Vertex to Present New Data on its Portfolio of Cystic Fibrosis Medicines at the 2022 North American Cystic Fibrosis Conference

November 3, 2022

- New clinical data show TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) continues to deliver significant benefit across a variety of outcomes and over the long term in people with CF -

BOSTON--(BUSINESS WIRE)--Nov. 3, 2022-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that multiple abstracts on the company's portfolio of cystic fibrosis (CF) medicines will be presented in posters and oral presentations at this year's North American Cystic Fibrosis Conference (NACFC), including studies demonstrating the clinical benefits and long-term safety of TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor).

Vertex will present new long-term safety and efficacy data on TRIKAFTA from an open-label 192-week extension study in people 12 years and older with CF and at least one *F508del* allele. Based on an interim analysis through Week 144 of the 192-week study, people receiving TRIKAFTA showed maintained improvements in lung function, respiratory symptoms and cystic fibrosis transmembrane conductance regulator (CFTR) function. TRIKAFTA also continues to be generally well tolerated (Poster #170 and Oral Workshop: W21.2). These data will also be discussed during the second plenary on November 4, 2022, at NACFC.

"These long-term data at 144 weeks demonstrate remarkable health effects in the longest study of TRIKAFTA. The data show sustainment of the historic improvements in lung function, respiratory symptoms and sweat chloride, a marker of CFTR function," said Deepika Polineni, M.D., MPH, Associate Professor of Pediatrics and Cystic Fibrosis Center Director at Washington University School of Medicine in St. Louis, and a co-investigator of the 445-105 study (Poster #170). "CFTR modulators like TRIKAFTA have pivotally changed standard of care therapy in CF, and the CF community continues to benefit from ongoing collection and evaluation of long-term data."

Vertex will also present data for the first time from its investigational Phase 3 open-label study designed to evaluate the safety, pharmacokinetics and efficacy of TRIKAFTA in children 2 through 5 years of age with CF and at least one *F508del* allele (Poster #693). The study shows that treatment with TRIKAFTA led to improvements in sweat chloride concentration and lung function, as measured by the lung clearance index, and stable nutritional status in children 2 through 5 years of age. TRIKAFTA was generally well tolerated, with a safety profile generally consistent with older age groups. Based on these results, Vertex recently submitted a New Drug Application (NDA) with the U.S. Food and Drug Administration for this age range and will be filing for approvals with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA) by the end of this year.

Additionally, Vertex will present data from a pooled analysis from multiple Phase 3 studies with CFTR modulators evaluating how the restoration of CFTR-mediated chloride transport, as reflected by changes in sweat chloride concentration, impacts clinical outcomes in people with CF treated with CFTR modulators (Poster #694). The study showed that people with CF ages 12 years and older treated with CFTR modulators achieved higher levels of CFTR activity, as reflected in lower levels of sweat chloride. Those with greater improvements in sweat chloride demonstrated greater improvements in lung function, respiratory symptoms, body mass index, pulmonary exacerbations, and had better lung function trajectory over time. These new data demonstrate that higher levels of CFTR function as measured by a reduction of sweat chloride are associated with improved clinical outcomes. The best outcomes were seen in those achieving a sweat chloride concentration <60 mmol/L.

In addition, Vertex will present findings from the first fully decentralized study in people with CF designed to explore the feasibility of wearable technology in evaluating clinical outcomes such as cough count and physical activity (Poster #169 and Oral Workshop: W30.1).

Vertex will also present interim results from Phase 3 open-label extension studies evaluating the long-term safety and efficacy of TRIKAFTA in children with CF ages 6 years and older (Poster #163 and Thematic Poster: TPS01.2) and people with CF 12 years and older with *F508del*-gating or *F508del*-residual function genotypes (Poster #185 and Thematic Poster: TPS01.5).

"These new data add to the growing body of evidence demonstrating the benefits of our CFTR modulators across multiple clinical measures over the long-term, and the significant impact these medicines are having on patients," said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer, Vertex.

