Vaxcyte Completes Enrollment of OPUS-1 and OPUS-2 Phase 3 Trials Evaluating VAX-31 for the Prevention of Invasive Pneumococcal Disease and Pneumonia in Adults

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OPUS-1 Phase 3 Study Designed to Establish a New Standard for Adult Pneumococcal Conjugate Vaccines (PCVs) Through Head-to-Head Safety, Tolerability and Immunogenicity Comparisons of VAX-31 with Capvaxive® (PCV21) and Prevnar 20® (PCV20), the Current Standard-of-Care PCVs

Topline Safety, Tolerability and Immunogenicity Data from OPUS-1 Phase 3 Study Expected in Fourth Quarter of 2026

OPUS-2 Phase 3 Study Evaluating Concomitant Administration of VAX-31 and Seasonal Influenza Vaccine Designed to Provide Real-World Performance Insights in Adults; Results Expected in First Half of 2027

OPUS-3 Phase 3 Study Enrollment Ongoing in Adults Previously Vaccinated with Pneumococcal Vaccines; Results Expected in First Half of 2027

SAN CARLOS, Calif., March 23, 2026 (GLOBE NEWSWIRE) -- Vaxcyte, Inc. (Nasdaq: PCVX), a clinical-stage vaccine innovation company, today announced the completion of enrollment in the VAX-31 OPUS-1 Phase 3 pivotal, noninferiority trial with approximately 4,000 participants and the OPUS-2 Phase 3 trial evaluating VAX-31 concomitantly administered with a seasonal influenza vaccine in approximately 1,300 participants. The Phase 3 program evaluating VAX-31, the Company's next-generation 31-valent pneumococcal conjugate vaccine (PCV) candidate, for the prevention of invasive pneumococcal disease (IPD) and pneumonia in adults was finalized in consultation and alignment with the U.S. Food and Drug Administration (FDA) and is intended to generate a broad and robust dataset to support a planned Biologics License Application (BLA) submission.

"Completing enrollment in the Phase 3 OPUS-1 and OPUS-2 trials represents two important milestones in the development of VAX-31 and reflects the disciplined execution of our comprehensive clinical program," said Grant Pickering, Chief Executive Officer and Co-founder of Vaxcyte. "With VAX-31, we are aiming to expand the breadth of disease and serotype coverage while ensuring immunogenicity levels remain high to support durable protection. Based on the strength of the unprecedented results from our VAX-31 Phase 1/2 study in adults and our carrier-sparing platform, we believe VAX-31 has the potential to set a new standard-of-care as a best-in-class, next-generation pneumococcal conjugate vaccine for both adults and children. We look forward to announcing topline data from the OPUS-1 trial in the fourth quarter of 2026 and results from the OPUS-2 and OPUS-3 trials in the first half of 2027, keeping us on track toward a planned BLA submission."

About OPUS-1, the VAX-31 Adult Pivotal Phase 3 Noninferiority Trial
The pivotal Phase 3 study of VAX-31 is now fully enrolled with approximately 4,000 adults. The randomized, double-blind, active-controlled trial is evaluating the safety, tolerability and immunogenicity of the VAX-31 High Dose, the adult formulation being evaluated in the OPUS Phase 3 program, in healthy, pneumococcal-naïve[1] U.S. adults aged 50 years and older, with a separate cohort of adults aged 18-49 years. In this formulation, all serotypes are dosed at 3.3 mcg, except serotypes 1, 5 and 22F, which are dosed at 4.4 mcg. The study is being conducted at approximately 50 sites across the United States. Additional information about the study can be found at www.clinicaltrials.gov under the identifier NCT07284654.

Participant Overview (age and randomization)

- **Adults aged ≥50 years:** Participants in this age group were randomized 1:1:1 to receive a single dose of VAX-31, Capvaxive® (PCV21) or Prevnar 20® (PCV20) on Day 1.
- **Adults aged 18-49 years:** Participants in this age group were randomized 3:1 to receive a single dose of VAX-31 or PCV20 on Day 1, with PCV20 serving as the safety comparator.

For all participants, safety and tolerability will be assessed for six months following initial vaccination of VAX-31, PCV21 or PCV20.

