Corporate Presentation





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; demand for Vaxcyte's vaccine candidates; the process and timing of anticipated future development and manufacture of Vaxcyte's vaccine candidates, including breadth of coverage; the timing and availability of topline data for the VAX-24 Phase 1/2 clinical proof-of-concept study in adults aged 18 to 64; the initiation and timing of the separate Phase 2 study in adults aged 65 and older; the submission of a VAX-24 pediatric IND application; the announcement of guidance for the VAX-XP IND application submission; the announcement of guidance for VAX-A1; the nomination of a final vaccine candidate for VAX-PG; the achievement of future funding milestones; the use and availability 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; 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 Annual Report on Form 10-K filed with the SEC on February 28, 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.

VAXCYTE

VAXCYTE MISSION STATEMENT

We are on a global mission to engineer highfidelity 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



LARGE MARKET OPPORTUNITY FOR PCV FRANCHISE

- Scalable PCV platform enabling broader-spectrum PCVs: VAX-24 & VAX-XP
- Lead candidate: VAX-24
 - 24-valent PCV with potential to replace SOC
 - Phase 1/2 clinical study in adults 18-64 now dosing participants in Phase 2 portion
 - Anticipate Phase 1/2 topline _ safety, tolerability and immunogenicity results in adults 18-64 by end of 2022⁽¹⁾



L-FREE	PROTE

0

CELL IN SYNTHESIS PLATFORM

- Leverages site-specific conjugation
- Permits production of "tough-to-make" antigens
- Demonstrated speed, flexibility and scalability



DISCIPLINED TARGET SELECTION

- Targets well-defined >\$7B market segment
- Honors well-understood **PCV MOA**
- Leverages established surrogate immune endpoints and clinical pathways



ROBUST DEVELOPMENT PIPELINE

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

(1) Guidance provided as of May 9, 2022.





ALIGNED CRITICAL RESOURCES

- Strategic alignment with Lonza (manufacturing)
- Seasoned management team, directors and advisors
- Cash, cash equivalents and investments of \$352.3M as of 3/31/22

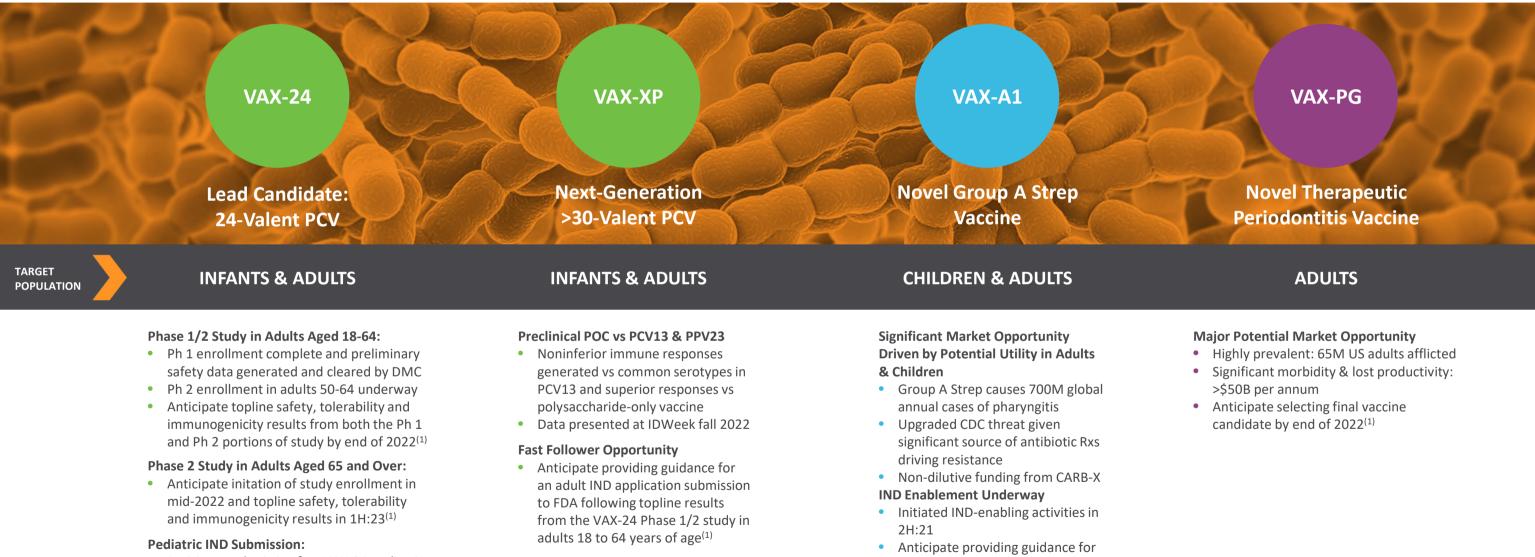
Experienced Team, Board of Directors and Scientific Advisors

Outstanding Track Record in Vaccines and Biopharma



Pipeline of High-Fidelity Vaccines

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



an adult IND application

submission to the FDA in 2H:22⁽¹⁾

• Anticipate submitting first VAX-24 pediatric IND application to FDA in 1H:23⁽¹⁾⁽²⁾

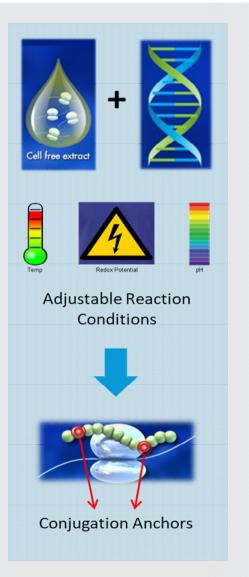
(1) Guidance provided as of May 9, 2022..

