Vertex Announces Inaxaplin (VX-147) Granted Breakthrough Therapy Designation by U.S. FDA and Priority Medicines (PRIME) Designation by the EMA

June 8, 2022

- Vertex granted nine Breakthrough Therapy Designations and three PRIME designations across its pipeline programs to date –

BOSTON--(BUSINESS WIRE)--Jun. 8, 2022-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced the U.S. Food and Drug Administration (FDA) has granted inaxaplin (VX-147) Breakthrough Therapy Designation for APOL1-mediated focal segmental glomerulosclerosis (FSGS) and the European Medicines Agency (EMA) has granted inaxaplin Priority Medicines (PRIME) designation for APOL1-mediated chronic kidney disease (AMKD). Inaxaplin is the first investigational therapy aimed at treating the underlying cause of AMKD.

The FDA's Breakthrough Therapy Designation 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. The Breakthrough Therapy Designation was granted based on the Phase 2 clinical study of inaxaplin in patients with APOL1-mediated FSGS, a form of AMKD.

The EMA's PRIME designation is a regulatory mechanism that provides early and proactive support to developers of promising medicines, to optimize the generation of robust data and enable accelerated assessment so these medicines can potentially reach patients faster. The goal of PRIME is to help patients benefit as early as possible from innovative new therapies that have the potential to significantly address an unmet medical need. PRIME designation was granted based on clinical proof-of-concept data from Vertex's Phase 2 study of inaxaplin in APOL1-mediated FSGS. Inaxaplin is only the second nephrology product to be granted PRIME designation.

Vertex now holds three of the approximately 70 non-oncological PRIME designations granted to date, including its two PRIME designations for exagamglogene autotemcel (exa-cel), formerly known as CTX001, one for transfusion-dependent beta thalassemia and one for sickle cell disease. In the US, this is the ninth breakthrough therapy designation granted to Vertex across its portfolio programs.

About the Inaxaplin (VX-147) Pivotal Program
A randomized, double-blind, placebo-controlled Phase 2/3 adaptive study is ongoing and will first evaluate two doses of inaxaplin for 12 weeks to select a dose for Phase 3 and subsequently evaluate the efficacy and safety of the single, selected dose in the Phase 3 portion of the study.

Patients aged 18 to 60 years, with two *APOL1* mutations, urine protein to creatinine ratio (UPCR) ≥0.7 g/g to <10 g/g, estimated glomerular filtration rate (eGFR) ≥25 to <75 mL/min/1.73m^2 and on stable doses of standard of care medications are eligible to enroll. Approximately 66 patients are planned to be enrolled in the Phase 2 dose-ranging portion of the study, and approximately 400 additional patients are planned to be enrolled in the Phase 3 portion of the study.

The primary efficacy endpoint for the final analysis is eGFR slope in patients receiving the inaxaplin selected dose 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 eGFR, the onset of end-stage kidney disease (i.e., maintenance dialysis for ≥28 days, kidney transplantation, or a sustained eGFR of <15 mL/min/1.73 m^2), 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 UPCR 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.

About APOL1-Mediated Kidney Disease
APOL1-mediated kidney disease is a form of chronic kidney disease caused by mutations in the *APOL1* gene. Approximately 100,000 people in the U.S. and Europe have two *APOL1* genetic mutations and proteinuric kidney disease. People who inherit two mutations in the *APOL1* gene have a course of disease that is far more aggressive than in the absence of *APOL1* genetic mutations. Inherited *APOL1* genetic mutations 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 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, alpha-1 antitrypsin deficiency and Duchenne muscular dystrophy.

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 12 consecutive years on Science magazine's Top Employers list and one of the 2021 Seramount (formerly Working Mother Media) 100 Best Companies. 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 regarding the expedited development of inaxaplin resulting from the FDA's Breakthrough Therapy Designation and the EMA's PRIME designation, the potential benefits of inaxaplin, the anticipated timelines and dosing associated with ongoing and future clinical trials, study design, including expectations on patient enrollment, expectations regarding efficacy endpoints, and 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 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.

(VRTX-GEN)

View source version on businesswire.com: https://www.businesswire.com/news/home/20220608005181/en/

Vertex Pharmaceuticals Incorporated
Investors:
Michael Partridge, +1 617-341-6108
or
Miroslava Minkova, +1 617-341-6135

Media:
mediainfo@vrtx.com
or
U.S.: +1 617-341-6992
or
Heather Nichols: +1 617-839-3607
or
International: +44 20 3204 5275

Source: Vertex Pharmaceuticals Incorporated