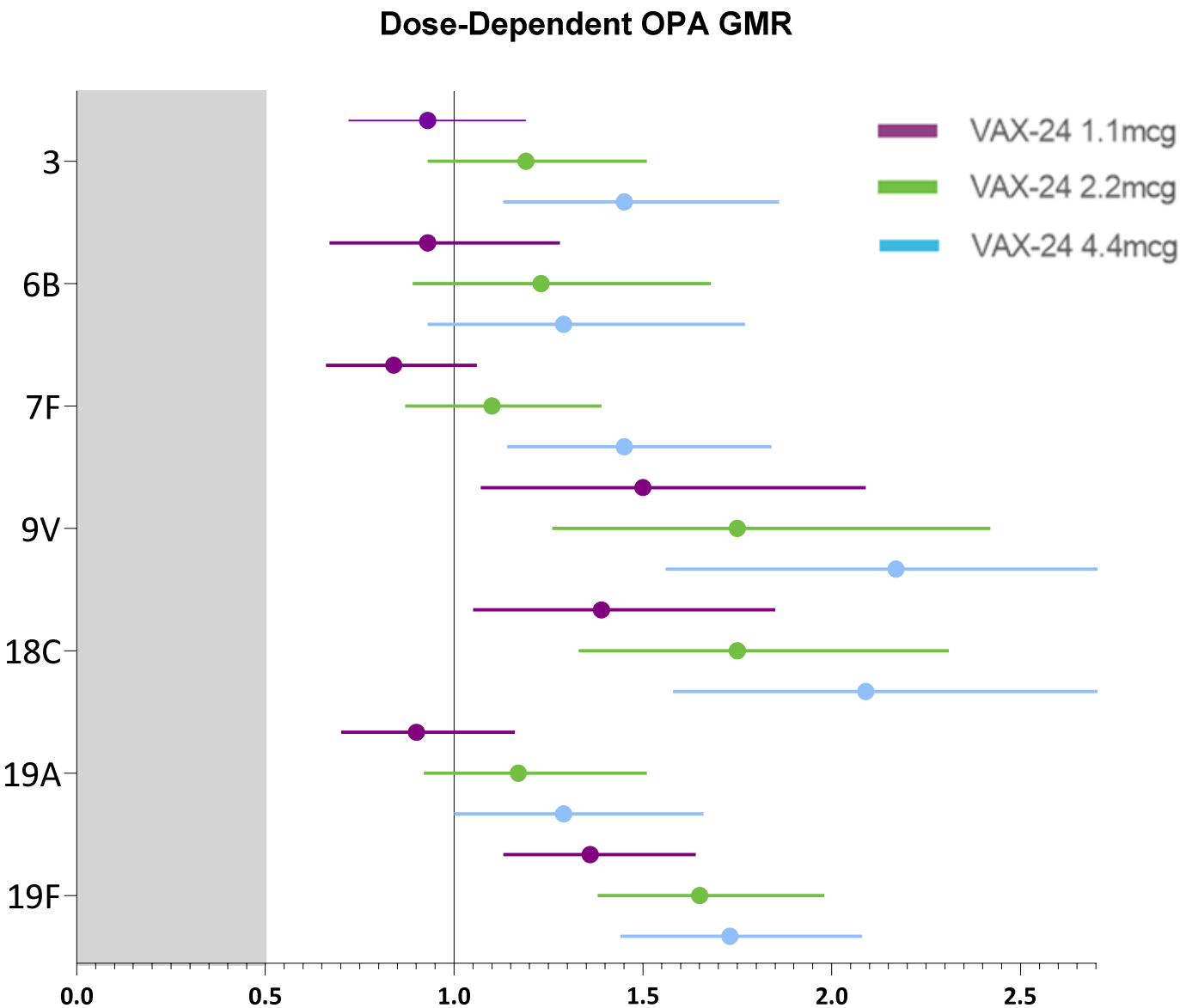


VAX-24 Mixed Dose (2.2mcg/4.4mcg)



