Vertex Presents New Data at the European Cystic Fibrosis Conference Demonstrating Significant Benefits of Treatment with TRIKAFTA®

June 7, 2024

- *Results from a randomized, placebo-controlled study of TRIKAFTA® in people with cystic fibrosis with rare, non-*F508del CFTR *mutations showed statistically significant and clinically meaningful improvements in the primary and all secondary endpoints -*

- *Interim results of largest real-world study of TRIKAFTA® showed sustained improvement in lung function at three years as well as lower rates of lung transplant and death in people with cystic fibrosis, compared to pre-TRIKAFTA® initiation -*

BOSTON--(BUSINESS WIRE)--Jun. 7, 2024-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that data on TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor), also known in the European Union and in the U.K. as KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) in combination with ivacaftor, were presented at this year's European Cystic Fibrosis Society's (ECFS) 47th European Cystic Fibrosis Conference held June 5-8, 2024, in Glasgow, Scotland.

Data from a randomized, double-blind, Phase 3 study (abstract WS06.04) demonstrated that people with CF who have rare, non-*F508del* mutations in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene responsive to TRIKAFTA® *in vitro* demonstrated clinical benefit from receiving TRIKAFTA®. Compared to placebo, lung function improved by 9.2 percentage points as measured by ppFEV$_1$, CFTR function improved (as measured by mean sweat chloride concentration reductions of 28.3 mmol/L), and pulmonary exacerbations were reduced by 72% per year. Safety and tolerability were generally consistent with the established safety profile of TRIKAFTA®.

Vertex also presented the interim analysis (IA) of a registry-based study of real-world data collected from people with CF initiating TRIKAFTA® from 2019-20 in the U.S. and KAFTRIO® plus ivacaftor from 2020-21 in Germany (abstract WS01.04). The ongoing five-year post-authorization study is the largest real-world study of people with CF treated with TRIKAFTA®/KAFTRIO® to date, including more than 16,000 people with CF from the U.S. Cystic Fibrosis Foundation Patient Registry (CFFPR) and approximately 3,000 people with CF from the German CF Registry. The IA showed clinically meaningful, disease-modifying benefits for TRIKAFTA®/KAFTRIO®, including a 76% and 70% reduction in the cumulative annual rate of pulmonary exacerbations in the U.S. and in Germany, respectively, compared to the year prior to TRIKAFTA®/KATRIO® treatment. In addition, there was a 62% lower rate of death in the U.S. and 84% lower in Germany; and an 86% lower rate of lung transplant in the U.S. and 96% lower in Germany compared to the 2019 U.S. CFFPR and German CF Registry populations (pre-TRIKAFTA®/KAFTRIO®). No new safety concerns were identified.

"The breadth of TRIKAFTA data presented at ECFS is further evidence of the significant potential of this disease-modifying medicine," said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. "These studies demonstrate that TRIKAFTA is changing the course of CF treatment and the lives of those living with CF."

Additional Presentations

Other Vertex presentations at the conference this year include:

- Abstract WS15.02, entitled "Real-World Effectiveness of Elexacaftor/Tezacaftor/Ivacaftor (ELX/TEZ/IVA) in People With Cystic Fibrosis and ELX/TEZ/IVA-Responsive, Non-*F508del CFTR* Genotypes"
- Abstract EPS10.08, entitled "LONGITUDE: An Observational Study of the Long-term Effectiveness of ELX/TEZ/IVA in People With CF Using Data From the UK CF Registry – Preliminary Results From the Subgroup Aged 6-11 Years"
- Abstract P096, entitled "Qualitative Interviews Confirming the Faithful Electronic Migration of the Preschool Pictorial Cystic Fibrosis Questionnaire-Revised (CFQ-R) and Parent Preschool CFQ-R"
- Abstract EPS6.05, entitled "Clinical Outcomes in Concurrent Elexacaftor/Tezacaftor/Ivacaftor (ELX/TEZ/IVA) Treated vs. Ineligible Cohorts in the US Cystic Fibrosis Foundation Patient Registry (CFFPR) During COVID-19"
- Abstract P063, entitled "ELX/TEZ/IVA has beneficial effects on clinical outcomes and quality of life in people with cystic fibrosis in the real-world TRAJECTORY study"
- Abstract P072, entitled "Real-World Impact of Elexacaftor/Tezacaftor/Ivacaftor (ELX/TEZ/IVA) in Italy: A Retrospective Study From a CF Center"

About Cystic Fibrosis

Cystic fibrosis (CF) is a rare, life-shortening genetic disease affecting more than 92,000 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 30s, but with treatment, projected survival is improving.

Today Vertex CF medicines are treating over 65,000 people with CF across 60 countries on six continents. This represents 2/3 of the diagnosed people with CF eligible for CFTR modulator therapy.

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.

TRIKAFTA U.S. INDICATIONS AND IMPORTANT SAFETY INFORMATION FOR INDICATIONS AND USAGE

TRIKAFTA (elexacaftor/tezacaftor/ivacaftor and ivacaftor) 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.

IMPORTANT SAFETY INFORMATION

Before taking TRIKAFTA, patients should tell their doctor about all of their medical conditions, including if they: are allergic to TRIKAFTA or any ingredients in TRIKAFTA, 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.

Patients should tell their doctor about all the medicines they 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 taking TRIKAFTA.

TRIKAFTA can cause serious side effects, including:

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

High liver enzymes in the blood, which is a common side effect in patients 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.

Serious allergic reactions have happened to patients who are treated with TRIKAFTA. Call your healthcare provider or go to the emergency room right away if you have any symptoms of an allergic reaction. Symptoms of an allergic reaction may include: rash or hives; tightness of the chest or throat or difficulty breathing; swelling of the face, lips and/or tongue; difficulty swallowing; and light-headedness or dizziness.

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 U.S. Prescribing Information for TRIKAFTA.

About KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) in Combination With 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. KAFTRIO® (ivacaftor/tezacaftor /elexacaftor) in combination with 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 by binding to different sites on the CFTR protein. 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 ivacaftor, tezacaftor and elexacaftor help hydrate and clear mucus from the airways.

KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) in combination with ivacaftor is approved in the European Union and in the U.K. 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 *CFTR* gene.

For complete product information, please see the Summary of Product Characteristics that can be found on www.ema.europa.eu and on https://products.mhra.gov.uk/.

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, IgA nephropathy, 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, as amended, including, without limitation, statements by Carmen Bozic, M.D. in this press release, and statements regarding our expectations for the benefits of TRIKAFTA/KAFTRIO. 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 studies may not be indicative of final clinical trial results, 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, that data may not be available on the anticipated timeline, or at all, that our development programs may experience delays, and other risks listed under the heading “Risk Factors” in Vertex's most recent annual report and subsequent filings 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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