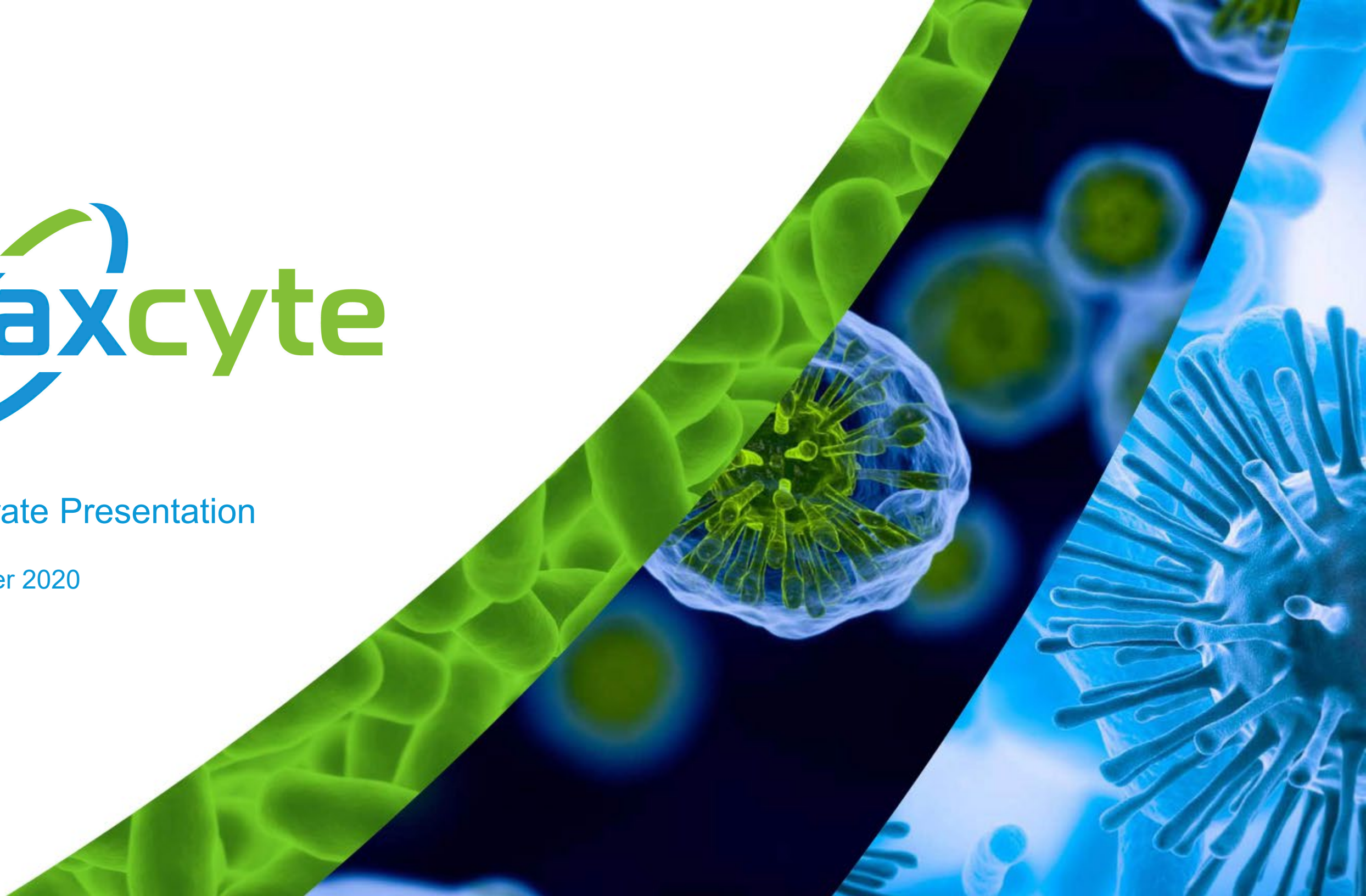




## Corporate Presentation

November 2020





# Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. These statements include but are not limited to, statements related to the process and timing of anticipated future development of Vaxcyte's vaccine candidates, including VAX-24, VAX-XP, VAX-A1 and 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 our ability to file an investigational new drug application for VAX-24 in the second half of 2021. 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, and the risks and uncertainties inherent with preclinical and clinical development processes; the success, cost and timing of all development activities and clinical trials; attainment of milestones, and sufficiency of cash and other funding to support Vaxcyte's development programs and other operating expenses. These and other risks are described more fully in Vaxcyte's filings with the Securities and Exchange Commission (SEC), including its Quarterly Report on Form 10-Q filed with the SEC on November 12, 2020 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.



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



# Key Corporate Highlights

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

<b>Large Market Opportunity for Lead PCV Franchise</b>	<ul style="list-style-type: none"><li>• Uniquely scalable PCV platform designed to deliver broadest spectrum vaccines in established &gt;\$7B category</li><li>• VAX-24 is a 24-valent PCV with preclinical POC demonstrating potential to replace SoC (Pneumovax 23<sup>®</sup> &amp; Prevnar 13<sup>®</sup>)</li><li>• Anticipate VAX-24 IND filing in 2H:21 and Phase 2 clinical POC data readout in 2022</li><li>• VAX-XP is a &gt;30-valent PCV with preclinical POC demonstrating potential to further expand spectrum, as necessary</li></ul>
<b>Cell-Free Protein Synthesis Platform</b>	<ul style="list-style-type: none"><li>• Site-specific conjugation enables development of more broad-spectrum and/or more immunogenic conjugate vaccines</li><li>• Permits production of “tough-to-make” antigens beyond reach of conventional technologies</li><li>• Demonstrated speed, flexibility, and scalability to facilitate discovery &amp; support rapid response initiatives</li></ul>
<b>Disciplined Target Selection</b>	<ul style="list-style-type: none"><li>• Honoring well-understood PCV mechanism of action to lower biological and development risk</li><li>• Leveraging established surrogate immune endpoints and clinical pathways</li><li>• Targeting well-defined commercial landscape with efficient market adoption dynamics</li></ul>
<b>Robust Pipeline</b>	<ul style="list-style-type: none"><li>• Platform underpins pipeline to unlock large market opportunities with significant unmet medical needs<ul style="list-style-type: none"><li>- VAX-A1: Novel Group A Strep conjugate vaccine</li><li>- VAX-PG: Novel periodontitis therapeutic vaccine</li></ul></li></ul>
<b>Aligned Critical Resources</b>	<ul style="list-style-type: none"><li>• Strategic alignment with Lonza to ensure robust, scalable manufacturing</li><li>• Seasoned management team, directors and advisors with significant vaccine experience</li><li>• IPO completed in June 2020</li><li>• Cash and cash equivalents of \$397M at September 30, 2020</li></ul>





