Vertex Presents Updated Phase 1/2 Data From RUBY-3 Study That Continue to Demonstrate Best-in-Class Potential for Povetacicept in Adults with IgA Nephropathy and Primary Membranous Nephropathy at American Society of Nephrology Kidney Week

November 8, 2025

- 48-week data show a 64% decrease from baseline in proteinuria in IgA nephropathy, 82% decrease from baseline in proteinuria in primary membranous nephropathy, and stabilization of estimated glomerular filtration rate across both diseases -

- Vertex on track to initiate rolling submission of Biologics License Application for potential accelerated approval to the U.S. Food and Drug Administration this year; full enrollment completed for Phase 3 RAINIER trial in IgA nephropathy -

- Povetacicept in primary membranous nephropathy granted Fast Track Designation by the U.S. Food and Drug Administration and Phase 2/3 pivotal trial initiated -

BOSTON--(BUSINESS WIRE)--Nov. 8, 2025-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced updated data for povetacicept (pove) in IgA nephropathy (IgAN) and primary membranous nephropathy (pMN) from the ongoing RUBY-3 trial at the American Society of Nephrology (ASN) Kidney Week 2025 in Houston, Texas. Pove is an investigational recombinant fusion protein therapeutic and dual inhibitor of the BAFF (B cell activating factor) and APRIL (a proliferation inducing ligand) cytokines. Pove is the only BAFF+APRIL inhibitor in pivotal trials for multiple kidney diseases.

Results were presented today as a late-breaking oral presentation (SA-OR091) and included interim data from the open-label Phase 1/2 RUBY-3 trial, where adults with IgAN and pMN received pove subcutaneously every 4 weeks. The analysis included 21 participants with IgAN and 10 participants with pMN treated with pove at the 80mg dose, of which 17 participants and 5 participants, respectively, completed the Week 48 study visit.

Results in IgAN

In IgAN, key efficacy findings for the pove 80mg cohort at 48 weeks showed a 64% decrease from baseline in mean 24-hour urine protein to creatinine ratio (UPCR), estimated glomerular filtration rate (eGFR) stabilization with change from baseline in eGFR (mean±SE) of 3.3±3.1 mL/min/1.73m^2, 90% (9/10) of participants achieving hematuria resolution (defined as a decrease to negative or small levels of urine blood in participants with baseline levels of urine blood of moderate or large), and 53% of participants achieving clinical remission (defined as UPCR <0.5 g/g, negative hematuria, and <25% reduction in eGFR vs. baseline).

Results in pMN

In pMN, key efficacy findings for the pove 80mg cohort at 48 weeks showed an 82% decrease from baseline in mean 24-hour UPCR, eGFR stabilization with change from baseline in eGFR (mean±SE) of -0.3±3.4 mL/min/1.73m^2, and 40% of participants achieving complete clinical remission (defined as UPCR <0.5 g/g).

Pove was generally safe and well tolerated with adverse events (AEs) that were mostly mild or moderate in severity. There were no serious adverse events related to povetacicept. The safety data is consistent with previous interim analyses, and the safety profile is similar between the IgAN and pMN cohorts.

“These impressive data demonstrate the viability of BAFF+APRIL inhibition to transform the treatment of serious kidney diseases such as IgAN and pMN, important areas of high unmet need,” said RUBY-3 Principal Investigator James Tumlin, M.D., Professor, Department of Medicine, Emory University School of Medicine, and Director of Clinical Research at Georgia Nephrology. “In IgAN, it is especially encouraging to see that at 48 weeks of follow up, a full two-thirds of the participants treated with pove achieved a complete response as defined by UPCR <0.5 g/g, which is in line with the most recent KDIGO guidelines.”

“The exceptionally fast pace of enrollment for the Phase 3 RAINIER trial demonstrates the unmet demand to find effective interventions in IgAN,” said RAINIER Steering Committee Member Richard Lafayette, M.D., Professor of Medicine (Nephrology) at the Stanford University Medical Center. “People living with IgAN and pMN indeed need additional disease-modifying treatments that address the specific drivers of nephron loss and will provide lasting disease control. Pove’s data from RUBY-3 in two serious kidney diseases support the utility of a dual BAFF+APRIL approach, and we are increasingly excited awaiting the RAINIER Phase 3 results.”

Next Steps for Pove Development

Vertex recently announced the U.S. Food and Drug Administration (FDA) granted Breakthrough Therapy Designation for pove in IgAN, and the Company expects to submit the first module of the Biologics License Application (BLA) rolling submission this year for potential accelerated approval. Vertex has notified the FDA of its intent to use a priority review voucher to expedite the review of the pove BLA in IgAN from ten months to six months. The Phase 3 RAINIER study is now fully enrolled.

Vertex also received Fast Track Designation from the FDA for pove in pMN, and recruitment for the pivotal Phase 2/3 OLYMPUS trial is currently underway. pMN is the second indication in which pove has demonstrated best-in-class potential.

Investor Event

Vertex will host an investor event at 7:00 p.m. CST (8:00 p.m. EST) 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.

Visit news.vrtx.com/asn-kidney-week for more information about Vertex's presence at ASN Kidney Week 2025.

About Povetacicept (Pove)

Pove is a dual inhibitor 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/or tissue penetration compared to other APRIL, BAFF, and dual BAFF+APRIL inhibitors in preclinical studies. This preclinical data, combined with clinical data observed to date and convenient dosing and administration, give pove best-in-class potential across a number of serious autoimmune diseases driven by uncontrolled B cells. Pove is an investigational agent and has not been approved by health authorities globally.

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 Fast Track Designation

Fast Track Designation is a program administered by the FDA to expedite the development and review of new drugs and biologics that treat serious or life-threatening conditions and have the potential to fill unmet medical needs. This designation is intended to facilitate development and expedite review of qualifying drugs.

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 RUBY-3

RUBY-3 is an ongoing, multiple-ascending dose, multi-cohort, open label, Phase 1/2 basket study of povetacicept in autoimmune glomerulonephritis, including IgAN, pMN, lupus nephritis and ANCA-associated vasculitis with glomerulonephritis, where povetacicept is being administered subcutaneously for up to 104 weeks.

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. The RAINIER study design was presented as a poster (FR-PO0813) during ASN Kidney Week.

About OLYMPUS

OLYMPUS is a global Phase 2/3 adaptive, randomized, active-controlled pivotal trial of pove in approximately 176 patients with pMN. In the Phase 2 portion, participants will be randomized to receive one of two different doses of pove and after the last participant 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 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 16 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 James Tumlin M.D., and Richard Lafayette, M.D., and statements about the expectations for the Company's BLA submission for pove in IgAN for potential accelerated approval in the U.S., 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 Phase 2/3 trial in pMN, 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, that the company may be unable to make the anticipated regulatory submissions on the expected timeline, or at all, 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 or the scientific data presented. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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