

### **Corporate Presentation**

November 10, 2021

# **Forward-Looking Statements**

2

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 benefits of Vaxcyte's vaccine candidates; the process and timing of anticipated future development of Vaxcyte's vaccine candidates, including the timing and submission of an IND application for VAX-24 and the initiation of the VAX-24 Phase 1/2 clinical proof-of-concept study thereafter; the timing and availability of topline data for VAX-24; the ability to complete the manufacturing of the GMP drug product; the successful testing and release of the final drug product for VAX-24 and documentation of stability; the achievement of future funding milestones; the use and availability of funds from CARB-X; the nomination of a final vaccine candidate for VAX-PG; the market opportunity for our vaccines; our expectations regarding the potential benefits, spectrum coverage and immunogenicity of our vaccine candidates; the timing of the initiation, progress and expected results of our preclinical studies, clinical trials and research and development plans; 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; Vaxcyte's reliance on third-party manufacturers; 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 10, 2021 or in other documents Vaxcyte subsequently files with or furnishes to the SEC. Vaxcyte undertakes no duty or obligation to update any forward-looking statements contained in this release as a result of new information, future events or changes in its expectations.

**Vaxcyte Mission Statement** 

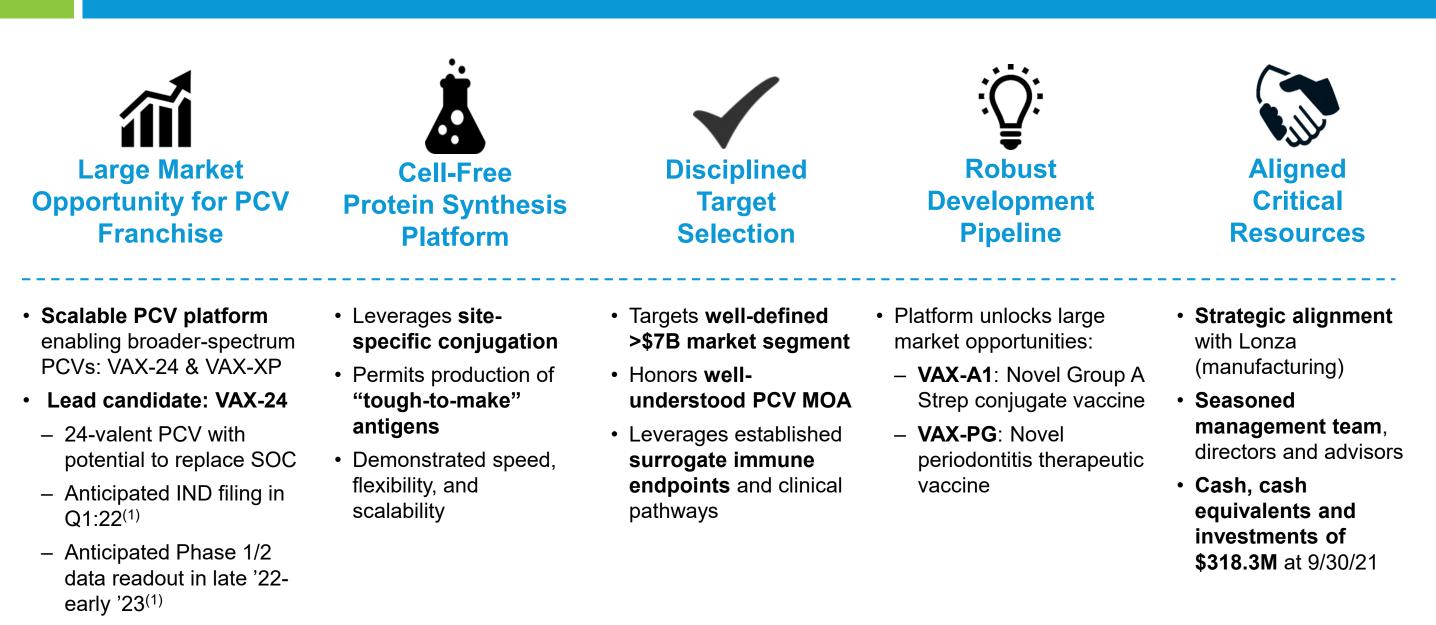




Seeking to improve global health by developing superior & novel vaccines designed to prevent or treat some of the most common & deadly infectious diseases worldwide.

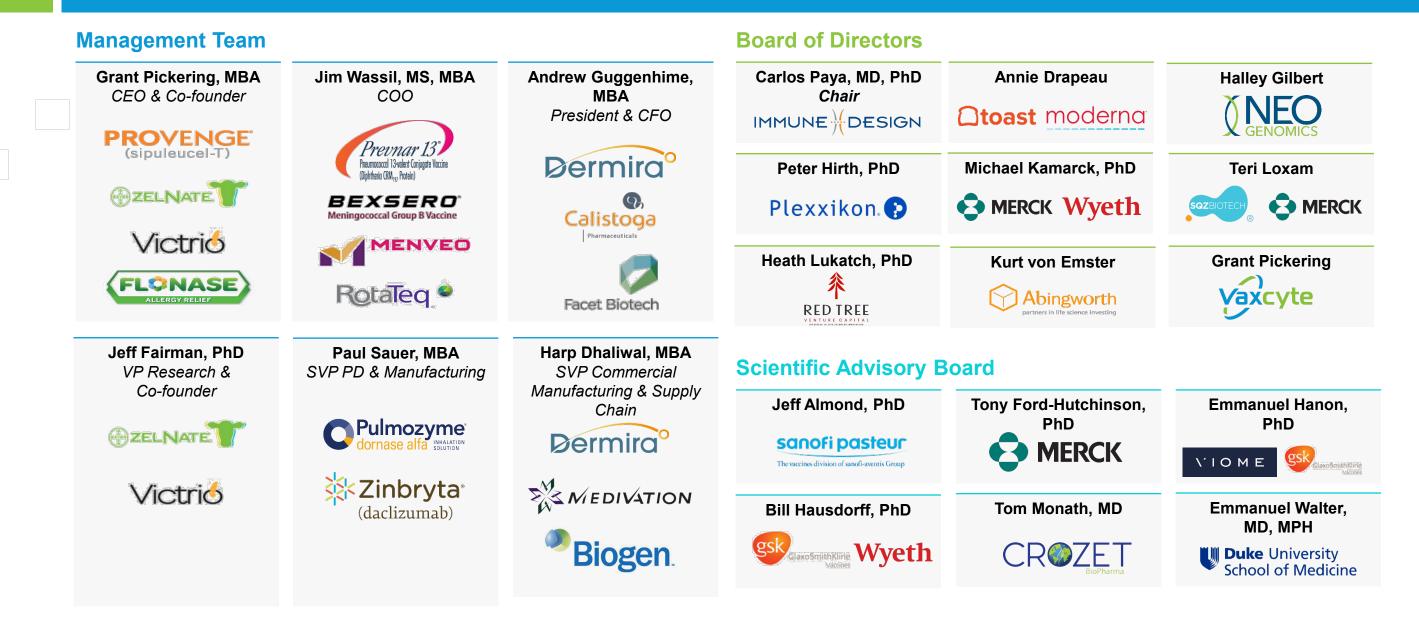
# Key Corporate Highlights

Next-Generation Vaccine Company – Led by Pneumococcal Conjugate Vaccine (PCV) Franchise



