UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): April 17, 2023

Vaxcyte, Inc.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**01-39323**	**46-4233385**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

825 Industrial Road **Suite 300** **San Carlos, California**	**94070**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's Telephone Number, Including Area Code: 650 837-0111

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	PCVX	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

On April 17, 2023, Vaxcyte, Inc. ("Vaxcyte") issued a press release announcing positive data from its Phase 2 study of its 24-valent pneumococcal conjugate vaccine candidate, VAX-24, in adults aged 65 and older and full six-month safety and tolerability data from its adult Phase 1/2 and Phase 2 studies. The press release is attached hereto as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

On April 17, 2023, Vaxcyte also made available the slide presentation attached as Exhibit 99.2 to this Current Report on Form 8-K, which is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Press Release, dated April 17, 2023.
99.2	Slide presentation, dated April 17, 2023.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

VAXCYTE, INC.

Date: April 17, 2023

By: /s/ Andrew Guggenhime
Andrew Guggenhime
President and Chief Financial Officer

Vaxcyte Reports Positive Data from Phase 2 Study of its 24-Valent Pneumococcal Conjugate Vaccine Candidate, VAX-24, in Adults Aged 65 and Older and Full Six-Month Safety Data from Adult Phase 1/2 and Phase 2 Studies

— VAX-24 Showed Robust Immune Responses Across all 24 Serotypes (ST) at All Doses, Confirming Prior Phase 2 Results in Adults Aged 50-64 —

— VAX-24 2.2mcg Dose Met Opsonophagocytic Activity (OPA) Response Non-Inferiority Criteria for 18 of 20 STs Common with Prevnar 20® (PCV20) and Superiority Criteria for the Four Additional VAX-24 STs —

— VAX-24 2.2mcg Dose Showed Further Improvement in Overall Immune Responses vs. PCV20 Relative to Results from Phase 2 Study in Adults Aged 50-64 —

— Full Six-Month Safety Data from Both Adult Studies Demonstrated VAX-24 Safety and Tolerability Results Similar to PCV20 at All Doses Studied —

— Prespecified Pooled Immunogenicity Analyses of Data from Both Adult Phase 2 Studies Showed the VAX-24 2.2mcg Dose Met OPA Non-Inferiority Criteria for All 20 STs Common with PCV20 and Superiority Criteria for the Four Additional VAX-24 STs —

— VAX-24 Well-Positioned for Adult Phase 3 Program with Topline Data Anticipated in 2025 —

— Company to Host Webcast/Conference Call Today at 7:30 a.m. ET / 4:30 a.m. PT —

SAN CARLOS, Calif., April 17, 2023 — Vaxcyte, Inc. (Nasdaq: PCVX), a clinical-stage vaccine innovation company engineering high-fidelity vaccines to protect humankind from the consequences of bacterial diseases, today announced positive results from the VAX-24 Phase 2 study in adults aged 65 and older, as well as data from the full six-month safety assessment and prespecified pooled immunogenicity analyses from both the Phase 2 study in adults aged 65 and older and the prior Phase 1/2 study in adults aged 18-64 (Phase 1 portion adults aged 18-49, Phase 2 portion adults aged 50-64). VAX-24, the Company's lead, broad-spectrum 24-valent pneumococcal conjugate vaccine (PCV) candidate, is being studied for the prevention of invasive pneumococcal disease (IPD).

In the Phase 2 study in adults aged 65 and older, VAX-24 demonstrated robust OPA immune responses for all 24 serotypes at all doses studied, confirming the prior adult study results. The VAX-24 2.2mcg dose, which Vaxcyte plans to advance to Phase 3, showed an overall improvement in immune responses vs. PCV20 relative to the results from the prior Phase 2 study in adults aged 50-64. The six-month safety data from both studies showed safety and tolerability results for VAX-24 similar to PCV20 at all doses studied.

“We believe the positive results from the Phase 2 study in adults aged 65 and older confirm the clinical potential of VAX-24 in the adult population. Based on the overall strength of our data and the well-established regulatory pathway, we look forward to meeting with regulators and advancing VAX-24 into a pivotal Phase 3 study for which we expect topline data in 2025,” said Grant Pickering, Chief Executive Officer and Co-Founder of Vaxcyte. “We developed VAX-24 with the goal of creating a best-in-class PCV that provides broader coverage and better immune responses compared to the standard-of-care vaccines. These data support that objective and also demonstrate the potential of our PCV franchise, including VAX-31, our 31-valent PCV candidate.”

“The data from both studies demonstrate VAX-24 safety and tolerability results similar to PCV20 and across cohorts, including older adults evaluated in this most recent study who are at increased risk for complications from IPD,” said Jim Wassil, Executive Vice President and Chief Operating Officer of Vaxcyte. “The immunogenicity results from our Phase 2 studies reinforce the potential utility of our carrier-sparing approach and give us confidence in the potential for VAX-24 to provide an additional 10-28 percent of coverage of IPD in adults compared to the standard-of-care PCVs.”

Immunogenicity Results from Phase 2 Study in Adults Aged 65 and Older (n=207)

- VAX-24 showed robust immune responses across all 24 STs at all three doses tested (1.1mcg, 2.2mcg, and 2.2mcg/4.4mcg), confirming the results from the prior Phase 2 study results in adults aged 50-64 (n=771).
- The VAX-24 2.2mcg dose:
  - Achieved target responses, as measured by the geometric mean ratio (GMR) of OPA responses for VAX-24 vs. PCV20, for all 24 STs, supporting the potential of VAX-24 to expand coverage and improve immunogenicity over the standard-of-care.
  - Met the OPA response non-inferiority criteria[(1)] for 18 of 20 STs common with PCV20 and met the superiority criteria[(2)] for all four additional STs unique to VAX-24. The two STs that did not reach the OPA response criteria had GMRs of 0.86 (15B) and 0.71 (22F).
  - Showed higher GMRs for 16 of 20 STs common with PCV20 and an overall improvement in immune responses vs. PCV20 relative to the results from the Phase 2 study in adults aged 50-64.

Full Six-Month Safety Data from Both Adult Studies

The Company also reported the full six-month safety results from the VAX-24 Phase 2 study in adults aged 65 and older and the VAX-24 Phase 1/2 study in adults aged 18-64.

- Through six months, VAX-24 demonstrated safety and tolerability results similar to PCV20 across all ages and doses studied.

- Frequently reported local and systemic reactions were generally mild-to-moderate, resolving within several days of vaccination, with no meaningful difference observed across the cohorts.
- No serious adverse events or new onset chronic illnesses were considered to be related to study vaccines. In a VAX-24 arm of the Phase 2 study in adults aged 65 and older, one participant with multiple pre-existing risk factors suffered a sudden cardiac death six months post-vaccination, which the Principal Investigator determined was not related to study vaccine due to the participant's history of hypertensive cardiovascular disease.

Prespecified Pooled Immunogenicity Analyses of Data from VAX-24 Adult Phase 2 Studies

The Company conducted prespecified pooled analyses of data from both adult Phase 2 studies to evaluate the immunogenicity of VAX-24 in participants aged 50 and older (n~225/group) and aged 60 and older (n~100/group), which are representative populations for the planned VAX-24 Phase 3 pivotal study.

At the VAX-24 2.2mcg dose:

- In both analyses, VAX-24 met the OPA response non-inferiority criteria for all 20 STs common with PCV20 and met the superiority criteria for the four additional STs unique to VAX-24.
- In the pooled group with participants aged 50 and older, VAX-24 met the OPA response non-inferiority criteria for all 20 STs common with PCV20, of which 16 achieved higher immune responses and four reached statistical significance.
- In the pooled group with participants aged 60 and older, VAX-24 met the OPA response non-inferiority criteria for all 20 STs common with PCV20, of which 17 achieved higher immune responses and three reached statistical significance.

Anticipated Key Milestones

Vaxcyte is advancing the clinical development of its PCV programs with several anticipated key upcoming milestones, including:

- ***VAX-24 Adult Program:***
  - Conduct End-of-Phase 2 meeting with the U.S. Food and Drug Administration (FDA) in the second half of 2023 to inform the conduct of the adult Phase 3 program.
  - Announce topline safety, tolerability and immunogenicity data from the Phase 3 pivotal non-inferiority study in adults in 2025.
- ***VAX-24 Infant Program:***
  - Announce topline safety, tolerability and immunogenicity data from the primary three-dose immunization series of the infant Phase 2 study by 2025.
- ***VAX-31 Adult Program:***
  - Submit adult Investigational New Drug (IND) application to FDA in the second half of 2023.
  - Announce topline safety, tolerability and immunogenicity data from Phase 1/2 study in adults in 2024.

Conference Call and Webcast

Vaxcyte will hold a webcast and conference call today, April 17, 2023, at 7:30 a.m. ET / 4:30 a.m. PT to discuss these results. To participate in the conference call, please dial (800) 267-6316 (domestic) or (203) 518-9783 (international) and refer to conference ID PCVX0417. A live webcast of the conference call will also be available on the investor relations page of the Vaxcyte corporate website at www.vaxcyte.com. After the live webcast, the event will remain archived on the Vaxcyte website for 30 days.

