Vertex Announces Progress in Povetacicept Development Program and Presentation of New Data at American Society of Nephrology Kidney Week

October 17, 2025

- Food and Drug Administration grants rolling review of Biologics License Application for povetacicept in IgA nephropathy; Vertex to submit first module before end of year -

- Second pivotal development program of povetacicept underway with Phase 2b/3 trial initiation in primary membranous nephropathy -

- Updated data from RUBY-3 trial of povetacicept accepted for late breaking oral presentation; inaxaplin study design and APOL1-mediated kidney disease related data accepted for poster presentation -

BOSTON--(BUSINESS WIRE)--Oct. 17, 2025-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced several important updates across its development program for povetacicept (pove), an investigational recombinant fusion protein therapeutic and dual antagonist of the BAFF (B cell activating factor) and APRIL (a proliferation inducing ligand) cytokines. Pove has demonstrated best-in-class potential in IgA nephropathy (IgAN) and primary membranous nephropathy (pMN) and has pipeline-in-a-product potential across a range of B cell-mediated diseases. Pove is the only BAFF+APRIL inhibitor in pivotal trials for multiple kidney diseases.

Next Steps for Pove Development

In IgAN

Following the announcement that the Food and Drug Administration (FDA) granted Breakthrough Therapy Designation (BTD) to pove for the treatment of IgAN, FDA recently granted a rolling review of the Biologics License Application (BLA) for pove for this indication. Vertex expects to submit the first module to FDA for potential accelerated approval before the end of 2025. The Company remains on track to complete the full BLA submission for accelerated approval in the U.S. in the first half of 2026, if results from the planned interim analysis are supportive.

In pMN

Vertex announced it has initiated OLYMPUS, a Phase 2b/3 pivotal study of pove for the treatment of pMN, the second indication in which pove has best-in-class potential. There are no therapies specifically approved for the treatment of pMN.

“We are very pleased with the continued momentum in our pove program across multiple indications,” said Carmen Bozic, M.D., Executive Vice President of Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. “Breakthrough designation, rolling submission for the IgAN BLA, and initiation of the second pivotal trial for pove, in pMN, bring us closer to getting this potential best-in-class therapy to patients with these serious diseases.”

The company also announced upcoming presentations at the American Society of Nephrology (ASN) Kidney Week 2025, November 6-9 in Houston, Texas highlighting data from more patients with longer duration of follow up with pove in IgAN and pMN as well as data on the burden of disease in patients with APOL1-mediated kidney disease (AMKD).

Data to be Presented at ASN

Vertex will present data on adults with IgAN and with pMN who received pove subcutaneously every 4 weeks (SC Q4W) in the RUBY-3 trial, in addition to its poster presentations on inaxaplin and AMKD.

- A late-breaking presentation #SA-OR091, entitled “Efficacy and Safety of Povetacicept in Patients with IgAN and Primary Membranous Nephropathy (pMN) at 48 Weeks of Treatment: The RUBY-3 Study,” will be presented during Late-Breaking Research Orals-3 session on November 8 from 5:06–5:18 p.m. CST.
- A presentation #FR-PO0813, entitled “Povetacicept for IgAN: Design of a Phase 3 Randomized, Placebo-Controlled Study,” will be presented during a poster session and via eposter on November 7 from 10:00 a.m. to 12:00 p.m. CST.
- A presentation #TH-PO0604, entitled “Inaxaplin for a Broad Population with APOL1-Mediated Kidney Disease and Comorbid Conditions: Phase 2 Proof-of-Concept Study,” will be presented during a poster session and via eposter on November 6 from 10:00 a.m. to 12:00 p.m. CST.
- A presentation #TH-PO0625, entitled “Clinical Characteristics and Disease Progression Among Nondiabetic Patients with

APOL1-Mediated Kidney Disease (AMKD) and Patients with Other Forms of Chronic Kidney Disease (CKD)," will be presented during a poster session and via eposter on November 6 from 10:00 a.m. to 12:00 p.m. CST.

Investor Event

Vertex will host an investor event on Saturday, November 8, 2025, from 7:00–8:15 p.m. CST in Houston, to discuss the updated data for pove in IgAN and pMN, and other highlights across its kidney disease portfolio. A live webcast of the presentation and Q&A portions can be accessed through the Investor Relations section of Vertex's website at https://investors.vrtx.com/. An archived webcast will be available on the company's website.

About Povetacicept (Pove)
Pove is a dual antagonist of the BAFF and APRIL cytokines, which promote B cell activation, differentiation and/or survival, and provides B cell control by inhibiting the ability of BAFF and APRIL to drive the pathogenesis of multiple autoimmune diseases. Due to its engineered TACI domain, pove has demonstrated greater binding affinity, potency and tissue penetration compared to other BAFF and/or APRIL inhibitors in preclinical studies. Based on this, pove has potential best-in-class efficacy in serious autoimmune diseases driven by uncontrolled B cells.

About IgA Nephropathy (IgAN)
IgAN is a serious, progressive, life-threatening kidney disease driven by uncontrolled autoreactive B cell activity and is the most common cause of primary glomerulonephritis, affecting approximately 300,000 people in the United States and Europe. It is estimated that there are approximately 33,000 diagnosed patients in Japan and approximately 750,000 diagnosed patients in China. IgAN results from the deposition of circulating immune complexes consisting of immunoglobulins and galactose-deficient immunoglobulin A (Gd-IgA1) in the renal glomerular mesangium, triggering kidney injury and fibrosis. Up to 72% of adult IgAN patients progress to end-stage renal disease within 20 years of diagnosis. There are no approved therapies that specifically target the underlying cause of IgAN.