Immunogenicity Analyses (1-month post vaccination)

Primary immunogenicity objectives:

- **Noninferiority** of VAX-31 compared with PCV21 and/or PCV20 for the 28 serotypes shared with either or both comparator vaccines in adults aged 50 years and older *(criterion: lower bound (LB) of the two-sided 95% confidence interval (CI) of the OPA GMR is >0.667).*
- **Superiority** of VAX-31 compared with PCV21 or PCV20 for the three serotypes unique to VAX-31 (2, 7C and 20C) and for serotype 20B in adults aged 50 years and older *(criterion: LB of the two-sided 95% CI of the OPA GMR is >2.0).*
- **Noninferiority** of VAX-31 immune responses in adults aged 18-49 years compared with those in adults aged 50-64 years *(criterion: LB of the two-sided 95% CI of the OPA GMR is >0.667).*

Key secondary immunogenicity objectives:

- **Noninferiority** of VAX-31 compared with both PCV21 and PCV20 for the 11 serotypes common to all three vaccines in adults aged 50 years and older *(criterion: LB of the two-sided 95% CI of the OPA GMR is >0.5).*
- **Statistically greater immune responses** elicited by VAX-31 compared with those elicited by PCV21 or PCV20 for the 28 shared serotypes in adults aged 50 years and older *(criterion: LB of the two-sided 95% CI of the OPA GMR is >1.0).*
- **Superiority** of VAX-31 compared with PCV20 for the eight serotypes common to VAX-31 and PCV21 but not included in PCV20 in adults aged 50 years and older *(criterion: LB of the two-sided 95% CI of the OPA GMR is >2.0).*
- **Superiority** of VAX-31 compared with PCV21 for the nine serotypes common to VAX-31 and PCV20 but not included in PCV21 in adults aged 50 years and older *(criterion: LB of the two-sided 95% CI of the OPA GMR is >2.0).*

VAX-31 Serotypes vs. Comparators:

- **VAX-31 serotypes (31):** 1, 2, 3, 4, 5, 6A, 6B, 7C, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15A, 15B, 16F, 17F, 18C, 19A, 19F, 20C, 22F, 23A, 23B, 23F, 31, 33F, 35B
- **Serotypes common to VAX-31, PCV21 and PCV20 (11):** 3, 6A, 7F, 8, 10A, 11A, 12F, 15B, 19A, 22F, 33F
- **Serotypes common to VAX-31 and PCV20 but not in PCV21 (9):** 1, 4, 5, 6B, 9V, 14, 18C, 19F, 23F
- **Serotypes common to VAX-31 and PCV21 but not in PCV20 (8):** 9N, 15A, 16F, 17F, 23A, 23B, 31, 35B
- **Serotypes unique to VAX-31 (3):** 2, 7C, 20C (20B is also being evaluated)

About OPUS-2, the Adult Phase 3 Trial of VAX-31 Concomitantly Administered with a Seasonal Influenza Vaccine
This Phase 3 study, which is now fully enrolled with approximately 1,300 adults, is a randomized, double-blind, placebo-controlled clinical trial designed to evaluate the safety, tolerability and immunogenicity of VAX-31 when administered either concomitantly with or one month following administration of a licensed seasonal influenza vaccine in pneumococcal-naïve, healthy U.S. adults aged 50 years and older. The results of this descriptive study are intended to inform the design of a potential post-licensure outcomes study that further evaluates VAX-31 in concomitant use with an influenza vaccine and to provide supportive evidence as part of the broader Phase 3 dataset. The study is being conducted at approximately 25 sites in the United States. Additional information about the study can be found at www.clinicaltrials.gov under the identifier NCT07365826.

Participant Overview

Participants were randomized 1:1 into one of two groups:

- **Concomitant Administration Group:** Participants received a seasonal influenza vaccine administered open-label and concomitantly with VAX-31 administered blinded on Day 1, followed by a blinded placebo injection at Month 1.
- **Sequential Administration Group:** Participants received a seasonal influenza vaccine administered open-label with a blinded placebo injection on Day 1, followed by VAX-31 administered blinded at Month 1. This sequential dosing approach allows for evaluation of immune responses to VAX-31 when administered alone, while preserving blinding and controlling for vaccination timing.

For all participants, safety and tolerability will be assessed for six months following initial vaccination.

Immunogenicity Analyses

Primary immunogenicity objectives:

- **Assessing serotype-specific immune responses** (opsonophagocytic activity (OPA) geometric mean titers (GMTs) and geometric mean fold rises (GMFRs)) elicited by VAX-31 across all 31 serotypes and serotype 20B in pneumococcal-naïve adults aged 50 years and older.
- **Comparing strain-specific immune responses** (hemagglutination inhibition (HAI) GMTs) elicited by a seasonal influenza vaccine when co-administered with VAX-31 to those elicited by a seasonal influenza vaccine alone.

Secondary immunogenicity objective:

- **Comparing immunoglobulin G (IgG) antibody responses** (IgG geometric mean concentrations (GMCs)) elicited by VAX-31 across all 31 serotypes and serotype 20B when VAX-31 is co-administered with a seasonal influenza vaccine to those elicited by VAX-31 alone.

