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

April 17, 2023

-- 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 (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 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.

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