About the VAX-24 Adult Clinical Program

Phase 2 Clinical Study in Adults Aged 65 and Older (VAX-24 Study 102, NCT05297578):

This Phase 2 study was a randomized, observer-blind, dose-finding, controlled study designed to evaluate the safety, tolerability and immunogenicity of a single injection of VAX-24 at three dose levels (1.1mcg, 2.2mcg and 2.2mcg/4.4mcg) and compared to a single injection of PCV20 in 207 healthy adults aged 65 and older. The prespecified immunogenicity endpoints of the study included an assessment of the induction of antibody responses, using OPA and Immunoglobulin G (IgG), at one month post-vaccination, for each of the three VAX-24 doses and compared to PCV20 and, for the additional four serotypes contained in VAX-24 and Pneumovax® 23 (PPSV23), but not in PCV20, the percentage of subjects that experienced a four-fold rise in antibody titers. Participants in the study were evaluated for safety through six months post-vaccination. The study enrolled subjects from 19 sites in the United States.

Phase 1/2 Clinical Proof-of-Concept Study in Adults 18-64 Years of Age (VAX-24 Study 101, NCT05266456):

The VAX-24 Phase 1/2 clinical proof-of-concept study was a randomized, observer-blind, dose-finding, controlled study designed to evaluate the safety, tolerability and immunogenicity of VAX-24 in healthy adults aged 18-64. The Phase 1 portion of the study evaluated the safety and tolerability of a single injection of VAX-24 at three dose levels (1.1mcg, 2.2mcg and 2.2mcg/4.4mcg) and compared to PCV20 in 64 healthy adults aged 18-49. The Phase 2 portion evaluated the safety, tolerability and immunogenicity of a single injection of VAX-24 at the same three dose levels and compared to a single injection of PCV20 in 771 healthy adults aged 50-64. The immunogenicity objectives of the Phase 2 portion of the study included an assessment of the induction of antibody responses, using OPA and IgG, at one month post-vaccination, for each of the three VAX-24 doses and compared to PCV20, and for the additional four serotypes contained in VAX-24 (and PPSV23), but not in PCV20, the percentage of subjects that experienced a four-fold rise in antibody titers. Participants in the study were evaluated for safety through six months post-vaccination. The study enrolled subjects from 13 sites in the United States.

About VAX-24

VAX-24 is an investigational 24-valent PCV candidate designed to prevent IPD, which can be most serious for infants, young children, older adults and those with immune deficiencies or certain chronic health conditions. The public health community continues to affirm the need for vaccines that offer broader protection to prevent IPD. VAX-24 is intended to improve upon the standard-of-care PCVs for both children and adults by covering the serotypes that are responsible for most of the pneumococcal disease currently in circulation. Vaxcyte aims to efficiently create and deliver high-fidelity, broad-spectrum vaccines, such as VAX-24, by using modern synthetic techniques, including advanced chemistry and the XpressCF™ cell-free protein synthesis platform. Vaxcyte is deploying this approach with VAX-24 in order to add more pneumococcal strains without compromising the overall immune response.

In January 2023, the FDA granted Breakthrough Therapy designation to VAX-24 for the prevention of IPD in adults. The Breakthrough Therapy designation process is designed to expedite the development and review of drugs that are intended to treat a serious or life-threatening condition.

About Pneumococcal Disease

Pneumococcal disease (PD) is an infection caused by Streptococcus pneumoniae (pneumococcus) bacteria. It can result in IPD, including meningitis and bacteremia, and non-invasive PD, including pneumonia, otitis media and sinusitis. In the United States, approximately 320,000 people get pneumococcal pneumonia each year, which is estimated to result in approximately 150,000 hospitalizations and 5,000 deaths. Pneumococci also cause over 50% of all cases of bacterial meningitis in the United States. Antibiotics are used to treat PD, but some strains of the bacteria have developed resistance to treatments. The morbidity and mortality due to PD are significant, particularly for young children and older adults, underscoring the need for a more broad-spectrum vaccine.

About Vaxcyte

Vaxcyte is a vaccine innovation company engineering high-fidelity vaccines to protect humankind from the consequences of bacterial diseases. The Company is developing broad-spectrum conjugate and novel protein vaccines to prevent or treat bacterial infectious diseases. Vaxcyte's lead candidate, VAX-24, is a 24-valent, broad-spectrum, carrier-sparing PCV being developed for the prevention of IPD. Vaxcyte is re-engineering the way highly complex vaccines are made through modern synthetic techniques, including advanced chemistry and the XpressCF™ cell-free protein synthesis platform, exclusively licensed from Sutro Biopharma, Inc. Unlike conventional cell-based approaches, the Company's system for producing difficult-to-make proteins and antigens is intended to accelerate its ability to efficiently create and deliver high-fidelity vaccines with enhanced immunological benefits. Vaxcyte's pipeline also includes VAX-31, a 31-valent PCV candidate; VAX-A1, a prophylactic vaccine candidate designed to prevent Group A Strep infections; VAX-PG, a therapeutic vaccine candidate designed to slow or stop the progression of periodontal disease; and VAX-GI, a vaccine program designed to prevent Shigella. Vaxcyte is driven to eradicate or treat invasive bacterial infections, which have serious and costly health consequences when left unchecked. For more information, visit www.vaxcyte.com.

Forward-Looking Statements

This press release 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 VAX-24, including breadth of coverage, the ability to deliver a potentially best-in-class PCV and the improvement upon the standard-of-care; the process and timing of anticipated future development of Vaxcyte's vaccine candidates; the timing of the initiation, progress and expected results of Vaxcyte's preclinical studies, clinical trials and research and development plans (including the submission of the IND application for VAX-31 and regulatory interactions and the availability of data for the VAX-24 adult, VAX-24 infant and VAX-31 studies); the demand for Vaxcyte's vaccine candidates; the potential benefits and opportunities available as a result of the Breakthrough Therapy designation for VAX-24 in adults; and other statements that are not historical fact. The words "anticipate," "believe," "could," "expect," "intend," "potential," "should," "would" and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) convey uncertainty of future events or outcomes and 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; 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, without limitation, 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. All forward-looking statements contained in this press release speak only as of the date on which they were made and are based on management's assumptions and estimates as of such date, and readers should not rely upon the information in this press release as current or accurate after its publication date. 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. Readers should not rely upon the information in this press release as current or accurate after its publication date.

(1) Lower bound of the 2-sided 95% confidence interval of the OPA geometric mean ratio is greater than 0.5.

(2) Lower bound of the 2-sided 95% confidence interval of the difference in the proportions of participants with a ≥4-fold increase from Day 1 to Day 29 is greater than 10%, and lower bound of the 2-sided 95% confidence interval of the OPA geometric mean ratio is greater than 2.0.

Contacts:

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VAX-24 Phase 2 Program Results, Including Adult 65+ Data and Full Six-Month Safety Data from Both Studies

April 17, 2023

Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. The
but are not limited to, statements related to the potential benefits of Vaxcyte's vaccine candidates, including breadth of coverage and
potentially best-in-class pneumococcal conjugate vaccine; demand for Vaxcyte's vaccine candidates; the process and timing of anticipa
development and manufacture of Vaxcyte's vaccine candidates; the growth and expansion of the pneumococcal vaccine market; the m
Vaxcyte's vaccines; Vaxcyte's expectations regarding the spectrum coverage, regulatory pathway, adoption speed and immunogenicity
candidates; the timing of the initiation, progress and expected results of Vaxcyte's preclinical studies, clinical trials and research and de
(including the submission of the IND application for VAX-31 and regulatory interactions and the availability of data for the VAX-24 adul
VAX-31 studies); and other statements that are not historical fact. The words "anticipate," "believe," "continue," "could," "designed," "
"intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to ide
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development programs, including development timelines, success and timing of chemistry, manufacturing and controls and related ma
potential delays or inability to obtain and maintain required regulatory approvals for its vaccine candidates; the risks and uncertainties
preclinical and clinical development processes; the success, cost and timing of all development activities and clinical trials; and the suf
other funding to support Vaxcyte's development programs and other operating expenses, any of which could materially and adversely
business and operations. These and other risks are described more fully in Vaxcyte's filings with the Securities and Exchange Commissi
Annual Report on Form 10-K filed with the SEC on February 27, 2023 or in other documents Vaxcyte subsequently files with or furnish
undertakes no duty or obligation to update any forward-looking statements contained in this release as a result of new information, fu
in its expectations.