About Cystic Fibrosis

Cystic fibrosis (CF) is a rare, life-shortening genetic disease affecting more than 83,000 people globally. CF is a progressive,

multi-organ disease that affects the lungs, liver, pancreas, GI tract, sinuses, sweat glands and reproductive tract. CF is caused by a defective and/or missing CFTR protein resulting from certain mutations in the *CFTR* gene. Children must inherit two defective *CFTR* genes — one from each parent — to have CF, and these mutations can be identified by a genetic test. While there are many different types of *CFTR* mutations that can cause the disease, the vast majority of people with CF have at least one *F508del* mutation. *CFTR* mutations lead to CF by causing CFTR protein to be defective or by leading to a shortage or absence of CFTR protein at the cell surface. The defective function and/or absence of CFTR protein results in poor flow of salt and water into and out of the cells in a number of organs. In the lungs, this leads to the buildup of abnormally thick, sticky mucus, chronic lung infections and progressive lung damage that eventually leads to death for many patients. The median age of death is in the early 30s.

About TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor)

U.S. INDICATION AND IMPORTANT SAFETY INFORMATION FOR TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) TABLETS

TRIKAFTA is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients aged 6 years and older who have at least one copy of the F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene or another mutation that is responsive to treatment with TRIKAFTA. Patients should talk to their doctor to learn if they have an indicated CF gene mutation. It is not known if TRIKAFTA is safe and effective in children under 6 years of age.

Patients should not take TRIKAFTA if they take certain medicines or herbal supplements, such as: antibiotics such as rifampin or rifabutin; seizure medicines such as phenobarbital, carbamazepine, or phenytoin; St. John's wort.

Before taking TRIKAFTA, patients should tell their doctor about all of their medical conditions, including if they: have kidney problems, have or have had liver problems, are pregnant or plan to become pregnant because it is not known if TRIKAFTA will harm an unborn baby, or are breastfeeding or planning to breastfeed because it is not known if TRIKAFTA passes into breast milk.

TRIKAFTA may affect the way other medicines work, and other medicines may affect how TRIKAFTA works. Therefore, the dose of TRIKAFTA may need to be adjusted when taken with certain medicines. Patients should especially tell their doctor if they take: antifungal medicines including ketoconazole, itraconazole, posaconazole, voriconazole, or fluconazole; antibiotics including telithromycin, clarithromycin, or erythromycin.

TRIKAFTA may cause dizziness in some people who take it. Patients should not drive a car, operate machinery, or do anything that requires alertness until they know how TRIKAFTA affects them.

Patients should avoid food or drink that contains grapefruit while they are taking TRIKAFTA.

TRIKAFTA can cause serious side effects, including:

Liver damage and worsening of liver function in people with severe liver disease that can be serious and may require transplantation. Liver damage has also happened in people without liver disease.

High liver enzymes in the blood, which is a common side effect in people treated with TRIKAFTA**.** These can be serious and may be a sign of liver injury. The patient's doctor will do blood tests to check their liver before they start TRIKAFTA, every 3 months during the first year of taking TRIKAFTA, and every year while taking TRIKAFTA. Patients should call their doctor right away if they have any of the following symptoms of liver problems: pain or discomfort in the upper right stomach (abdominal) area; yellowing of the skin or the white part of the eyes; loss of appetite; nausea or vomiting; dark, amber-colored urine.

Abnormality of the eye lens (cataract) has been noted in some children and adolescents treated with TRIKAFTA. If the patient is a child or adolescent, their doctor should perform eye examinations before and during treatment with TRIKAFTA to look for cataracts.

The most common side effects of TRIKAFTA include headache, diarrhea, upper respiratory tract infection (common cold) including stuffy and runny nose, stomach (abdominal) pain, inflamed sinuses, increase in liver enzymes, increase in a certain blood enzyme called creatine phosphokinase, rash, flu (influenza), and increase in blood bilirubin.

These are not all the possible side effects of TRIKAFTA.

Please click here to see the full U.S. Prescribing Information for TRIKAFTA (elexacaftor/tezacaftor/ivacaftor and ivacaftor).

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 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. Carmen Bozic and Dr. Deepika Polineni in this press release, statements regarding the potential benefits, safety and efficacy of TRIKAFTA, our plans to present data about our portfolio of CF medicines at the NACFC, including data from our TRIKAFTA Phase 3 open-label studies and data from a pooled analysis from multiple Phase 3 studies with CFTR modulators, and additional scientific presentations regarding TRIKAFTA, including long-term safety and efficacy data, expectations to present findings from a study designed to explore wearable technology in evaluating clinical outcomes, and expectations to file regulatory approvals with the EMA and MHRA by the end of this year. 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 company may not be able to submit the anticipated regulatory filings on the expected timeline, or at all, 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 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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