Vertex Announces U.S. FDA Approval for TRIKAFTA® (elexacaftor/tezacaftor /ivacaftor and ivacaftor) in Children With Cystic Fibrosis Ages 6 through 11 With Certain Mutations

June 9, 2021

- With this approval approximately 1,500 children with one minimal function mutation and one F508del mutation have a medicine to treat the underlying cause of their disease for the first time -

BOSTON--(BUSINESS WIRE)--Jun. 9, 2021-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced the U.S. Food and Drug Administration (FDA) approved expanded use of TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) to include children with cystic fibrosis (CF) ages 6 through 11 years who have at least one *F508del* mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene or a mutation in the *CFTR* gene that is responsive to TRIKAFTA based on *in vitro* data. TRIKAFTA was previously approved by the FDA for use in people with cystic fibrosis 12 years and older with at least one copy of the *F508del* mutation or one copy of a mutation that is responsive *in vitro*. An additional dosage strength of TRIKAFTA tablets is now available (elexacaftor 50 mg/tezacaftor 25 mg/ivacaftor 75 mg and ivacaftor 75 mg) in connection with this approval.

"Today's approval is a critical milestone in our efforts to deliver medicines that help treat the underlying cause of this devastating disease as early in life as possible," said Reshma Kewalramani, M.D., Chief Executive Officer and President, Vertex. "We can now reach approximately 1,500 newly eligible children in the U.S., and we continue to pursue approval for this expanded indication in other countries."

Vertex completed a 24-week Phase 3 open-label, multicenter study which enrolled 66 children ages 6 through 11 years old with cystic fibrosis (CF) who have either two copies of the *F508del* mutation or one copy of the *F508del* mutation and one minimal function mutation to evaluate the safety, pharmacokinetics and efficacy of TRIKAFTA. The regimen was generally well tolerated, and safety data were similar with those observed in previous studies of patients ages 12 years and older. The full data from this study were recently published in *American Journal of Respiratory and Critical Care Medicine*.

"Clinical experience with TRIKAFTA in patients 12 and older over the past 20 months has demonstrated this medicine has a meaningful and unprecedented clinical benefit for patients. I look forward to now being able to treat younger patients with this breakthrough medicine, including those who have not presented major signals of disease progression," said Terri Laguna M.D., M.S.C.S., Associate Director of the Cystic Fibrosis Center and Division Head, Pulmonary and Sleep Medicine, Ann & Robert H. Lurie Children's Hospital of Chicago. "In addition to bringing TRIKAFTA to a younger patient population, patients not previously eligible for any CFTR modulator will now be able to access a treatment that targets the underlying cause of their disease."

TRIKAFTA® is already approved for the treatment of patients with CF ages 12 years and older with certain mutations in the U.S. Switzerland, Australia and Israel, as well as in the EU and the U.K. as KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) in a combination regimen with KALYDECO® (ivacaftor). Vertex has submitted applications for use of TRIKAFTA/KAFTRIO in children ages 6 through 11 years to the European Medicines Agency (EMA) and the Medicines & Healthcare products Regulatory Agency (MHRA) and plans to file for this expanded use in Switzerland, Australia and Israel this year.

For more information on TRIKAFTA, patient assistance programs or to find additional eligibility details, visit TRIKAFTA.com, VertexGPS.com or vertextreatments.com.

About Cystic Fibrosis

Cystic Fibrosis (CF) is a rare, life-shortening genetic disease affecting more than 80,000 people globally. CF is a progressive, multi-system disease that affects the lungs, liver, GI tract, sinuses, sweat glands, pancreas 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. While there are many different types of *CFTR* mutations that can cause the disease, the vast majority of all people with CF have at least one *F508del* mutation. These mutations, which can be determined by a genetic test, or genotyping test, lead to CF by creating non-working and/or too few CFTR proteins 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 that can cause chronic lung infections and progressive lung damage in many patients that eventually leads to death. The median age of death is in the early 30s.

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

What is TRIKAFTA?

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; or 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 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:

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

These are not all the possible side effects of TRIKAFTA. **Please click the product link to see the full Prescribing Information for** TRIKAFTA**.**

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 medicines in other serious diseases where it has deep insight into causal human biology, including pain, alpha-1 antitrypsin deficiency and APOL1-mediated kidney diseases. In addition, Vertex has a rapidly expanding pipeline of cell and genetic therapies for diseases such as sickle cell disease, beta thalassemia, Duchenne muscular dystrophy and type 1 diabetes mellitus.

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 11 consecutive years on Science magazine's Top Employers list and a best place to work for LGBTQ equality by the Human Rights Campaign. 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, including, without limitation, statements made by Dr. Reshma Kewalramani and Dr. Terri Laguna in this press release, statements regarding our expectations for the number of patients newly eligible for TRIKAFTA, and statements regarding the potential benefits

of TRIKAFTA and our expectations regarding global regulatory filings for the expanded use of TRIKAFTA. 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 our regulatory filings may not be approved on a timely basis, 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.

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