Agenda

- **INTRODUCTION AND VAX-24 RESULTS OVERVIEW**
- **VAX-24 PHASE 2 STUDY RESULTS IN ADULTS AGED 65 AND OLDER (65+)**
  - Disposition and Demographics
  - Safety and Tolerability Data
  - Immunogenicity Data
- **PRESPECIFIED POOLED IMMUNOGENICITY ANALYSES OF BOTH PHASE 2 ADULT STU**
- **FULL SIX-MONTH SAFETY DATA FROM BOTH ADULT STUDIES**
- **PROGRAM CONCLUSIONS, STATUS AND NEXT STEPS**

Introduction and VAX-24 Results Overview

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Summary: VAX-24 Adult 65+ Study Results Confirm Prior Phase 2 Re

Positive Results Support Best-in-Class Potential for VAX-24 and Set Stage for Phase 3 Design and A

SAFETY: Full six-month safety data from Phase 2 study in adults aged 65+ and prior Phase 1/2 study in ad demonstrate VAX-24 safety and tolerability results similar to Prevnar 20® (PCV20) at all doses studied

IMMUNOGENICITY: 65+ study achieved target responses for all 24 serotypes at 2.2mcg dose, demonstrati VAX-24 to expand coverage and improve immunogenicity over standard-of-care

- Phase 2 65+ study results (n~45/arm): VAX-24 met OPA response non-inferiority criteria for 18/20 STs com and met the superiority criteria for all four additional STs unique to VAX-24
- VAX-24 showed overall improvement in immune responses vs. PCV20 relative to results from Phase 2 in a higher GMRs for 16/20 STs common with PCV20

VAX-24 WELL-POSITIONED FOR ADULT PHASE 3 PIVOTAL PROGRAM

- 2.2mcg confirmed as optimal VAX-24 dose to advance to Phase 3 pivotal study, which will include adults 5
- Prespecified pooled analyses of both Phase 2 adult studies for adults 50+ (n~225/group) and 60+ (n~100/ response non-inferiority criteria for all 20 common STs and met superiority criteria for four additional STs
- End-of-Phase 2 meeting with FDA to confirm study size and population (anticipate n~750/arm)

PLATFORM: New data further support potential of our carrier-sparing PCV franchise and cell-free platform

ANTICIPATED PCV FRANCHISE MILESTONES:

- VAX-24 Adults: End-of-Phase 2 meeting with FDA 2H:23; Phase 3 pivotal immunogenicity data in 2025
- VAX-24 Infants: Phase 2 study enrolling subjects, topline data from the primary three-dose immunization
- VAX-31 Adults: IND application submission 2H:23; topline data from Phase 1/2 study in 2024

OPA = Opsonophagocytic Activity; STs = serotypes; GMR = Geometric Mean Ratio

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Global Impact of Pneumococcal Disease Remains Significant

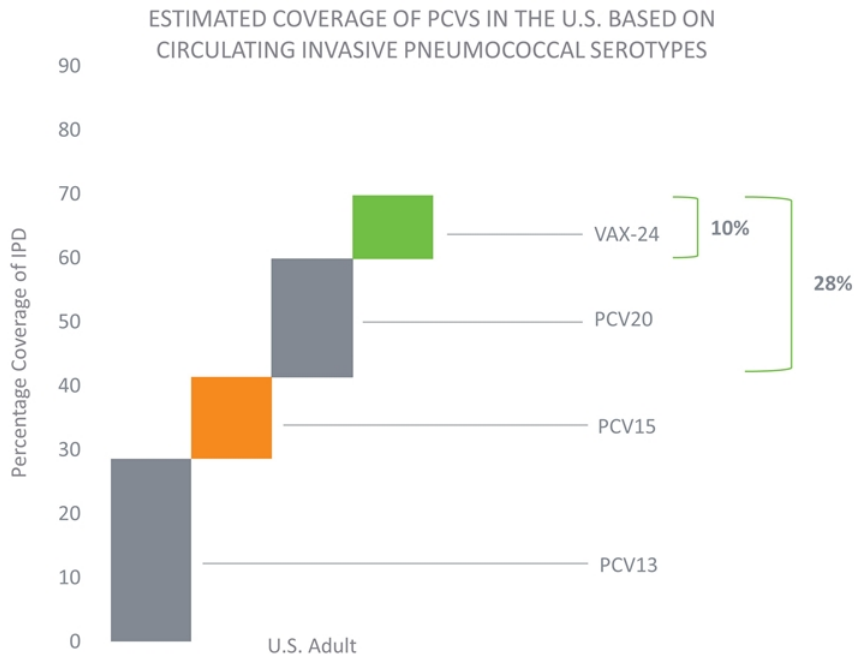
Circulating Disease Driven by Serotypes Outside of Current PCVs

- *Streptococcus pneumoniae* is the most common pathogen causing pneumococcal disease (PD).
  - In the U.S. alone, there are ~320K pneumococcal pneumonia cases per year resulting in ~150K hospitalizations.
  - Invasive pneumococcal disease (IPD) is a leading cause of invasive disease in children two years of age and under.
- Circulating strains of PD in the U.S. and globally are associated with high case-fatality rates, antibiotic resistance and/or meningitis.

Gierke 2015
https://www.cdc.gov/pneumococcal/clinicians/clinical-features.html

Spectrum of Coverage Drives Adoption in PCV Segment

Significant Unmet Needs Remain Despite Available Vaccines



VAX-24 TARGET PRODUCT

- Designed to provide broa coverage of any currently PCV, including an increme 10-28% coverage of IPD ir adults vs. the SOC PCVs (PCV20/PCV15) today.
- Designed to provide the b a conjugate vaccine while surpassing the coverage c Pneumovax 23.

(1) Data in the US is for 2017, inclusi
(2) Varghese et al. Clin Micro and Inf
PCV13 = Prevnar 13®, PCV15 = VAXNE

VAXCYTE

Carrier-Sparing Approach for PCV Franchise Validated By Phase 2 Pr

Site-Specific Conjugation Using Cell-Free Platform to Go Beyond Limits of Conventional Chemistry

LIMITATIONS OF CONVENTIONAL CONJUGATION CHEMISTRY

- Random conjugation masks “on-target” T-cell epitopes on the protein carrier
- Higher ratio of protein carrier to polysaccharide required
- Overabundance of protein carrier and its “off-target” effects exacerbates competition for CD4+ T-cell leading to carrier suppression

VAXCYTE’S UNIQUE CARRIER-SPARING CONJUGATE V

- Site-specifically attach conventional antigens carriers designed to:
  - Enable consistent exposure of T-cell epitopes (a epitopes) on protein carrier to drive class-defin
  - Avoid “off-target” effects from protein carrier t the CD4+ help
  - Enable use of less protein carrier per conjugate sacrificing immunogenicity
- Enable broader-spectrum carrier-sparing co

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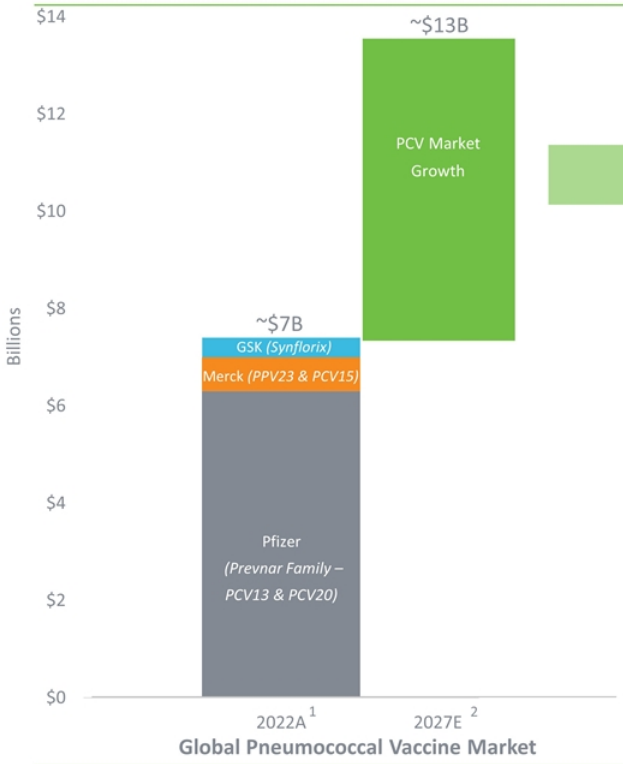
Pneumococcal Vaccine Market Poised for Significant Growth

Expected to Reach ~$13B by 2027 Driven Primarily by Growth in Adult Market



PCV Market Growth Driver

- Strong ACIP consideration to expand U.S. universal adu >50 years from >65 would significantly expand market
- Would necessitate prime-boost for effective long-term which has been limited by continued availability of Pne

- ACIP recently voted to support PCV20 “catch-up” for a previously received PCV13 and Pneumovax 23
- “At risk” adults recently added to U.S. universal PCV va recommendation, which includes >25% of 50-64 year

- Premium price for PCV20 and PCV15 shows value of ad serotype coverage

(1) Sources: Company websites; includes Merck’s PCV15 sales disclosed for Q4 2022.
(2) Global Pneumococcal Vaccine Market (2022-2027), Infogence Global Research.
(3) Shea KM, Edelsberg J, Weycker D et al. (2014), Open Forum Infect Dis 1(1): ofu024.
ACIP = Advisory Committee on Immunization Practices

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VAX-24 Phase 2 Study in Adults 65+

