# Vaxcyte Doses First Participants in the OPUS Phase 3, Noninferiority Trial Evaluating VAX-31 for the Prevention of Invasive Pneumococcal Disease and Pneumonia in Adults

December 8, 2025

***Trial Design Finalized in Consultation and Alignment with U.S. Food and Drug Administration***

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

***Company Expects to Report Topline Safety, Tolerability and Immunogenicity Data for OPUS Phase 3, Noninferiority Trial in the Fourth Quarter of 2026 and Initiate Additional Phase 3 Studies in 2026 with Readouts in 2027, Supporting Planned BLA Submission***

***VAX-31 is Designed to Cover ~95% of Invasive Pneumococcal Disease (IPD) and ~88% of Pneumococcal Pneumonia in U.S. Adults Aged 50+, with Potential to Provide an Incremental 14-34% Broader IPD Coverage and 19-31% Broader Pneumonia Coverage than Standard-of-Care Vaccines***

***VAX-31 Aims to Advance Adult Pneumococcal Protection by Maintaining Critical Pressure on Both Currently Circulating and Long-Established, Historically Disease-Causing Serotypes, While Maintaining or Improving Immune Responses***

SAN CARLOS, Calif., Dec. 08, 2025 (GLOBE NEWSWIRE) -- Vaxcyte, Inc. (Nasdaq: PCVX), a clinical-stage vaccine innovation company, today announced that the first participants were dosed in the OPUS (OPA-based Pivotal U.S. Study) Phase 3 pivotal, noninferiority trial evaluating VAX-31 for the prevention of invasive pneumococcal disease (IPD) and pneumonia in adults. The design of the trial, which is expected to enroll approximately 4,000 participants, was finalized in consultation and alignment with the U.S. Food and Drug Administration (FDA). Topline safety, tolerability and immunogenicity results from the OPUS trial, which are expected to serve as the cornerstone of the VAX-31 Biologics License Application (BLA), are anticipated in the fourth quarter of 2026.

Building on the unprecedented results from the Company's VAX-31 adult Phase 1/2 study, which demonstrated both broader serotype coverage and stronger overall immune responses than Prevnar 20 (PCV20), the OPUS trial represents the next step in setting a new standard for adult pneumococcal vaccines. This trial is evaluating the safety, tolerability and immune responses of VAX-31 in adults aged 50 and older through direct, head-to-head comparisons with both Capvaxive (PCV21) and PCV20, the current standard-of-care pneumococcal conjugate vaccines (PCVs), with the objective of establishing a best-in-class profile for VAX-31.

The key primary immunogenicity objectives of the OPUS trial are to demonstrate 1) noninferiority if the lower bound of the two-sided 95% confidence interval (CI) for the opsonophagocytic activity (OPA) geometric mean ratio (GMR) of VAX-31 exceeds 0.667 compared with PCV21 and/or PCV20 for the 28 serotypes shared with one or both comparators and 2) superiority if the lower bound of the two-sided 95% CI of the OPA GMR exceeds 2.0 for the three serotypes unique to VAX-31 and serotype 20B versus the comparator vaccines. The trial is also evaluating the safety, tolerability and immune responses of VAX-31 in adults aged 18-49. Key secondary immunogenicity objectives are included to evaluate VAX-31 based on additional measures of noninferiority, superiority and statistically greater immune responses.

"The initiation of our adult Phase 3 program marks a major milestone in the development of VAX-31 as the program enters the final phase of clinical development, advancing toward potential licensure," said Grant Pickering, Chief Executive Officer and Co-founder of Vaxcyte. "On the strength of the unprecedented results from our VAX-31 Phase 1/2 study in adults and our carrier-sparing platform, we are uniquely positioned to set a new standard by which future adult pneumococcal vaccines will be measured. Through this program, we are aiming to expand the breadth of disease and serotype coverage while ensuring immunogenicity levels remain high to ensure durable protection. To this end, VAX-31 has the potential to provide a 14-34% increase in coverage for IPD and a 19-31% increase in coverage for pneumococcal pneumonia over current standard-of-care vaccines for U.S. adults. We expect to announce topline data from the OPUS noninferiority trial in the fourth quarter of 2026 and the results of additional Phase 3 studies in 2027, keeping our timelines to both potential BLA filing and U.S. launch on track. Consistent with precedent, we would also plan to generate post-licensure real-world evidence in the adult population."

"Pneumococcal disease remains one of the most significant vaccine-preventable threats in adults, with a growing prevalence of disease from serotypes not covered by existing vaccines," said Jim Wassil, Executive Vice President and Chief Operating Officer of Vaxcyte. "By leveraging our carrier-sparing, site-specific conjugation technology and deep understanding of adult immunobiology, our next-generation VAX-31 PCV is intended to provide the broadest coverage by maintaining critical pressure on both currently circulating as well as long-established, historically disease-causing serotypes that remain controlled largely because of ongoing vaccination."

**About OPUS, the VAX-31 Adult Pivotal Phase 3 Noninferiority Trial (n~4,000)**
The pivotal Phase 3 study of VAX-31 is a randomized, double-blind, active-controlled clinical trial evaluating the safety, tolerability and immunogenicity of the High Dose formulation of VAX-31 in which all serotypes are dosed at 3.3 mcg, except serotypes 1, 5 and 22F which are dosed at 4.4 mcg, in healthy, pneumococcal-naïve[1] U.S. adults aged 50 years and older with a separate cohort of adults aged 18-49 years. The study is being conducted at approximately 50 sites in the United States.

**Participant Overview (age and randomization)**

- **Adults aged ≥50 years (n~3,560):** Participants in this age group will be randomized 1:1:1 to receive a single dose of VAX-31, PCV21 or PCV20 on Day 1.
- **Adults aged 18-49 years (n~440):** Participants in this age group will be 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 (to occur 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)

**Anticipated Key PCV Program Milestones**
Vaxcyte is advancing the clinical development of its PCV programs with several anticipated key upcoming milestones:

**PCV Franchise Adult Indication**

**VAX-31**

- Announce topline safety, tolerability and immunogenicity data for the OPUS Phase 3 pivotal, noninferiority study in the fourth quarter of 2026.
- Initiate remaining Phase 3 studies in 2026 and announce data from these studies in 2027 (details of each study to be announced upon commencement).

**PCV Franchise Infant Indication**

**VAX-31**

- Announce topline safety, tolerability and immunogenicity data for the VAX-31 infant Phase 2 randomized, dose-finding study from both the primary three-dose immunization series and booster dose either sequentially or together by the end of the first half of 2027.

**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 over 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." 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 a Phase 3 adult clinical program and in a Phase 2 infant 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 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, the VAX-31 High Dose 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 a 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 and the ability to improve upon the standard-of-care; 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 Quarterly Report on Form 10-Q filed with the SEC on November 4, 2025 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.

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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. IPD cases with missing serotype data were*

*excluded, non-typeable cases were included in the denominator.*

[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.