Vaxcyte Reports Positive Topline Data from Phase 1/2 Proof-of-Concept Study of its 24-Valent Pneumococcal Conjugate Vaccine Candidate Being Investigated for the Prevention of Invasive Pneumococcal Disease in Adults Aged 18-64

October 24, 2022

-- In the Study, VAX-24 Demonstrated a Safety and Tolerability Profile Similar to Prevnar 20™ (PCV20) at All Doses Studied --

-- All 24 Serotypes of VAX-24 at Conventional 2.2mcg PCV Dose Met or Exceeded Regulatory Immunogenicity Standards --

-- All 20 VAX-24 Serotypes Common with PCV20 Met Standard OPA Response Non-Inferiority Criteria, of Which 16 Achieved Higher Immune Responses, at 2.2mcg VAX-24 Dose --

-- All 4 Serotypes Unique to VAX-24 Exceeded Standard Superiority Criteria --

-- Vaxcyte to Advance Potential Best-in-Class VAX-24 Clinical Program in Adult and Pediatric Populations --

-- Company to Host Webcast/Conference Call Today at 8:00 a.m. ET / 5:00 a.m. PT --

SAN CARLOS, Calif., Oct. 24, 2022 (GLOBE NEWSWIRE) -- 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 topline results from the Phase 1/2 clinical proof-of-concept study evaluating the safety, tolerability and immunogenicity of VAX-24, the Company's investigational 24-valent pneumococcal conjugate vaccine (PCV), in healthy adults aged 18-64. In this study, VAX-24 met the primary safety and tolerability objectives, demonstrating a safety profile similar to Prevnar 20™ (PCV20) for all doses studied.

In the study, VAX-24 met or exceeded the established regulatory immunogenicity standards for all 24 serotypes at the conventional 2.2mcg dose, which the Company intends to move forward into a Phase 3 program. At this dose, VAX-24 met the standard opsonophagocytic activity (OPA) response non-inferiority criteria for all 20 serotypes common with PCV20, of which 16 achieved higher immune responses. Additionally, at all three doses, VAX-24 met the standard superiority criteria for all four serotypes unique to VAX-24. These four incremental serotypes cover 10-15 percent of strains causing invasive pneumococcal disease (IPD) over the current standard-of-care in adults.

"We are thrilled with these positive topline results from our Phase 1/2 proof-of-concept study, which met all of our objectives. The findings indicate a potential best-in-class profile for VAX-24 and validate our carrier-sparing approach to enable the development of broader-spectrum PCVs," said Grant Pickering, Chief Executive Officer and Co-Founder of Vaxcyte. "The study results demonstrate that VAX-24 has the potential to provide broader coverage and better immune responses relative to the standard-of-care. We believe this presents an opportunity to set a new bar for immunogenicity standards for pneumococcal vaccines."

Key Topline Study Results
Safety and Tolerability Findings:

- VAX-24 demonstrated a safety and tolerability profile similar to PCV20 at all doses studied.
- Frequently reported local and systemic reactions were generally mild-to-moderate, resolving within several days of vaccination, with no difference observed across the cohorts. No serious adverse events or new onset chronic illnesses were considered to be related to study vaccines.
- The full six-month safety follow-up is ongoing for the Phase 2 portion of the study.

Immunogenicity Findings:

- VAX-24 demonstrated robust OPA and immunoglobulin G (IgG) immune responses for all 24 serotypes at all doses studied (1.1mcg, 2.2mcg, 2.2mcg/4.4mcg), each of which could advance into Phase 3.
- The VAX-24 2.2mcg dose met or exceeded the established regulatory immunogenicity standards for all 24 serotypes and is the dose the Company expects to advance into Phase 3.
- At the 2.2mcg dose, VAX-24 met the standard OPA response non-inferiority criteria[(1)] for all 20 serotypes common with PCV20, of which 16 serotypes (3, 4, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 23F and 33F) achieved higher immune responses and four serotypes (9V, 18C, 19F and 33F) reached statistical significance.
- At all three doses, VAX-24 met the standard superiority criteria[(2)] for all four serotypes (2, 9N, 17F and 20B) unique to VAX-24.