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Study Design

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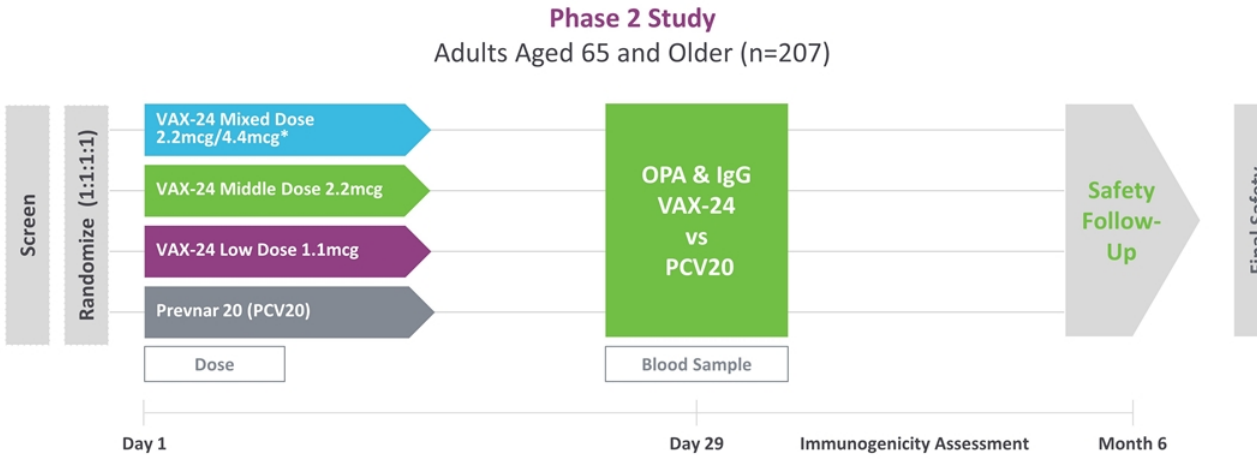
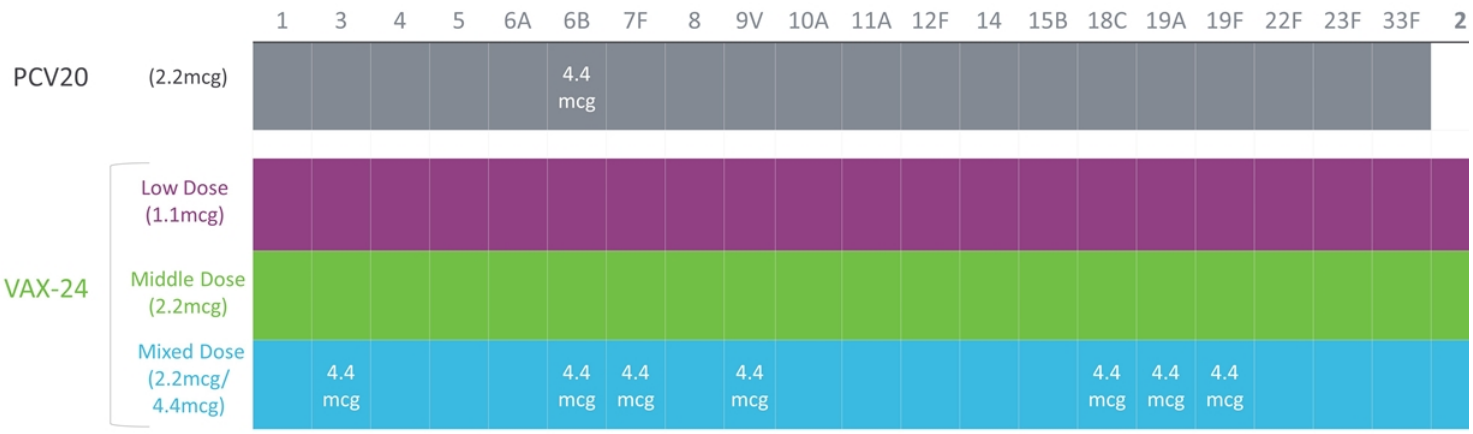
Overview of VAX-24 Phase 2 Clinical Study in Adults 65+

Design: Randomized, Observer-Blind, Dose-Finding, Controlled Clinical Study to Evaluate Safety, Tolerability Immunogenicity of VAX-24 vs. Standard-of-Care (PCV20) in Healthy Adults Aged 65 and Older



** 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.*

Study Evaluated Three VAX-24 Doses Consistent with Prior Phase 2



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

Study Safety, Tolerability and Immunogenicity Key Outcome Measu

	DAY 7	DAY 29	DAY 180
SAFETY AND TOLERABILITY OUTCOME MEASURES	• Solicited local reactions • Solicited systemic events	• Unsolicited adverse events (AE) • Serious adverse events (SAE)	• SAE, new onset of ch illnesses (NOCI) and attended adverse ev
IMMUNOGENICITY OUTCOME MEASURES		• Opsonophagocytic assay (OPA) geometric mean titer (GMT) • IgG geometric mean concentration (GMC) • % of subjects achieving a 4-fold rise in OPA • Geometric Mean Ratios (GMR) in serotype-specific OPA	

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Disposition and Demographics

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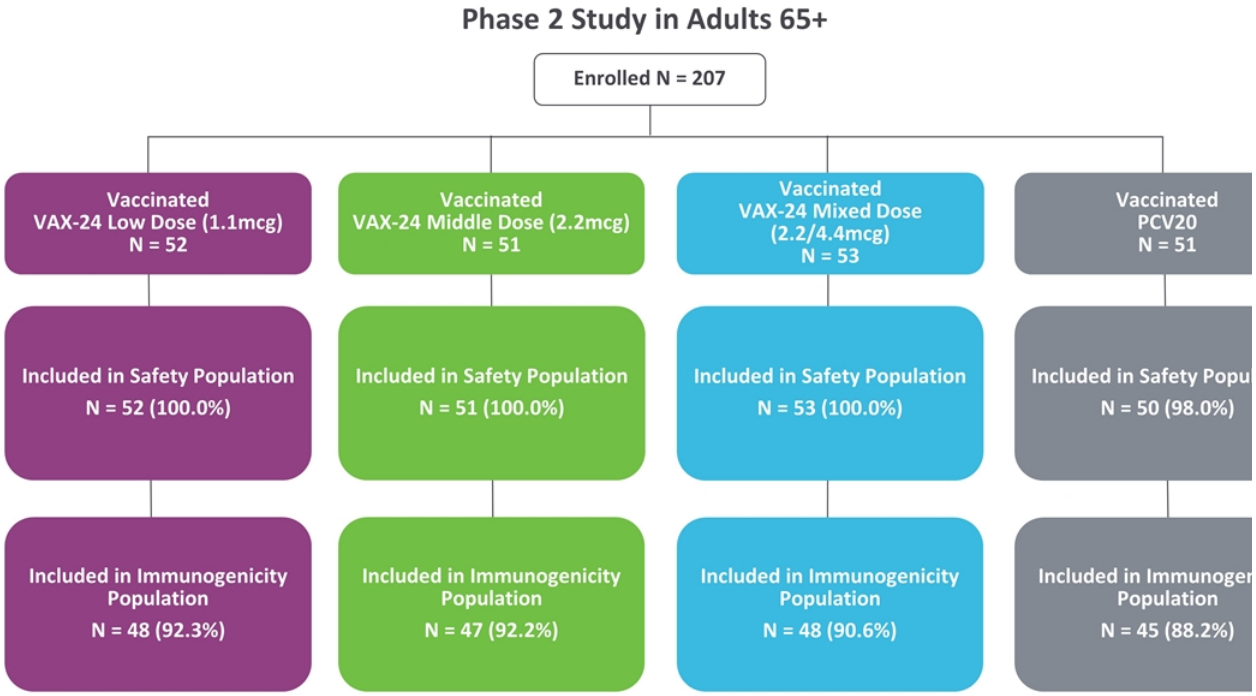
Study Disposition

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



7 Subjects (3.4%) Discontinued

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Demographic Population

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

	VAX-24 Low Dose (1.1mcg)		VAX-24 Middle Dose (2.2mcg)		VAX-24 Mixed Dose (2.2mcg/4.4mcg)		
	Safety	Immunogenicity	Safety	Immunogenicity	Safety	Immunogenicity	Safety
Number of Subjects	52	48	51	47	53	48	50
Median Age, Years (range)	67.5 (65-80)	67.5 (65-80)	66.0 (65-79)	66.0 (65-79)	67.0 (65-88)	67.0 (65-88)	67.0 (65-
Sex, n (%) Female	38 (73.1)	35 (72.9)	34 (66.7)	32 (68.1)	37 (69.8)	33 (68.8)	30 (60.
Male	14 (26.9)	13 (27.1)	17 (33.3)	15 (31.9)	16 (30.2)	15 (31.3)	20 (40.
Race, n (%) White	44 (84.6)	40 (83.3)	40 (78.4)	37 (78.7)	38 (71.7)	33 (68.8)	35 (70.
Black	7 (13.5)	7 (14.6)	10 (19.6)	9 (19.1)	14 (26.4)	14 (29.2)	14 (28.
Asian	0 (0)	0 (0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0
Native Hawaiian	0 (0)	0 (0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0
American Indian or Native Alaskan	1 (1.9)	1 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0
Other	0 (0)	0 (0)	1 (2.0)	1 (2.1)	1 (1.9)	1 (2.1)	0 (0.0
Multiracial	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.0
Median Height, cm (range)	165.5 (146-183)	165.5 (146-183)	166.6 (151-194)	166.6 (151-194)	167.6 (145-188)	167.6 (145-188)	166.5 (150-18
Median Weight, kg (range)	75.05 (50.6-161.9)	74.91 (50.6-161.9)	80.01 (48.5-150.0)	80.70 (48.5-150.0)	86.32 (53.5-130.2)	85.35 (53.5-130.2)	81.33 (47.7-14
Median BMI, kg/m² (range)	27.42 (20.4-50.7)	27.36 (20.4-50.7)	28.92 (19.9-49.2)	29.04 (19.9-49.1)	29.64 (20.1-44.9)	28.99 (20.1-44.9)	29.38 (17.6-52

