4Q & FY 2022 Financial Results and Business Update

February 27, 2023

VAXCYTE
protect humankind™

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 potential benefits of Vaxcyte's vaccine candidates, including breadth of coverage and the ability to deliver a potentially best-in-class pneumococcal conjugate vaccine and the improvement upon the standard-of-care; the VAX-24 Phase 2 study designs; the process and timing of anticipated future development of Vaxcyte's vaccine candidates; the timing and availability of data for the VAX-24 Phase 2 and Phase 3 studies and related regulatory interactions; the timing of the initiation of the VAX-24 Phase 2 infant study and the availability of Phase 2 topline results; the timing and submission of an IND application for the VAX-31 adult program and the timing and availability of the Phase 1/2 topline data for such program; the announcement of guidance for VAX-A1; the market opportunity for Vaxcyte's vaccines; the ability of Vaxcyte's strategic partnerships to deliver commercial, scalable manufacturing capabilities; changes to Vaxcyte's operating expenses, including potential rational; 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 27, 2023 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

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

2022 Key Accomplishments & Recent Highlights

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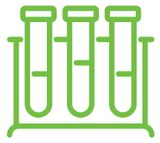
2022 Key Accomplishments

- Reported positive topline safety, tolerability and immunogenicity data from Phase 1/2 poof-of-concept study of VAX-24 in adults aged 18-64; data indicate potential best-in-class profile
- Completed enrollment of Phase 2 study evaluating the safety, tolerability and immunogenicity of VAX-24 in adults 65 years and older
- Revealed the additional seven serotypes in VAX-31 (formerly VAX-XP), a 31-valent PCV, the broadest-spectrum PCV the Company believes to be in development
- Further solidified manufacturing foundation, including a new agreement with Sutro Biopharma for expanded rights to develop and manufacture cell-free extract
- Successfully raised ~$805 million in gross proceeds in two follow-on equity offerings; $957.9 million in cash, cash equivalents and investments as of December 31, 2022
- Strengthened leadership team with key appointments