(2) Subject to a pre-IND meeting with the FDA and successful topline results from the VAX-24 Phase 1/2 study in adults 18 to 64 years of age.

VAXCYTE

Cell-Free Protein Synthesis Platform Unlocks Multiple Vaccine Applications

Design and Produce Proteins Beyond Reach of Conventional Methods



VAXCYTE

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 nnAA conjugation anchors
- Permits protein production in nonphysiological 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 broaderspectrum vaccines

NOVEL PROTEIN VACCINES

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

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PCV Opportunity





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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.



GLOBAL INCIDENCE & 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.
- The CDC estimates that 150K hospitalizations from pneumococcal pneumonia occur annually in the U.S.
- Among children < age 5, PD is a leading cause of death globally.

In the U.S.:

- Infants: PCV13 (4 doses).
- Pneumovax[®] 23 (PPV23) (1 dose/each).

¹ Gierke 2015

² https://www.cdc.gov/abcs/reports-findings/survreports/spneu18.pdf CDC 2018 ³ https://www.cdc.gov/pneumococcal/clinicians/clinical-features.html



CURRENT GLOBAL STANDARD-OF-CARE

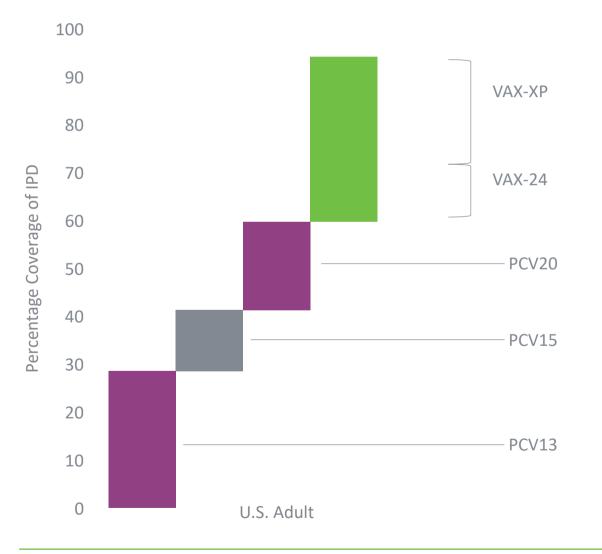
Vaccinations are recommended globally for infants and adults to prevent PD.

• Adults: Prevnar 20[™] (PCV20) (1 dose) or Vaxneuvance[™] (PCV15) and

Significant Unmet Needs Despite Recent Coverage Expansion in Adults

Resulting in Spectrum of Coverage Driving Adoption of Pneumococcal Vaccines

ESTIMATED COVERAGE OF PCVS BASED ON CIRCULATING INVASIVE PNEUMOCOCCAL SEROTYPES



Most IPD is caused by strains above and beyond Prevnar 13[®], driving need for broader-spectrum PCVs.

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

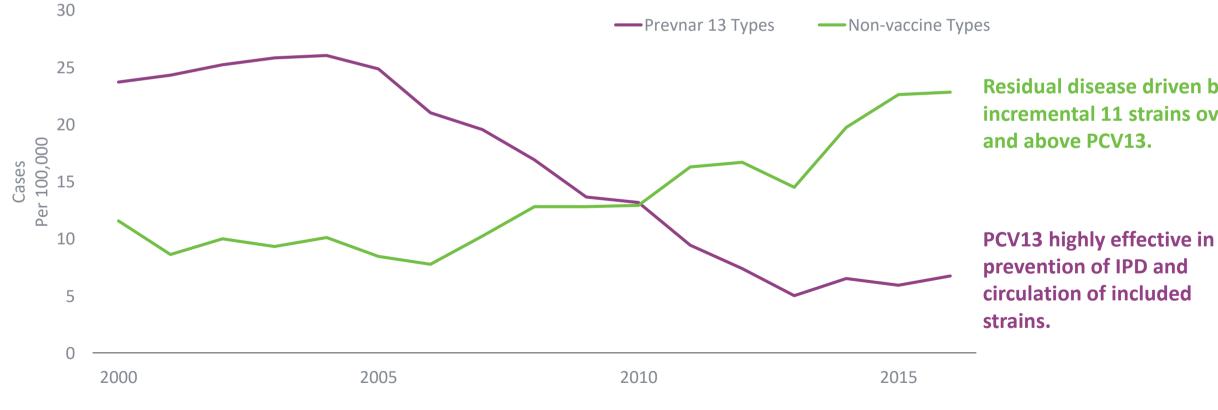
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Serotype Replacement Drives Need for Broader-Spectrum Vaccines

