Vaxcyte Reports Positive Topline Data from Phase 1/2 Study of VAX-31, its 31-Valent Pneumococcal Conjugate Vaccine Candidate, in Adults Aged 50 and Older

September 3, 2024

-- At All Doses Studied, VAX-31 Demonstrated Robust Opsonophagocytic Activity Immune Responses for All 31 Serotypes --

-- At Middle and High Doses, VAX-31 Met or Exceeded Regulatory Immunogenicity Criteria for All 31 Serotypes --

-- At All Doses Studied, VAX-31 Was Observed to be Well Tolerated and Demonstrated a Safety Profile Similar to Prevnar 20® --

-- Topline Results Further Validate Potential of Vaxcyte's Carrier-Sparing Platform to Deliver Broadest-Spectrum Pneumococcal Conjugate Vaccine Candidates that Provide Protection Against Both Currently Circulating and Historically Prevalent Serotypes --

-- For Adult Indication, VAX-31 Selected to Advance to Phase 3 Program; Vaxcyte Plans to Initiate Phase 3 Pivotal, Non-Inferiority Study by Mid-2025 and Announce Topline Safety, Tolerability and Immunogenicity Data in 2026 --

-- For Pediatric Indication, in Parallel with Ongoing VAX-24 Study, Company Plans to Initiate VAX-31 Infant Phase 2 Study in First Quarter of 2025 Following IND Application Submission and Clearance --

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

SAN CARLOS, Calif., Sept. 03, 2024 (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 study evaluating the safety, tolerability and immunogenicity of VAX-31, the Company's 31-valent pneumococcal conjugate vaccine (PCV) candidate designed to prevent invasive pneumococcal disease (IPD), in 1,015 healthy adults aged 50 and older. Based on the strength of the results from this study, the Company has selected VAX-31 to advance to an adult Phase 3 program.

In this Phase 1/2 study, VAX-31 was observed to be well tolerated and demonstrated a safety profile at all doses studied through the full six-month evaluation period similar to Prevnar 20® (PCV20). VAX-31 showed robust opsonophagocytic activity (OPA) immune responses for all 31 serotypes at all doses studied. At the middle and high doses, VAX-31 met or exceeded the OPA response non-inferiority criteria(1) for all 20 serotypes common with PCV20. At the VAX-31 high dose, average OPA immune responses were greater for 18 of 20 serotypes compared to PCV20 (geometric mean ratio (GMR) greater than 1.0), with seven of these serotypes achieving statistically higher immune responses(2) compared to PCV20. At the middle dose, 13 of 20 serotypes had a GMR greater than 1.0 and five serotypes achieved statistically higher immune responses compared to PCV20. For all 11 incremental serotypes unique to VAX-31, and not in PCV20, all three doses met the superiority criteria(3). The Company plans to select the VAX-31 dose prior to the initiation of the adult Phase 3 program.

"We believe the positive safety, tolerability and immunogenicity results from the VAX-31 Phase 1/2 study affirm the potential of our site-specific, carrier-sparing platform to deliver the broadest-spectrum PCVs that provide protection against both currently circulating and historically prevalent strains," said Grant Pickering, Chief Executive Officer and Co-Founder of Vaxcyte. "Based on the strength and clarity of these data, we have selected VAX-31 for the adult indication and plan to initiate the pivotal, non-inferiority Phase 3 study by mid-2025 and announce topline data in 2026. We intend to initiate the remaining VAX-31 Phase 3 studies in 2025 and 2026 and submit a Biologics License Application subject to the results of these studies."

"We are exceptionally proud to share these results, which we believe validate VAX-31's potential as a best-in-class pneumococcal vaccine capable of raising the bar for immunogenicity standards," said Jim Wassil, Executive Vice President and Chief Operating Officer of Vaxcyte. "The public health community continues to highlight the need for broader-protection vaccines to prevent IPD, which is associated with high case-fatality rates, antibiotic resistance and meningitis. To address this need, VAX-31 was designed to increase coverage to more than 95% of IPD circulating in adults 50 and older in the United States, with the potential to provide significantly greater coverage relative to today's standard-of-care adult PCVs. We want to extend our sincere gratitude to everyone involved in this program, especially the study participants, trial investigators and sites, and the entire Vaxcyte team."

Key Topline Study Results

Safety and Tolerability Findings:

- Based on the full six-month safety data, VAX-31 was observed to be well tolerated and demonstrated a safety 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 meaningful differences observed across the cohorts. No serious adverse events were considered to be related to study vaccines.

Immunogenicity Findings:

VAX-31 showed robust OPA immune responses for all 31 serotypes at all doses studied, and all three doses would be advanceable to Phase 3.

- At the high and middle doses, VAX-31 met or exceeded the regulatory immunogenicity criteria for all 31 serotypes and, at the low dose, for 29 of 31 serotypes.
- For the 20 serotypes common with PCV20 (1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, 33F):
    - At the high dose, all 20 serotypes met the OPA response non-inferiority criteria, 18 of 20 serotypes had a GMR greater than 1.0 and seven serotypes achieved statistically higher immune responses.
    - At the middle dose, all 20 serotypes met the OPA response non-inferiority criteria, 13 of 20 serotypes had a GMR greater than 1.0 and five serotypes achieved statistically higher immune responses.
    - At the low dose, 18 of 20 serotypes met the OPA response non-inferiority criteria, 8 of 20 serotypes had a GMR greater than 1.0 and three serotypes achieved statistically higher immune responses.
- For all 11 additional serotypes unique to VAX-31 (2, 7C, 9N, 15A, 16F, 17F, 20B, 23A, 23B, 31, 35B), and not in PCV20, all three doses met the superiority criteria.