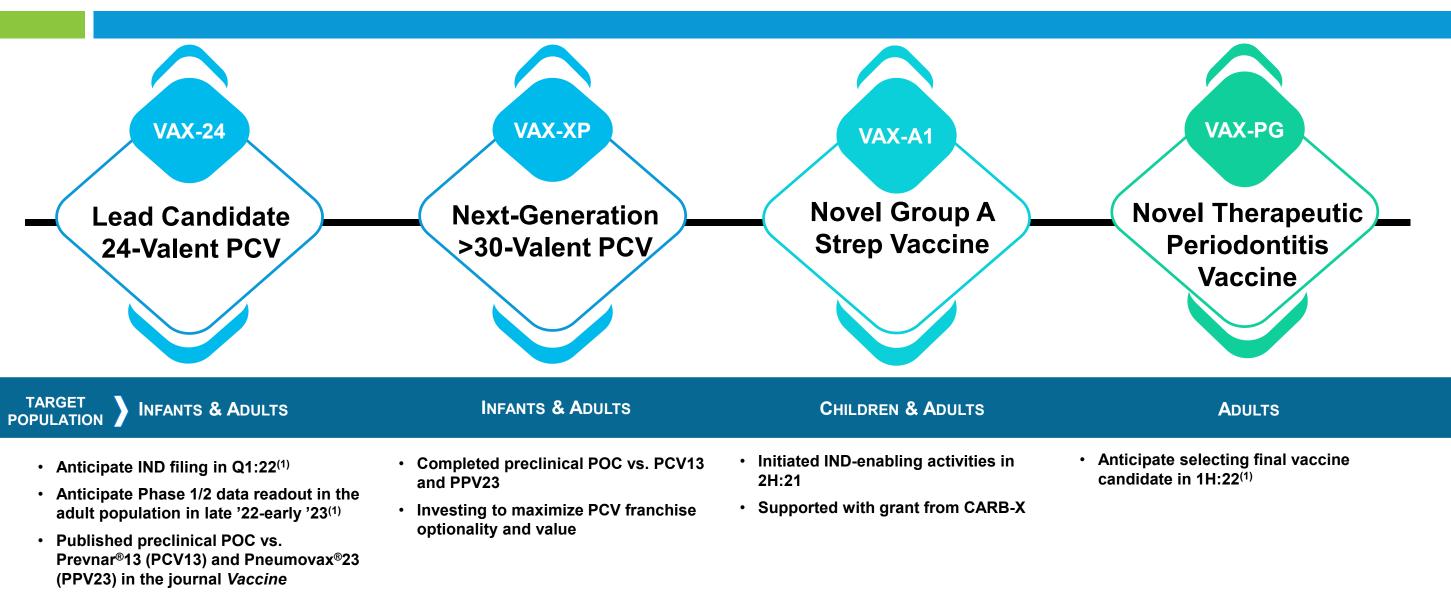
# Experienced Team, Board of Directors, and Scientific Advisors

Outstanding Track Record in Vaccines and Biopharma



### **Next-Generation Vaccine Pipeline**

Focus on Superior PCV Franchise with Novel, Early Stage Pipeline to Follow



### Cell-Free Protein Synthesis Platform Unlocks Multiple Vaccine Applications Design and Produce Proteins Beyond Reach of Conventional Methods



### **XpressCF** Platform<sup>(1)</sup>

### **Cell-Free Protein Synthesis (CFPS):**

- Transcriptional & translational (ribosomal) machinery from *E coli* stored as a frozen "extract"
- Produces singular protein of interest at high yields
- Uniquely enables site-specific conjugation via insertion of multiple nnAA conjugation anchors
- Uniquely permits protein production in nonphysiological conditions

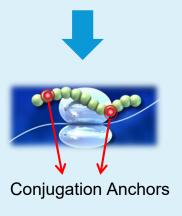
### Speed, Flexibility, Scalability:

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





Adjustable Reaction Conditions



### **Platform Capabilities**

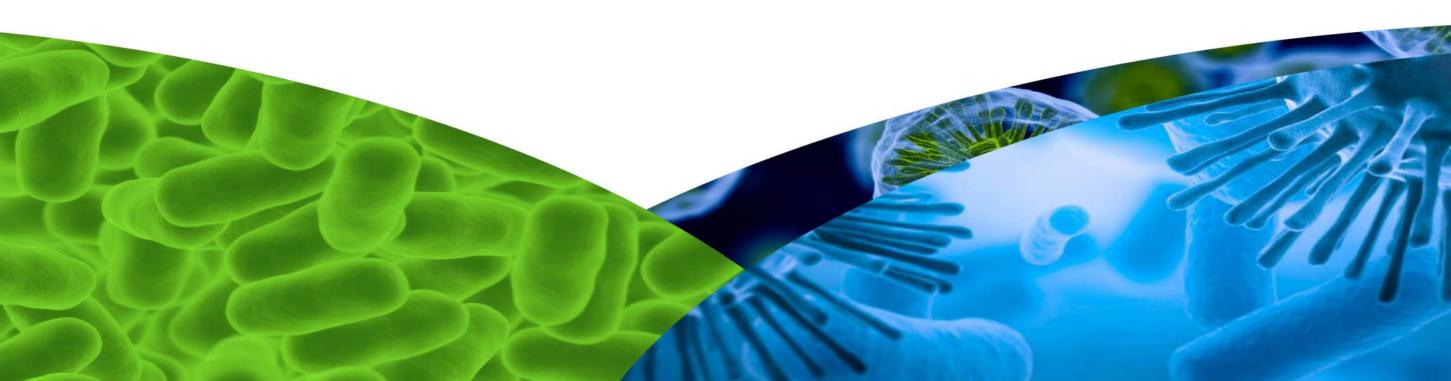
#### **Superior Conjugate Vaccines:**

- 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
- Designed to enable use of less protein carrier without sacrificing immunogenicity
- Enables 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







# 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 all cases of bacterial meningitis in the U.S.

Global Incidence and Impact of PD

Global incidence of PD is driven by emerging serotypes not covered by currently available vaccines.

