Vertex Announces U.S. FDA Approval for TRIKAFTA® (elexacaftor/tezacaftor /ivacaftor and ivacaftor) in Children With Cystic Fibrosis Ages 2 Through 5 With Certain Mutations

April 26, 2023

-About 900 children with cystic fibrosis will now have a medicine to treat the underlying cause of their disease for the first time-

BOSTON--(BUSINESS WIRE)--Apr. 26, 2023-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced the U.S. Food and Drug Administration (FDA) approved the expanded use of TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) to include children with cystic fibrosis (CF) ages 2 through 5 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 CF 6 years and older with at least one *F508del* mutation or a mutation in the *CFTR* gene that is responsive to TRIKAFTA® based on *in vitro* data.

“Since its initial approval, TRIKAFTA has had a significant impact on the CF community, transforming the lives of thousands of people living with cystic fibrosis,” said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer, Vertex. “We remain steadfast in our commitment to bringing highly effective CF treatments to people of all ages living with this disease.”

This label expansion was supported by a 24-week Phase 3 open-label study which enrolled 75 children ages 2 through 5 years old with CF to evaluate the safety, pharmacokinetics and efficacy of TRIKAFTA®. The regimen was generally well tolerated, with a safety profile consistent with that observed in older age groups, and led to improvements in sweat chloride concentration, a measure of CFTR function, and lung function. The data from this study were recently published in the American Journal of Respiratory and Critical Care Medicine.

“Early intervention with CFTR modulator therapies like TRIKAFTA can offer the potential to improve the trajectory of CF lung disease,” said Jennifer Goralski, M.D., Assistant Professor of Medicine and Pediatrics, Co-Director, Adult Cystic Fibrosis Center, University of North Carolina School of Medicine, and a lead Principal Investigator in the TRIKAFTA® 2- to 5-year-old pivotal clinical trial. “With this approval, we now have the ability to treat young children with TRIKAFTA and can proactively address the underlying cause of their disease.”

TRIKAFTA® was previously approved for the treatment of people with CF ages 6 years and older with certain mutations in the U.S., Canada, Switzerland, Australia, New Zealand and Israel, as well as in the EU, the U.K., Iceland, Liechtenstein and Norway as KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) in a combination regimen with KALYDECO® (ivacaftor). Additionally, Vertex has submitted applications for the use of TRIKAFTA®/KAFTRIO® in children ages 2 through 5 years of age to other global regulatory authorities, including the European Medicines Agency (EMA) and the Medicines and Healthcare Products Regulatory Agency (MHRA).

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 88,000 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)

In people with certain types of mutations in the *CFTR* gene, the CFTR protein is not processed or folded normally within the cell, and this can prevent the CFTR protein from reaching the cell surface and functioning properly. TRIKAFTA® (elexacaftor/tezacaftor /ivacaftor and ivacaftor) is an oral medicine designed to increase the quantity and function of the CFTR protein at the cell surface. Elexacaftor and tezacaftor work together to increase the amount of mature protein at the cell surface. Ivacaftor, which is known as a CFTR potentiator, is designed to facilitate the ability of CFTR proteins to transport salt and water across the cell membrane. The combined actions of elexacaftor, tezacaftor and ivacaftor help hydrate and clear mucus from the airways.

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

TRIKAFTA is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients aged 2 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 2 years of age.

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.

Tell your doctor about all the medicines you take, including prescription and over-the- counter medicines, vitamins, and herbal supplements.

TRIKAFTA may affect the way other medicines work, and other medicines may affect how TRIKAFTA works. The dose of TRIKAFTA may need to be adjusted when taken with certain medicines. Patients should ask their doctor or pharmacist for a list of these medicines if they are not sure.

Patients should especially tell their doctor if they take: antibiotics such as rifampin or rifabutin; seizure medicines such as phenobarbital, carbamazepine, or phenytoin; St. John's wort; antifungal medicines including ketoconazole, itraconazole, posaconazole, voriconazole, or fluconazole; antibiotics including telithromycin, clarithromycin, or erythromycin.

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, 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.

Patients should tell their doctor if they have any side effect that bothers them or that does not go away. These are not all the possible side effects of TRIKAFTA. For more information, patients should ask their doctor or pharmacist. **Please click here 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 clinical pipeline of investigational small molecule, mRNA, cell and genetic therapies (including gene editing) in other serious diseases where it has deep insight into causal human biology, including sickle cell disease, beta thalassemia, APOL1-mediated kidney disease, acute and neuropathic pain, type 1 diabetes and alpha-1 antitrypsin deficiency.

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 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 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. Carmen Bozic and Dr. Jennifer Goralski in this press release, statements regarding the eligible patient population for TRIKAFTA®, including newly eligible patient population, and statements regarding the potential benefits 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 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 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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Vertex Pharmaceuticals Incorporated
Investors:
InvestorInfo@vrtx.com
or
Manisha Pai, +1 617-961-1899

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

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