# Experienced Team, Board of Directors, and Scientific Advisors

## Outstanding Track Record in Vaccines and Biopharma

### Management Team

**Grant Pickering, MBA**  
CEO & Founder

**PROVENGE**  
(sipuleucel-T)



**Victrio**



**Jim Wassil, MS, MBA**  
COO



**BEXSERO**  
Meningococcal Group B Vaccine



**Andrew Guggenhime, MBA**  
CFO & CBO



### Board of Directors

**Moncef Slaoui, PhD**  
Chairman



**Peter Hirth, PhD**



**William Newell**



**Halley Gilbert**



**Robert Hopfner, PhD**



**Grant Pickering**



**Patrick Heron**



**Heath Lukatch, PhD**  
(Red Tree Venture Capital)



**Kurt von Emster**



**Rom Colindres, MD, MPH, MBA**  
CMO



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



**Paul Sauer, MBA**  
SVP PD Manufacturing



### Scientific Advisory Board

**Jeff Almond, PhD**



**Trevor Hallam, PhD**



**Tony Ford-Hutchinson, PhD**



**Tom Monath, MD**



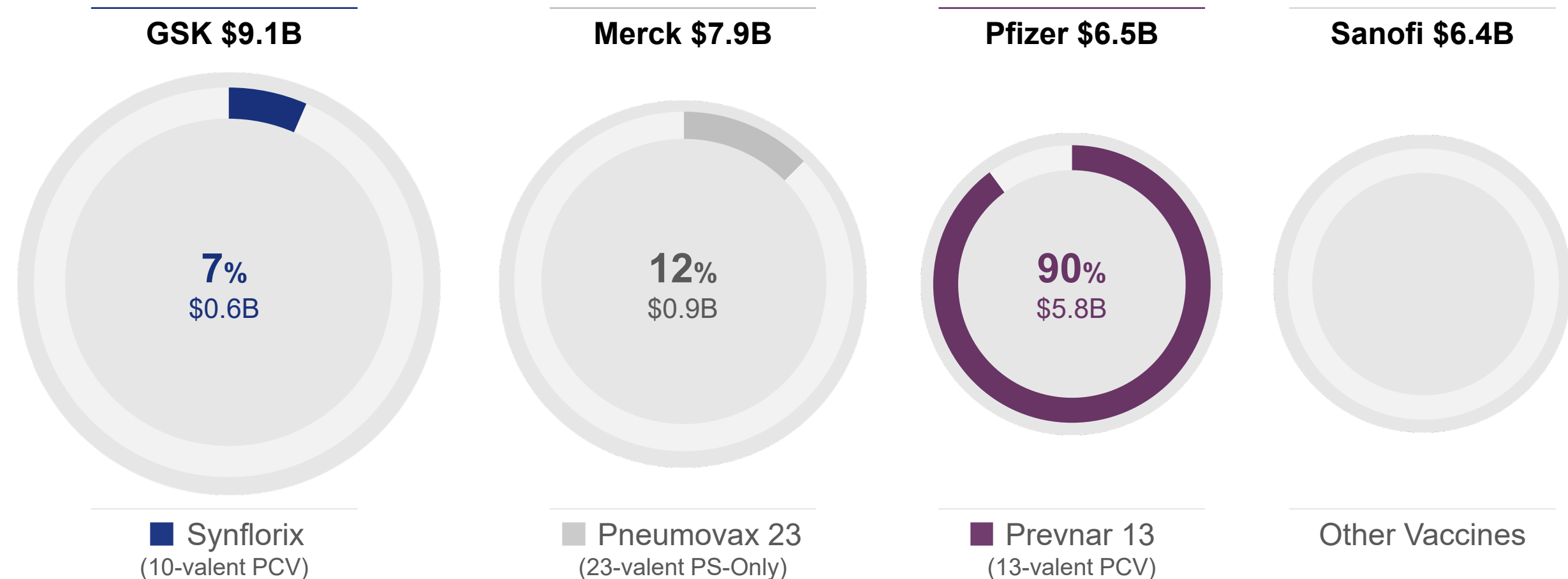


# The Vaxcyte Opportunity

*Develop Broad-Spectrum, Potentially Category Leading PCV Franchise in >\$7B Market Segment*

**Global Vaccine Sales of ~\$36B and Projected to Grow to ~\$58B by 2025 <sup>(1)</sup>**

**>\$7B Pneumococcal Vaccine Segment – led by Prevnar 13 – Industry's Largest Selling Vaccine <sup>(2)</sup>**



<sup>(1)</sup> Companies' Filings and Industry Research (BIS Research 2018: Global Vaccine Market).

<sup>(2)</sup> 2019 Earnings releases. Sanofi revenues based on average 2019 EUR/USD exchange rate of 1.12. GSK revenues based on average 2019 GBP/USD exchange rate of 1.277.

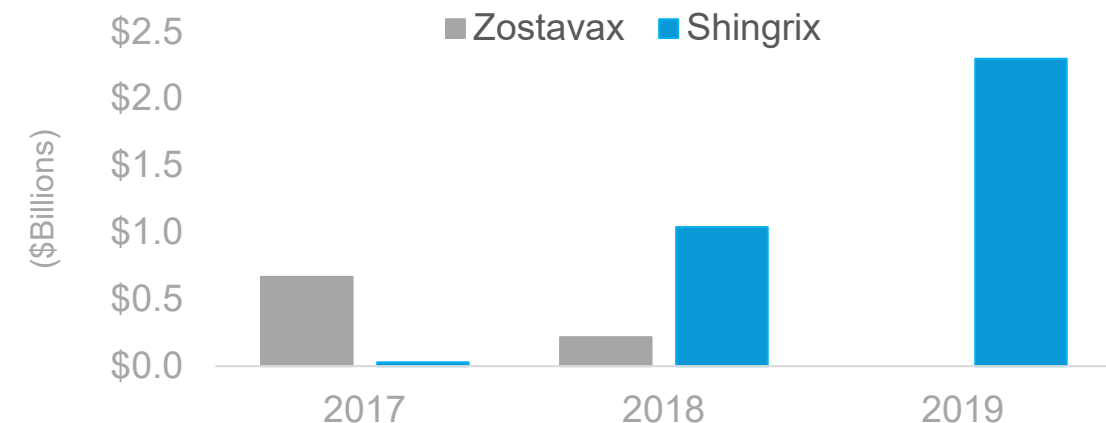


# Pneumococcal Vaccine Market is Highly Attractive

## *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® vs Zostavax®



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

# Cell-Free Protein Synthesis Platform Unlocks Multiple Vaccine Applications

## *Design and Produce Proteins Beyond Reach of Conventional Methods*



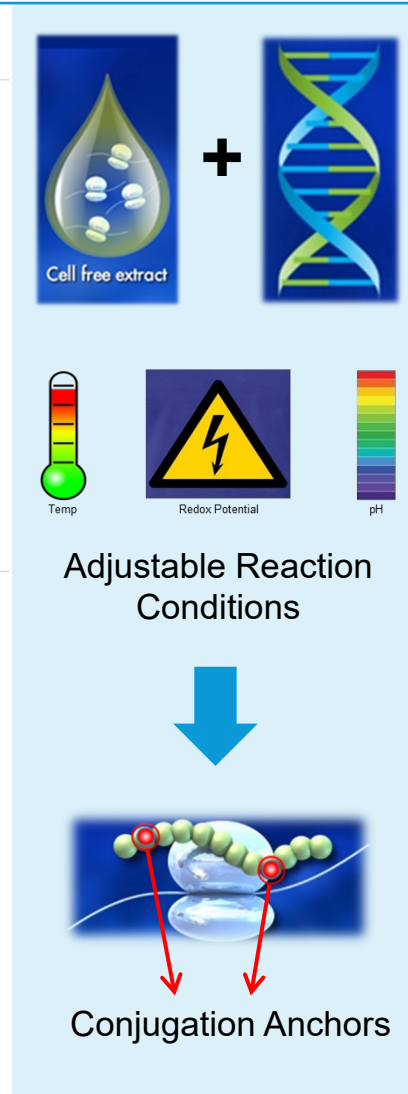
### XpressCF Platform<sup>(1)</sup>

#### 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 non-physiological conditions

#### Speed, Flexibility, Scalability:

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



### 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







(1) Exclusively licensed from Sutro Biopharma for the field of vaccines addressing infectious diseases.





# Next-Generation Vaccine Pipeline

## Targeting 2H:21 IND Filing for Lead VAX-24 Program

Program	Profile / Type	Vaccine Description	Target Population	Disease	Status	Next Anticipated Milestone
VAX-24	Superior Conjugate Vaccine	24-valent PCV		Invasive Pneumococcal Disease (IPD)	Preclinical POC vs Prevnar 13 and Pneumovax 23 (IND-enabling stage)	IND in 2H:21 Phase 1/2 Topline Data in 2022
				IPD and Otitis Media	Preclinical POC vs Prevnar 13 (IND-enabling stage)	Phase 1 Initiation (post-Clinical POC in adults)
VAX-XP	Superior Conjugate Vaccine	Next-generation >30-valent PCV		IPD	Preclinical POC vs Prevnar 13 and PS/Alum <sup>(1)</sup>	CMC Optimization
				IPD and Otitis Media	Preclinical POC vs Prevnar 13	
VAX-A1	Novel Conjugate Vaccine	Monovalent conjugate / complex protein-based vaccine		Group A Strep Infections	Preclinical POC & Grant Funded	Final Vaccine Nomination
VAX-PG	Novel Protein Vaccine	Tough-to-make protein-based therapeutic vaccine		Periodontitis	Preclinical POC	Final Vaccine Nomination



Adults



Children

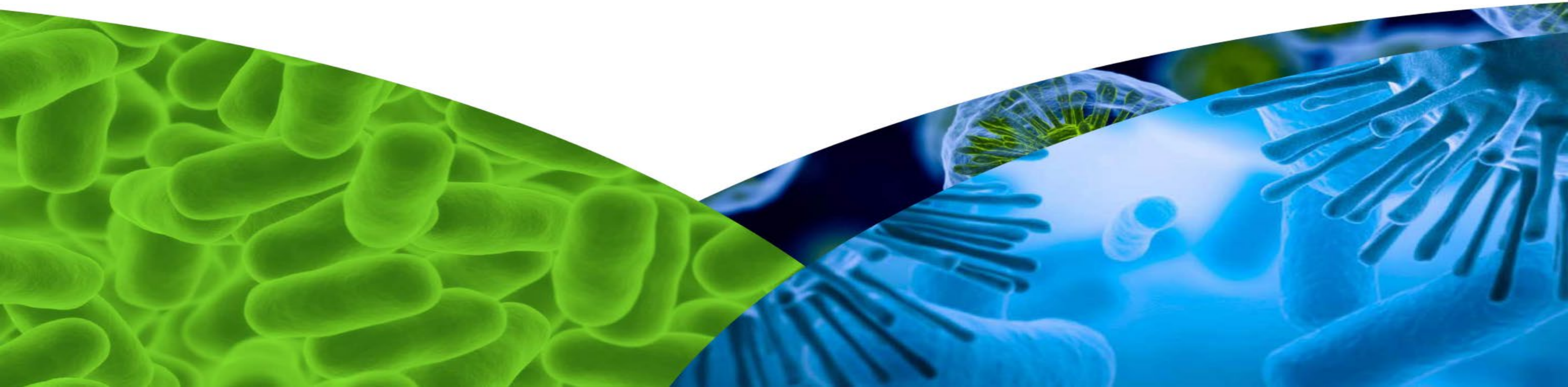


Infants

(1) For the Polysaccharide/Alum comparator, we used 23 polysaccharides in Pneumovax 23 and 9 additional polysaccharides with alum for comparison.



