Vertex Announces Publication in New England Journal of Medicine of Results from Phase 2 Study of Inaxaplin (VX-147)

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BOSTON--(BUSINESS WIRE)--Mar. 16, 2023-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced publication in the *New England Journal of Medicine* (NEJM) of results from preclinical studies and a Phase 2 study evaluating the efficacy and safety of inaxaplin (VX-147) on top of standard-of-care in people with focal segmental glomerulosclerosis (FSGS) and two *APOL1* variants, a severe, rapidly progressive form of chronic kidney disease also known as APOL1-mediated kidney disease (AMKD). AMKD is caused by variants of the *APOL1* gene and affects approximately 100,000 people in the U.S. and Europe. Inaxaplin is an APOL1 inhibitor aimed at treating the underlying cause of AMKD.

The manuscript presents results from the Phase 2 study of inaxaplin, demonstrating a statistically significant and clinically meaningful mean reduction in proteinuria of 47.6% (95% CI: 60.0%, 31.3%) at 13 weeks compared to baseline, which was the primary endpoint of the study. Reduction in proteinuria was observed early and continued throughout the 13-week treatment period. Results were consistent regardless of baseline proteinuria or background standard-of-care therapy. Inaxaplin was generally well tolerated in the study. The most common adverse events (occurring in >15% of subjects) were headache, back pain and nausea. These results provide the first clinical evidence that an oral small molecule APOL1 inhibitor can decrease proteinuria in patients with AMKD.

“Inaxaplin has the potential to be a breakthrough for people living with AMKD by addressing the underlying cause of this devastating disease,” said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. “We look forward to exploring the full potential of this molecule in the ongoing Phase 2/3 pivotal trial and bringing this potential therapy to patients who are waiting.”

“The results from the Phase 2 inaxaplin study show real promise for patients suffering from AMKD,” said Glenn Chertow, M.D., M.P.H., Professor of Medicine, Stanford University School of Medicine and Chair of Vertex’s APOL1 Program Steering Committee. “APOL1-mediated kidney disease can progress swiftly to kidney failure, and the potential for inaxaplin to precisely target the underlying cause of AMKD should bring hope and excitement to persons living with AMKD and those of us who care for them.”

About Inaxaplin
Earlier last year, Vertex initiated a pivotal Phase 2/3, randomized, double-blind, placebo-controlled study to assess the impact of inaxaplin, on top of standard-of-care, on kidney function and proteinuria in people with AMKD. The primary endpoint of the study is reduction in the rate of decline of kidney function as measured by estimated glomerular filtration rate (eGFR) slope in patients receiving inaxaplin compared to placebo after a minimum follow-up of approximately two years. The study is also designed to have a pre-planned interim analysis at Week 48 evaluating eGFR slope, supported by a percent change from baseline in proteinuria, in the inaxaplin arm versus placebo. If positive, the interim analysis may serve as the basis for Vertex to seek accelerated approval of VX-147 in the U.S. for patients with AMKD. Enrollment in the study is ongoing, with more than 100 sites open in the U.S. and internationally, with 250 planned sites in total globally.

The U.S. Food and Drug Administration (FDA) recently granted inaxaplin Breakthrough Therapy Designation (BTD) for APOL1-mediated FSGS. The European Medicines Agency (EMA) has also granted inaxaplin Priority Medicines (PRIME) and Orphan Drug designation for AMKD.

About APOL1-Mediated Kidney Disease
APOL1-mediated kidney disease (AMKD) is a form of chronic kidney disease caused by variants in the *APOL1* gene. Approximately 100,000 people in the U.S. and Europe have two *APOL1* genetic variants and proteinuric kidney disease. People who inherit two variants in the *APOL1* gene have a course of disease that is far more aggressive than in the absence of APOL1 genetic variants. Inherited *APOL1* genetic variants cause kidney disease through a toxic gain of function, which leads to podocyte injury. This injury disrupts filtration, resulting in proteinuria and rapidly progressive kidney disease. Progressive kidney disease can result in dialysis, kidney transplant or death.

About Vertex

Vertex is a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious diseases. The company has multiple approved medicines that treat the underlying cause of cystic fibrosis (CF) — a rare, life-threatening genetic disease — and has several ongoing clinical and research programs in CF. Beyond CF,Vertex has a robust clinical pipeline of investigational small molecule, cell and genetic therapies in other serious diseases where it has deep insight into causal human biology, including sickle cell disease, beta thalassemia, APOL1-mediated kidney disease, pain, type 1 diabetes

and alpha-1 antitrypsin deficiency.

Founded in 1989 in Cambridge, Mass., Vertex's global headquarters is now located in Boston's Innovation District and its international headquarters is in London. Additionally, the company has research and development sites and commercial offices in North America, Europe, Australia and Latin America. Vertex is consistently recognized as one of the industry's top places to work, including 13 consecutive years on Science magazine's Top Employers list and one of Fortune's Best Workplaces in Biotechnology and Pharmaceuticals and Best Workplaces for Women. For company updates and to learn more about Vertex's history of innovation, visit www.vrtx.com or follow us on Facebook, Twitter, LinkedIn, YouTube and Instagram.

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 Dr. Bozic and Dr. Chertow in this press release and statements regarding the potential benefits of inaxaplin, including the aim for it to treat the underlying cause of AMKD, the anticipated timelines and dosing associated with ongoing and future clinical trials, study design, including expectations on patient enrollment, expectations regarding efficacy endpoints, plans for interim evaluation, and plans for submission for regulatory approval in the U.S. 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 the trial may not be completed in the expected timeframe, or at all, that patient enrollment in our trials may be delayed, that data from the company's development programs may not support registration or further development of its compounds due to safety, efficacy, or other reasons, and other risks listed under the heading "Risk Factors" in Vertex's most recent annual report filed with the Securities and Exchange Commission (SEC) and available through the company's website at www.vrtx.com and on the SEC's website at www.sec.gov. 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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