"We are very excited to share these strong clinical results from our proof-of-concept study, which validate the potential for VAX-24 to improve upon the standard-of-care for adults by potentially providing 10-15 percent incremental protection for this serious disease. The 24 serotypes included in VAX-24

cover a significant portion of the IPD currently in circulation and are associated with high case-fatality rates, antibiotic resistance and meningitis," said Jim Wassil, Executive Vice President and Chief Operating Officer of Vaxcyte. "On behalf of our team at Vaxcyte, we would like to gratefully acknowledge the efforts of everyone involved in this program, especially the trial investigators, trial sites and study participants."

About the Phase 1/2 Clinical Proof-of-Concept Study
The VAX-24 Phase 1/2 clinical proof-of-concept study is a randomized, observer-blind, dose-finding, controlled study designed to evaluate the safety, tolerability and immunogenicity of VAX-24 in healthy adults 18-64 years of age.

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 18 to 49 years of age.

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 50 to 64 years of age. The immunogenicity objectives of the Phase 2 portion of the study include an assessment of the induction of antibody responses, using OPA and IgG, at each of the three VAX-24 doses and compared to PCV20, and for the additional four serotypes contained in VAX-24 (and Pneumovax® 23), but not in PCV20, the percentage of subjects that experience a four-fold rise in antibody titers. Participants in the study will be evaluated for safety through six months after vaccination. Additional information about the study can be found at www.clinicaltrials.gov under the identifier NCT05266456.

Key Anticipated PCV Franchise Milestones
Vaxcyte is advancing the clinical development of its PCV programs with several anticipated key milestones, including:

VAX-24 Adult Program

- Topline safety, tolerability and immunogenicity data from the Phase 2 study in adults 65 and older are anticipated in the first half of 2023.
- Final results with the 6-month safety data of the Phase 2 adult studies are anticipated in the first half of 2023.
- Regulatory interactions to inform the Phase 3 program are anticipated in the second half of 2023.
- Topline safety, tolerability and immunogenicity data from the Phase 3 non-inferiority study in adults are expected in 2025.

VAX-24 Pediatric Program

- The infant Investigational New Drug (IND) application submission and the Phase 2 study initiation are both anticipated in first half of 2023.
- Topline safety, tolerability and immunogenicity data from the infant Phase 2 study primary 3-dose immunization series are expected by 2025.

VAX-XP Adult Program

- The IND application submission for VAX-XP, Vaxcyte's PCV candidate with 31 strains, is anticipated in the second half of 2023.
- Topline safety, tolerability and immunogenicity data from a Phase 1/2 study in adults are expected in 2024.

Conference Call and Webcast
Vaxcyte will hold a webcast and conference call today, Monday, October 24 at 8:00 AM ET to provide topline results from its VAX-24 Phase 1/2 proof-of-concept study. Those who would like to participate may access the live webcast here, or register in advance for the teleconference here. 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 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 August 2022, the FDA granted Fast Track Designation to VAX-24 for the adult indication. The Fast Track designation is an FDA process that has been designed to expedite the development and review of drugs, including vaccines, that treat or prevent serious conditions and fill an important unmet medical need.

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 900,000 people get pneumococcal pneumonia each year, which is estimated to result in approximately 150,000 hospitalizations and 28,000 deaths. Pneumococci also cause over 50% of all cases of bacterial meningitis in the United States. Antibiotics are used to treat pneumococcal disease, but some strains of the bacteria have developed resistance to treatments. The morbidity and mortality due to pneumococcal disease are highly 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 pneumococcal conjugate vaccine 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-XP, a PCV with coverage of 31 strains; VAX-A1, a prophylactic vaccine candidate designed to prevent Group A Strep infections; and VAX-PG, a therapeutic vaccine candidate designed to slow or stop the progression of periodontal disease. 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 improvement upon the standard-of-care; 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 and submission of an IND application for 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-XP adult program and the timing and availability of the Phase 1/2 topline data for such program; the demand for Vaxcyte's vaccine candidates; 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; impacts of COVID-19; 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 Quarterly Report on Form 10-Q filed with the SEC on August 8, 2022 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

(1) Lower bound of the 2-sided 95% confidence interval of the OPA geometric mean titer 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 titer ratio is greater than 2.0.

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