PCV Opportunity





# Largest Vaccine Market Segment, but Significant Unmet Needs Remain

## *Pneumococcal Vaccine Market Currently Dominated by Prevnar 13 Despite Coverage Limitations*

- Most disease caused by strains above and beyond Prevnar 13, demonstrating need for a broader-spectrum PCV
- ~900K pneumococcal pneumonia cases in the US per year
  - World's leading cause of death among children under five years
  - Caused by Strep pneumoniae: 90+ strains (1/3<sup>rd</sup> pathogenic)
- Current ACIP Recommendation:
  - Infants: Prevnar 13
  - Adults: Prevnar 13 & Pneumovax 23



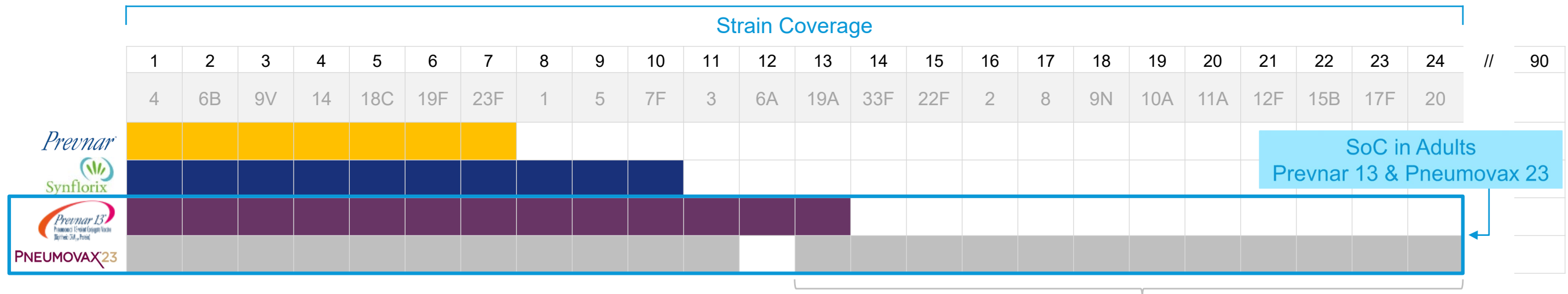
- 13v PCV from Pfizer
- Highly efficacious, but limited coverage



- 10v PCV from GSK
- Highly efficacious, but inferior coverage



- Polysaccharide-only vaccine from Merck
- Poor immunogenicity and not boostable

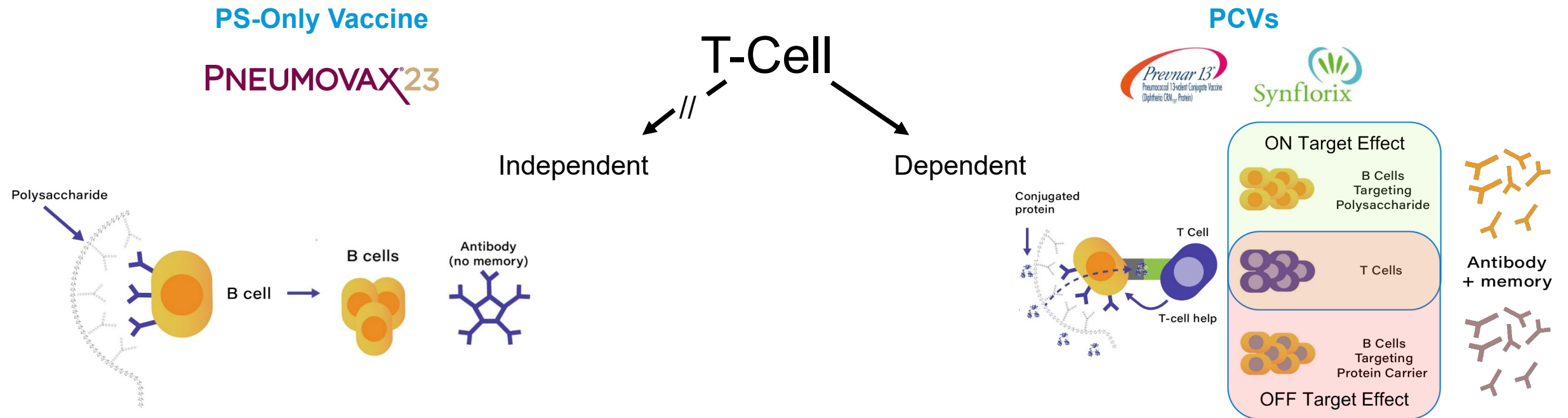


Incremental 11 strains cause majority of residual disease in US & EU, resulting in continued need for older, PS-only vaccine (Pneumovax 23)



# 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

## 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 13 is a modified form of diphtheria toxin (CRM<sub>197</sub>).



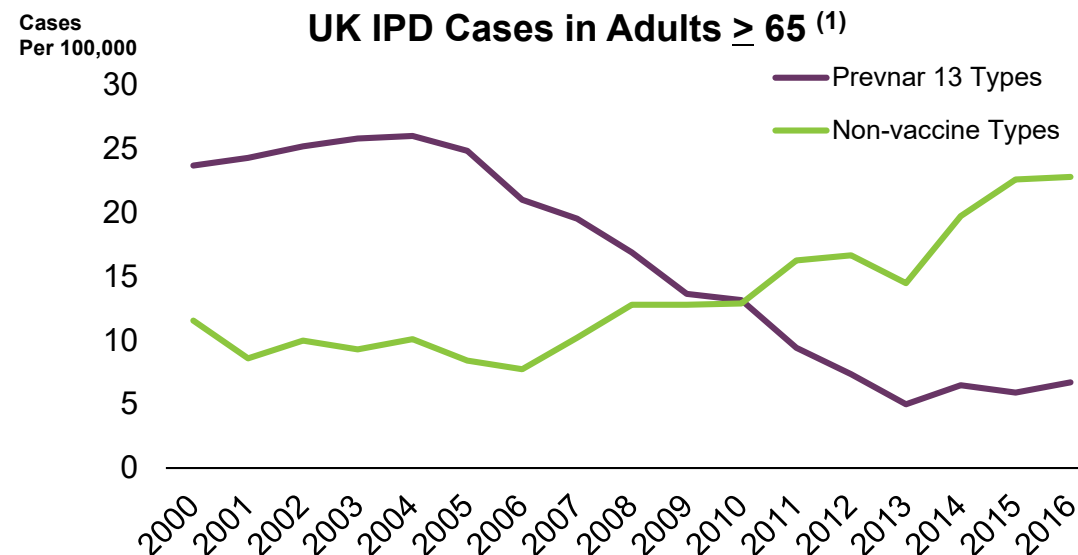
# Limitations of Current Pneumococcal Conjugate Vaccines (PCVs)

## *Coverage Expansion Necessary to Address Circulating Pneumococcal Disease*

1

### Serotype Replacement

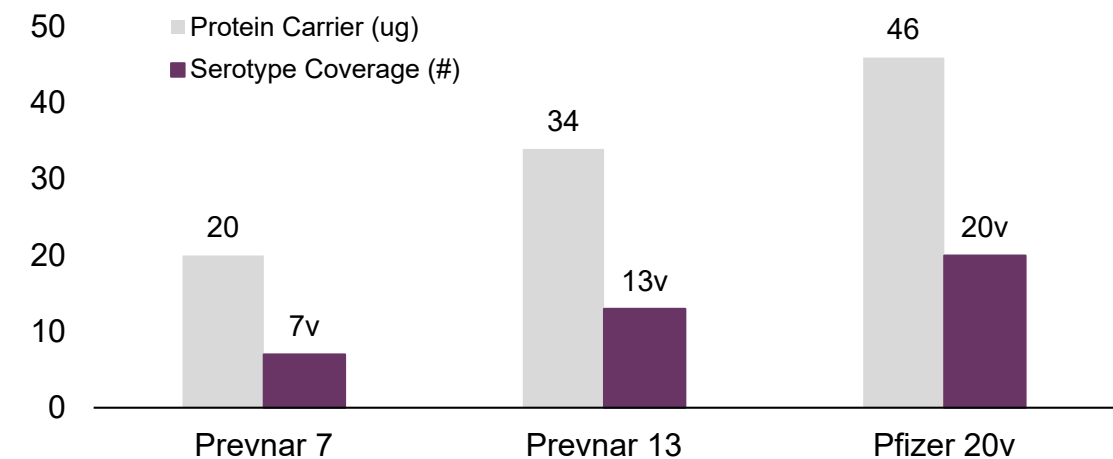
- Phenomenon whereby non-PCV strains increase in disease prevalence after widespread PCV use
  - Prevnar 13 highly effective in prevention of Invasive Pneumococcal Disease (IPD) for included strains
  - Most residual disease caused by incremental 11 strains over and above Prevnar 13



2

### Limitations of Conventional Chemistry

- Random conjugation
- Higher ratio of protein carrier to polysaccharide
- Further exacerbates carrier suppression



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

(2) Pfizer Patent Application: US 2015/0202309 A1 published Jul. 23, 2015.