About Primary Membranous Nephropathy (pMN)
pMN is a rare and serious autoimmune glomerular disease which is driven by uncontrolled autoreactive B cell activity, resulting in autoantibody production against glomerular antigens including protein phospholipase A2 receptor (PLA2R). pMN affects approximately 150,000 people in the United States and Europe. Over-production of these autoantibodies against glomerular antigens results in kidney damage, fibrosis and renal failure. There are no therapies specifically approved for the treatment of pMN.

About RAINIER
RAINIER is a global Phase 3 randomized, placebo-controlled pivotal trial of pove 80 mg administered subcutaneously every four weeks vs. placebo on top of standard of care in approximately 480 people with IgAN. The study is designed to have a pre-planned interim analysis evaluating the percent change from baseline in urine protein to creatinine ratio (UPCR) for the pove arm vs. placebo after a pre-specified number of patients reach 36 weeks of treatment. If positive, the interim analysis may serve as the basis for Vertex to seek accelerated approval in the U.S. Final analysis will occur at two years of treatment, with a primary endpoint of total estimated glomerular filtration rate (eGFR) slope through Week 104.

About OLYMPUS
OLYMPUS is a global Phase 2b/3 adaptive, randomized, active-controlled pivotal trial of pove in approximately 176 patients with pMN. In the Phase 2b portion, participants will be randomized to receive one of two different doses of pove and after the last subject completes 12 weeks of treatment, the Phase 3 dose will be selected. In the Phase 3 portion, participants will be randomized to receive either the selected dose of pove or a calcineurin inhibitor. Final analysis will occur at two years of treatment, with a primary endpoint of proportion of participants with complete clinical remission at Week 104.

About APOL1-Mediated Kidney Disease (AMKD)
AMKD is a rapidly progressive, proteinuric kidney disease caused by two variants in the *APOL1* gene. It occurs in people of African ancestry. AMKD occurs when inherited *APOL1* genetic variants cause kidney cell injury, cell death and damage to the glomeruli, which filter blood in the kidney. This leads to proteinuria and decreased kidney function, which can lead in turn to dialysis, transplant or death. AMKD affects an estimated patient population of approximately 250,000 in the U.S. and Europe, including AMKD patients with comorbidities. There are no therapies approved for AMKD.

About Inaxaplin
Inaxaplin is a first-in-class, investigational small molecule inhibitor of APOL1 aimed at addressing the underlying cause of AMKD.

About Vertex
Vertex is a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious diseases and conditions. The company has approved therapies for cystic fibrosis, sickle cell disease, transfusion-dependent beta thalassemia and acute pain, and it continues to advance clinical and research programs in these areas. Vertex also has a robust clinical pipeline of investigational therapies across a range of modalities in other serious diseases where it has deep insight into causal human biology, including neuropathic pain, APOL1-mediated kidney disease, IgA nephropathy, primary membranous nephropathy, autosomal dominant polycystic kidney disease, type 1 diabetes and myotonic dystrophy type 1.

Vertex was founded in 1989 and has its global headquarters in Boston, with international headquarters in London. Additionally, the company has research and development sites and commercial offices in North America, Europe, Australia, Latin America and the

Middle East. Vertex is consistently recognized as one of the industry's top places to work, including 15 consecutive years on Science magazine's Top Employers list and one of Fortune's 100 Best Companies to Work For. For company updates and to learn more about Vertex's history of innovation, visit www.vrtx.com or follow us on LinkedIn, Facebook, Instagram, YouTube and X.

Special Note Regarding Forward-Looking Statements

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements by Carmen Bozic, M.D., and statements about the expectations for the Company's BLA submission for pove in IgAN, including expectations for the timing of the submission of the first module and the completion of the full BLA submission, expectations for pove's best-in-class potential in IgAN and pMN and pipeline-in-a-product potential across a range of diseases, clinical status of and expectations for the OLYMPUS trial in pMN, plans to present data during presentations at ASN and plans for an investor event to discuss updated data for pove in IgAN and pMN and other highlights across the Company's kidney disease portfolio, expectations for the RAINIER study design and data expectations, including timing of data availability, and expectations that the Company will seek accelerated approval in the U.S., if the RAINIER interim analysis is positive. While Vertex believes the forward-looking statements contained in this press release are accurate, these forward-looking statements represent the company's beliefs only as of the date of this press release and there are a number of risks and uncertainties that could cause actual events or results to differ materially from those expressed or implied by such forward-looking statements. Those risks and uncertainties include, among other things, that data from a limited number of patients may not be indicative of final clinical trial results, that clinical trial data might not be available on the expected timeline, that data from the company's research and development programs may not support registration or further development of its compounds due to safety, efficacy, and other risks, and other risks listed under the heading "Risk Factors" in Vertex's most recent annual report and subsequent quarterly reports filed with the Securities and Exchange Commission at www.sec.gov and available through the company's website at www.vrtx.com. You should not place undue reliance on these statements. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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