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





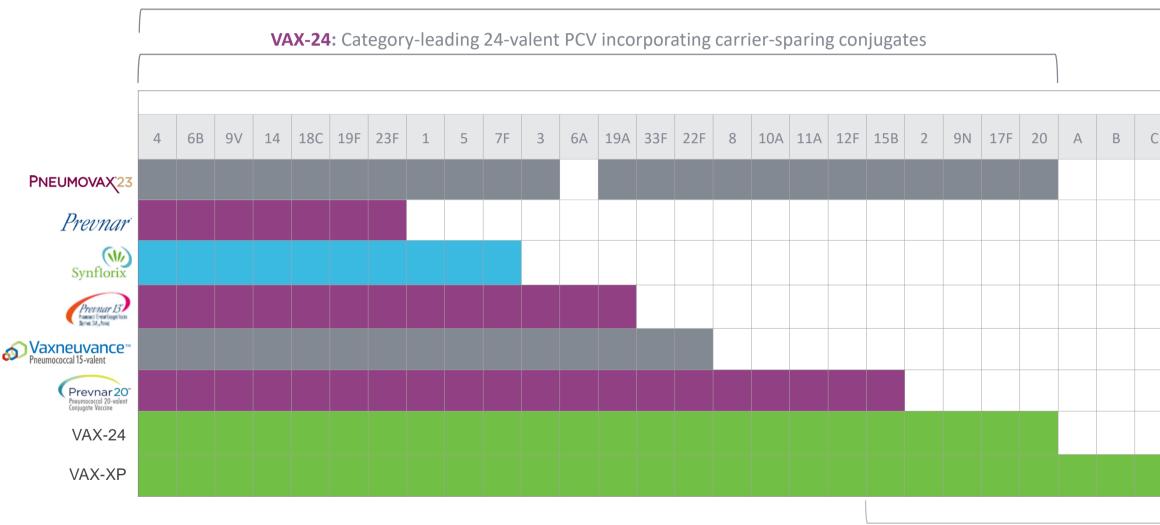
(1) Ladhani et al, Lancet Infect Dis 2018 Apr;18(4):441-45 inclusive of unpublished raw data.

VAXCYTE

Residual disease driven by incremental 11 strains over

Vaxcyte PCV Franchise Designed to Offer Broader Protection

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



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

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

VAXCYTE

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				TBD			

Spectrum of Coverage Drives Adoption

Pneumococcal Vaccine Market is Highly Attractive

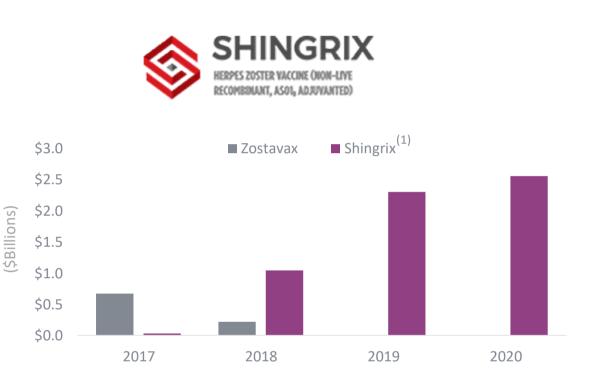
VAX-24 has the Potential to Become the Most Broad-Spectrum PCV

Pneumococcal Vaccine Market Dynamics

- Spectrum of coverage drives adoption
- Highly attractive margins:
 - PCV13 & PPV23 are premium priced in the US
- Durable revenue stream:
 - PCV13 & PPV23 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
 - PCV13 vs Prevnar 7

VAXCYTE

Shingrix[®] vs Zostavax[®]



- 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.

Potential for Adult Pneumococcal Market to Grow Substantially

October 2021 ACIP Vote Reinforced Need for PCVs with Broader Spectrum of Coverage and Paves Way for Substantial Expansion for Adult Population



- ACIP issued universal recommendation for Pfizer's PCV20 or Merck's PCV15 along with continued use of Pneumovax 23 (PPV23) in adults ≥ 65 years of age
- Value of incremental strains vs Prevnar 13 demonstrated by a **premium price** for Prevnar 20 and Merck's PCV15
- Added "at risk" population to universal recommendation for population aged 19 to 64 substantially expanding adult market
- First time ACIP has recommended a PCV for risk groups ages 19 to 64



- Strong desire expressed to expand
- prime-boost in adult population

By preserving Pneumovax 23, ACIP decision reinforces need for 24-valent PCV Significant immediate expansion of adult population





universal adult vaccination to >50 years

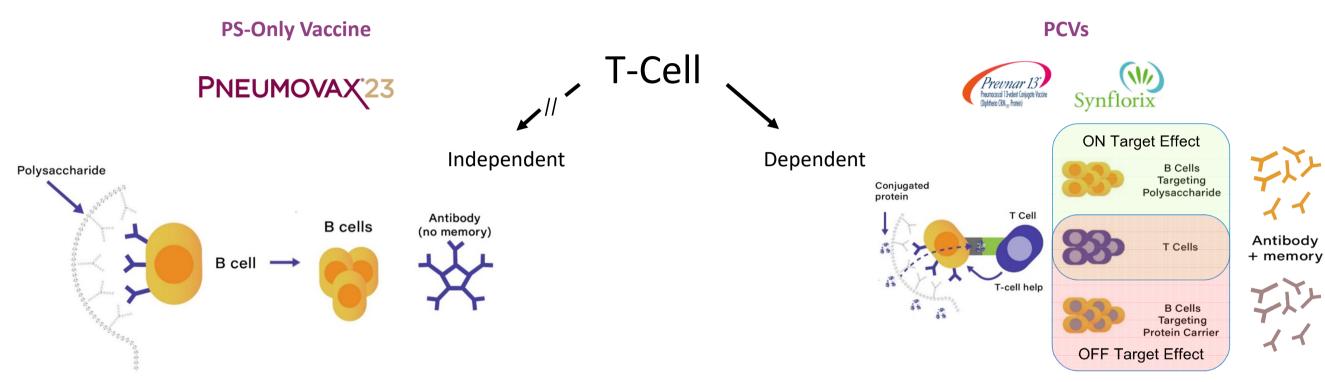
• Shift to >50 years will potentially drive

CDC committed to gathering more data and revisiting topic at a future meeting

Opportunity for substantial expansion of adult market to address unmet needs

PCVs Designed to Overcome the Limitations of Polysaccharide-Only Vaccines

PCV Efficacy Driven by T-Cell Epitopes on Diphtheria Toxin Protein Carrier – CRM₁₉₇⁽¹⁾



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 (CRM₁₉₇).