# Limitations of Current Pneumococcal Conjugate Vaccines (PCVs)

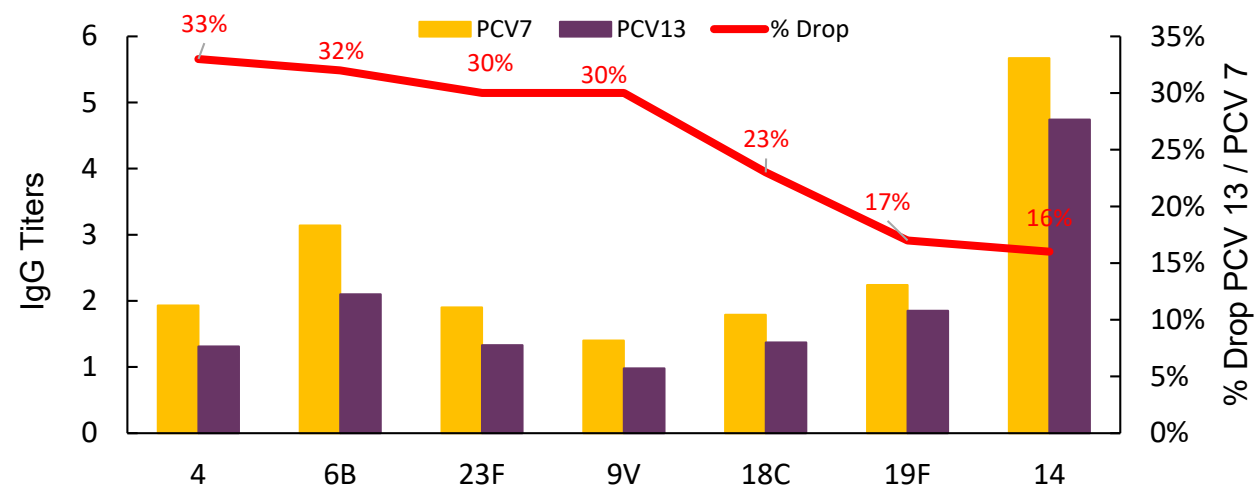
## Coverage Expansion Using Conventional Chemistry Has Led to Carrier-Induced Immune Suppression

3

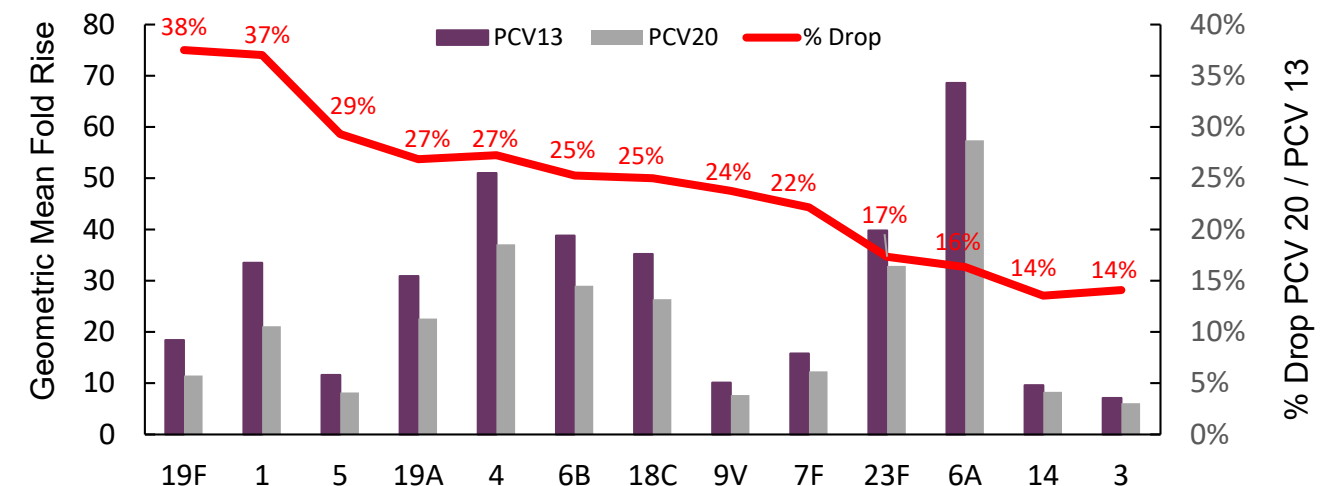
### Carrier Suppression

- Reduced immune response to the target PSs 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

Infant Immune Responses (IgG): Prevnar 7 vs Prevnar 13 <sup>(1)</sup>



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

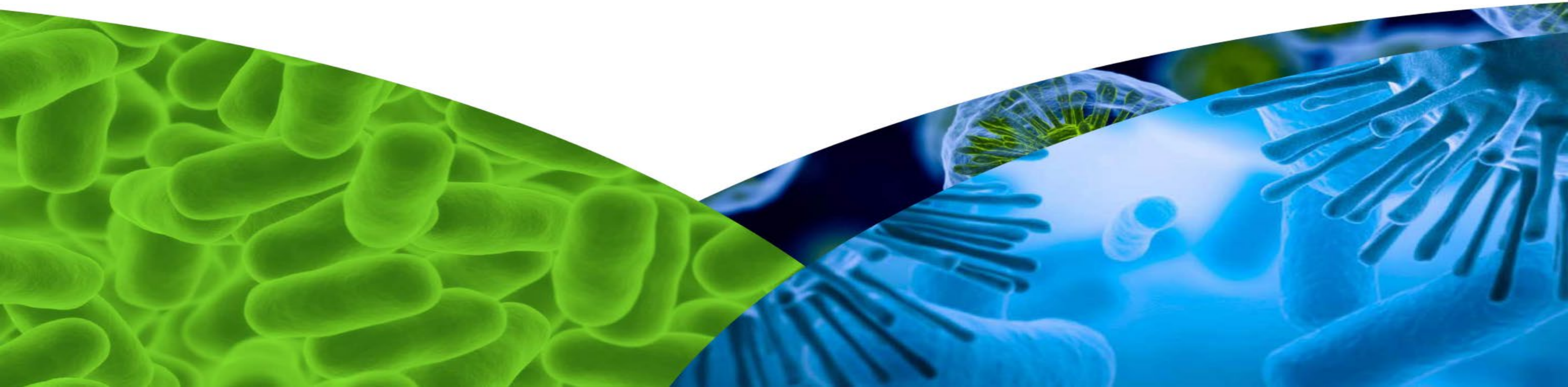


(1) Yeh et al, *Pediatrics*. 126: e493 (2010).

(2) Hurley et al, *Safety, tolerability, & immunogenicity of PCV20 (PF-06482077) in adults 60-64 years of age*, presented at 29<sup>th</sup> European Congress of Clinical Microbiology & Infectious Disease, April 13-16, 2019, Amsterdam.