In the U.S. alone, there are ~900K pneumococcal pneumonia cases annually.

For IPD, adult mortality rates in the U.S. range from 11% to 30%.

Among children under age 5, PD is a leading cause of death globally.

### Current Global Standard-of-Care (SOC)

Vaccinations are recommended globally for infants and adults to prevent PD.

In the U.S.:

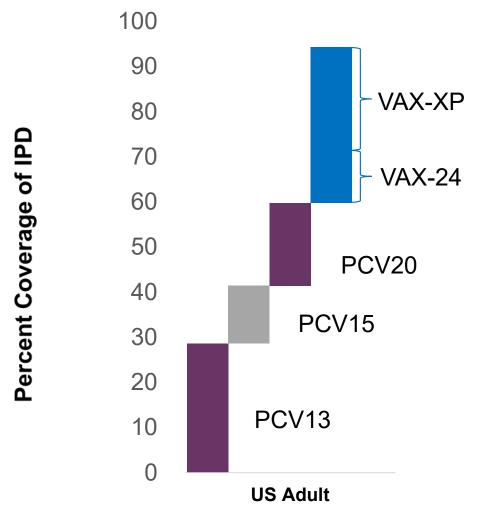
Infants: PCV13 (4 doses)

Adults: Prevnar 20<sup>™</sup> (PCV20) (1 dose) or Vaxneuvance<sup>™</sup> (PCV15) and Pneumovax 23<sup>®</sup> (PPV23) (1 dose/each)

# Significant Unmet Needs Remain Despite SOC Today

Resulting in Spectrum of Coverage Driving Adoption of Pneumococcal Vaccines

### Estimated coverage of PCVs based on circulating invasive pneumococcal serotypes.



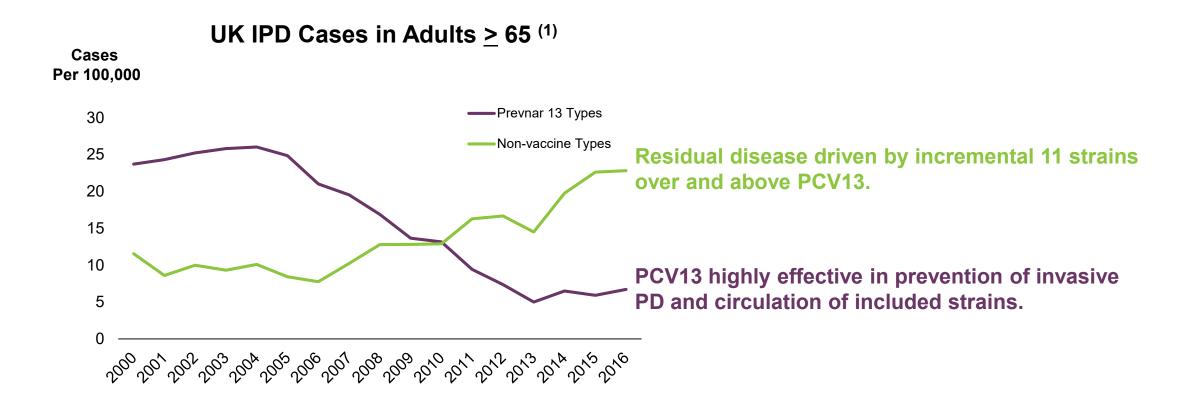
Most disease caused by strains above and beyond Prevnar 13<sup>®</sup>, driving need for broaderspectrum PCVs.

<sup>1</sup>Data in the US is for 2017, inclusive of those > 5 yrs of age <sup>2</sup>Varghese et al. Clin Micro and Infect (2020) 26(4): 512.e1-512.e10



### 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

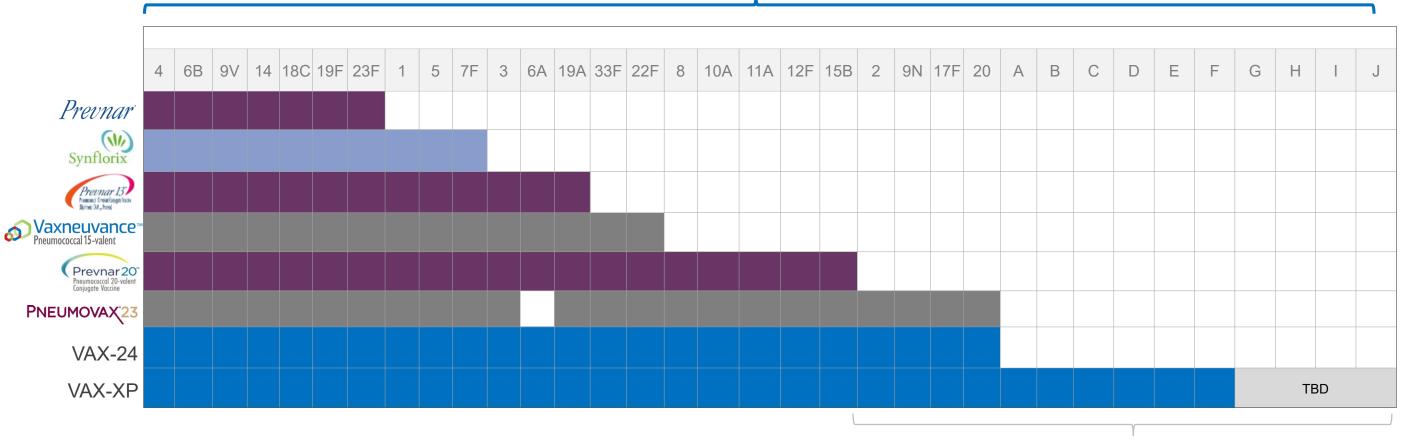


# Vaxcyte PCV Franchise Designed to Offer Broader Protection

Potential for Sustained Leadership in the Established >\$7B Pneumococcal Vaccine Market

VAX-24: Category-leading 24-valent PCV incorporating carrier-sparing conjugates

**VAX-XP**: Next-generation >30-valent PCV showcases franchise approach and scalability of carrier-sparing conjugates



Spectrum of Coverage Drives Adoption

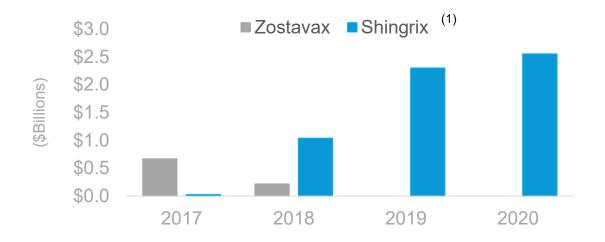
12

### 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
- Highly attractive margins:
  - Prevnar 13 & Pneumovax 23 are premium priced in the US
- Durable revenue stream:
  - Prevnar 13 & Pneumovax have generated >\$100B in revenues
- 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 now adequate for full approval for follow-on PCVs
- Potential for rapid adoption: Governing body ACIP recommendation drives uptake
  - Prevnar 13 vs Prevnar 7
  - Shingrix<sup>®</sup> vs Zostavax<sup>®</sup>