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Narrow Coverage But Highly Effective in Adults & Infants - Boostable

Conjugation of PS to protein carrier leads to:

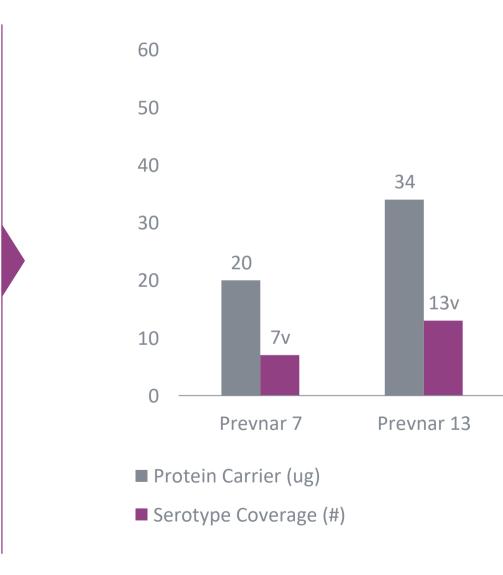
- Enhanced Ab responses (IgG) that protect against pneumonia
- T cell-mediated memory to provide boostable, durable protection
- Characteristic interstrand crosslinked matrix-like structures

Limitations of Current PCVs

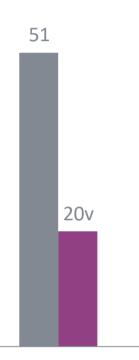
Coverage Expansion Needed to Address Circulating Disease, but Protein Carrier Backbone Problematic

LIMITATIONS OF CONVENTIONAL CHEMISTRY

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







Prevnar 20

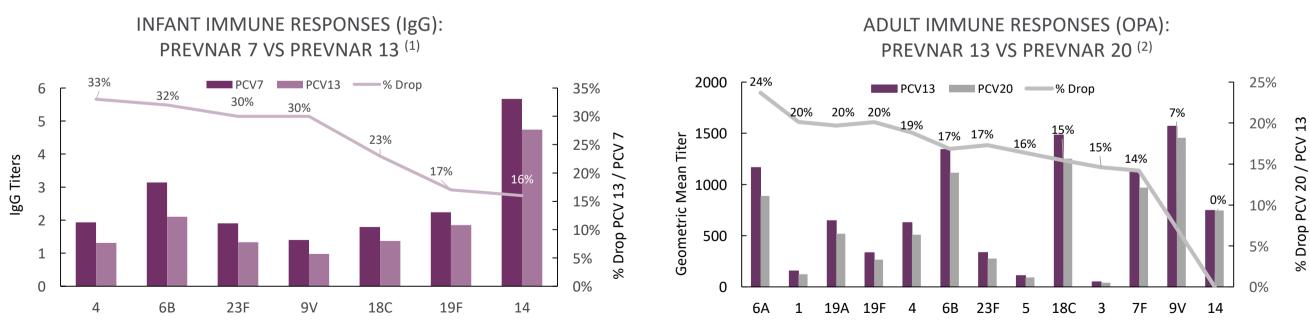
Limitations of Current PCVs

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



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

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

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Differentiated PCV Franchise Led by VAX-24

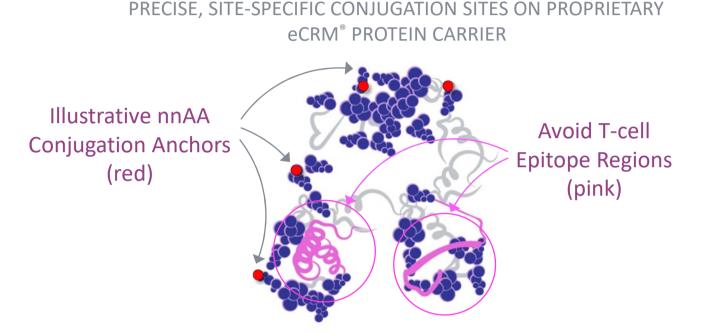




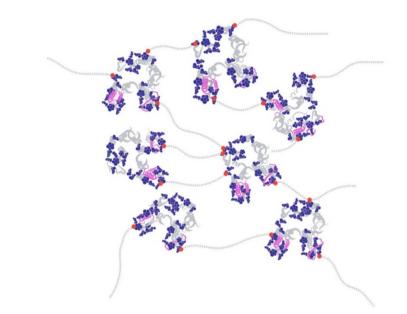
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VAX-24 Employs Carrier-Sparing Conjugates

XpressCF Enables Precise Conjugation to Enhance Potency of Standard Protein Carrier



FINAL VAX-24 CONJUGATES IN CUSTOMARY MATRIX FORM



eCRM: Enhanced Potency Potential

- Avoids masking sites on CRM₁₉₇ carrier responsible for T-cell help
- Optimized sites for conjugation using copper-free click chemistry
- More consistent antigenic presentation