VAXCYTE

Safety and Tolerability Data

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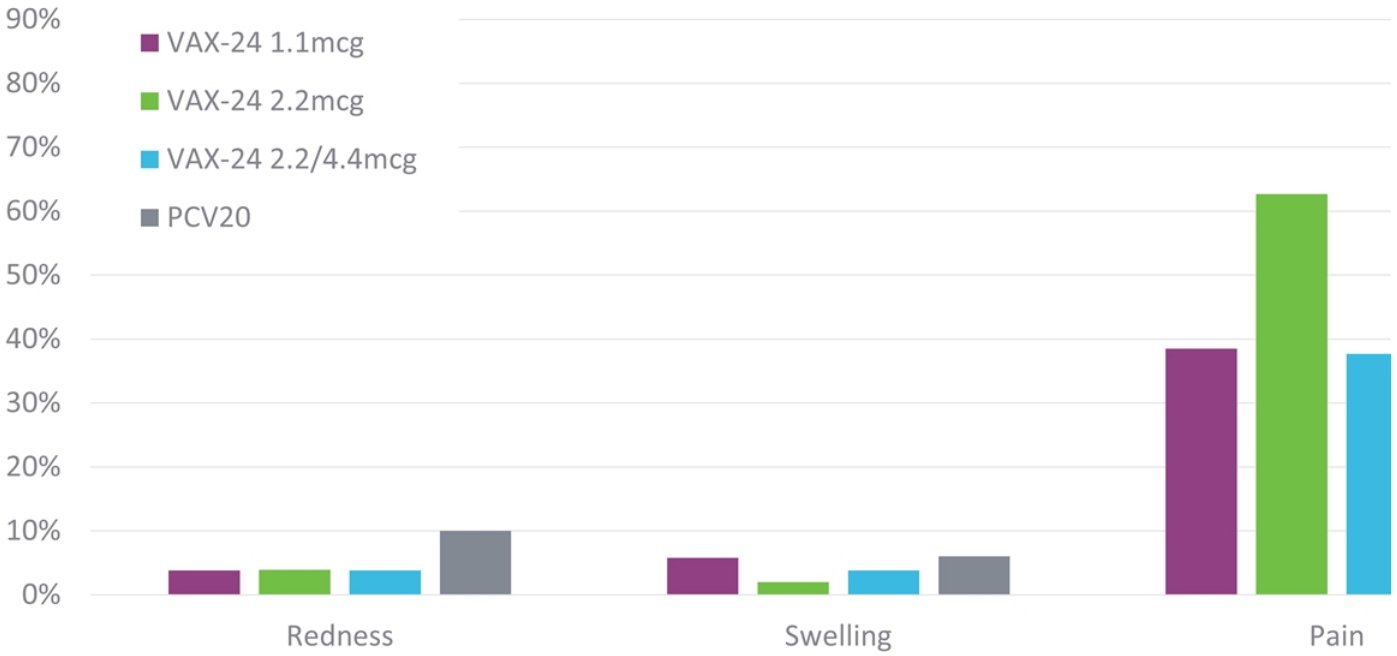
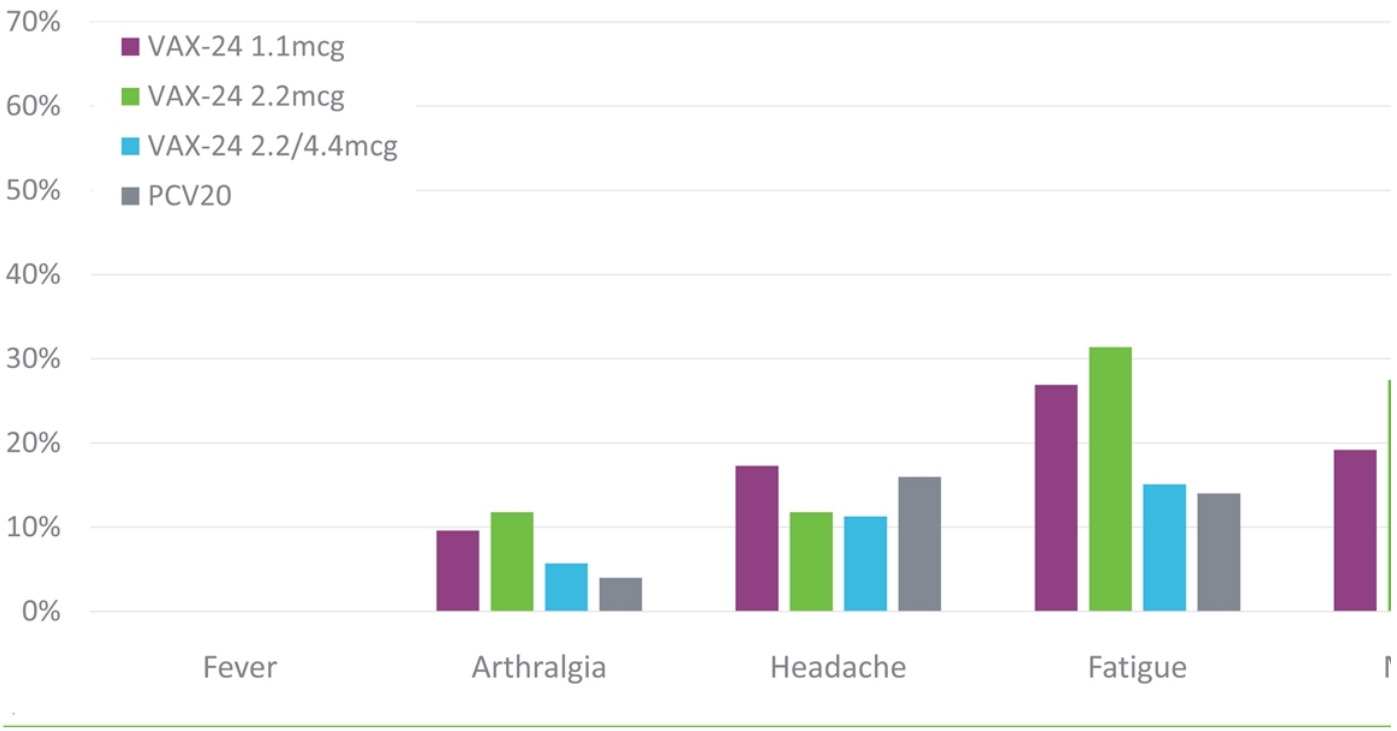
Local Solicited AEs Similar to PCV20 and Across Cohorts Through Da



VAXCYTE

Systemic Solicited AEs Similar to PCV20 and Across Cohorts Throug



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Immunogenicity Data

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Precedent Regulatory Criteria for Phase 2/3 PCV Immunogenicity St

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

Non-inferiority:

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

Superiority:

- Lower bound of 2-sided 95% CI of the OPA GMR is greater than 1.2
- Lower bound of the 2-sided 95% CI of the difference in proportions of participants with a ≥4-fold increase from Day 1 to Day 29 is greater than 0

CRITERIA FOR FOUR INCREMENTAL SEROTYPES IN VAX-24:

Superiority:

- Lower bound of the 2-sided 95% CI of the difference in the proportions of participan with a ≥4-fold increase from Day 1 to Day greater than 10%
- Lower bound of the 2-sided 95% CI of the GMR is greater than 2.0

CI = confidence interval

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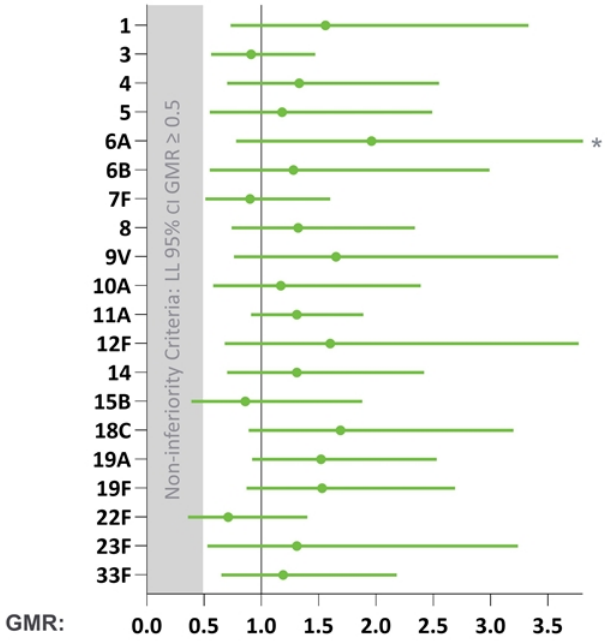
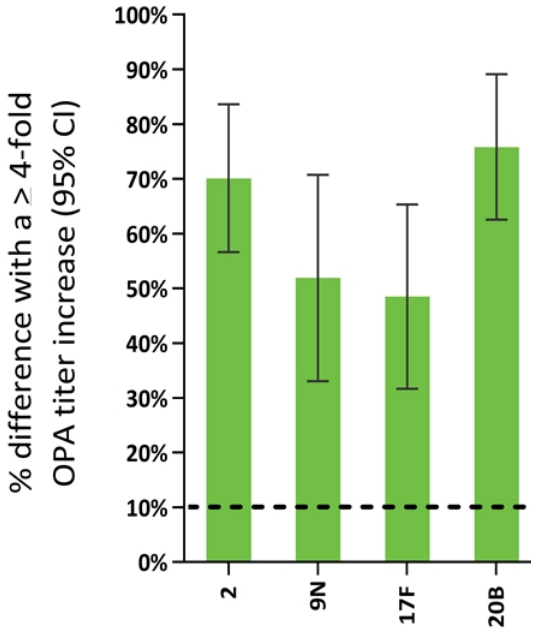
VAX-24 2.2mcg Dose Showed Robust Immune Responses for All 24

Met non-inferiority criteria for 18 of 20 common STs for the OPA GMR of VAX-24 : PCV20 (n~45)