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

# $\mathcal{O}$

# Potential for Global Pneumococcal Market to Grow Beyond the \$7B Today

The Oct. 2021 ACIP Vote Reinforced Need for PCVs with Broader Spectrum of Coverage and for Use in Expanded Adult Population

 ACIP supported use of either Pfizer's PCV20 or Merck's PCV15 plus Pneumovax23 in adults ≥65 years of age

By preserving PPV23, ACIP decision reinforces the need for a 24-valent PCV

- Age-based recommendation remains at age 65, per ACIP
- This is the first time ACIP has recommended a PCV for risk groups ages 19 to 64

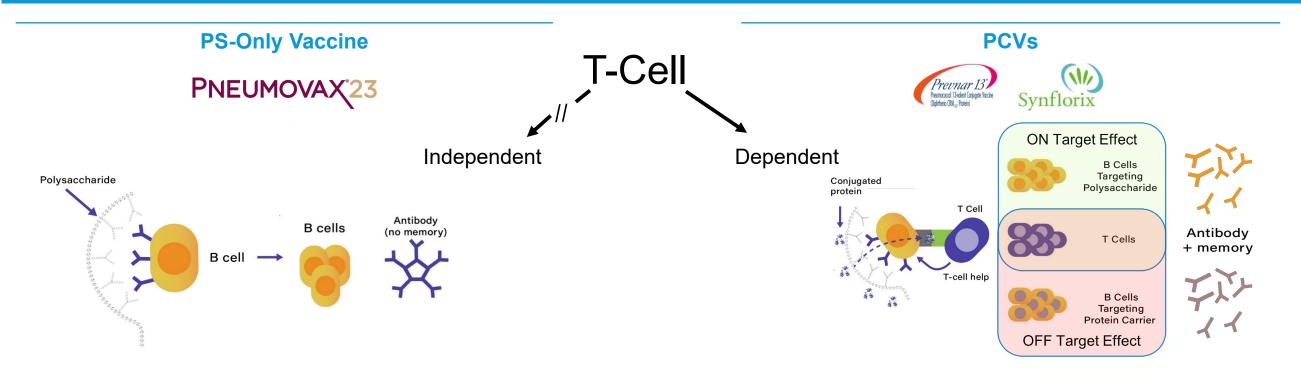
Significantly expands adult population and increases overall PCV market

- Strong desire expressed by several ACIP committee members to move adult vaccination to 50 years of age
- CDC committed to gathering more data and revisiting at a future meeting

Provides important opportunity to address unmet needs in adults



### PCVs 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

Note: Graphics adapted from Strugnell et al, Understanding Modern Vaccines, Vol 1, Issue 1, 61-88.
(1) Protein carrier in Prevnar 13 is a modified form of diphtheria toxin (CRM<sub>197</sub>).

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

# Limitations of Current PCVs

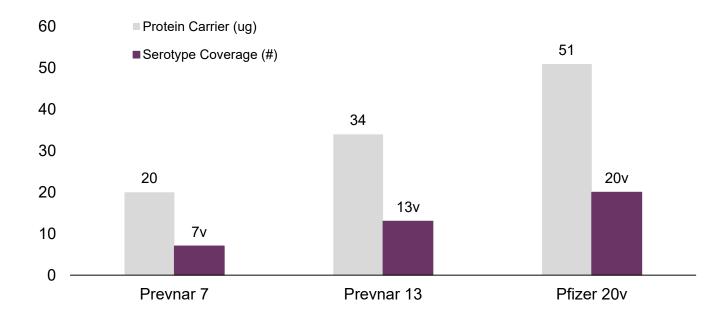
Coverage Expansion Needed to Address Circulating Disease, but Protein Carrier Backbone Problematic

**Limitations of Conventional Chemistry** 

Random conjugation

Higher ratio of protein carrier to polysaccharide

Further exacerbates carrier suppression



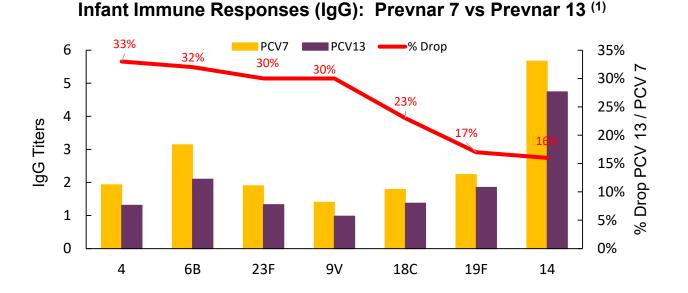
# Limitations of Current PCVs



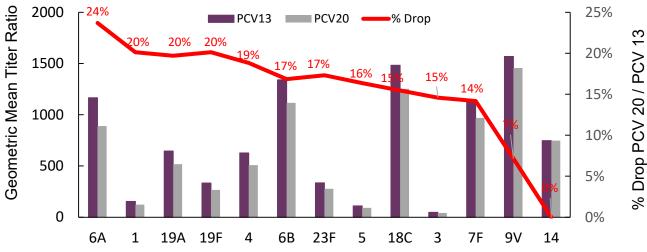
Coverage Expansion Using Conventional Chemistry Has Led to Carrier-Induced Immune Suppression

### **Carrier Suppression**

- Reduced immune response to the target polysaccharides due to the cumulative amount of the protein carrier
  - Expanded spectrum of coverage requires increasing protein carrier burden
  - Reduced immune responses demonstrated in both infants and adults



Adult Immune Responses (OPA): Prevnar 13 vs PCV20<sup>(2)</sup>



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

17

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



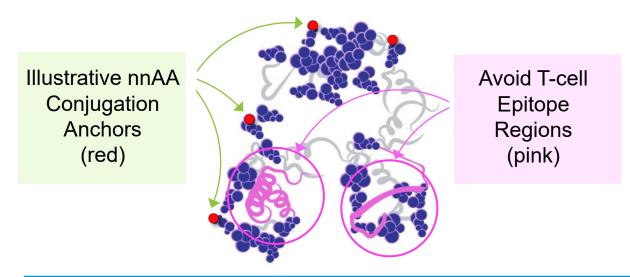
# Differentiated PCV Franchise Led by VAX-24