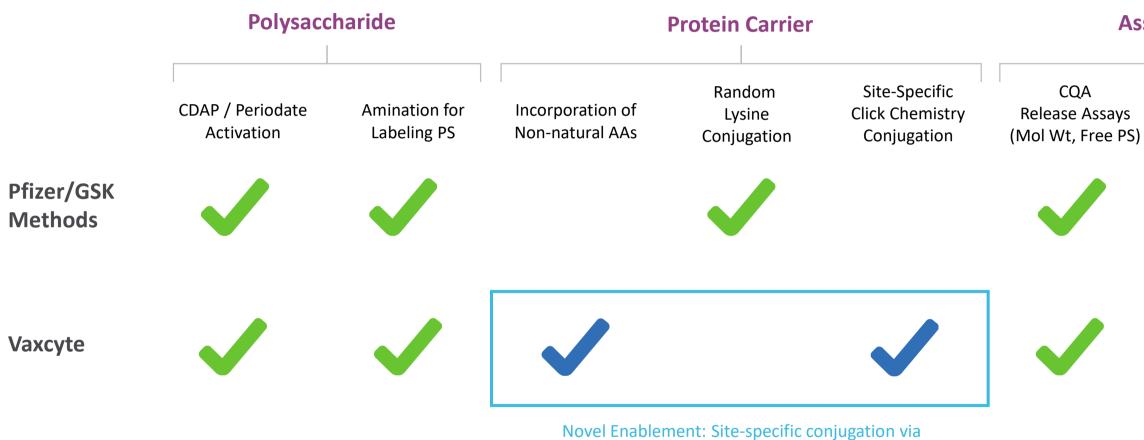
VAXCYTE

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 and serological assays

VAX-24 Design Leverages Many Standard PCV Conventions

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



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)

VAXCYTE

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Serological Assays (IgG & OPA)

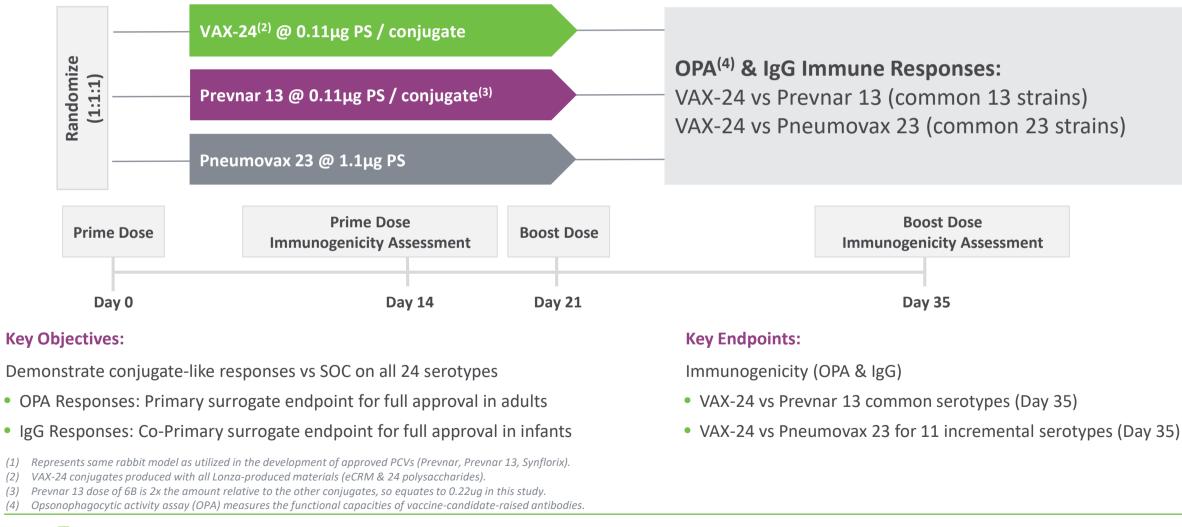


VAX-24 Preclinical POC Study

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

Study Design: Vaccination of rabbits⁽¹⁾ 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



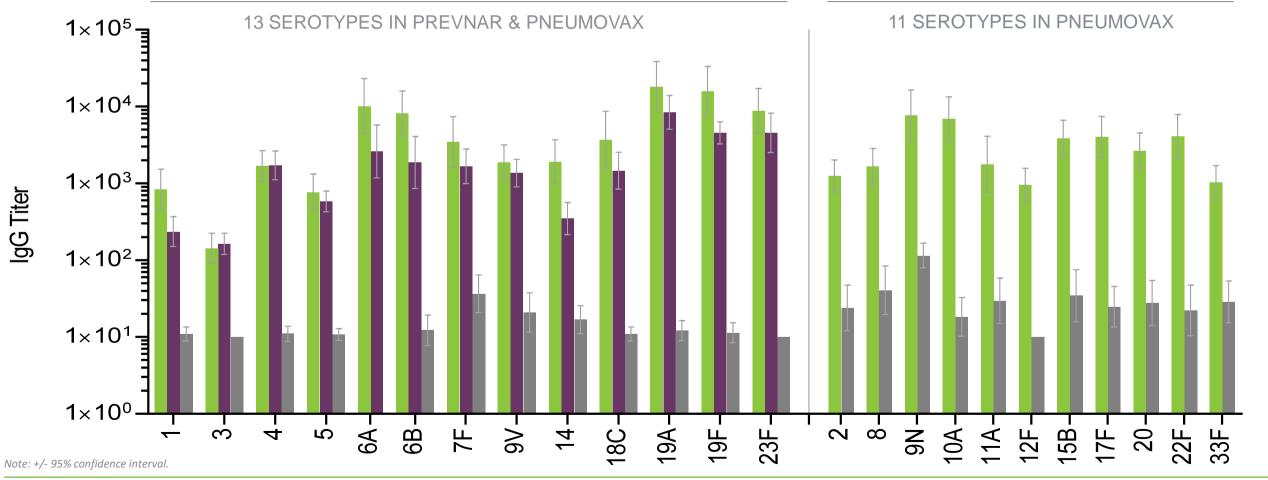


(1)