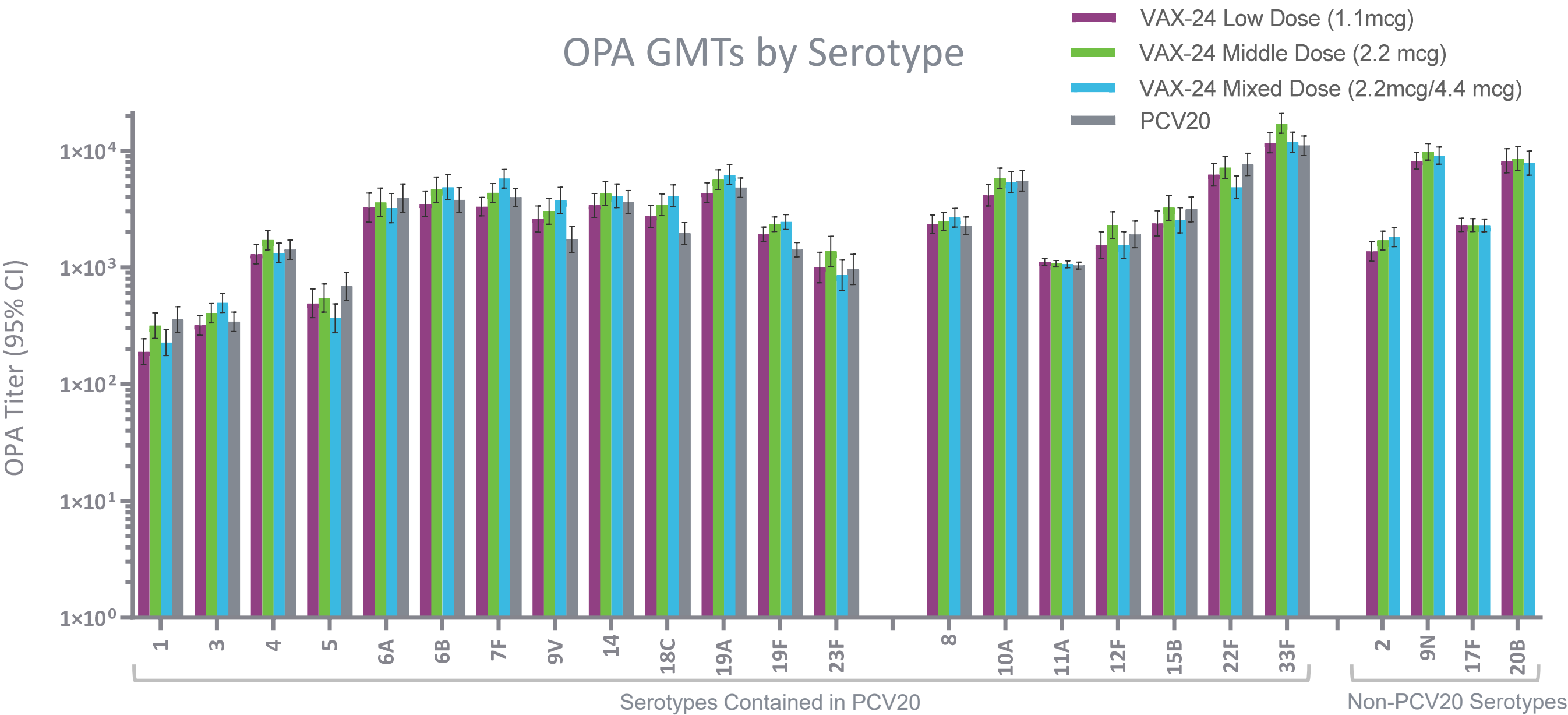
X = 7 VAX-24 serotypes at the 4.4mcg dose; GMR = Geometric Mean Ratio; LL= Lower Limit; CI = Confidence Interval