# VAX-24 Employs Carrier-Sparing Conjugates

*XpressCF Enables Precise Conjugation to Enhance Potency of Standard Protein Carrier* 

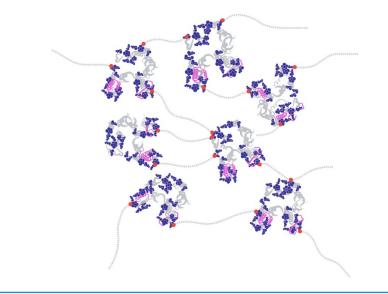
Precise, Site-Specific Conjugation Sites on Proprietary eCRM<sup>®</sup> Protein Carrier



### 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

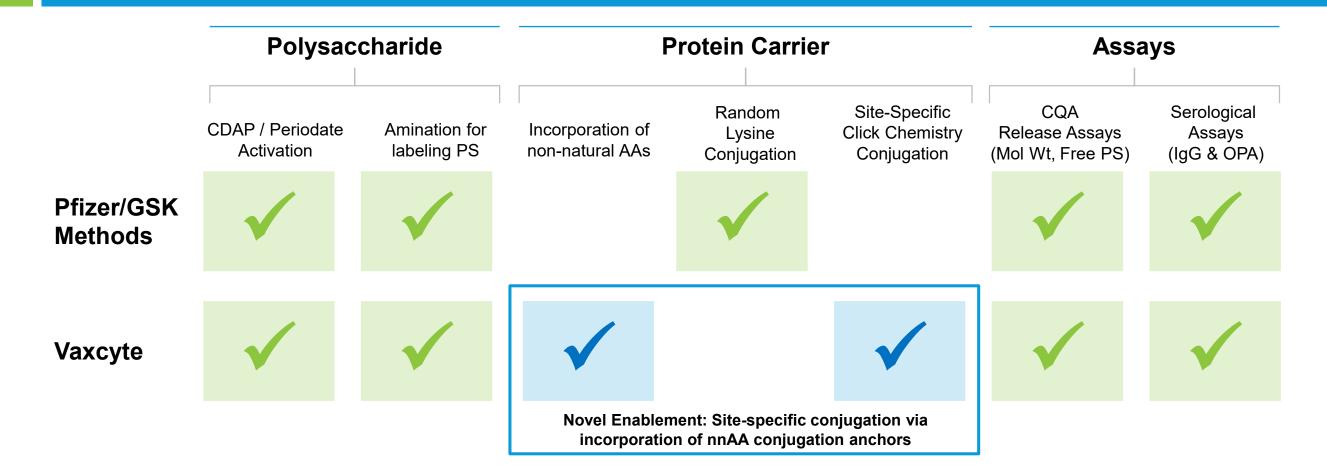


#### **Carrier-Sparing Conjugates**

- 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 attribute & serological assays

# VAX-24 Design Leverages Many Standard PCV Conventions

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



• 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

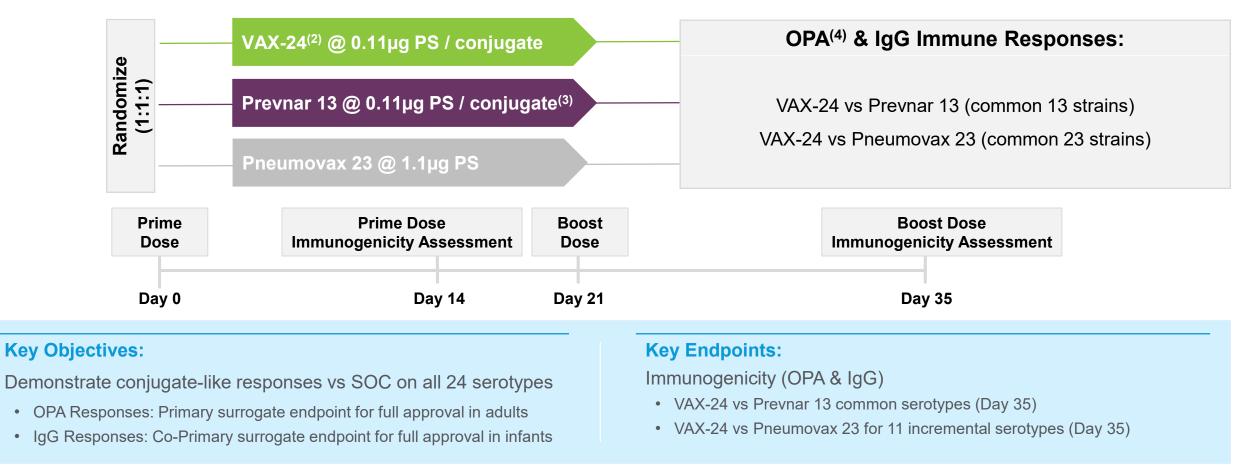
• Vaxcyte has leveraged the same animal models utilized in the development of both approved PCVs (Prevnar and Synflorix)

# VAX-24 Preclinical POC Study

Designed to Assess Conjugate-Like Immune Responses vs Standard of Care

Study Design: Vaccination of rabbits<sup>(1)</sup> with doses matching weight-to-weight allometric scaling to marketed human dose

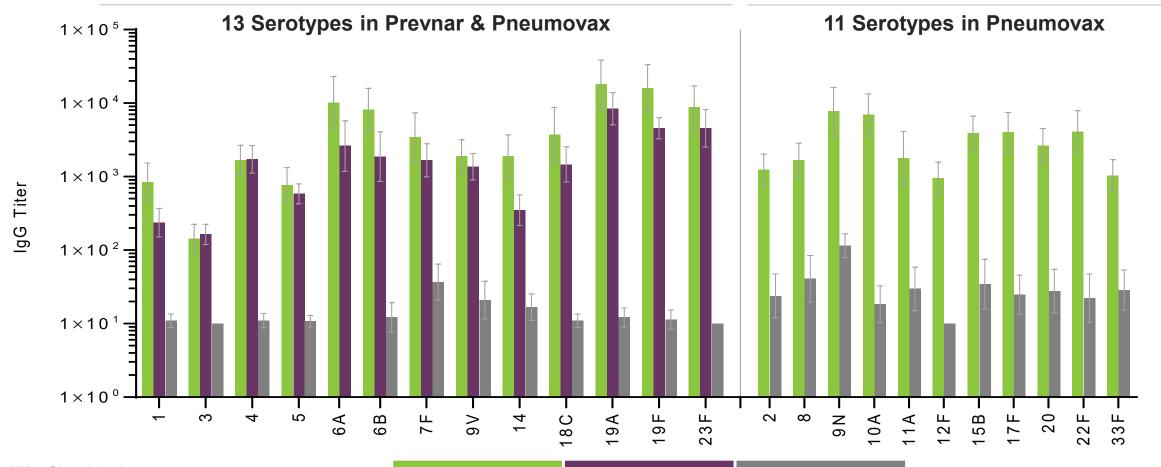
### Preclinical POC Study: Rabbits (n=10/cohort) Dosed at Day 0 & Day 21