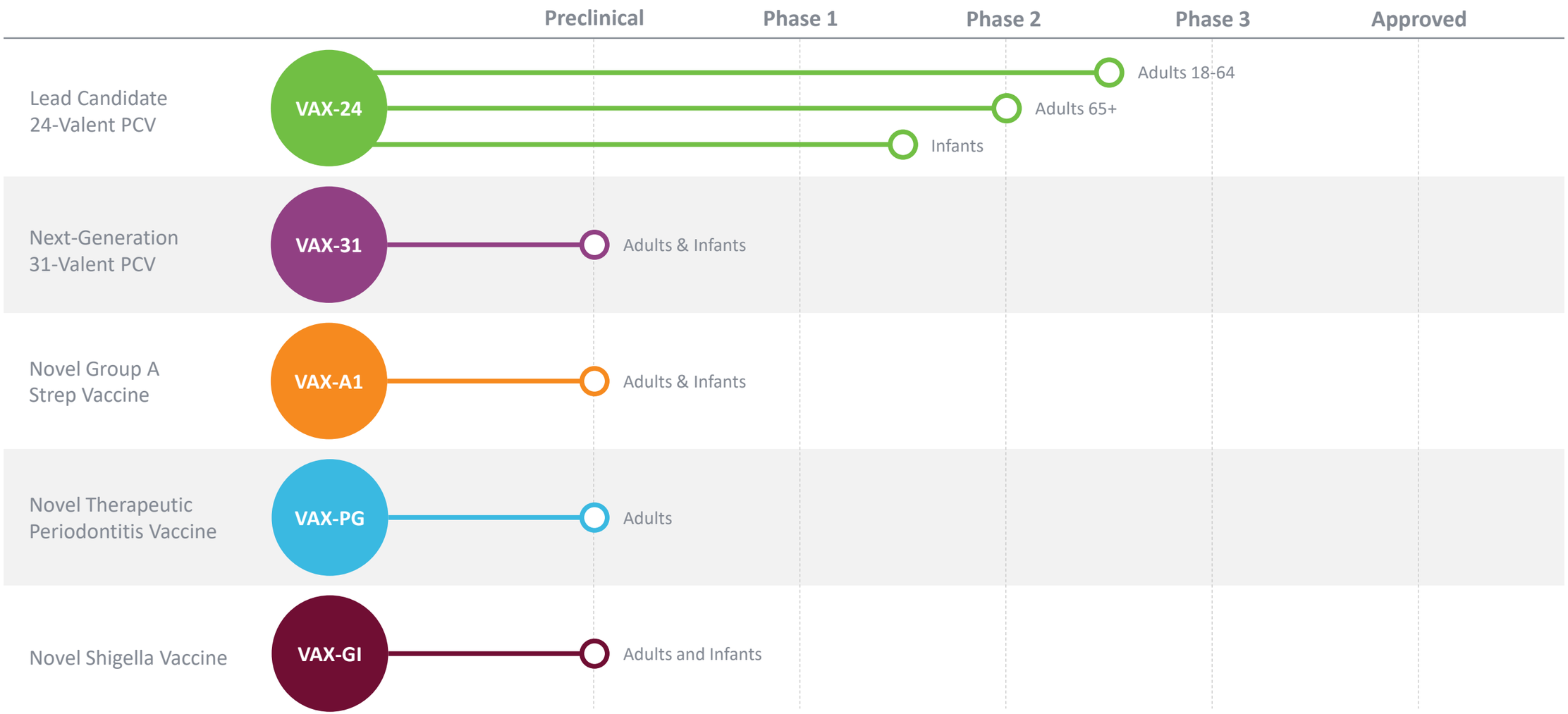


Recent Highlights

- VAX-24 granted Breakthrough Therapy designation from FDA for the prevention of IPD in adults aged 18 and older
- VAX-24 infant Investigational New Drug (IND) application for the prevention of invasive pneumococcal disease (IPD) cleared by the U.S. Food and Drug Administration (FDA)
- Added VAX-GI, a novel Shigella vaccine program, to the pipeline

Pipeline of High-Fidelity Vaccines

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



Critical Manufacturing Foundation Established for PCV Franchise

Long-term Investment and Strategic Partnerships to Deliver Commercial, Scalable Manufacturing Capabilities

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STRATEGIC ALIGNMENT WITH WORLD-CLASS CDMO

- End-to-end “turn-key” GMP supply established at marquee Swiss facility
- Existing infrastructure is well-positioned to support U.S. adult launch for VAX-24
- Plans to ensure expanded commercial manufacturing footprint to support infant indication and ex-U.S. demand are underway

SUTRO BIOPHARMA

LONGSTANDING RELATIONSHIP WITH SUPPLIER OF KEY VACCINE COMPONENT

- December 2022 agreement provides expanded rights related to the supply of cell-free extract and an option to acquire additional rights to develop and manufacture cell-free extract
- Enables direct oversight and control of cell-free extract manufacturing for our products and provides additional flexibility going forward

PCV Franchise

Topline VAX-24 Phase 1/2 Proof-of-Concept Safety, Tolerability and Immunogenicity Results in Adults 18-64