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

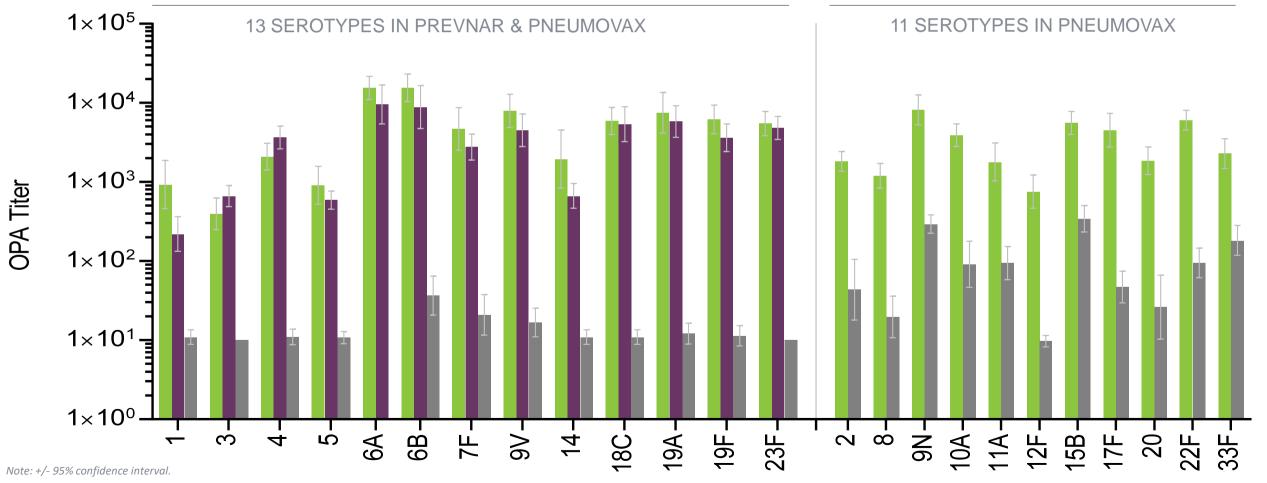


VAXCYTE

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

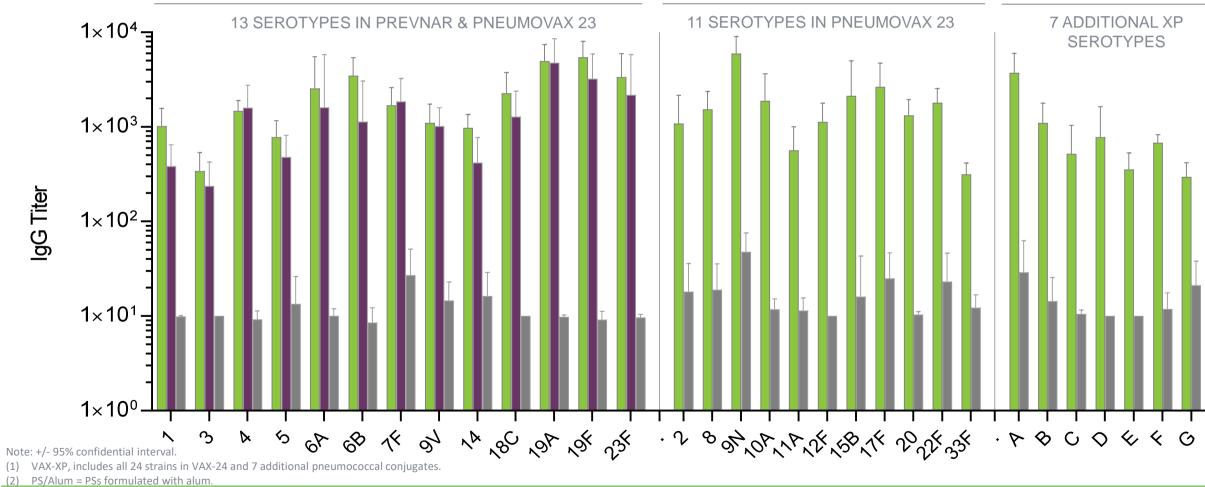


VAXCYTE

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.