# Strong Evidence of a Dose-Dependent Response for the 7 VAX-24 Serotypes Tested at 1.1mcg, 2.2mcg and 4.4mcg



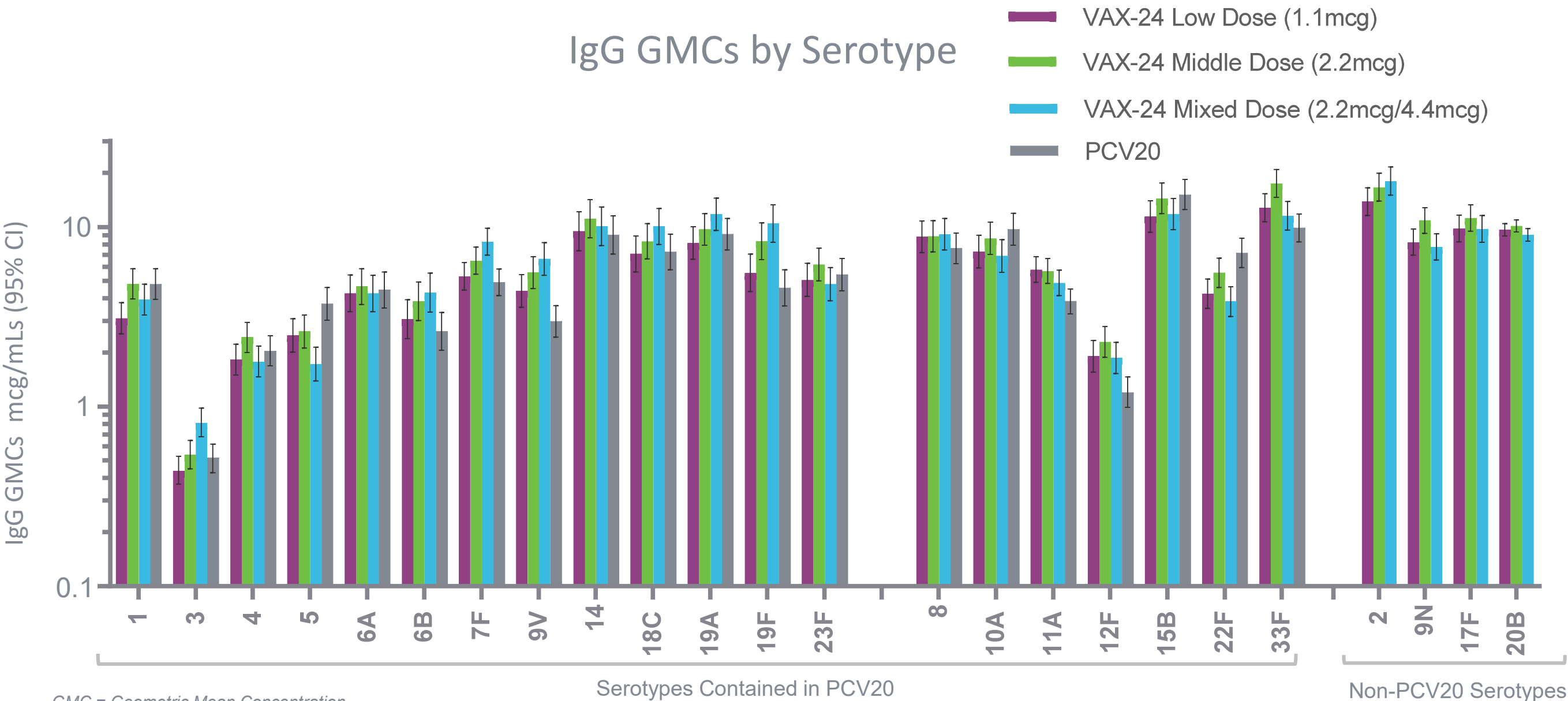
4.4mcg dose deemed not necessary as 2.2mcg dose demonstrated higher OPA GMRs for all 7 serotypes tested versus PCV20.

# All 24 Serotypes in VAX-24 Demonstrated Robust OPA Immune Responses





# All 24 Serotypes in VAX-24 Demonstrated Robust IgG Responses



# Vaxcyte PCV Franchise Leverages Established Regulatory Pathway

## Well-Trodden Clinical Plan Aligned with Current FDA, EMA and WHO Guidance and Precedent PCVs

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### CURRENT FDA, EMA & WHO GUIDANCE AND PRECEDENT

- Well-defined established surrogate immune endpoints
- No anticipated requirement for field efficacy trials

- Licensure via non-inferior immune responses vs. SOC <sup>(1)</sup>
- Consistent with Merck (PCV15) & Pfizer (PCV20) BLAs <sup>(2)(3)</sup>










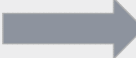





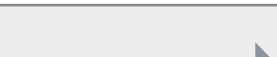


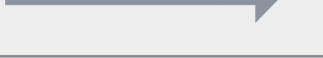





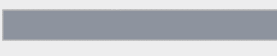




- Consistency across Ph 2 POC and Ph 3 pivotal studies for immune response in adult and infant programs <sup>(4)(5)(6)</sup>