- (1) Represents same rabbit model as utilized in the development of approved PCVs (Prevnar, Prevnar 13, Synflorix).
- (2) VAX-24 conjugates produced with all Lonza-produced materials (eCRM & 24 polysaccharides)
- (3) Prevnar 13 dose of 6B is 2x the amount relative to the other conjugates, so equates to 0.22ug in this study.
- (4) Opsonophagocytic activity assay (OPA) measures the functional capacities of vaccine-candidate-raised antibodies.

### VAX-24 Preclinical POC Study Supports Potential to Deliver Broader-Spectrum PCV IgG Antibody Titer Comparisons (Current Standard for Approval in Pediatrics)

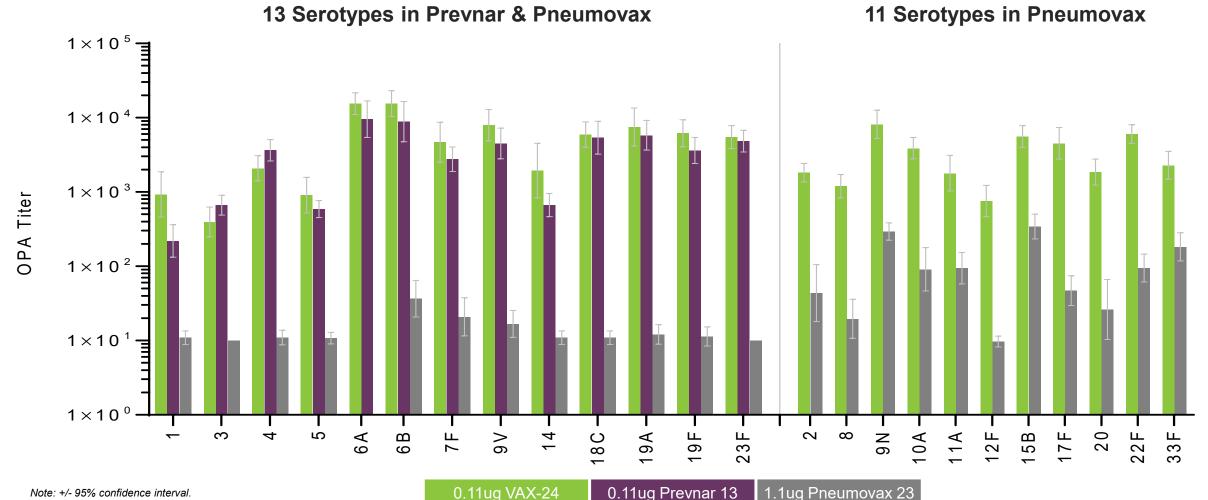
❖ Comparable or better immune responses for VAX-24 relative to Prevnar 13 and Pneumovax 23 across common strains.
 ❖ Potential for approval in pediatrics based on non-inferiority relative to standard of care (≥ 50% of IgG titers one month post-boost).



0.11ug VAX-24 0.11ug Prevnar 13 1.1ug Pneumovax 23

# VAX-24 Preclinical POC Study Supports Potential to Deliver Broader-Spectrum PCV Functional Antibody (OPA) Responses (Current Standard for Approval in Adults)

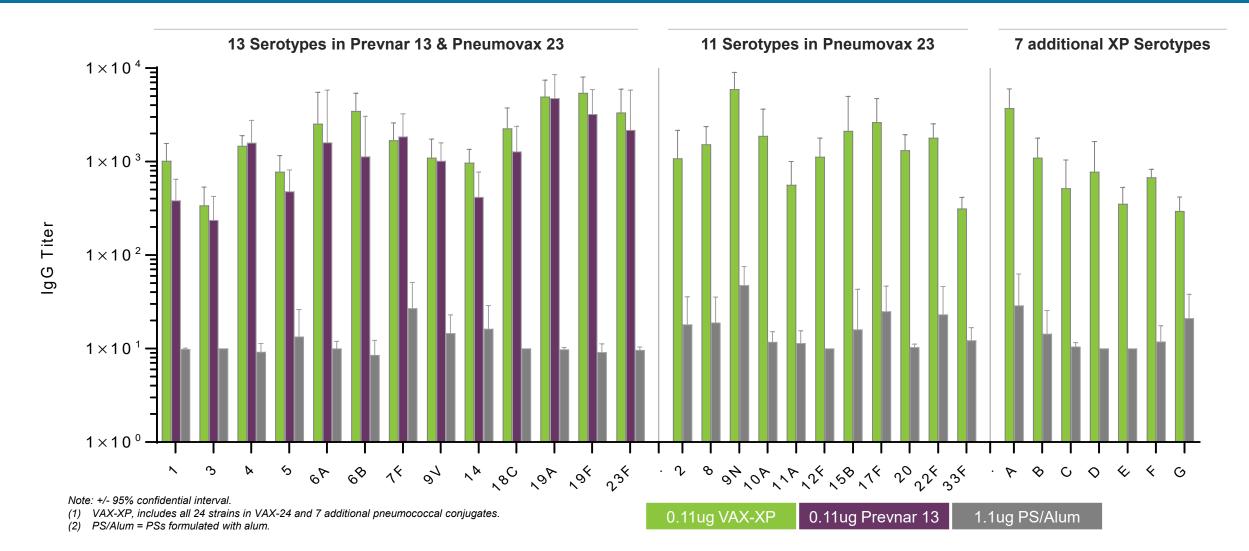
Comparable or better immune responses for VAX-24 relative to Prevnar 13 and Pneumovax 23 across all common strains. ◆ Potential for approval in adults based on non-inferiority relative to standard of care (≥ 50% of OPA titers one month postvaccination).



# VAX-XP: Further Evidence of Potential for Platform Scalability

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.