PCV Franchise Leverages Established Regulatory Pathway

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

Well-defined, established surrogate immune endpoints

No anticipated requirement for field efficacy trials

Licensure based on demonstration of non-inferior immune responses vs. SOC⁽¹⁾

Consistent with Merck (PCV15) and Pfizer (PCV20) BLA filings⁽²⁾⁽³⁾

Vaxcyte's Approach for VAX-24

Surrogate immune endpoints⁽⁴⁾⁽⁵⁾⁽⁶⁾ have been consistent between Ph 2 POC and Ph 3 pivotal studies for adult and infant programs

CLINICAL APPROACH

Clinical development plan designed to follow precedent of Merck (PCV15) and Pfizer (PCV20) clinical studies

ADULT POC

Ph 2 clinical POC study to include ~800 healthy adults aged 50-64 (200/arm); topline results expected by end of $2022^{(7)}$

Potential for Fast Track, Priority Review and Breakthrough Designation - granted for other increased spectrum PCVs

e.g., Prevnar 13 vs 7, 20 vs 13, and Merck PCV15 vs Prevnar 13)

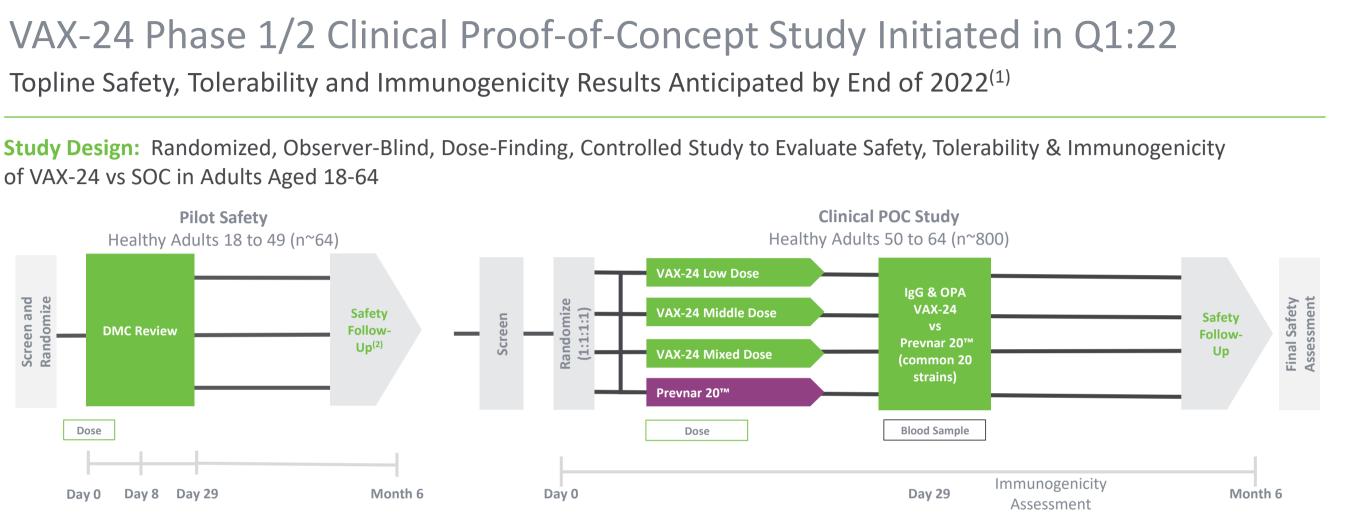
- (1) For adults: Lower limit of the 95% CI for the OPA GMR \geq 0.5 for each serotype comparison. For infants: Lower limit of the 95% CI for the IgG GMC ratio post dose 4 is \geq 0.5 and LL of the 95% CI for % of subjects achieving an IgG concentration \geq 0.35 μ g/mL 1 month after dose 3 is < -10%.
- (2) Clinicaltrials.gov: Pfizer clinical studies for 20vPnC NCT03512288, NCT03550313, NCT03313050, NCT03313037, NCT03760146, NCT03835975, and NCT03828617.
- Clinicaltrials.gov: Merck clinical studies for V114 (PCV15) NCT02987972, NCT03620162, NCT03692871, NCT03731182, NCT03480763, NCT03615482, NCT03547167, NCT03480802, and NCT03565900. (3)
- WHO. Recommendations to assure the quality, safety and efficacy of pneumococcal conjugate vaccines, in WHO Expert Committee on Biological Standardization, 60th report. Geneva, Switzerland: WHO; 2013:91-521. (4)
- 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. (5)
- 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. (6) (7) Guidance provided as of May 9, 2022.



REGULATORY ACCELERANTS

Topline Safety, Tolerability and Immunogenicity Results Anticipated by End of 2022⁽¹⁾

of VAX-24 vs SOC in Adults Aged 18-64



- Phase 1 portion of the study is evaluating safety and tolerability of a single injection of VAX-24 at three dose levels and compared to Prevnar 20[™] in 64 healthy adults 18 to 49 years of age. Participants were randomized equally in four separate arms and were evaluated for safety 8 and 29 days after dosing.
- Phase 2 portion of the study will evaluate safety, tolerability and immunogenicity of a single injection of VAX-24 at three dose levels and compared to Prevnar 20[™] in ~800 healthy adults 50 to 64 years of age. Participants will be randomized equally in four separate arms and approximately 28 days after participants are dosed, serology samples collected to assess immunogenicity.
- All participants in the Phase 1/2 study will be followed for a total of six months after dosing to assess safety and tolerability.