About the VAX-31 Phase 1/2 Clinical Study
The VAX-31 Phase 1/2 clinical study was a randomized, observer-blind, active-controlled, dose-finding clinical study designed to evaluate the safety, tolerability and immunogenicity of a single injection of VAX-31 at three dose levels (low, middle and high) and compared to PCV20 in 1,015 healthy adults aged 50 and older. In the low, middle and high doses, all serotypes were dosed at 1.1mcg, 2.2mcg and 3.3mcg, respectively, except serotypes 1, 5 and 22F, which were dosed at 1.65mcg, 3.3mcg, and 4.4mcg, respectively. The Phase 1 portion of the study included 64 healthy adults 50 to 64 years of age and the Phase 2 portion included 951 healthy adults 50 years of age and older. The immunogenicity objectives of the study included an assessment of the induction of antibody responses at Month 1, based on OPA and immunoglobulin G (IgG), at each of the three VAX-31 doses and compared to PCV20 for the 20 serotypes in common, as well as for the additional 11 serotypes contained in VAX-31, but not in PCV20. The study enrolled subjects from 25 sites in the United States. Additional information about the study can be found at www.clinicaltrials.gov under the identifier NCT06151288.

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

Adult:
VAX-31

- Following an FDA End-of-Phase 2 meeting, initiate Phase 3 pivotal, non-inferiority study by mid-2025 and announce topline safety, tolerability and immunogenicity data in 2026.
- Initiate remaining Phase 3 studies in 2025 and 2026.

Infant:
VAX-24

- Announce topline safety, tolerability and immunogenicity data from primary three-dose immunization series of the Phase 2 study, which is fully enrolled with 802 healthy infants, by the end of the first quarter of 2025, followed by topline data from the booster dose by the end of 2025.

VAX-31

- Initiate Phase 2 study in the first quarter of 2025 following IND submission and clearance.
- Announce topline safety, tolerability and immunogenicity data from the VAX-31 infant Phase 2 study primary three-dose immunization series in mid-2026, followed by topline data from the booster dose approximately nine months later.

Conference Call and Webcast
Vaxcyte will hold a webcast and conference call today, September 3 at 8:00 a.m. ET to discuss the results from the VAX-31 Phase 1/2 study. To participate in the conference call, please dial 800-225-9448 (domestic) or 203-518-9708 (international) and refer to conference ID PCVX0903. 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 Pneumococcal Disease
Pneumococcal disease (PD) is an infection caused by *Streptococcus pneumoniae* (pneumococcus) bacteria. It can result in invasive pneumococcal disease (IPD), including meningitis and bacteremia, and non-invasive PD, including pneumonia, otitis media and sinusitis. In the United States, pneumococcal pneumonia is estimated to result in approximately 150,000 hospitalizations each year. *Streptococcus pneumoniae* is among the World Health Organization's top antibiotic-resistant pathogens to be urgently addressed, and the U.S. CDC lists drug-resistant *Streptococcus pneumoniae* as a "serious threat." *Streptococcus pneumoniae* is the leading cause of vaccine-preventable deaths in children under five globally. 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 broader-spectrum vaccine.

About VAX-31
VAX-31, a 31-valent PCV candidate advancing to a Phase 3 adult clinical program, is designed to prevent IPD, which is especially serious in infants, young children, older adults and those with immune deficiencies or certain chronic health conditions. IPD is associated with high case-fatality rates, antibiotic resistance and meningitis. VAX-31 is the broadest-spectrum PCV in the clinic and has the potential to provide protection against both

currently circulating and historically prevalent serotypes. VAX-31 was designed to increase coverage to more than 95% of IPD circulating in adults in the United States aged 50 and older, with the potential to provide an incremental 12-40% of coverage over current standard-of-care adult PCVs.

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. VAX-31 is a Phase 3-ready 31-valent, carrier-sparing PCV being developed for the prevention of IPD in adults and infants and is the broadest-spectrum PCV candidate in the clinic today. VAX-24, the Company's 24-valent PCV candidate, is designed to cover more serotypes than any infant PCV on-market and is currently being evaluated in a Phase 2 infant study. Both VAX-31 and VAX-24 are designed to improve upon the standard-of-care PCVs by covering the serotypes in circulation that are responsible for a significant portion of IPD and are associated with high case-fatality rates, antibiotic resistance and meningitis, while maintaining coverage of previously circulating strains that are currently contained through continued vaccination practice.

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-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 candidate 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 and VAX-31, including breadth of coverage, the ability to deliver a potentially first-in-class PCV franchise and the potential to improve upon the standard-of-care and raise the bar for immunogenicity standards; the process and timing of anticipated future development of Vaxcyte's vaccine candidates; the timing and availability of data for the VAX-24 infant Phase 2 study; the timing and availability of data for the VAX-31 adult Phase 3 studies and infant Phase 2 study; the demand for Vaxcyte's vaccine candidates; the ability of Vaxcyte's cell-free platform to deliver the broadest-spectrum PCVs that provide protection against both currently circulating and historically prevalent strains; and other statements that are not historical fact. The words "anticipate," "believe," "could," "expect," "intend," "may," "on track," "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 its Quarterly Report on Form 10-Q filed with the SEC on August 6, 2024 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 OPA geometric mean ratio is greater than 1.0.

(3) 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 Month 1 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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