Met superiority criteria for all four inc VAX-24 based on 4-fold rise vs. P

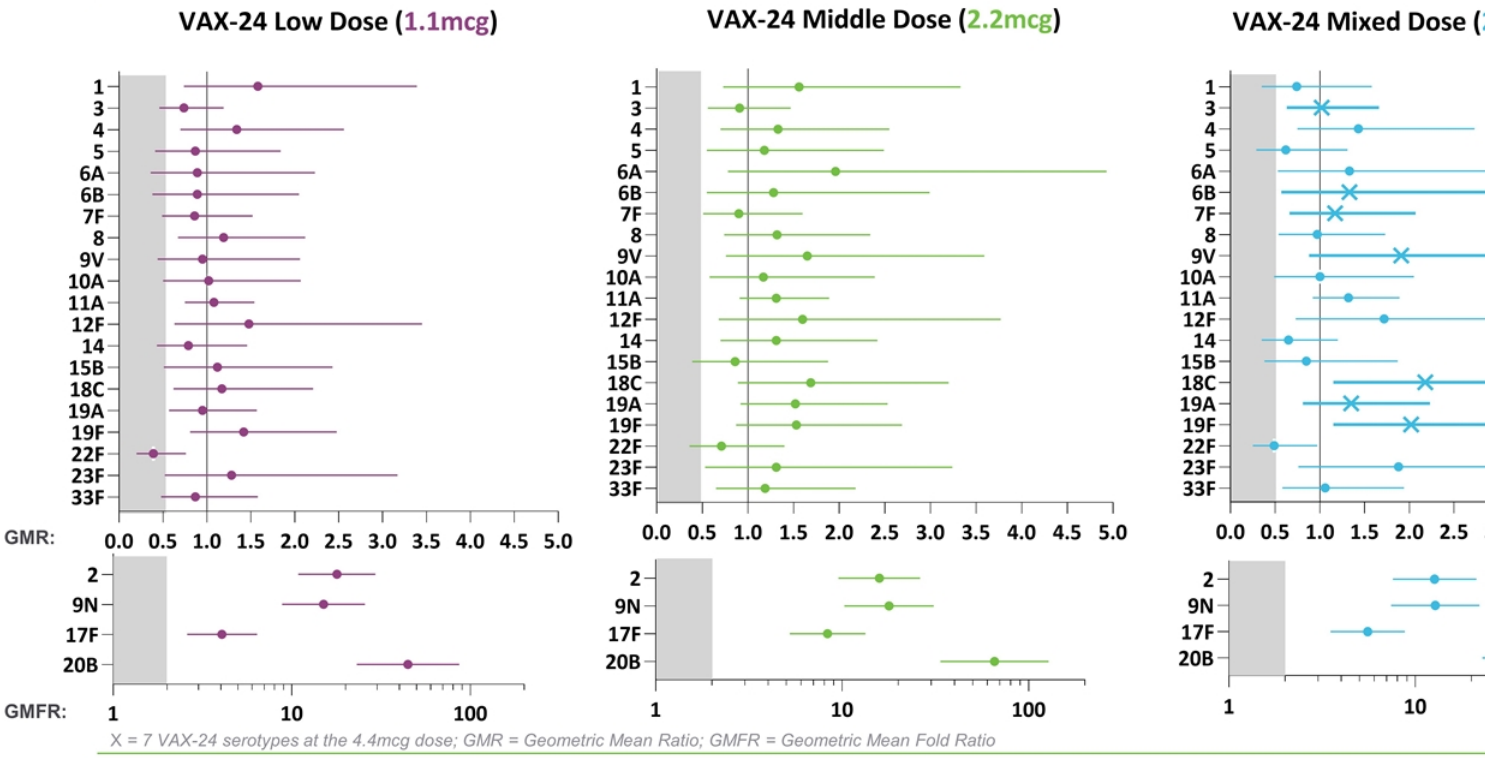


VAXCYTE

* *Upper Limit = 4.93; sample size of 45 calculated as median between immunogenicity evaluable VAX-24 n=47 and PCV20 n=45 rounded to nearest 5*

65+ Study Results Confirm 2.2mcg is Optimal Dose to Advance to P

Consistent with Prior Phase 2 Study, 2.2mcg Dose Demonstrated Higher OPA GMR for 16/20 Share



X = 7 VAX-24 serotypes at the 4.4mcg dose; GMR = Geometric Mean Ratio; GMFR = Geometric Mean Fold Ratio

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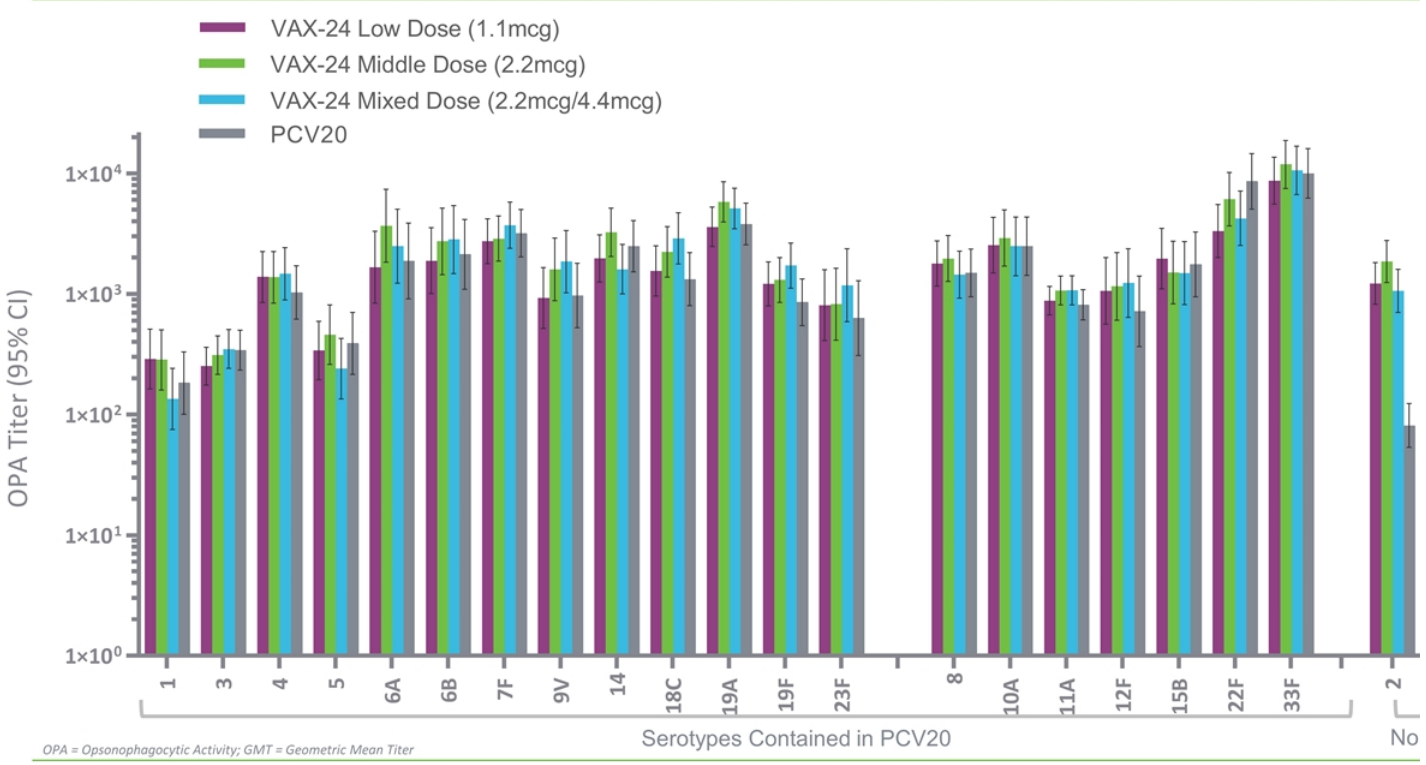
All 24 Serotypes in VAX-24 Demonstrated Robust OPA GMT Immun