POSITIVE RESULTS SUPPORT BEST-IN-CLASS POTENTIAL FOR VAX-24 AND CARRIER-SPARING PCV FRANCHISE

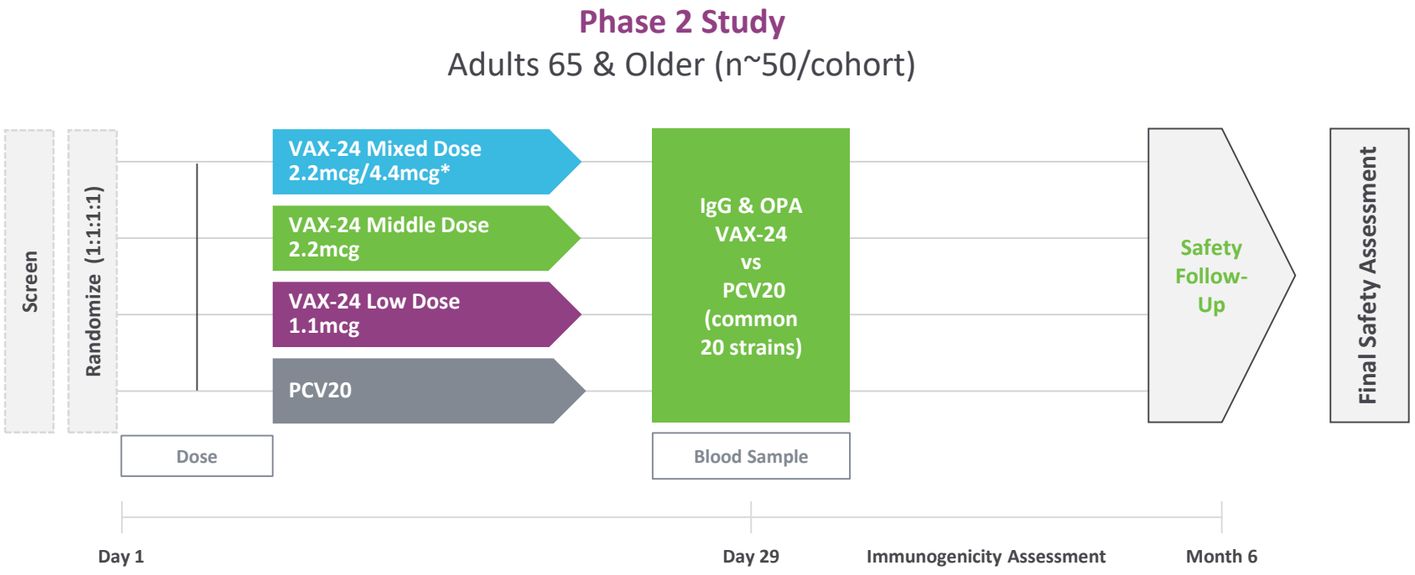
- VAX-24 demonstrated a safety and tolerability profile similar to PCV20 at all three doses studied

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

- Optimal 2.2mcg dose being advanced to Phase 3:
  - Met the standard opsonophagocytic activity (OPA) response non-inferiority criteria for all 20 STs in common with PCV20, of which 16 achieved higher immune responses
  - Met the standard superiority criteria for all 4 additional STs unique to VAX-24

Design of VAX-24 Phase 2 Clinical Study in Adults 65 Years & Older

Design: Randomized, Observer-Blind, Dose-Finding, Controlled Study to Evaluate Safety, Tolerability & Immunogenicity of VAX-24 vs SOC in Adults Aged 65 and Older



- The study is evaluating safety, tolerability and immunogenicity of a single injection of VAX-24 at three dose levels and compared to PCV20 in ~200 healthy adults 65 years of age and older
- Participants were randomized equally in four separate arms and 28 days after participants are dosed, serology samples collected to assess immunogenicity
- All participants will be followed for a total of six months after dosing to assess safety and tolerability
- Designed to inform Phase 3 powering; not powered to show non-inferiority

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

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Key Objectives & Expectations for VAX-24 Phase 2 Study in Adults 65+

Topline safety, tolerability and immunogenicity data expected in Q2 2023

KEY CONSIDERATIONS

- Smaller study with ~50 subjects per cohort vs. ~200 per cohort in the Phase 2 study in adults aged 50-64
- Importantly, study not powered to demonstrate non-inferiority
- Designed to further inform powering of pivotal Phase 3 non-inferiority study and add to existing VAX-24 body of research
- Age-stratified data from Phase 2 study in adults 50-64 provide directional insights into upcoming Phase 2 results in adults aged 65+
- Topline data announcement for Phase 2 study in adults 65+ to include additional pooled data analysis combining data from both 60-64 and 65+ adult populations

