Vertex Announces FDA Clearance of Investigational New Drug Application for VX-407 for the Treatment of Autosomal Dominant Polycystic Kidney Disease (ADPKD)

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– ADPKD is the most common inherited kidney disease, with no treatments currently available that address the underlying cause of disease –

– Vertex to initiate a Phase 1 clinical trial in healthy volunteers this month –

– ADPKD is Vertex's 10th disease area in the clinic, further expanding the company's pipeline of potentially transformative medicines for serious diseases –

BOSTON--(BUSINESS WIRE)--Mar. 21, 2024-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that the U.S. Food and Drug Administration (FDA) has cleared the Investigational New Drug Application (IND) for VX-407, an investigational first-in-class small molecule corrector that targets the underlying cause of autosomal dominant polycystic kidney disease (ADPKD) in patients with a subset of *PKD1* genetic variants. ADPKD is the most common inherited kidney disease, with an estimated 250,000 people in the U.S. and Europe living with ADPKD; however, there are no treatments currently available that address the underlying causal biology of the disease.

ADPKD is a life-shortening genetic kidney disease characterized by the growth of numerous kidney-enlarging cysts that impair kidney function and can ultimately lead to kidney failure, requiring dialysis or kidney transplantation, and premature death.

The majority of ADPKD cases are caused by variants in the *PKD1* gene, which encodes the polycystin 1 (PC1) protein. These inherited variants lead to a loss of PC1 function that results in cyst growth. VX-407 is a first-in-class small molecule corrector that is designed to target the underlying cause of ADPKD in a subset of patients with *PKD1* variants, estimated at ~25,000 (or ~10%) of the overall ~250,000 ADPKD patient population, by restoring function to the variant PC1 protein. Vertex plans to initiate a Phase 1 clinical trial of VX-407 in healthy volunteers this month.

"The advancement of VX-407, a first-in-class molecule for the treatment of ADPKD, into the clinic represents another important opportunity to transform the treatment of a serious disease," said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. "Just as our approach in cystic fibrosis allowed us to reach more patients over time, our goal here is to serially innovate to reach the 250,000 people suffering from ADPKD."

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 250,000 diagnosed people in the U.S. and Europe. As an autosomal dominant disease, 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.

About VX-407

VX-407 is a first-in-class small molecule corrector that is designed to treat ADPKD in patients with a subset of *PKD1* variants, estimated at ~25,000 (or ~10%) of the overall ~250,000 ADPKD patient population, by correcting defective PC1 folding to restore function. In doing so, the aim is to stop growth of kidney cysts and reduce kidney volume, thereby preventing progression to kidney failure.

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., in this press release, statements regarding plans to initiate a Phase 1 clinical trial of VX-407 in healthy volunteers this month, and estimates regarding the potential eligible patient population. 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 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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