Vertex Announces Key Advancements Across Kidney Portfolio

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- Food and Drug Administration granted Breakthrough Therapy Designation for povetacicept in IgA nephropathy; on track to file for accelerated approval in the U.S. in H1 2026 if 36-week interim analysis data positive -

- Enrollment completed for interim analysis cohort of AMPLITUDE global Phase 2/3 trial evaluating inaxaplin in APOL1-mediated kidney disease; potential to file for accelerated approval in the U.S. if 48-week interim analysis data positive -

- Phase 2 proof-of-concept study initiated for VX-407 in patients with autosomal dominant polycystic kidney disease -

BOSTON--(BUSINESS WIRE)--Sep. 25, 2025-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced several important advancements across its programs in immunoglobulin A Nephropathy (IgAN), APOL1-mediated kidney disease (AMKD) and autosomal dominant polycystic kidney disease (ADPKD). These updates represent significant progress toward reaching the Company's goal of bringing forward first-in-class or best-in-class therapies that target the underlying cause of these serious kidney diseases.

Povetacicept in IgAN

Vertex announced today that the Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation (BTD) to povetacicept (pove) for the treatment of IgAN. Pove is an investigational recombinant fusion protein therapeutic and dual antagonist of the BAFF (B cell activating factor) and APRIL (a proliferation inducing ligand) cytokines with best-in-class potential in IgAN and other B cell-driven diseases. BTD is for a drug that treats a serious condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on one or more clinically significant endpoints over existing treatments.

Pove is currently being studied in RAINIER, a global Phase 3 clinical trial in patients with IgAN. The study is designed to have a pre-planned interim analysis (IA) evaluating urine protein to creatinine ratio (UPCR) for the pove arm versus placebo after a specified number of patients reach 36 weeks of treatment. The IA cohort has been fully enrolled, and Vertex remains on track to file for accelerated approval in the U.S. in H1 2026 if results are supportive.

Inaxaplin in AMKD

Vertex also announced today enrollment completion of the IA cohort of AMPLITUDE, a global Phase 2/3 clinical trial designed to assess the impact of inaxaplin on kidney function and proteinuria for people living with AMKD. Inaxaplin is a first-in-class, investigational small molecule inhibitor of APOL1 aimed at addressing the underlying cause of AMKD. The AMPLITUDE study is designed with an interim analysis at Week 48 in a pre-specified number of patients to assess percent change from baseline in proteinuria and eGFR slope in the inaxaplin arm versus placebo. If positive, the IA will serve as the basis for Vertex to seek accelerated approval of inaxaplin in the U.S.

VX-407 in ADPKD

The Company also announced it has initiated AGLOW, a Phase 2 proof-of-concept study of VX-407 for the treatment of ADPKD. VX-407 is a first-in-class investigational small molecule corrector that is designed to treat ADPKD in patients with a subset of *PKD1* variants, estimated at up to approximately 10% of the overall ADPKD population. VX-407 is designed to target the underlying cause of ADPKD by correcting defective PC1 folding to restore function, thereby potentially reducing total kidney volume and preventing progression to kidney failure. AGLOW is a 52-week single-arm study that will evaluate the effect of VX-407 on height-adjusted total kidney volume (htTKV) in patients with a subset of variants of the *PKD1* gene.

"Our pursuit of breakthrough science and serial innovation has changed the treatment landscape for cystic fibrosis, acute pain, sickle cell disease and beta thalassemia by advancing transformative therapies that target the underlying cause of these diseases. We are excited to bring the same level of pioneering science and potentially transformative benefit to patients with serious kidney diseases," said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. "Today's announcements on BTD for pove in IgAN, completion of enrollment in the IA cohort in our AMKD study setting up the potential for accelerated approval of inaxaplin and initiation of the VX-407 POC study in ADPKD mark significant milestones toward bringing the next wave of promising medicines to patients who are waiting."

About IgA Nephropathy (IgAN)

IgAN is a serious, progressive, life-threatening, B cell-mediated chronic kidney disease that is the most common cause of primary (idiopathic) 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 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 RAINIER

RAINIER is a global Phase 3 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 versus 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 eGFR slope through Week 104.

About Breakthrough Therapy Designation

The FDA's BTD is intended to expedite development and review of medicines that aim to address a serious condition with preliminary clinical evidence indicating that the drug may demonstrate substantial improvement over existing treatments on one or more clinically significant endpoints. BTD was granted for pove in IgAN based on data from the Phase 2 RUBY-3 clinical trial.

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 protein in the urine (known as “proteinuria”) and decreased ability of the kidney to 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 currently approved for AMKD.

About AMPLITUDE

AMPLITUDE is a global Phase 2/3 clinical trial designed to assess the impact of inaxaplin on kidney function and proteinuria for people living with AMKD. Inaxaplin is being evaluated as a 45 mg once-daily oral dose compared to placebo, on top of standard of care. The primary efficacy endpoint for the final analysis is estimated glomerular filtration rate (eGFR) slope in patients receiving inaxaplin compared to placebo. The secondary efficacy endpoint is time to composite clinical outcome, which will also be assessed at the final analysis and is defined as a sustained decline of ≥30% from baseline in the eGFR, the onset of end-stage kidney disease or death. The final study analysis will occur when subjects have at least two years of eGFR data and when approximately 187 composite clinical outcomes have occurred.

About Autosomal Dominant Polycystic Kidney Disease (ADPKD)

ADPKD is the most common inherited kidney disease and one of the most common severe Mendelian genetic diseases, affecting approximately 300,000 diagnosed people in the U.S. and Europe. As the disease is autosomal dominant, one affected parent can pass on the disease to their children.

In most cases, ADPKD is caused by variants in the *PKD1* and *PKD2* genes, which express proteins known as polycystins. The majority of ADPKD patients (~80%) have a variant in the *PKD1* gene, resulting in a loss of function of polycystin 1 (PC1). This leads to the proliferation of kidney epithelial cells, increased fluid secretion and the formation and expansion of numerous fluid-filled cysts. The progressive cyst formation causes an increase in kidney size and decline in kidney function. Around half of patients with ADPKD experience kidney failure by the age of 60. Kidney cysts can also lead to severe abdominal pain, cyst infection, blood in the urine and kidney stones, all of which significantly impair quality of life. There are no approved therapies that specifically address the underlying cause of ADPKD.

About AGLOW

AGLOW is a global Phase 2 proof-of-concept study of VX-407 for the treatment of ADPKD. It is a single-arm, open-label, 52-week study that will evaluate the effect of VX-407 treatment on height-adjusted total kidney volume (htTKV) in a subset of patients with variants of the *PKD1* gene.

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 potential benefits of VX-407 for patients with ADPKD and for the initiated AGLOW study, including study design, expectations for the potential benefits of pove for patients with IgAN, including the preliminary clinical evidence, the study designs for the RAINIER study, and plans to file for accelerated approval in the U.S. in H1 2026 if results are supportive, expectations for the potential benefits of the BTD for pove in IgAN, expectations for the potential benefits of inaxaplin for patients with AMKD, the study designs for the AMPLITUDE study and plans for the IA to serve as the basis for Vertex to seek accelerated approval of inaxaplin in the U.S., if results are positive, and expectations for the significant progress toward reaching the Company’s goal of bringing forward first-in-class or best-in-class therapies that target the underlying cause of these serious kidney diseases. 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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