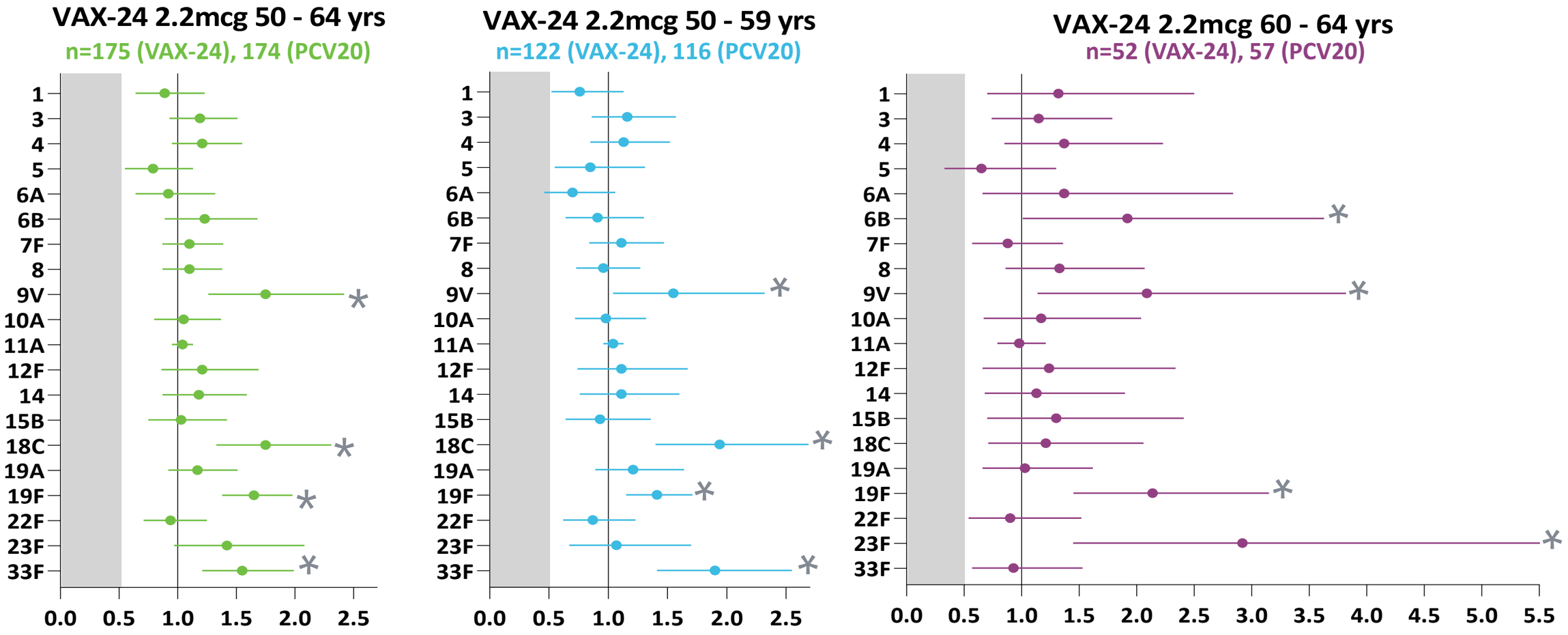
IMMUNOGENICITY FOCUS AREAS

- Key immunogenicity readouts are point estimates for OPA geometric mean ratios (GMRs) for each serotype and comparability to results from Phase 2 study in adults 50-64
- If GMRs are between 0.60-0.75 or higher per serotype, prior studies have shown that is adequate to achieve the non-inferiority threshold in larger Phase 3 studies
- Lower limit of 95th percent confidence intervals not the focus of this study
- Given smaller study size, confidence intervals will be substantially wider; some may cross 0.50 threshold

OPA = opsonophagocytic activity

Age Stratified OPA GMR for 2.2mcg VAX-24 Dose Compared to PCV20

Similar Results Between Age Groups With Higher Variability in Older Population Due to Smaller Sample Size