(1) For adults: Lower limit of the 95% CI for the OPA GMR  $\geq 0.5$  for each serotype comparison. For infants: Lower limit of the 95% CI for the IgG GMC ratio post dose 4 is  $\geq 0.5$  and LL of the 95% CI for % of subjects achieving an IgG concentration  $\geq 0.35 \mu\text{g/mL}$  1 month after dose 3 is  $< -10\%$ .  
(2) Clinicaltrials.gov: Pfizer clinical studies for 20vPnC NCT03512288, NCT03550313, NCT03313050, NCT03313037, NCT03760146, NCT03835975, and NCT03828617.  
(3) Clinicaltrials.gov: Merck clinical studies for V114 (PCV15) NCT02987972, NCT03620162, NCT03692871, NCT03731182, NCT03480763, NCT03615482, NCT03547167, NCT03480802, and NCT03565900.  
(4) WHO. Recommendations to assure the quality, safety and efficacy of pneumococcal conjugate vaccines, in WHO Expert Committee on Biological Standardization, 60<sup>th</sup> report. Geneva, Switzerland: WHO; 2013:91-521.  
(5) Prevenar 13 FDA Summary Basis for Regulatory Action. BLA/STN: 125324, 2010. <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM206140.pdf>. Accessed January 10, 2020.  
(6) Guidelines on clinical evaluation of vaccines. EMEA/CHMP/VWP/164653/05, April 2018. [https://www.ema.europa.eu/en/documents/scientific-guideline/draft-guideline-clinical-evaluation-vaccines-revision-1\\_en.pdf](https://www.ema.europa.eu/en/documents/scientific-guideline/draft-guideline-clinical-evaluation-vaccines-revision-1_en.pdf), Accessed Feb 11, 2020.

# The Pneumococcal Vaccine Landscape

## Vaxcyte PCV Franchise Designed to Offer Broadest Spectrum of Coverage

### PCV

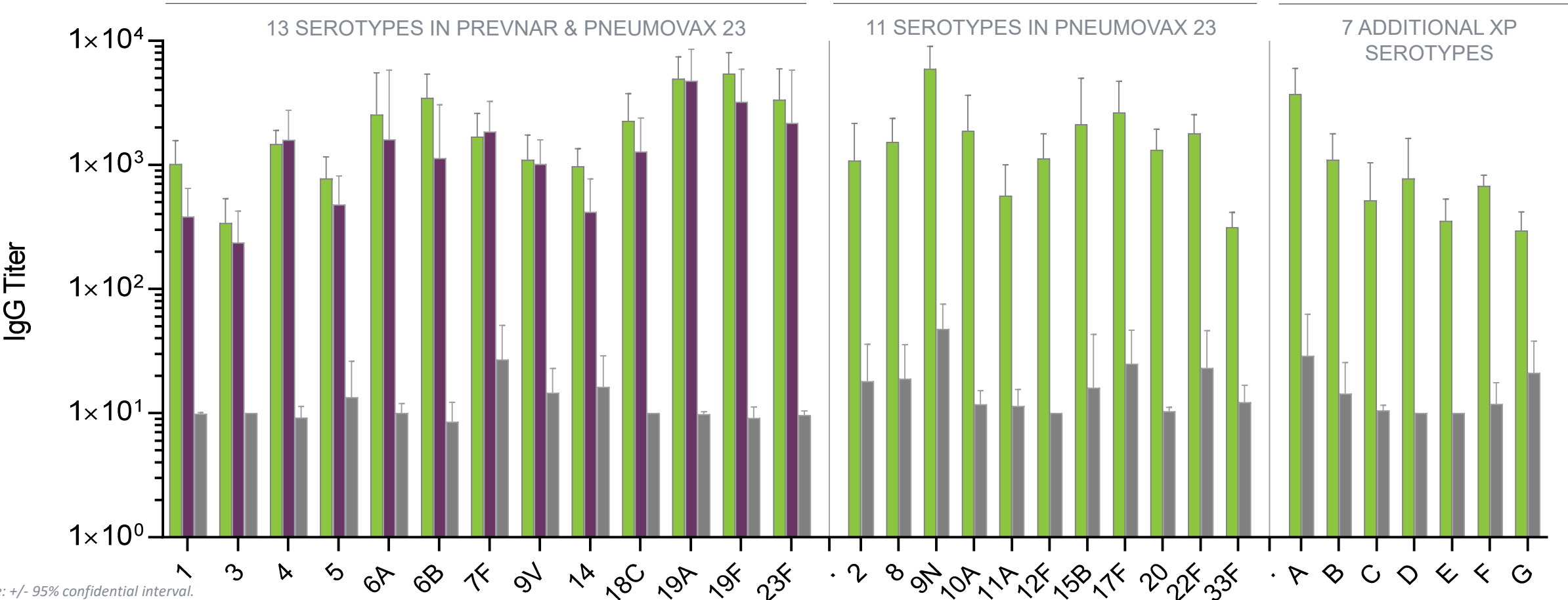
DEVELOPER	VACCINE NAME	SPECTRUM OF COVERAGE		STATUS	TARGET POPULATION: INFANTS /ADULTS	
GSK	SYNFLORIX		10-VALENT	• Approved ex-US		
MERCK	VAXNEUVANCE		15-VALENT	• Approved in adults & infants		
	MERCK V116		21-VALENT	• Phase 3 in adults		
	MERCK V117		21-VALENT	• Phase 1 in pediatrics		
PFIZER	PREVNAR 13		13-VALENT	• Approved in infants		
	PREVNAR 20		20-VALENT	• Approved in adults • Phase 3 in infants		
SK BIOSCIENCE/ SANOFI-PASTEUR	PCV21		21-VALENT	• Phase 2 in adults, toddlers and infants		
VAXCYTE	VAX-24 (SITE-SPECIFIC CONJUGATION)		24-VALENT	• Phase 2 in adults		
	VAX-XP (SITE-SPECIFIC CONJUGATION)		31-VALENT	• Preclinical POC		
MERCK	PNEUMOVAX 23 (PS ONLY)		23-VALENT	• SOC as follow-on in adults after PCV15		
GSK (24/30+)	AFX3772 (AFFINITY-BOUND PS TO NOVEL PNEUMO PROTEINS)		24-VALENT	• Phase 2		