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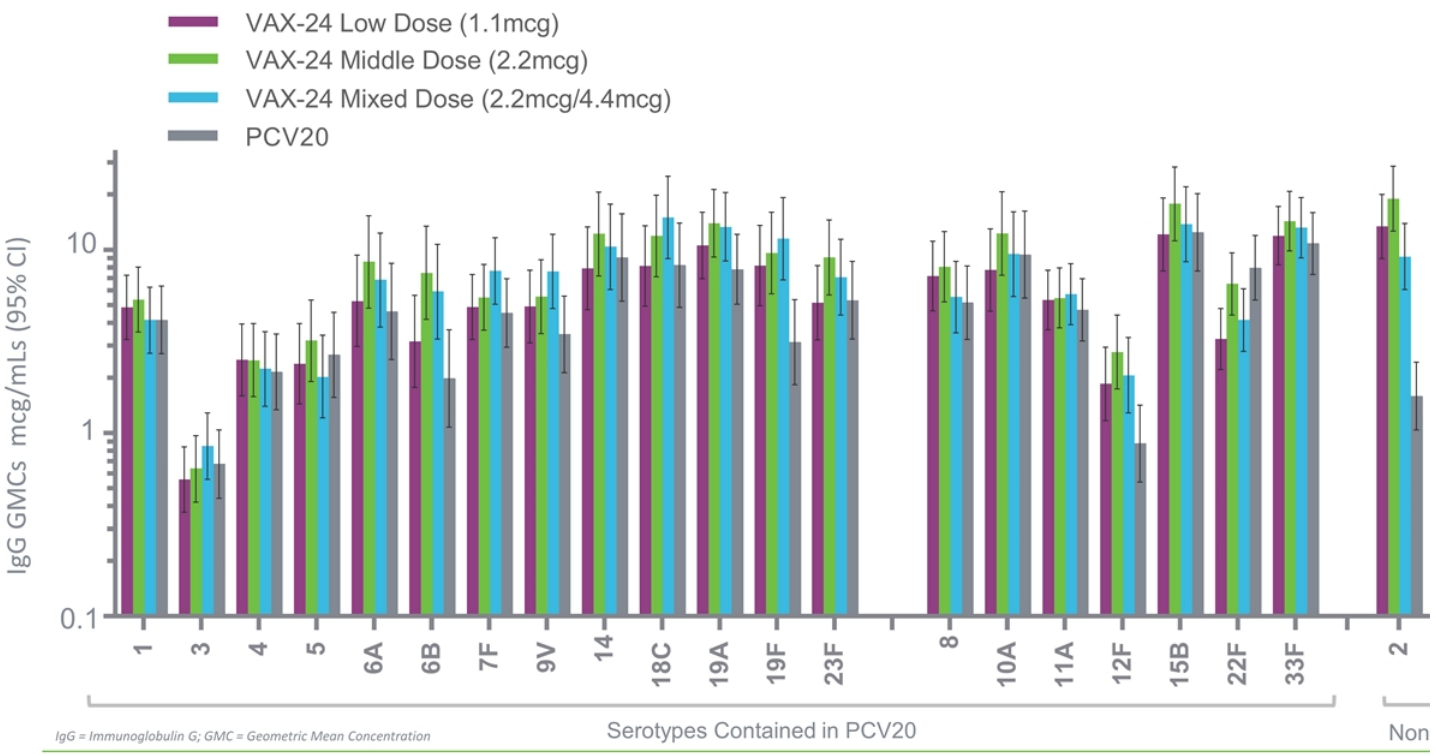
All 24 Serotypes in VAX-24 Demonstrated Robust IgG GMC Respons



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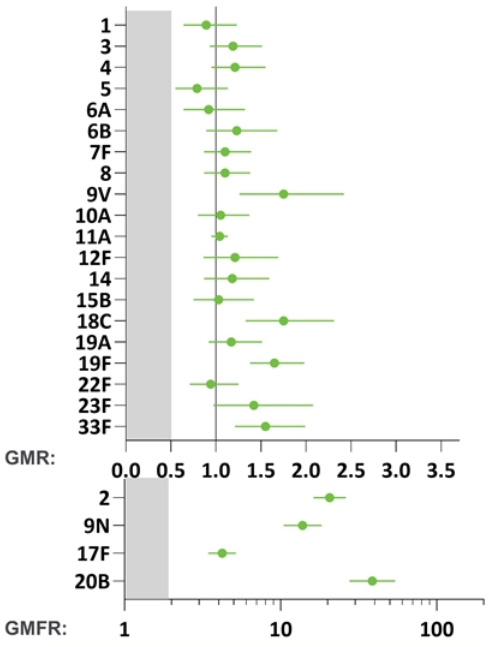
Prespecified Pooled Immunogenicity Analyses of Both VAX-24 Phase 2 Adult Studies

VAXCYTE

Phase 2 Program Confirms 2.2mcg as Optimal Dose in Adult Popula

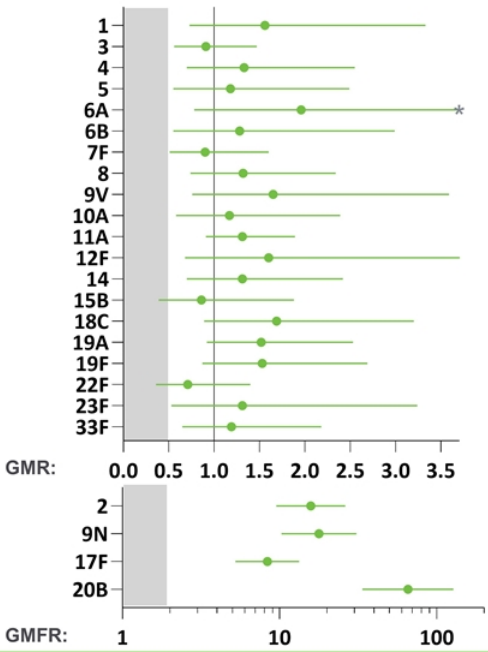
65+ Study Data Show Further Improvement in Overall Immune Response vs. PCV20

VAX-24 Phase 2 Study in Adults Aged 50-64
2.2mcg (n~180)



ST	GMR	95%CI	
1	0.89	1.23	0.64
3	1.19	1.51	0.93
4	1.21	1.55	0.95
5	0.79	1.13	0.55
6A	0.92	1.32	0.64
6B	1.23	1.68	0.89
7F	1.1	1.39	0.87
8	1.1	1.38	0.87
9V	1.75	2.42	1.26
10A	1.05	1.37	0.8
11A	1.04	1.13	0.95
12F	1.21	1.69	0.86
14	1.18	1.59	0.87
15B	1.03	1.42	0.75
18C	1.75	2.31	1.33
19A	1.17	1.51	0.92
19F	1.65	1.98	1.38
22F	0.94	1.25	0.71
23F	1.42	2.08	0.97
33F	1.55	1.99	1.21

VAX-24 Phase 2 Study in Adults Aged 65+
2.2mcg (n~45)



ST
1
3
4
5
6A
6B
7F
8
9V
10A
11A
12F
14
15B
18C
19A
19F
22F
23F
33F

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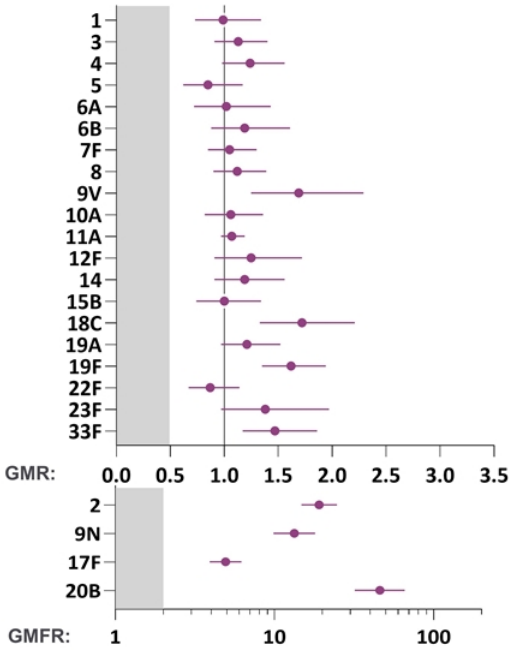
* *Upper Limit = 4.93; sample size of 180 calculated as median between immunogenicity evaluable VAX-24 n=179 and PCV20 n=181 rounded to nearest 10.*

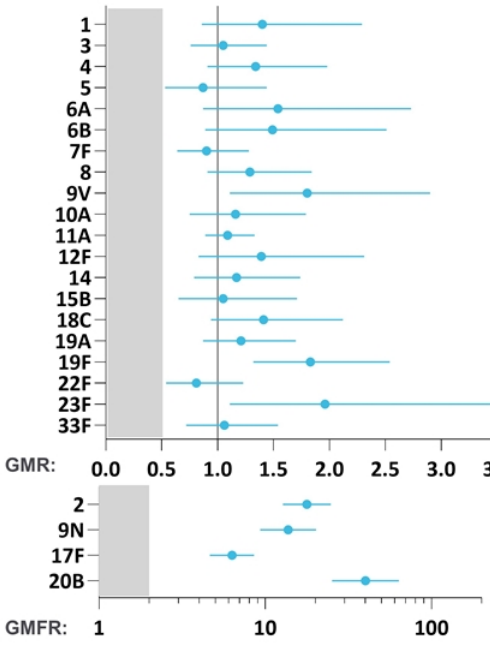
Prespecified Pooled Analyses Support Advancement of VAX-24 to P

Met Standard OPA Response Non-Inferiority Criteria for All 20 Common STs

Prespecified Pooled Data From VAX-24 2.2mcg Phase 2 Studies in Adults Aged 50+ (n~225)



Prespecified Pooled Data From VAX-24 Phase 2 Studies in Adults Aged 60+ (n



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Sample size of ~225 calculated as median between immunogenicity evaluable VAX-24 n=228 and PCV20 n=224 rounded to nearest 5 for 50+ and ~100 calculated as median between immunogenicity evaluable VAX-24 n=101 and PCV20 n=104 rounded to nearest 5 for 60+.

Full Six-Month Safety and Tolerability Data from Both VAX-24 Adult Studies

VAXCYTE

Six-Month Safety Data from VAX-24 Phase 2 Study in Adults Aged 6

Safety Results Similar to PCV20 and Across Cohorts

	VAX-24 – Low Dose (1.1mcg)	VAX-24 – Middle Dose (2.2mcg)	VAX-24 – Mixed Dose (2.2mcg/4.4mcg)	P
Number of Subjects with	52	51	53	
Unsolicited TEAE, n (%)	6 (11.5)	4 (7.8)	4 (7.5)	8
Related Unsolicited TEAE, n (%)	1 (1.9)	4 (7.8)	2 (3.7)	5
MAAE, n (%)	5 (9.6)	3 (5.9)	3 (5.7)	6
Related MAAE, n (%)	0	0	1 (1.9)	
NOCI, n (%)	1 (1.9)	1 (2.0)	1 (1.9)	
Related NOCI, n (%)	0	0	0	
SAE, n (%)	1 (1.9)	1 (2.0)	1 (1.9)	
Related SAE, n (%)	0	0	0	
Death, n (%)	0	1 (2.0)[1]	0	
Related Death, n (%)	0	0	0	

(1) 66-year-old white, obese male (BMI:47.4) with hypertension. No solicited AEs were reported after vaccination. Participant suffered sudden cardiac death six months post-vacci Principal Investigator to be not related to study product due to participant's history of hypertensive cardiovascular disease.