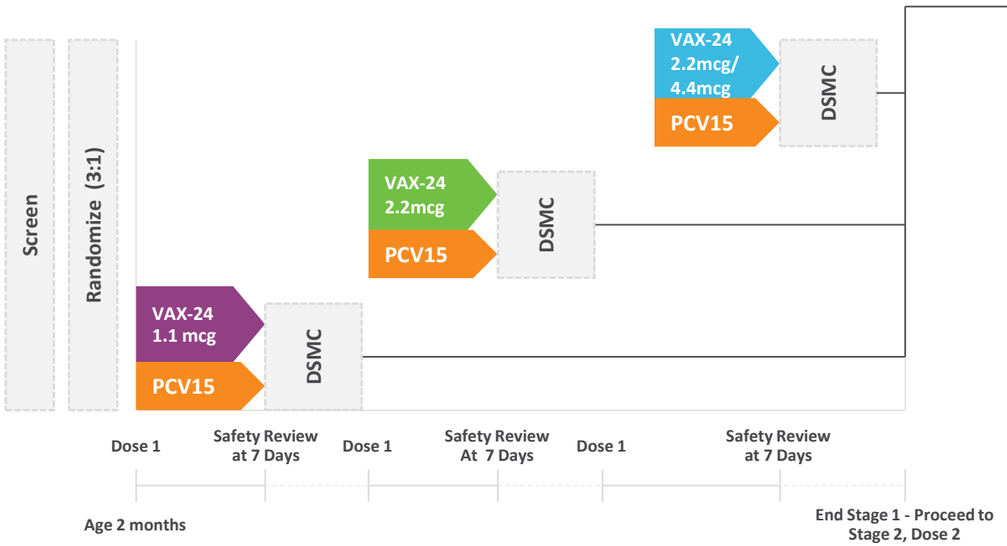
*Reached statistical significance for superiority.

Note: n represents the lowest number of evaluable subjects among all serotypes.

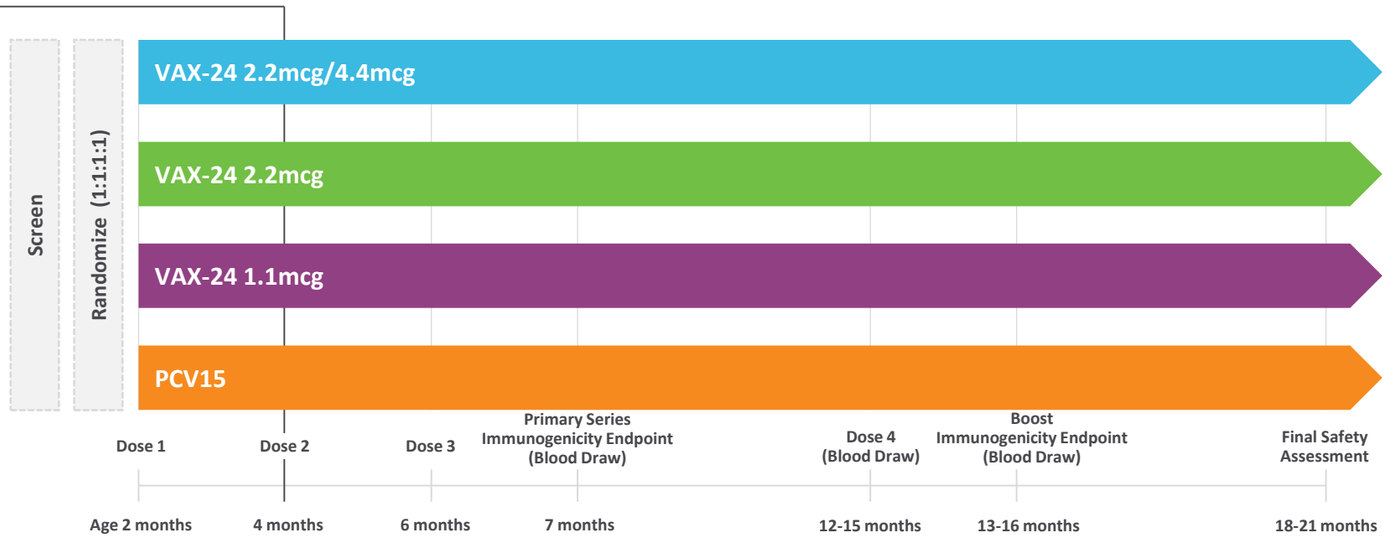
Design of VAX-24 Phase 2 Clinical Study in Infants; Initiation Expected in Q2:23[1]