SOC = standard of care; PS = polysaccharides.

# VAX-XP Preclinical Data: Further Evidence of Potential for Platform

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

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



Note: +/- 95% confidential interval.

(1) VAX-XP, includes all 24 strains in VAX-24 and 7 additional pneumococcal conjugates.

(2) PS/Alum = PSs formulated with alum.



# Non-PCV Pipeline

# VAX-A1: Group A Strep Conjugate Vaccine Program

## Novel Conjugate Vaccine Designed to Provide Universal Protection

### UNMET NEED

- Group A Strep causes 700M global annual cases of pharyngitis (strep throat) and increases risk of severe invasive infections such as sepsis, necrotizing fasciitis and toxic shock syndrome
- 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)

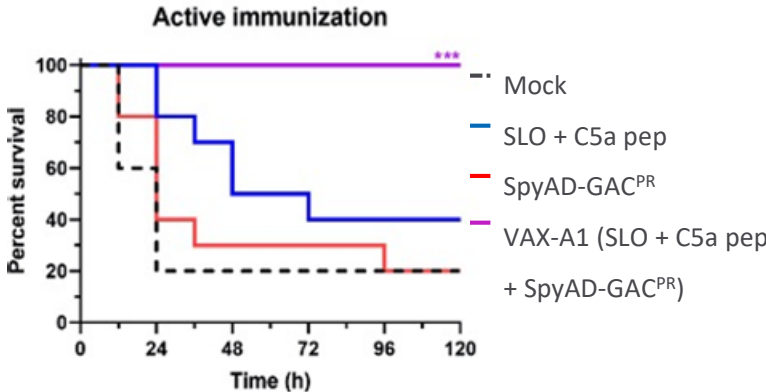
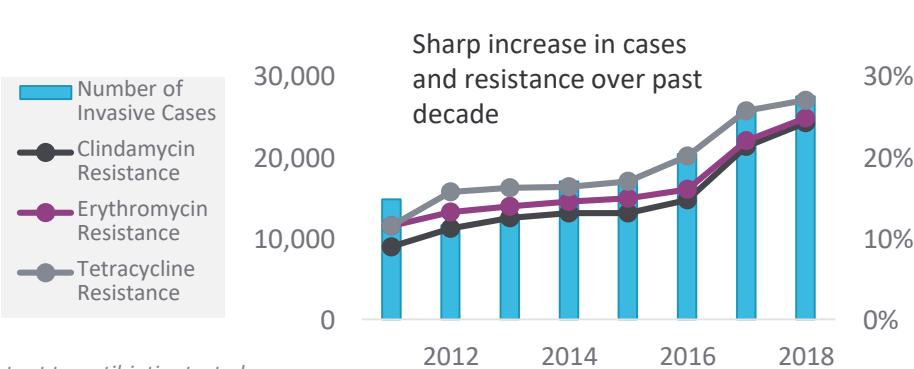
### VAX-A1: BROAD-SPECTRUM, MONOVALENT CONJUGATE VX