PCV Franchise Led by VAX-24

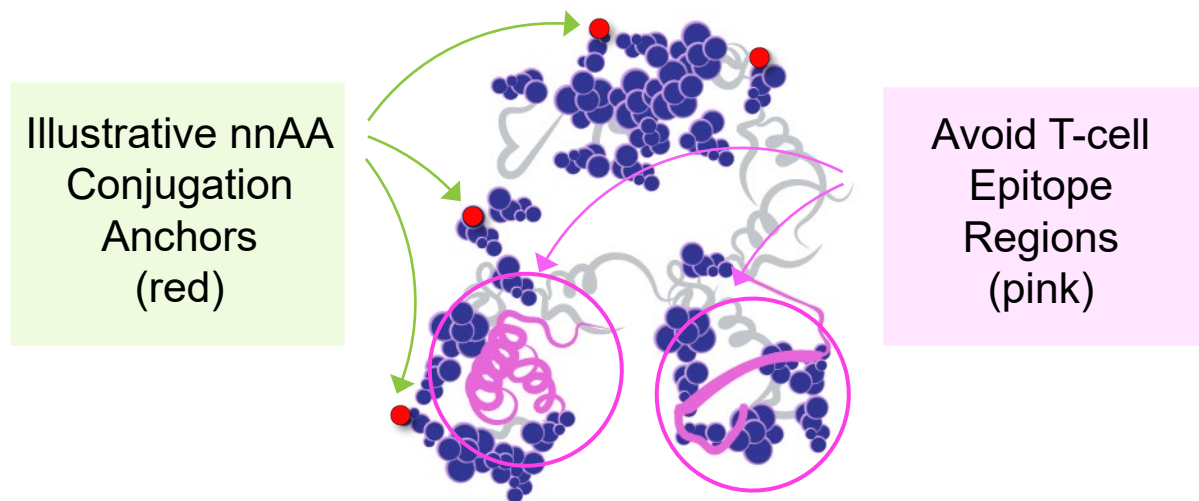




# VAX-24 Employs Carrier-Sparing Conjugates

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

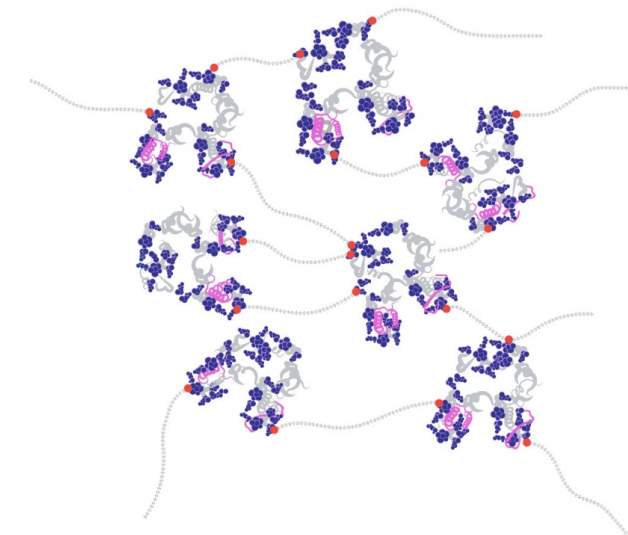
## Precise, Site-Specific Conjugation Sites on Proprietary eCRM Protein Carrier



### 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*

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

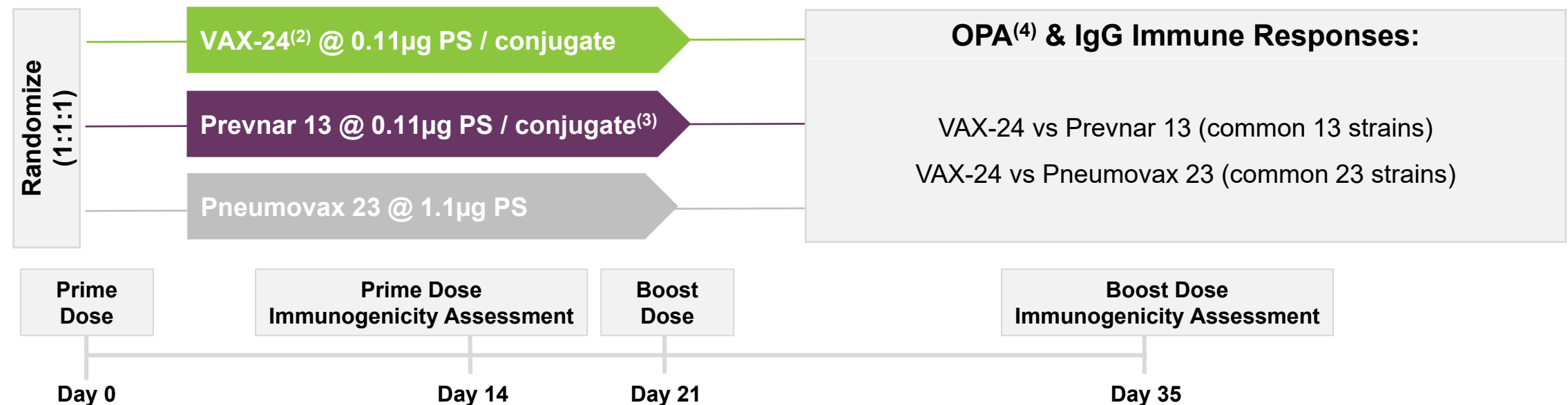


# VAX-24 Preclinical POC Study

*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



### Key Objectives:

Demonstrate conjugate-like responses vs SoC on all 24 serotypes

- OPA Responses: Primary surrogate endpoint for full approval in adults
- IgG Responses: Co-Primary surrogate endpoint for full approval in infants

### Key Endpoints:

Immunogenicity (OPA & IgG)

- VAX-24 vs Prevnar 13 common serotypes (Day 35)
- VAX-24 vs Pneumovax 23 for 11 incremental serotypes (Day 35)

(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.

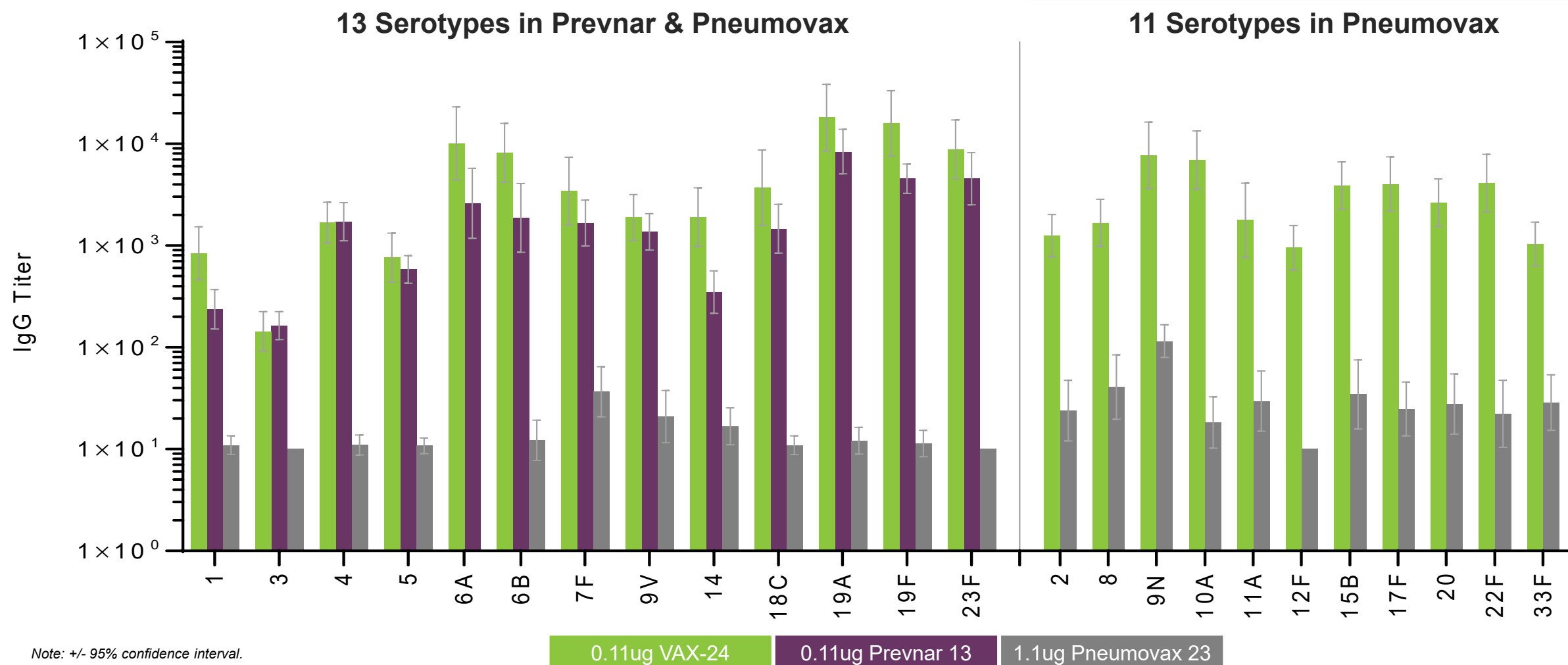




# VAX-24 Preclinical POC Study: IgG Antibody Titers

*VAX-24 > Pneumovax 23 and VAX-24 ≥ Prevnar 13*

- 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 ( $\geq 50\%$  of IgG titers one month post-boost)

