



Vertex Advances Inaxaplin (VX-147) into Phase 3 Portion of Adaptive Phase 2/3 Clinical Trial for the Treatment of APOL1-Mediated Kidney Disease

April 1, 2024

– 45 mg once daily oral dose selected for Phase 3 –

– Results support trial expansion to lower age group and study will now include adolescents ages 10-17 years –

– If positive, pre-planned interim analysis at Week 48 may serve as the basis for accelerated approval in the U.S. –

BOSTON--(BUSINESS WIRE)--Apr. 1, 2024-- [Vertex Pharmaceuticals Incorporated](#) (Nasdaq: VRTX) today announced that inaxaplin (VX-147) has advanced into the Phase 3 portion of the global Phase 2/3 pivotal clinical trial in APOL1-mediated kidney disease (AMKD), where a 45 mg once daily oral dose will be compared to placebo, on top of standard of care. The clinical trial is designed to assess the impact of inaxaplin on kidney function and proteinuria for people living with proteinuric kidney disease mediated by two variants in the *APOL1* gene, known as AMKD. In addition, the trial has been expanded to include adolescents with AMKD ages 10 to 17 years.

Previously reported Phase 2a proof-of-concept data demonstrated that inaxaplin led to a statistically significant and clinically meaningful mean reduction in the urine protein to creatinine ratio (UPCR) of 47.6% at 13 weeks of treatment compared to baseline, providing the first clinical evidence that an oral small molecule APOL1 inhibitor can decrease proteinuria in people with AMKD.

"Inaxaplin, a first-in-class molecule that addresses the underlying cause of APOL1-mediated kidney disease, has already shown impressive results in the Phase 2a proof-of-concept study," said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. "Advancing this trial into Phase 3 and broadening the trial to include younger patients is a critical step forward in bringing this potential therapy to patients who are waiting."

"AMKD is a rapidly progressing condition and often remains silent until the disease reaches an advanced stage. We have no approved disease-specific therapies for this truly devastating condition, and inaxaplin has the potential to transform the care of AMKD and significantly improve the lives of patients," noted Glenn M. Chertow, M.D., M.P.H., Professor of Medicine, Stanford University School of Medicine, and Chair of Vertex's APOL1 Program Steering Committee. "The kidney community is strongly encouraged by inaxaplin's potential, which energizes those of us caring for patients with AMKD."

An Independent Data Monitoring Committee (IDMC) reviewed blinded and unblinded Phase 2 safety and efficacy data from the Phase 2/3 pivotal trial, which evaluated two different doses of inaxaplin compared to placebo for 12 weeks of treatment in patients ages 18 to 65 years and recommended the selection of a single inaxaplin dose of 45 mg once daily in the Phase 3 portion of the Phase 2/3 study. The IDMC also recommended enrolling adolescents with AMKD ages 10 to 17 years in the Phase 3 portion of the study.

The U.S. Food and Drug Administration (FDA) has granted inaxaplin Rare Pediatric Disease Designation (RPD) and Breakthrough Therapy Designation (BTD) for APOL1-mediated focal segmental glomerulosclerosis (FSGS). The European Medicines Agency (EMA) has also granted inaxaplin Priority Medicines (PRIME) and Orphan Drug designations for AMKD.

About the Phase 2/3 AMPLITUDE Study

Inaxaplin is a potential first-in-class, investigational small molecule inhibitor of APOL1 with the goal of targeting the underlying cause of APOL1-mediated kidney disease (AMKD).

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 $\geq 30\%$ 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.

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 inaxaplin in the U.S. for patients with AMKD.

Enrollment in the study is ongoing, with more than 200 sites open in the U.S. and internationally.

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 may lead to 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 to dialysis, 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 approved medicines that treat the underlying causes of multiple chronic, life-shortening genetic diseases — cystic fibrosis, sickle cell

disease and transfusion-dependent beta thalassemia — and continues to advance clinical and research programs in these diseases. 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 acute and neuropathic pain, APOL1-mediated kidney disease, autosomal dominant polycystic kidney disease, type 1 diabetes, myotonic dystrophy type 1 and alpha-1 antitrypsin deficiency.

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 14 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 [Twitter/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, including, without limitation, statements made by Carmen Bozic, M.D., and Glenn Chertow, M.D., M.P.H., in this press release, statements regarding Vertex's plans for and study design of the Phase 3 portion of the clinical trial for inaxaplin, including the study's expansion to include adolescents with AMKD, expectations that the pre-planned interim analysis at Week 48 may serve as the basis for Vertex to seek accelerated approval in the U.S., and our expectations for the benefits of inaxaplin. 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 factors that could cause actual events or results to differ materially from those indicated by such forward-looking statements. Those risks and uncertainties include, among other things, 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 listed under the heading "Risk Factors" in Vertex's annual report and in subsequent filings filed with the Securities and Exchange Commission and available through the company's website at www.vrtx.com and 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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