24



### PCV Franchise Leverages Established Regulatory Pathway

### Potential FDA Approval Path Supported by Current WHO Guidance & Precedent PCVs

Well-defined, validated surrogate immune endpoints = no anticipated requirement for field efficacy trials Demonstration of non-inferior ( $\geq$  50%)<sup>(1)</sup> immune responses vs. SOC consistent with Merck (V114) and Pfizer (PCV20) BLA filings<sup>(2)(3)</sup> Surrogate immune endpoints<sup>(4)(5)(6)</sup> have been consistent between Ph 2 POC and Ph 3 pivotal studies for adult and infant programs

Vaxcyte's Approach for VAX-24

Anticipate VAX-24 IND filing in Q1:22 with Phase 1/2 clinical topline data readout in late '22-early '23<sup>(7)</sup>

> Pre-IND FDA meeting completed (Dec 2019)

Ph 2 clinical POC study to include ~800 healthy adults aged 50-64

Potential for Fast Track, Priority Review and Breakthrough Designation

(1) 95% CI lower limit of the OPA GMT ratio  $\geq$ 0.5 for each serotype comparison.

Clinicaltrials.gov: Pfizer clinical studies for 20vPnC NCT03512288, NCT03550313, NCT03313050, NCT03313037, NCT03760146, NCT03835975, and NCT03828617

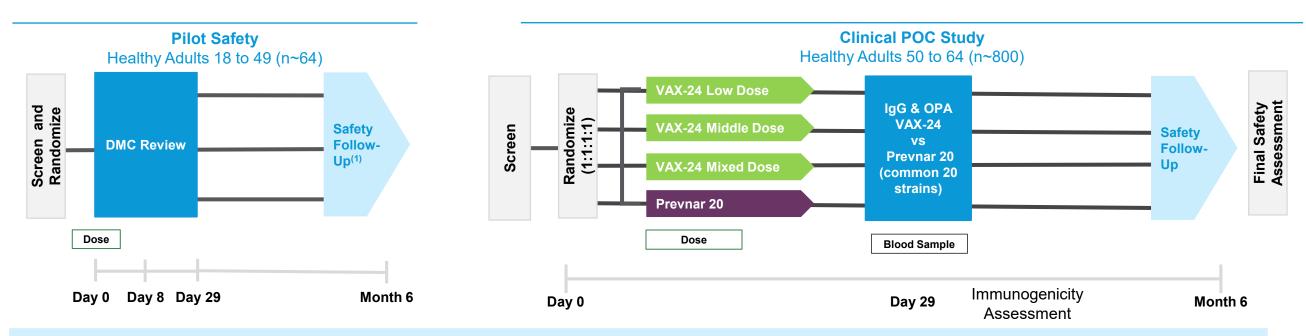
- (3) Clinicaltrials.gov: Merck clinical studies for V114 (PCV15) NCT02987972, NCT03620162, NCT03692871, NCT03731182, NCT03480763, NCT03615482, NCT03547167, NCT03480802, and NCT03565900.
- (4) WHO. Recommendations to assure the quality, safety and efficacy of pneumococcal conjugate vaccines, in WHO Expert 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. ttps://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, Accessed Feb 11, 2020.
   (7) Guidance provided as of November 10, 2021.

24 <sup>(7)</sup> Guidance pro

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

Designed to Demonstrate Non-Inferiority to SOC on Approvable Endpoint in Adults (OPA)

Study Design: Randomized, Observer-Blind, Dose-Finding, Controlled Study to Evaluate Safety & Immunogenicity of VAX-24 in Adults



#### **Key Objectives:**

- Evaluate safety & tolerability of single injection of VAX-24 in healthy adults 18 to 49 yrs (n~64)
- Comparative safety & tolerability of 3 different dose formulations of VAX-24 in healthy adults 50 to 64 yrs versus Prevnar 20

#### **Key Endpoints:**

- Immunogenicity (OPA & IgG)
  - VAX-24 vs Prevnar 20 common serotypes
  - VAX-24 incremental 4 serotypes not in Prevnar 20 GMT 4-fold rise
- 50 to 64 yr old cohort powered at >85% to detect OPA response of ≥50% across treatment groups & dose cohorts on a per serotype basis

### Critical Manufacturing Foundation Established for PCV Franchise Designed to Provide Robust & Scalable Capacity to Independently Supply Market



### Strategic Alignment with Best-in-Class CDMO

# Lonza 🗗

#### **Overview / Structure:**

- End-to-end "turnkey" supply established at marquee Swiss facility
- Fee-for-service relationship with risk sharing to align the parties

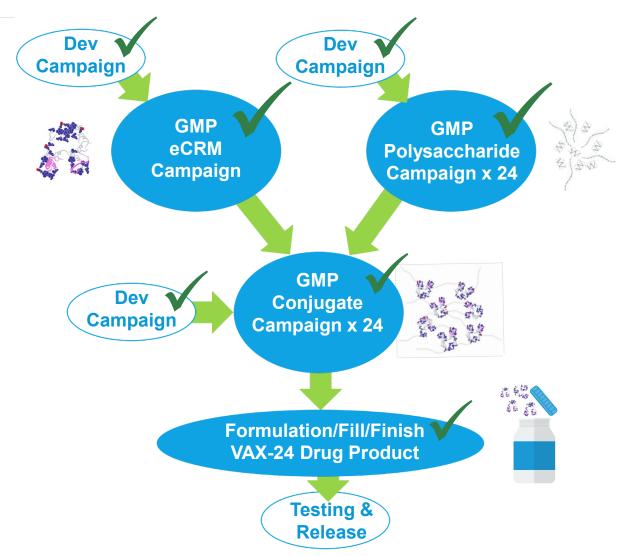
#### Status:

- Manufactured, tested and released GMP critical raw materials (eCRM<sup>®</sup> & 24 polysaccharides)
- Manufactured, tested and released the 24 GMP conjugated drug substances (DS)
- Completed GMP drug product (DP) manufacture (formulation, fill and finish)
- Anticipated completion of remaining DP testing and release, as well as documentation of stability, is expected prior to IND application filing and supply for VAX-24 Phase 1/2 clinical development
- Commercial production capacity available at same site using existing infrastructure or lbex capacity coming on-line

# Exclusive License to Cell-Free Protein Synthesis Platform

- Exclusive, worldwide, royalty-bearing, sub-licensable license for field of vaccines to treat or prevent infectious disease (4% royalty)
- Sutro Biopharma source of cell-free extract and custom reagents