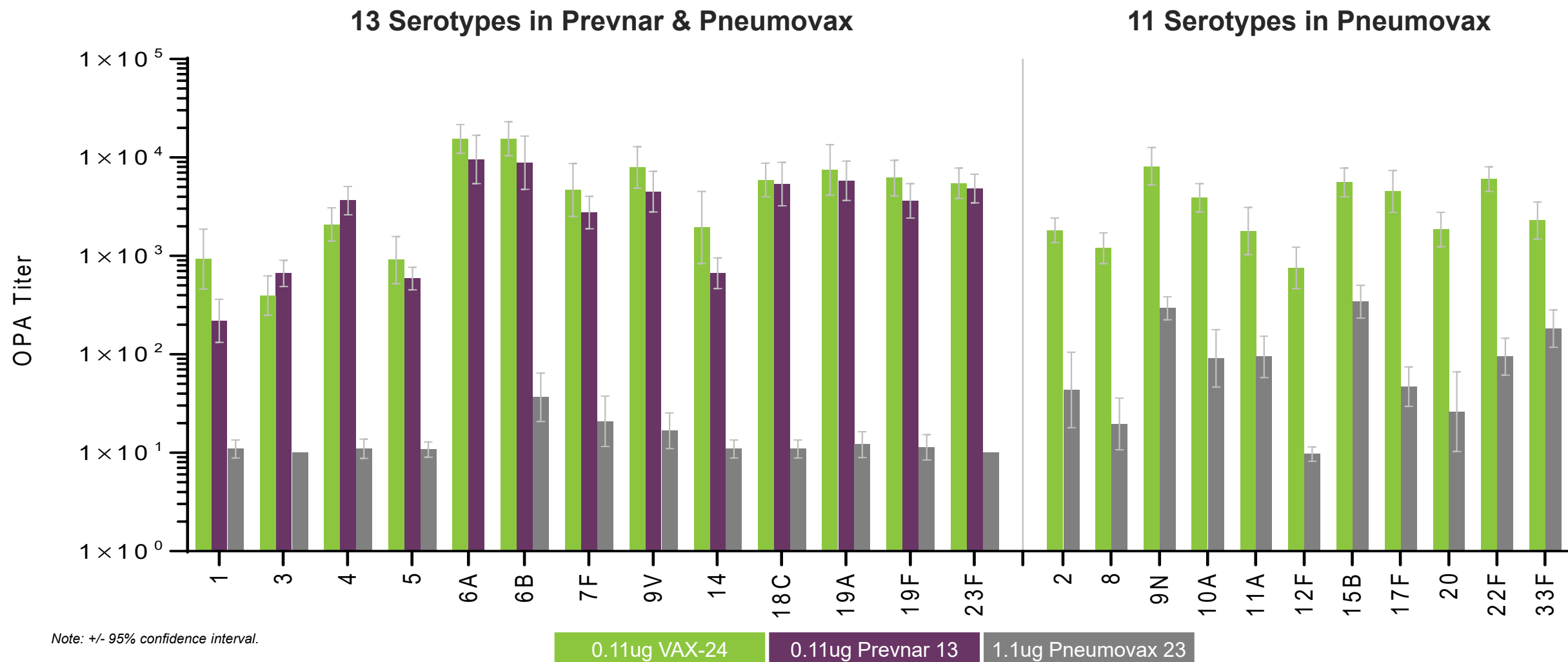




# VAX-24 Preclinical POC Study: Functional Antibody (OPA) Responses

*VAX-24 > Pneumovax 23 and VAX-24 ≥ Prevnar 13*

- 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 ( $\geq 50\%$  of OPA titers one month post-vaccination)

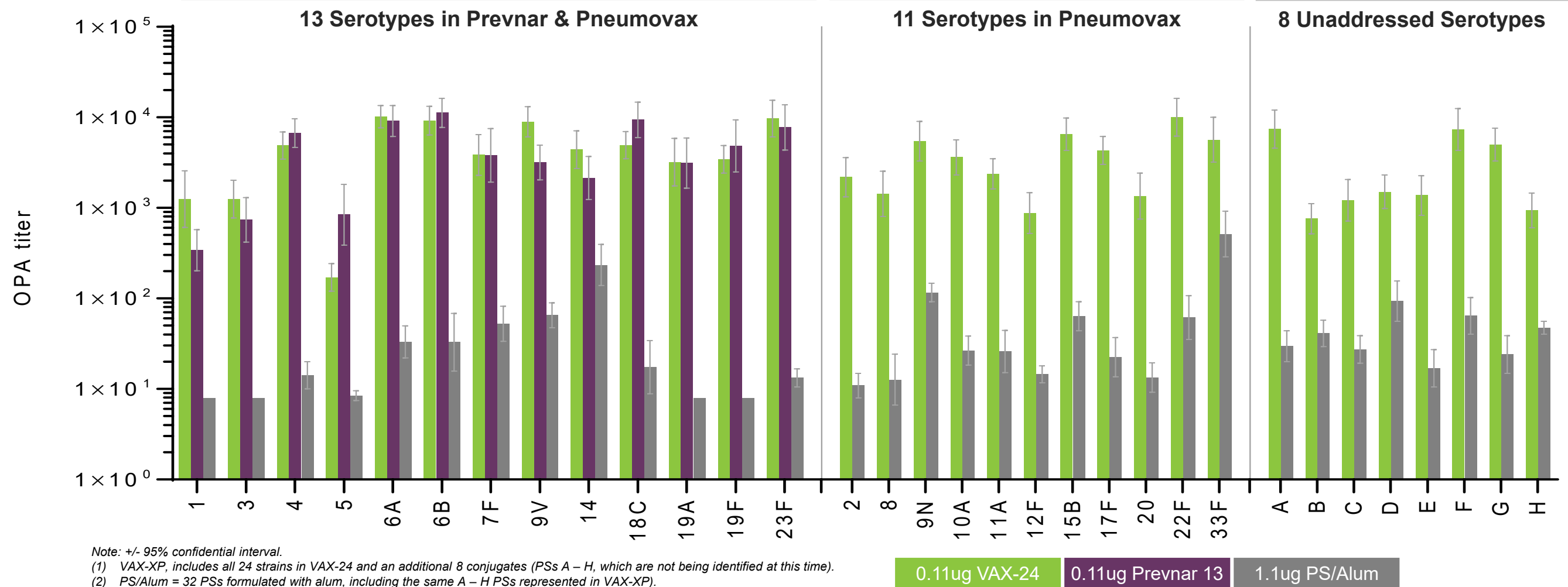




# VAX-XP Preclinical POC – Demonstrates Potential for Platform Scalability

*Functional Ab (OPA) Responses: Conjugate-Like Immune Responses in Rabbits for All Serotypes*


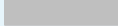
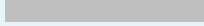






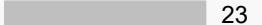

- PCV standard of care drives serotype replacement and continuing need for broader spectrum PCVs over time
- VAX-XP incorporates emerging serotypes responsible for significant IPD & antibiotic resistance





# Pneumococcal Vaccine Competitive Landscape

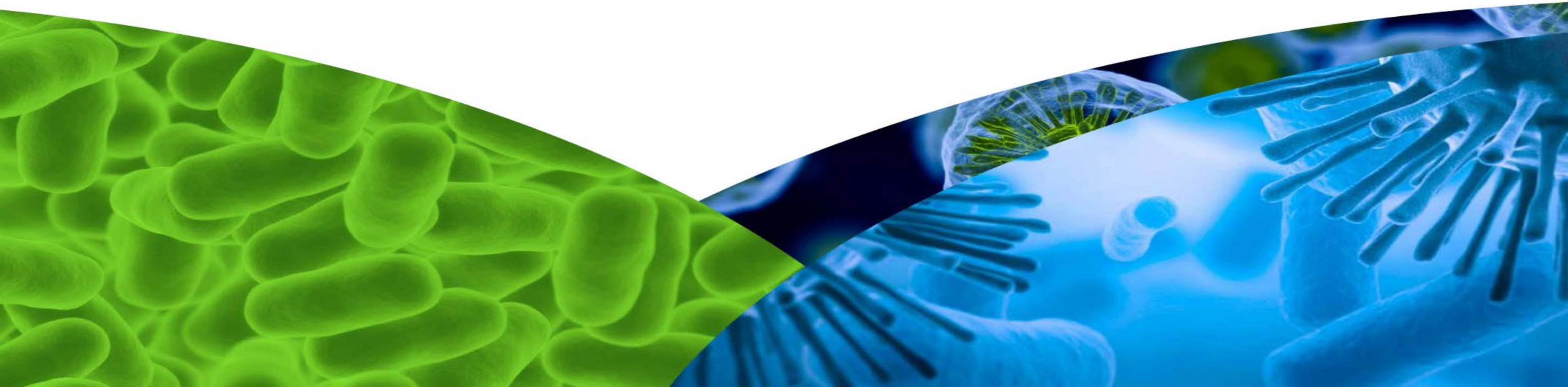
*VAX-24 & VAX-XP: Employing Carrier-Sparing Technology Designed to Enable Coverage Expansion*

	Key Attributes for Pneumococcal Vaccines									
	Sponsor / Program	Status	Spectrum of Coverage	Technology	Target Population		Prime + Boost	Safety	Carrier Sparing	Anti-Linker Antibodies
					Adults	Infants				
Marketed Vaccines	Synflorix	Not Competitive in US/EU	 10	PCV		✓	✓	✓	N	N
	Prevnar 13	SoC in Adults & Infants	 13	PCV	✓	✓	✓	✓	N	N
	Pneumovax 23	SoC in Adults post-Prevnar 13	 23	PS-Only	✓		N	✓	n/a	n/a
PCV Development Pipeline	Merck V114	Ph 3 in Adults & Infants	 15	PCV	✓	✓	✓		N	N
	Pfizer 20v	Ph 3 in Adults Ph 3 in Infants	 20	PCV	✓	✓	✓		N	N
	SK Bioscience / Sanofi-Pasteur	Ph 1/2 in Adults	Unknown	PCV	✓	✓	✓		N	N
	VAX-24	IND-Enabling	 24	PCV (site-specific conjugation)	✓	✓	✓		Y	N
	VAX-XP	Preclinical POC	 30+	PCV (site-specific conjugation)	✓	✓	✓		Y	N
Non-PCV Approaches	Affinivax / Astellas - ASP3772	Ph 1/2 in Adults	 24	Affinity-Bound PSs to Novel Pneumo Proteins	✓	✓			N	Y
	Glycovaxyn / GSK	Terminated Post-Ph 1 in 2018	 1	Bioconjugated PSs to Novel Pneumo Proteins	✓				N	
	Genoceia	Terminated Post-(+) Ph 1 in 2014	Universal	Novel Pneumo Proteins	✓				n/a	n/a
	Immbio / CNBG - PnuBioVax	Ph 1 In 2017	Universal	Novel Pneumo Proteins	✓				n/a	n/a
	Matrivax	Terminated (preclinical)	 23	Entrapped PSs by Cross-linked Proteins					N	
	Liquidia / PATH	Terminated (preclinical)	 13	Nano-particulate PS:PC Conjugates					N	