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

Stage 1: Dose Escalation (n~48)



Stage 2: Main Study (n~750)



STAGE 1 OVERVIEW

- Stage 1 will evaluate safety and tolerability of a single injection of VAX-24 at three dose-escalating levels compared to PCV15 in ~48 healthy infants.
- Infants will be enrolled and dosed at two months of age and evaluated seven days post-dose. Following satisfactory Data Safety Monitoring Committee (DSMC) review of safety data, the study will proceed to the next dose.
- If DSMC approves moving forward, all participants from Stage 1 will be part of the Stage 2 study starting at dose two (four months).

STAGE 2 OVERVIEW

- Stage 2 will evaluate safety, tolerability and immunogenicity of VAX-24 at three dose levels and compared to PCV15 in ~750 healthy infants. Per ACIP guideline, the primary immunization series includes three doses given at two months, four months and six months of age, followed by a booster dose at 12-15 months of age.
- The key prespecified immunogenicity study endpoints include an assessment of the induction of immunoglobulin G (IgG) antibody responses 30 days post-dose three (proportion of participants achieving accepted IgG threshold of ≥0.35ug/ml) and IgG geometric mean titer ratios 30 days post-dose 4 on a serotype-by-serotype basis for all three VAX-24 dose levels and compared to PCV15.
- All participants will be evaluated for safety six months following the booster dose at 12-15 months of age.

SOC = standard-of-care
ACIP = Advisory Committee on Immunization Practices

(1) Guidance provided as of February 27, 2023.

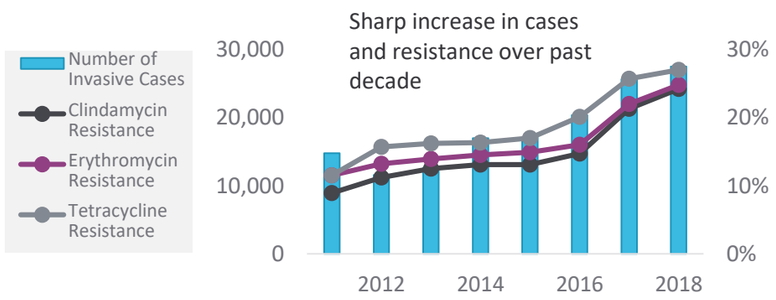
Early-Stage Pipeline Programs

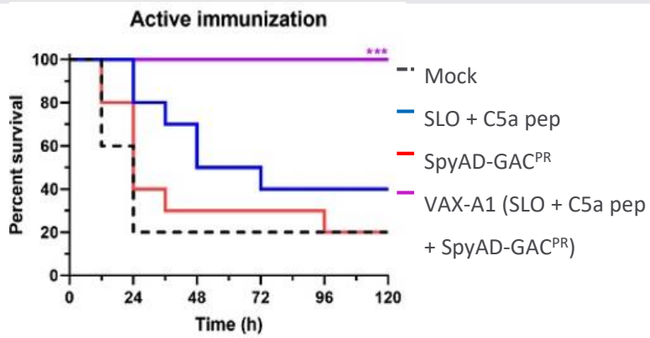
VAX-A1: Group A Strep Conjugate Vaccine Program

Novel Conjugate Vaccine Designed to Provide Universal Protection

UNMET NEED	• Group A Strep results in 700M cases of illness annually worldwide, including pharyngitis, or strep throat, and certain severe invasive infections such as sepsis, necrotizing fasciitis and toxic shock syndrome. • Upgraded CDC threat given significant source of antibiotic Rxs driving resistance which has nearly tripled in past decade • Responsible for post-infectious immune-mediated rheumatic heart disease leading to over 300K deaths in 2015 • Highly prevalent in children and rate of invasive disease in adults > 65 has more than doubled (exceeding IPD rate in adults)
VAX-A1: BROAD-SPECTRUM, MONOVALENT CONJUGATE VX	• Designed to confer robust, boostable and durable protection against a broad spectrum of subtypes of Group A Strep • Leverages site-specific conjugation to disease-specific carrier to expose mapped T- and B-cell epitopes • Proprietary conserved antigen – Polyrhamnose – conjugated to an immunogenic disease-specific carrier along with two conserved virulence factors
PROGRAM STATUS	• Partially funded by grant from CARB-X (consortium of BMGF, Wellcome Trust, US Biodefense Agency (BARDA)); received $6.6M to date, with total potential funding of up to $14.6M inclusive of grants to date • Initiated IND-enabling activities in 2H:21 • Development of VAX-A1 continues to advance and further information about the anticipated timing of an IND application will be provided as the program progresses[1]