VAX-24 Manufacturing Process / Status



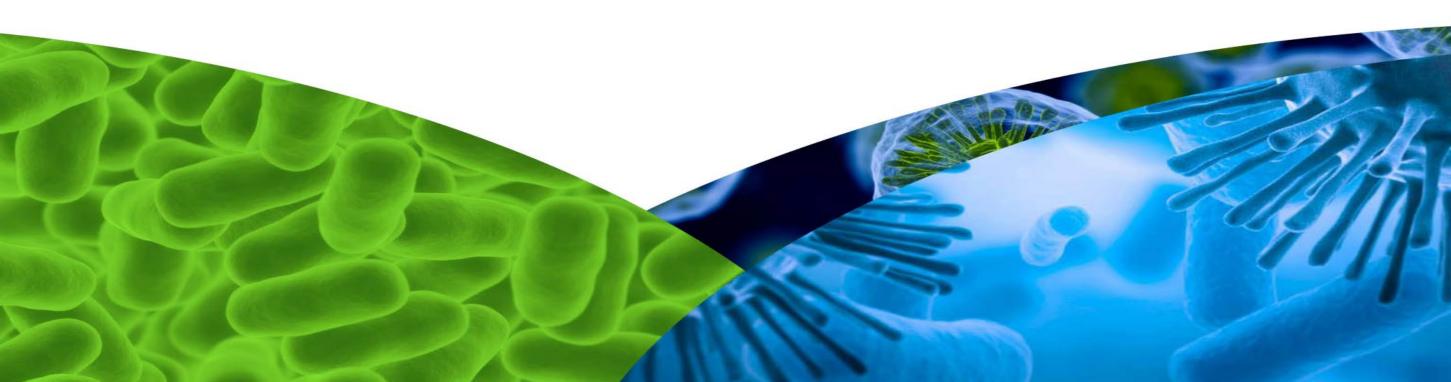


# The Pneumococcal Vaccine Landscape

Vaxcyte PCV Franchise Designed to Offer Broadest Spectrum of Coverage

<b>PCV</b> Approaches	DEVELOPER	VACCINE NAME	SPECTRUM OF COVERAGE	STATUS	TARGET POPULATION: INFANTS ADULTS	
	GSK	Synflorix	10-valent	APPROVED EX-US	$\checkmark$	
	Merck	VAXNEUVANCE	15-VALENT	<ul><li>FDA APPROVED IN ADULTS</li><li>PHASE 3 IN INFANTS</li></ul>	$\checkmark \checkmark$	
		MERCK V116	21-VALENT	PRECLINICAL	$\checkmark$	
		Merck V117	Unknown	PRECLINICAL	$\checkmark$	
	PFIZER	Prevnar 13	13-VALENT	SOC IN INFANTS AND ADULTS	$\checkmark$	
		PREVNAR 20	20-VALENT	<ul><li>FDA APPROVED IN ADULTS</li><li>PHASE 3 IN INFANTS</li></ul>	$\checkmark$	
	SK BIOSCIENCE / SANOFI-PASTEUR	твр	TBD	PH 1/2 IN ADULTS	$\checkmark \checkmark$	
	VAXCYTE	VAX-24 (SITE-SPECIFIC CONJUGATION)	24-valent	• IND-ENABLING	$\checkmark$	
		VAX-XP (SITE-SPECIFIC CONJUGATION)	30 PLUS- VALENT	PRECLINICAL POC	$\checkmark \checkmark$	
Non-PCV Approaches	Merck	PNEUMOVAX 23 (PS ONLY)	23-VALENT	<ul> <li>SOC IN ADULTS POST- PCV13</li> </ul>	$\checkmark$	
	AFFINIVAX / ASTELLAS	ASP3772 (AFFINITY-BOUND PSs TO NOVEL PNEUMO PROTEINS)	24-valent	PHASE 1/2 IN ADULTS	$\checkmark \checkmark$	





# VAX-A1: Group A Strep Conjugate Vaccine Program

Monovalent Conjugate Vaccine Designed to Provide Universal Protection

Unmet Need	<ul> <li>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</li> <li>Upgraded CDC threat given significant source of antibiotic Rxs driving resistance which has nearly tripled in past decade</li> <li>Responsible for post-infectious immune-mediated rheumatic heart disease leading to over 300K deaths in 2015</li> <li>Highly prevalent in children and rate of invasive disease in adults &gt; 65 has more than doubled (exceeding IPD rate in adults)</li> </ul>
VAX-A1: Broad-spectrum, Monovalent Conjugate Vx	<ul> <li>Designed to confer robust, boostable and durable protection against a broad spectrum of subtypes of Group A Strep</li> <li>Leverages site-specific conjugation to disease-specific carrier to expose mapped T- and B-cell epitopes</li> <li>Proprietary conserved antigen – Polyrhamnose – conjugated to an immunogenic disease-specific carrier along with two conserved virulence factors</li> </ul>
Program Status	<ul> <li>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 \$29.7M inclusive of grants to date</li> <li>Nominated final vaccine candidate in 1Q 2021</li> <li>Initiated IND-enabling activities in 2H 2021</li> </ul>
Key Data	Active immunization *** Mock Mock Mock Sblo + C5a pep SpyAD-GAC <sup>PR</sup> VAX-A1 (SLO + C5a pep + SpyAD-GAC <sup>PR</sup> )
CDC. Antibiotic Resistance Threats in the United BMGF = Bill & Melinda Gates Foundation.	a States, 2019. Atlanta, GA: US Department of Health and Human Services, CDC; 2019.

# VAX-PG: Periodontitis Vaccine Program

Therapeutic Vaccine Targeting Gingipains to Address Large, Underserved Market

Unmet Need	<ul> <li>Periodontal disease is a chronic oral inflammatory disease leading to destruction of soft &amp; hard tissues supporting the teeth</li> <li>Highly prevalent: 65 million US adults afflicted</li> <li>Significant morbidity and lost productivity: &gt;\$50B in lost productivity in 2010</li> <li>Associated with increased risk of heart attack, stroke, cardiovascular disease, and Alzheimer's Disease</li> </ul>				
VAX-PG: Multivalent Therapeutic Vaccine	• Preclinical model demonstrated protein-specific IgG response following immunization and protected mice from P. gingivalis- elicited oral bone loss				
Program Status	<ul> <li>Preclinical proof of concept published in Journal of Clinical Periodontology</li> <li>Next milestone: Nominate final vaccine candidate in 1H 2022<sup>(1)</sup></li> </ul>				
MOA & Key Data	<ul> <li>Restoration of balanced microbiota by interrupting underlying inflammatory condition</li> <li>Immunization with all formulations of VAX-PG provided significant protection against oral bone loss compared to the unvaccinated control (p&lt;0.01)</li> </ul>				

(1) Guidance provided as of November 10, 2021. Huang et.al. J Clin Periodontol. 2019 Feb;46(2):197-205

### Key Corporate Highlights Next-Generation Vaccine Company



Large Market Opportunity for Lead PCV Franchise

**Cell-Free Protein Synthesis Platform** 



**Disciplined Target Selection** 

**Robust Pipeline with Multiple Novel Vaccines** 

**Aligned Critical Resources**