About Pneumococcal Disease
Pneumococcal disease (PD) is an infection caused by *Streptococcus pneumoniae* bacteria. It can result in 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 225,000 adult 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." In children under five, *Streptococcus pneumoniae* is the leading cause of vaccine-preventable deaths 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 being evaluated in the OPUS Phase 3 adult clinical program and in a Phase 2 infant clinical program, is designed to prevent serious and sometimes fatal infections caused by *Streptococcus pneumoniae*, including IPD, pneumonia and otitis media. Specifically, IPD

is associated with high case-fatality rates, antibiotic resistance and meningitis. VAX-31 is the broadest-spectrum PCV candidate in the clinic today and has the potential to provide protection against both currently circulating and historically prevalent serotypes. VAX-31 is designed to increase coverage, in a single vaccine, to approximately 95% of IPD and approximately 88% of pneumococcal pneumonia circulating in adults in the United States aged 50 and older. This disease coverage has the potential to result in VAX-31 providing an incremental 14-34% of coverage for IPD and an incremental 19-31% of coverage for pneumococcal pneumonia over current standard-of-care adult PCVs. In U.S. children, it is designed to cover approximately 92% of IPD[2] and approximately 96% of acute otitis media[3] due to *Streptococcus pneumoniae*. This disease coverage has the potential to result in VAX-31 providing an incremental 23-44% of coverage for IPD and an incremental 35-62% of coverage for otitis media over current standard-of-care infant PCVs.

In May 2025, the FDA expanded the Breakthrough Therapy designation (BTD) for VAX-31 to include the prevention of pneumonia caused by *Streptococcus pneumoniae* in addition to the prevention of IPD in adults based on the positive topline results from the VAX-31 adult Phase 1/2 study indicating that VAX-31 may demonstrate substantial improvement over existing therapies. In this study, VAX-31 was observed to be well tolerated, demonstrated a safety profile similar to PCV20 and showed robust OPA immune responses for all 31 serotypes. With the VAX-31 High Dose, all 11 incremental serotypes unique to VAX-31, and not in PCV20, met the superiority criteria,[4] and it delivered greater average OPA immune responses for 18 of the 20 serotypes in common with PCV20, and seven of these serotypes achieved statistically higher immune responses.[5]

About Vaxcyte
Vaxcyte is a vaccine innovation company engineering high-fidelity vaccines to protect humankind from the consequences of bacterial diseases. VAX-31, a 31-valent PCV candidate being evaluated in the OPUS Phase 3 adult clinical program and in a Phase 2 infant clinical program, is being developed for the prevention of IPD and is the broadest-spectrum PCV candidate in the clinic today. VAX-24, a 24-valent PCV candidate, is designed to cover more serotypes than any infant PCV on-market. VAX-31 and VAX-24 are designed to improve upon standard-of-care PCVs by covering the serotypes in circulation that cause a significant portion of IPD and are associated with high case-fatality rates, antibiotic resistance and meningitis, while maintaining coverage of previously circulating strains. VAX-XL, in earlier-stage development, also leverages the Company's carrier-sparing, site-specific conjugation technology with the aim of further expanding coverage to deliver the broadest-spectrum candidate in the Company's PCV franchise.

Vaxcyte is re-engineering the way highly complex vaccines are made through XpressCF®, its 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 develop 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, and VAX-GI, a vaccine candidate designed to prevent Shigella. 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 Vaxcyte's carrier-sparing platform and PCV candidates, including breadth of coverage, the ability to deliver potentially best-in-class PCVs, the ability to improve upon the standard-of-care, and the ability to significantly reduce the burden of disease by expanding coverage against currently and historically circulating strains while maintaining robust immune response; the design, timing of initiation, progress and expected results of Vaxcyte's clinical trials and regulatory plans; the demand for Vaxcyte's vaccine candidates; 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 Annual Report on Form 10-K filed with the SEC on February 24, 2026 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.

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[1]Pneumococcal-naïve is defined as having no known prior history of IPD, pneumococcal pneumonia, or receipt of any licensed or investigational pneumococcal vaccine.

[2]In U.S. children under five years of age: *CDC 2023 Active Bacterial Core (ABC) Surveillance data.*

[3]In U.S. children five years of age or under: *Grant LR et al., FrontPediatr.2024;12:1383748.* Serotype percentages reflect 2017–2021 data (Supplemental Table 1).

[4]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.
[5]Lower bound of the 2-sided 95% confidence interval of the OPA geometric mean ratio is greater than 1.0.