KEY DATA





(1) Guidance provided as of February 27, 2023.

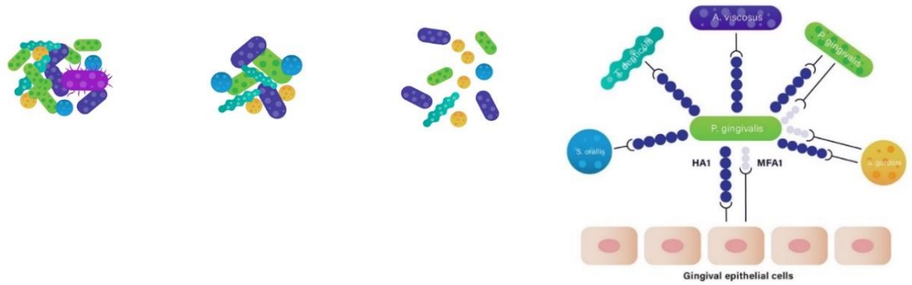
CDC. Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: US Department of Health and Human Services, CDC; 2019.

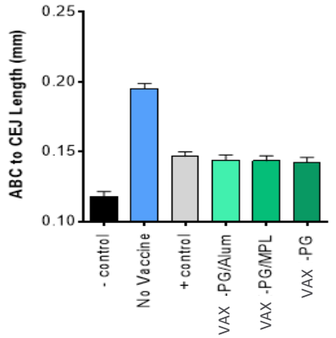
BMGF = Bill & Melinda Gates Foundation.

VAX-PG: Periodontitis Vaccine Program

Therapeutic Vaccine Targeting Gingipains to Address Large, Underserved Market

UNMET NEED	• Periodontal disease is a chronic oral inflammatory disease leading to destruction of soft & hard tissues supporting the teeth • Highly prevalent: estimated 65 million US adults afflicted • Periodontal disease caused an estimated loss of $330.6 billion in the US and Europe in 2018 with the direct costs exceeding $6 billion • Associated with increased risk of heart attack, stroke, cardiovascular disease and Alzheimer's Disease
VAX-PG: MULTIVALENT THERAPEUTIC VACCINE	• Incorporates proprietary combination of known virulence factors of keystone pathogen • Preclinical model demonstrated protein-specific IgG response following immunization and protected mice from P. gingivalis-elicited oral bone loss • Initial goal to develop therapeutic vaccine that slows or stops disease progression
PROGRAM STATUS	• Preclinical proof of concept published in Journal of Clinical Periodontology • A final vaccine candidate for VAX-PG was nominated in Q4 2022 and the program continues to advance[1]
MOA & KEY DATA	• Restoration of balanced microbiota by interrupting underlying inflammatory condition





Challenge Study Results

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

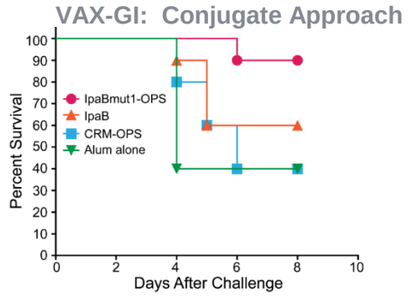
(1) Guidance provided as of February 27, 2023

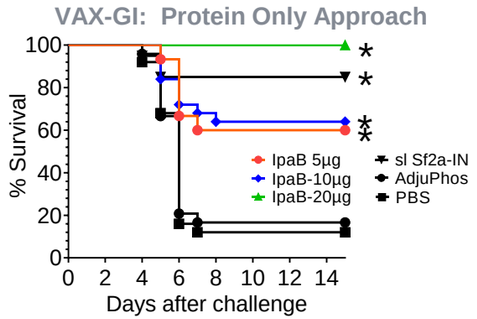
Huang et.al. J Clin Periodontol. 2019 Feb;46(2):197-205.