- 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 – Polyrhamnose – 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, US Biodefense Agency (BARDA)); add'l August 2021 award of \$3.2M toward IND-enabling activities; total potential funding of up to \$13.9M inclusive of grants to date
- Initiated IND-enabling activities in 2H:21
- Anticipate providing guidance on the expected timing for adult IND application submission in 2H:22<sup>(1)</sup>

### KEY DATA



(1) Guidance provided as of November 7, 2022.

Resistant includes those isolates intermediate or fully resistant to antibiotics tested.

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 & hard tissues supporting the teeth
- Highly prevalent: 65 million US adults afflicted
- Significant morbidity and lost productivity: >\$50B in lost productivity in 2010
- Associated with increased risk of heart attack, stroke, cardiovascular disease and Alzheimer's Disease

### VAX-PG: MULTIVALENT THERAPEUTIC VACCINE

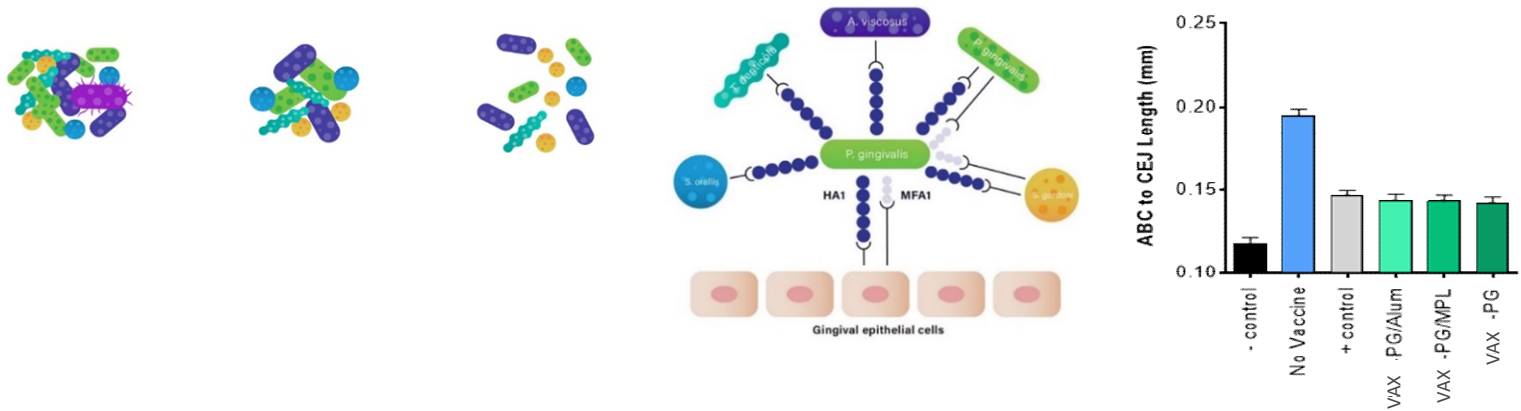
- Incorporates proprietary combination of known virulence factors of keystone pathogen
- Preclinical model demonstrated protein-specific IgG response following immunization and protected mice from *P. gingivalis*-elicited oral bone loss
- Initial goal to develop therapeutic vaccine that slows or stops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

### PROGRAM STATUS

- Preclinical proof of concept published in Journal of Clinical Periodontology
- Next milestone: Nominate final vaccine candidate by the end of 2022<sup>(1)</sup>

### 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) Guidance provided as of November 7, 2022.  
Huang et.al. J Clin Periodontol. 2019 Feb;46(2):197-205.

# Key Corporate Highlights

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Large Market Opportunity for Lead PCV Franchise

Cell-Free Protein Synthesis Platform

Disciplined Target Selection

Robust Pipeline with Multiple Novel Vaccines

Aligned Critical Resources