TEAE = Treatment emergent adverse events

Excludes Solicited AEs

VAXCYTE

Six-Month Safety Data from VAX-24 Phase 1/2 Study in Adults Aged

Safety Results Similar to PCV20 and Across Cohorts

	VAX-24 – Low Dose (1.1mcg)	VAX-24 – Middle Dose (2.2mcg)	VAX-24 – Mixed Dose (2.2mcg/4.4mcg)	P
Number of Subjects with	209	207	207	
Unsolicited TEAE, n (%)	32 (15.3)	24 (11.6)	26 (12.6)	34
Related Unsolicited TEAE, n (%)	4 (1.9)	9 (4.3)	5 (2.4)	8
MAAE, n (%)	27 (12.9)	26 (12.6)	24 (11.6)	31
Related MAAE, n (%)	0	0	0	
NOCI, n (%)	3 (1.4)	3 (1.4)	6 (2.9)	5
Related NOCI, n (%)	0	0	0	
SAE, n (%)	2 (1.0)	3 (1.4)	1 (0.5)	4
Related SAE, n (%)	0	0	0	
Death, n (%)	0	0	0	
Related Death, n (%)	0	0	0	

TEAE = Treatment emergent adverse events
Excludes Solicited AEs

VAXCYTE

Combined Six-Month Safety Data from Both Adult VAX-24 Studies

Safety Results Similar to PCV20 and Across Cohorts

	VAX-24 – Low Dose (1.1mcg)	VAX-24 – Middle Dose (2.2mcg)	VAX-24 – Mixed Dose (2.2mcg/4.4mcg)	
Number of Subjects with	261	258	260	
Unsolicited TEAE, n (%)	38 (14.6)	28 (10.9)	30 (11.5)	
Related Unsolicited TEAE, n (%)	5 (1.9)	13 (5.0)	7 (2.7)	
MAAE, n (%)	32 (12.2)	29 (11.2)	27 (10.4)	
Related MAAE, n (%)	0	0	1 (0.4)	
NOCI, n (%)	4 (1.5)	4 (1.6)	7 (2.7)	
Related NOCI, n (%)	0	0	0	
SAE, n (%)	3 (1.1)	4 (1.6)	2 (0.77)	
Related SAE, n (%)	0	0	0	
Death, n (%)	0	1 (0.39)[1]	0	
Related Death, n (%)	0	0	0	

(1) 66-year-old white, obese male (BMI:47.4) with hypertension. No solicited AEs were reported after vaccination. Participant suffered sudden cardiac death six months post-vacci Principal Investigator to be not related to study product due to participant's history of hypertensive cardiovascular disease.

TEAE = Treatment emergent adverse events

Excludes Solicited AEs

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Phase 2 Program Conclusions, Status & Next Steps

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Positive Phase 2 Program Results Support Best-in-Class Potential fo and Set Stage for Phase 3 Program

SUCCESSFUL VAX-24 PHASE 2 PROGRAM MET ALL KEY OBJECTIVES

- Full six-month VAX-24 data (n=779) showed safety and tolerability results similar to PCV20
- Improved immunogenicity vs. PCV20 with no evidence of dose-dependent safety and tolerability issues
- Confirmed 2.2mcg as optimal dose to advance to Phase 3 pivotal study
  - Achieved target immune responses for all 24 serotypes in both Phase 2 studies
  - Met non-inferiority criteria for all 24 STs in prespecified pooled analyses, with sample sizes expected to increase in Phase 3 program (n~750/arm)

WELL-POSITIONED FOR PHA PIVOTAL PROGRAM

- Well-established regulatory pathwa multiple precedents of approval ba surrogate immune endpoints
- Historically, consistent study design across Phase 2 and pivotal Phase 3
- Precedent Phase 3 programs and V data support flexibility of choice in age range for pivotal study
- With positive Phase 2 data, Vaxcyte advance VAX-24 into Phase 3

Anticipated PCV Franchise Milestones for 2023-2025[1]

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

VAX-24 Adult

- Conduct FDA End-of-Phase 2 meeting to finalize adult Phase 3 program in **2H:23**
- Announce topline safety, tolerability and immunogenicity data from the Phase 3 pivotal non-inferiority study in adults in **2025**

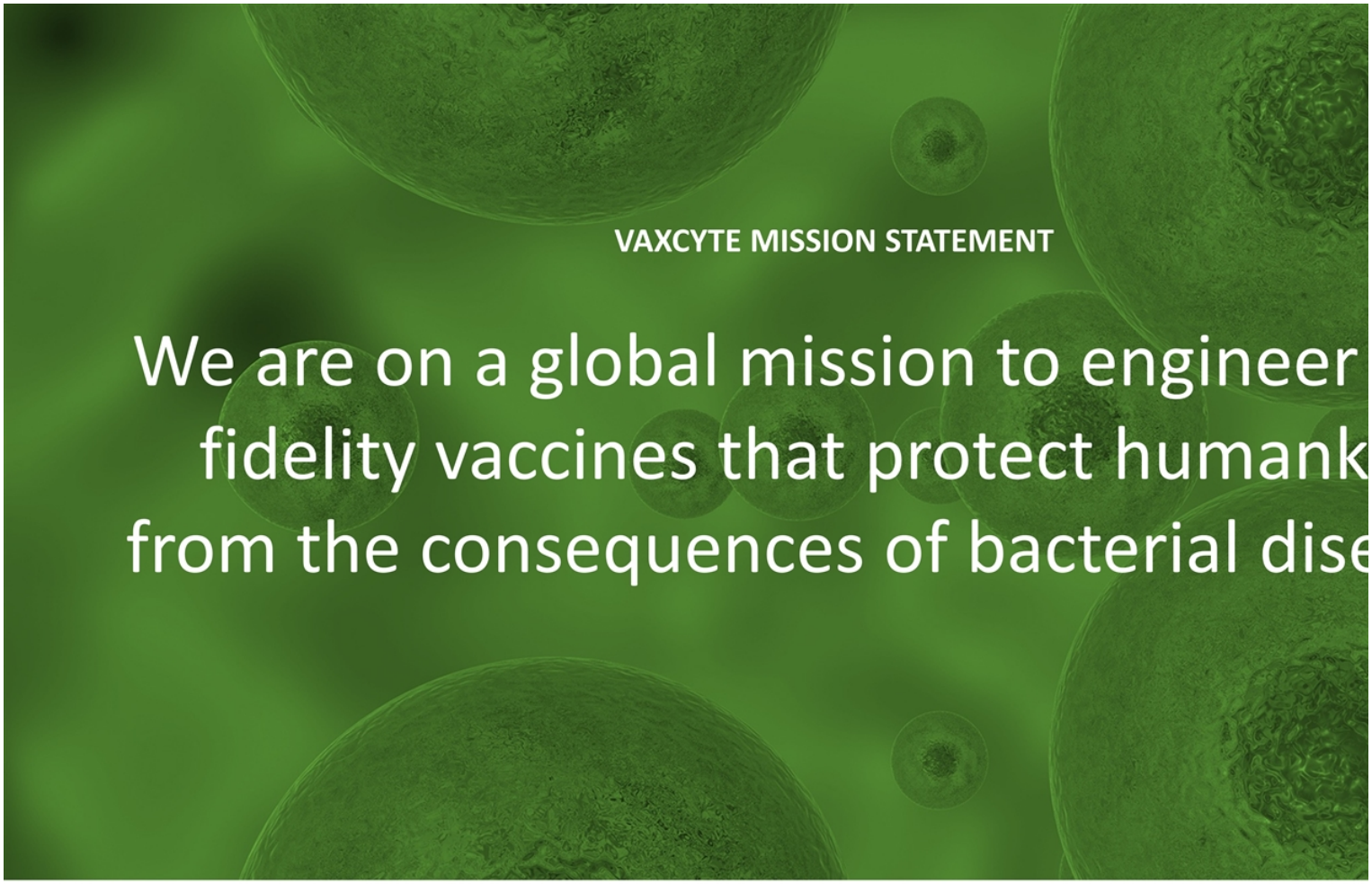
VAX-24 Infant

- Announce topline safety, tolerability and immunogenicity data from the primary three-dose immunization series of the Phase 2 study by **2025**

VAX-31 Adult

- Submit adult IND ap
  FDA in **2H:23**
- Announce topline sa
  tolerability and imm
  data from adult Pha
  in **2024**

(1) Guidance provided as of April 17, 2023.


VAXCYTE MISSION STATEMENT
We are on a global mission to engineer
fidelity vaccines that protect humank
from the consequences of bacterial dise

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Q&A with Management

Grant Pickering
Chief Executive Officer, Director and Founder

Jim Wassil
Executive Vice President and Chief Operating Officer

Andrew Gugge
President and Chief


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protect humankind