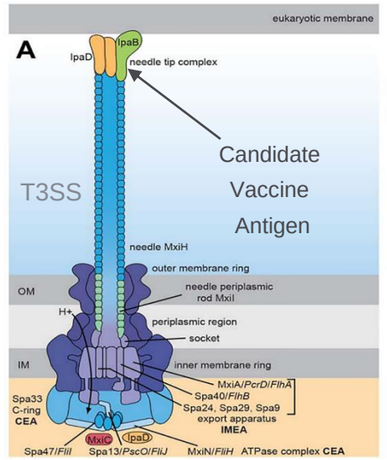
VAX-GI: Shigella Vaccine Program

Novel Shigella Vaccine

UNMET NEED	• Shigella is a bacterial illness with no available preventative treatment • Affects an estimated 180 million people worldwide each year and results in approximately 164,000 deaths annually, mostly among children under five years of age in low-income and middle-income settings[1] • With the aim of reducing morbidity and mortality due to the disease, the World Health Organization lists Shigella vaccine development as a priority goal[2]
VAX-GI: NOVEL SHIGELLA VACCINE	• Development collaboration with the University of Maryland, Baltimore; supported with funding by two NIH R01 grants for five years • Will pursue conjugate and protein-only approaches simultaneously • Conjugate approach: IpaB-LPS/IpaH/VirG; Protein-only approach: IpaB/IpaH/VirG
PROGRAM STATUS	• New program added to preclinical pipeline • Decision on final candidate to be determined by a human challenge study conducted at the University of Maryland, Baltimore • Currently optimizing process for scale-up and production
MOA & KEY DATA	• Targeting IpaB inhibits assembly of T3SS and toxin delivery to immune cells • Opsonophagocytosis and killing of bacteria







(1) *Lancet. 2018 Feb 24;391(10122):801-812.*
(2) *https://www.who.int/publications/i/item/9789240036741.*

Financial Update

Financial Update

(in millions)	FY 2022	FY 2021
Cash, Cash Equivalents and Investments	$957.9	$273.1
R&D Expenses	$169.5	$78.4
Acquired Manufacturing Expenses	23.0	-
SG&A Expenses	39.8	25.3
Total Operating Expenses	232.3	103.7
Net Loss	$(223.5)	$(100.1)

For 2023:

- Expect substantial increase in total operating expenses over full year and Q4 2022 annualized levels (excluding Acquired Manufacturing Expenses), particularly in R&D
- Expected significant increase in R&D expenses a function of:
  - Primarily, investment to make required clinical trial materials for planned VAX-24 Phase 3 program which will consist of multiple trials
  - To a lesser extent, expenses related to executing VAX-24 infant Phase 2 study, preparing for planned VAX-31 adult Phase 1/2 study, supporting a future BLA for VAX-24 and an increase in employees to support anticipated growth

Upcoming Milestones

Anticipated PCV Franchise Milestones for 2023-2025[1]

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

VAX-24 Adult

- Topline safety, tolerability and immunogenicity data from Phase 2 study in adults 65 and older in **Q2:23**
- Final results with six-month safety data for both Phase 2 adult studies in **1H:23**
- Following receipt of final safety reports, regulatory interactions to inform adult Phase 3 program in **2H:23**
- Topline safety, tolerability and immunogenicity data from the Phase 3 pivotal non-inferiority study in adults in **2025**

VAX-24 Infant

- Infant Phase 2 study initiation in **Q2:23**
- Topline safety, tolerability and immunogenicity data from Phase 2 study in infants following the primary 3-dose immunization series by **2025**

VAX-31 Adult

- Adult IND application submission to FDA in **2H:23**
- Topline safety, tolerability and immunogenicity data from Phase 1/2 study in adults in **2024**

(1) Guidance as of February 27, 2023

Thank you

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