SoC = standard of care; PS = polysaccharides, PC = protein carrier



## VAX-24 – Development Plan







# VAX-24 Regulatory Strategy Leverages Established Licensure Precedent

## *Consistent Endpoints Across Phases 2 & 3 Could Deliver Key Readout Upon Phase 1/2 Data Receipt*

- Current WHO guidance and precedent PCVs support potential FDA regulatory approval based on:
  - Well-defined and validated surrogate immune endpoints without the requirement for field efficacy trials
  - Demonstration of non-inferior ( $\geq 50\%$ )<sup>(1)</sup> immune responses vs standard of care (SoC) consistent with Merck (V114) and Pfizer (PCV20) late-stage clinical programs<sup>(2)(3)</sup>
- Surrogate immune endpoints<sup>(4)(5)(6)</sup> consistent between Ph 2 POC and Ph 3 pivotal studies for adult and infant programs
  - **Adults:** Non-inferior functional opsonophagocytic antibody (OPA) responses vs Prevnar 13 and Pneumovax 23<sup>(1)</sup>
  - **Infants:** Co-primary immunogenicity endpoints based on non-inferiority of anti-pneumococcal IgG antibody concentrations<sup>(7)</sup>
- Merck (V114) and Pfizer (PCV20) late-stage clinical programs based on immunological non-inferiority comparisons<sup>(2)(3)</sup>
- CMC, non-clinical and Phase 1/2 clinical plan discussed at December 2019 pre-IND FDA meeting
- Potential for Fast Track, Priority Review and Breakthrough Designation consistently granted for broader spectrum PCVs
- Anticipate VAX-24 IND filing in 2H:21 and Phase 2 clinical POC data readout in 2022

**Target Indication:** Active immunization for the prevention of invasive disease, pneumonia, and otitis media<sup>(8)</sup> caused by the 24 pneumococcal serotypes included in VAX-24

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

(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) Prevnar 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.

(7) Non-inferior seroconversion rates, based on IgG titers  $\geq 0.35\mu\text{g/ml}$  responses after the primary vaccination series; Non-inferior IgG responses vs Prevnar 13 (95% CI lower limit of the IgG GMT ratio  $\geq 0.5$  for each serotype comparison).

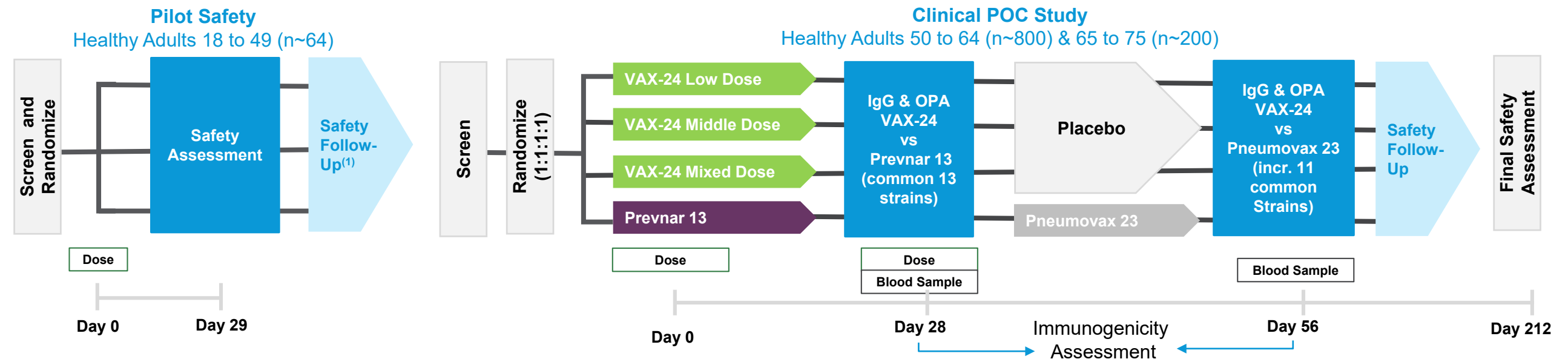
(8) Indication to be sought for the prevention of otitis media caused by *S. pneumoniae* serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F. No otitis media data are available for incremental 17 serotypes.



# 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 single injection of VAX-24 (3 doses) in healthy adults 50 to 75 yrs vs Pevnar 13 & Pneumovax 23

## Key Endpoints:

- Immunogenicity (OPA & IgG)
  - VAX-24 vs Pevnar 13 common serotypes (Week 4 vs 4)
  - VAX-24 vs Pneumovax 23 for 11 incremental serotypes (Week 4 vs 8)
- 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
- Older cohort enrolled in parallel to extrapolate immune responses in adults 65+ yrs

(1) Pilot Safety Follow-up will continue thru Day 212 in parallel upon initiation of Clinical POC Study after Day 29 safety observation.

# 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:

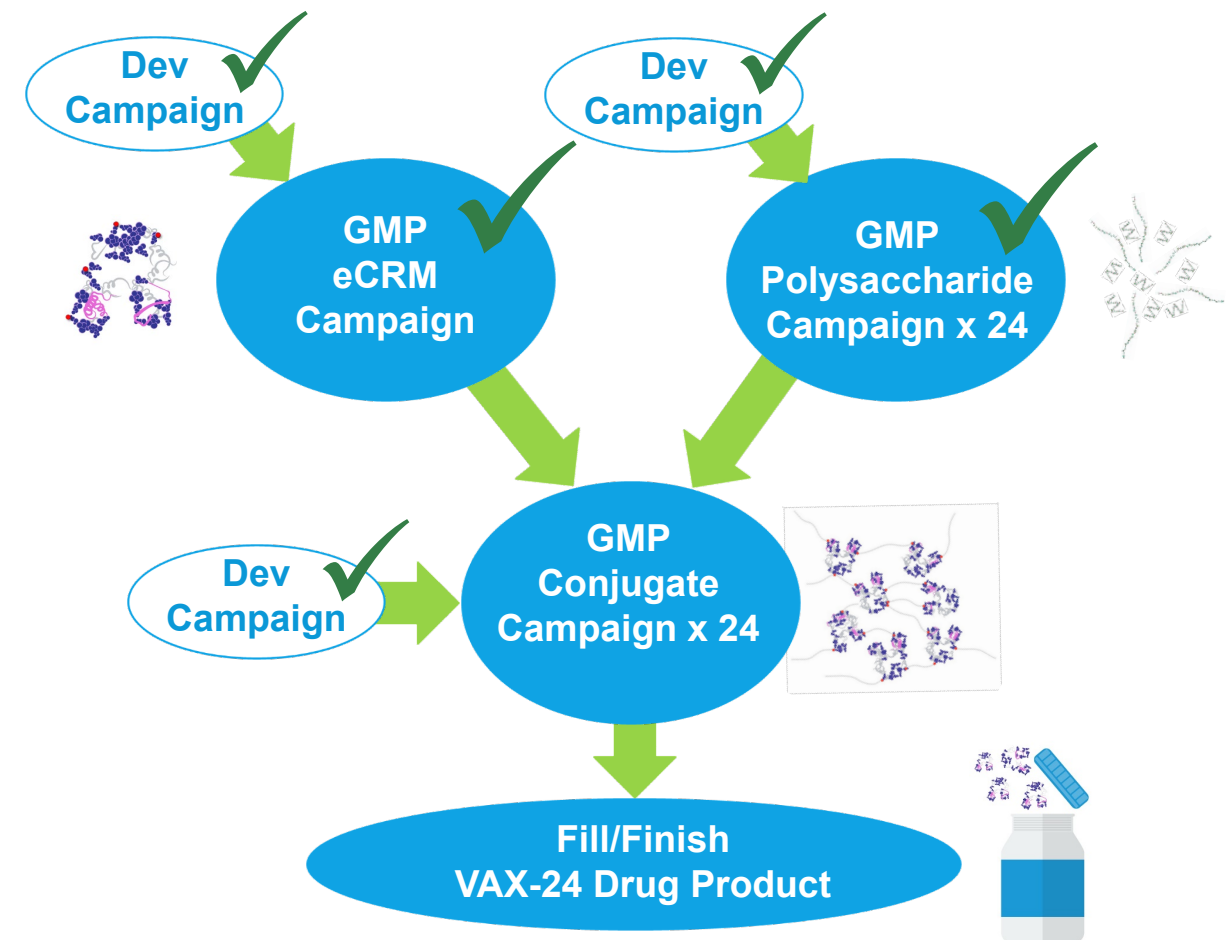
- GMP critical raw materials produced (eCRM & 24 polysaccharides)
- Entering final GMP production phase to facilitate IND and Phase 1/2 clinical supply for VAX-24
- Commercial production capacity available at same site using existing infrastructure or Ibex capacity coming on-line