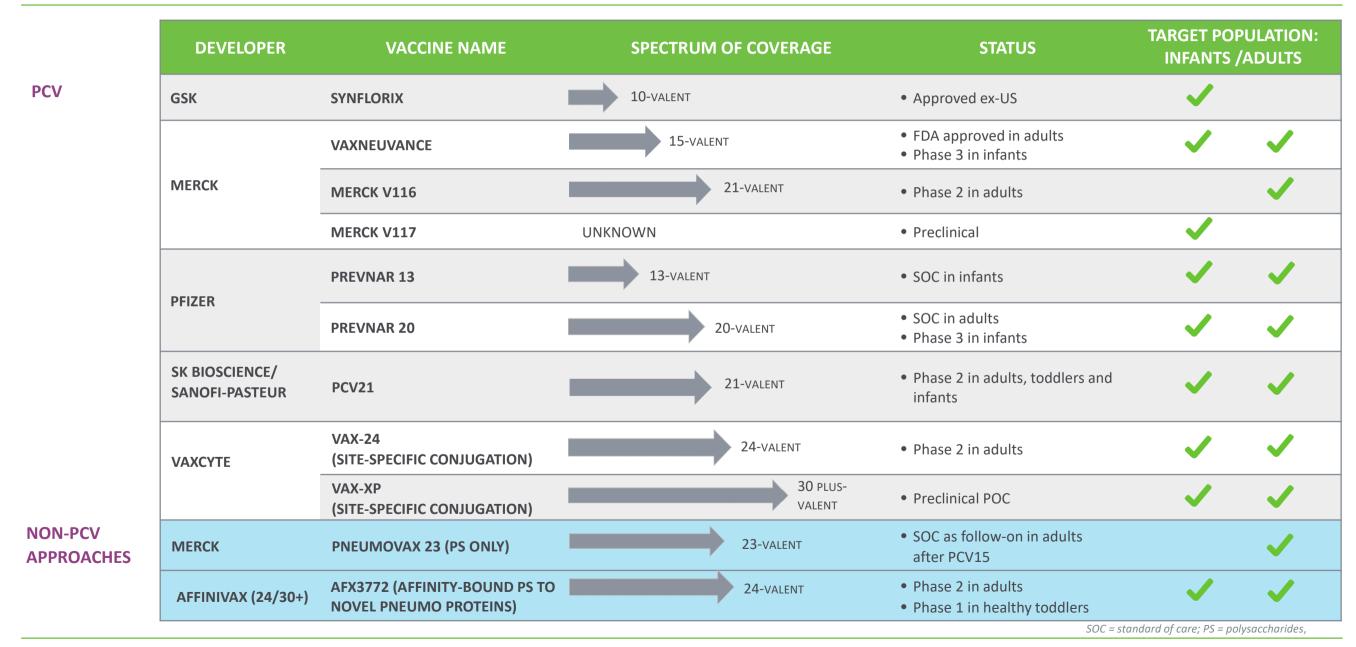
(1) Guidance provided as of February 28, 2022.

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



The Pneumococcal Vaccine Landscape

Vaxcyte PCV Franchise Designed to Offer Broadest Spectrum of Coverage



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Non-PCV Pipeline





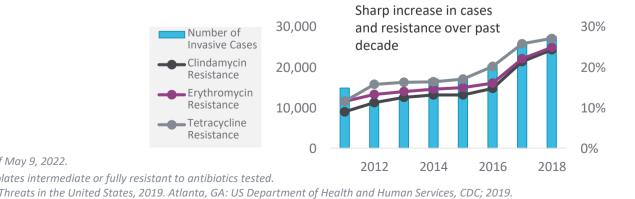
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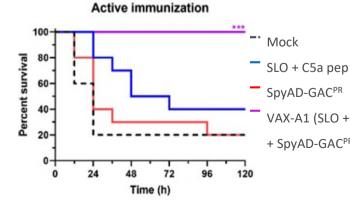
VAX-A1: Group A Strep Conjugate Vaccine Program

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 invinecrotizing fasciitis and toxic shock syndrome Upgraded CDC threat given significant source of antibiotic Rxs driving resistance which has nearly tripled in Responsible for post-infectious immune-mediated rheumatic heart disease leading to over 300K deaths in 2 Highly prevalent in children and rate of invasive disease in adults > 65 has more than doubled (exceeding IP)
VAX-A1: BROAD-SPECTRUM, MONOVALENT CONJUGATE VX	 Designed to confer robust, boostable and durable protection against a broad spectrum of subtypes of Group 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 alo factors
PROGRAM STATUS	 Partially funded by grant from CARB-X (consortium of BMGF, Wellcome Trust, US Biodefense Agency (BARDA \$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⁽¹⁾

KEY DATA





(1) Guidance provided as of May 9, 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



vasive infections such as sepsis,

past decade

2015

PD rate in adults)

ip A Strep

ong with two conserved virulence

A)); add'l August 2021 award of

SpyAD-GAC^{PR}

VAX-A1 (SLO + C5a pep

+ SpyAD-GAC^{PR})

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 support of the second secon					
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 fro 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⁽¹⁾ 					
MOA & KEY DATA	 Restoration of balanced microbiota by interrupting underlying inflammatory condition Chall Imm form provide the second seco					

(1) Guidance provided as of May 9, 2022. Huang et.al. J Clin Periodontol. 2019 Feb;46(2):197-205



orting the teeth

om P. gingivalis-elicited oral

llenge Study Results

ABC to (

0.1

- control

No Vaccine

+ control PG/Alum VAX -PG

-PG/MPL

VAX

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

Key Corporate Highlights

Large Market Opportunity for Lead PCV Franchise

Cell-Free Protein Synthesis Platform

Disciplined Target Selection

Robust Pipeline with Multiple Novel Vaccines

Aligned Critical Resources