## Exclusive License to Cell-Free Protein Synthesis Platform

**SUTRO**  
BIOPHARMA

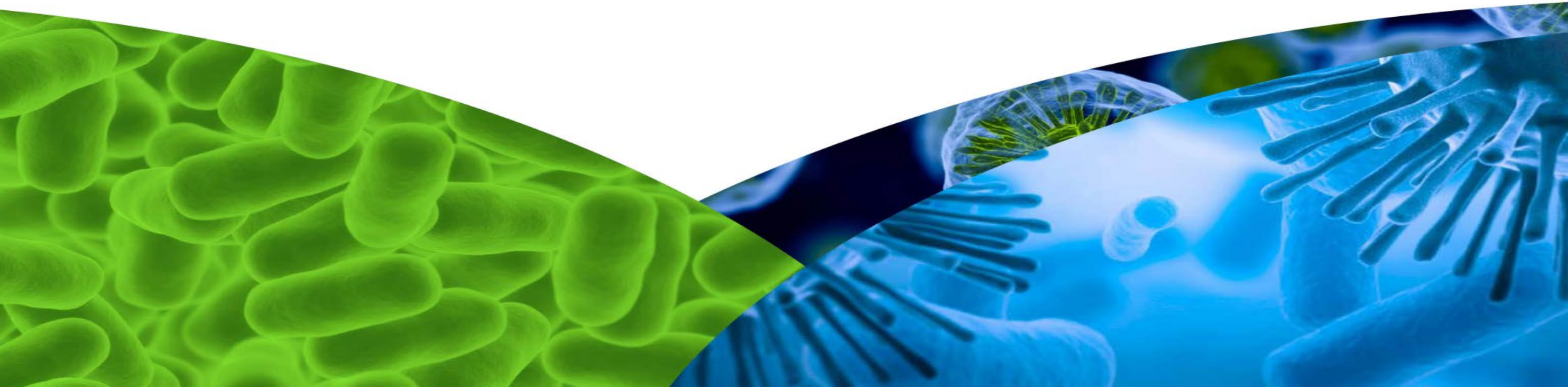
- Exclusive, worldwide, royalty-bearing, sub-licensable license for field of vaccines to treat or prevent infectious disease (4% royalty)
- Sutro Biopharma source of cell-free extract and custom reagents

## VAX-24 Manufacturing Process / Status





## Non-PCV Pipeline





# VAX-A1: Group A Strep Conjugate Vaccine Program

## *Monovalent 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 threat by CDC given antibiotic resistance having tripled over past decade
- Responsible for post-infectious immune-mediated rheumatic heart disease leading to over 300K deaths in 2015
- Highly prevalent in school-age children and a significant source of pediatric antibiotic Rx's driving resistance

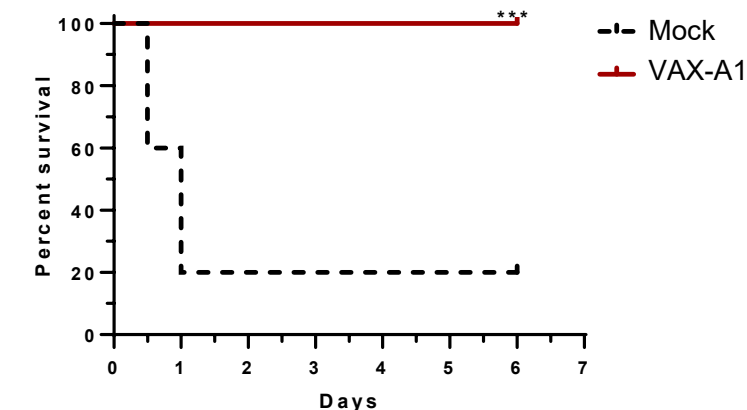
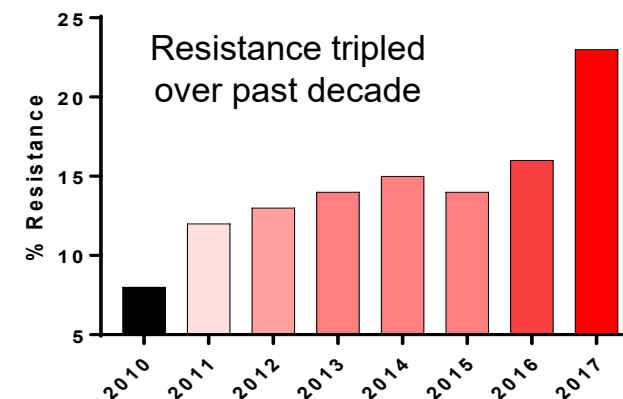
### VAX-A1: Broad-spectrum, Monovalent Conjugate Vx

- Designed to confer broad protection against 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

### Program Status

- Partially funded by grant from CARB-X (consortium of BMGF, Wellcome Trust, US Biodefense Agency (BARDA)); 90% funding for initial period and up to \$15.1M+ in total over ~4 years (through Phase 1 trial)
- Next milestone: Final vaccine composition in 2021

### Key Data







# 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

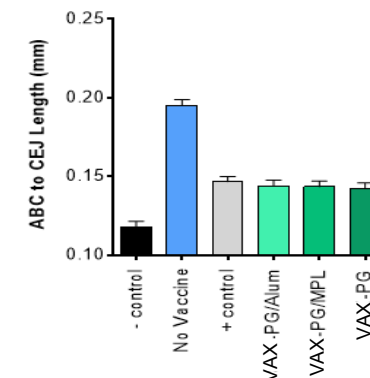
## VAX-PG: Multivalent Therapeutic Vaccine

- 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: Final vaccine composition in 2021

## MOA & Key Data



## Challenge Study Results

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



# Intellectual Property Overview

## *Multi-Pronged Approach to IP Protection*

- **Sutro Biopharma IP – Platform Coverage**

- Large patent portfolio on cell-free protein manufacturing & nnAA conjugation exclusively licensed to Vaxcyte for vaccines to infectious diseases
- Includes license to background IP from Stanford University

- **Vaxcyte Conjugate Vaccine IP – Platform Coverage**

- Multiple patent applications filed claiming novel protein carriers and conjugates as well as methods of producing these conjugates
- Strong global coverage with currently filed US and PCT applications

- **Disease-specific applications to PCV, periodontitis, and self-adjuvanted vaccines**

- **Licensed applications from UCSD directed to Group A Strep polysaccharide antigen**



# Accomplishments & Anticipated Key Milestones

## Progressing Toward IND Filing and Phase 2 Clinical Results

	2015	2016	2017	2018	2019	2020	2021	2022
Pipeline	Optimized eCRM Protein Carrier	VAX-24: Produced all 24 Conjugates  Achieved 16v PCV POC	VAX-24 Preclinical POC	VAX-XP Produced all 32 Conjugates	VAX-24 Successful FDA Pre-IND Mtg & New POC Data VAX-XP Preclinical POC VAX-A1 Preclinical POC VAX-PG Preclinical POC Published	VAX-24 Abstract Accepted at ISPPD <sup>(1)</sup>  VAX-XP Enablement (PSs & DS prep)	VAX-24 File IND in 2H & Initiate Ph 1/2 in Adults  VAX-A1 & VAX-PG Final Vx Nomination	Phase 2 Clinical POC in Adults
IND-Enablement / CMC	Licensed rights to XpressCF Platform	Lonza Development & Manufacturing Agreement		Lonza scope expanded creating End-to-End VAX-24 Supply Chain	VAX-24 Completed PD/Optimization, Tech Transfer, and Scale-up at Lonza:  eCRM PS x 24 Conjugates x 24	GMP Production of VAX-24 Phase 1/2 Conjugates (Drug Substance)	Scale up to support Phase 3 & Commercial	
Corporate <sup>(2)</sup>	Series A (\$26M)		Series B (\$60M)	Series C (\$85M)	VAX-A1 CARB-X grant (\$15M)	Series D (\$110M) & IPO (\$287.5M)		

(1) ISPPD = International Symposium on Pneumococci and Pneumococcal Diseases  
(2) Amounts represent gross proceeds.

Denotes Completed Milestone

Denotes Upcoming Milestone

# Key Corporate Highlights

*Next-Generation Vaccine Company*



**Large Market Opportunity for Lead PCV Franchise**

**Cell-Free Protein Synthesis Platform**

**Disciplined Target Selection**

**Robust Pipeline**

**Aligned Critical Resources**