Vertex Announces Publication in The New England Journal of Medicine of Phase 3 Results for TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) in People With Cystic Fibrosis

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BOSTON--(BUSINESS WIRE)--Aug. 26, 2021-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced publication in *The New England Journal of Medicine (NEJM)* of results from a Phase 3 study of TRIKAFTA® (elexacaftor/tezacaftor /ivacaftor and ivacaftor) in people with cystic fibrosis (CF) ages 12 years and older who have one copy of the *F508del* mutation and one gating (F/G) or residual function (F/RF) mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene. The manuscript includes data on primary and key secondary endpoints, which were previously reported and showed statistically significant and clinically meaningful improvements in lung function and sweat chloride, when compared to active control (either ivacaftor or tezacaftor/ivacaftor), as well as more detailed efficacy and safety data, including subgroup efficacy analyses.

“This study is the third of three Phase 3 clinical trials in the TRIKAFTA program in the 12 years and older age group. Consistent with the prior outcomes, these results show clinically meaningful improvements in pulmonary function, sweat chloride and Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain scores," said Carmen Bozic, M.D., Executive Vice President and Chief Medical Officer, Vertex. “These results are especially notable given that all patients were treated with a CFTR modulator prior to initiating TRIKAFTA.”

“The outcomes within this study, in particular those from the subgroup efficacy analysis by F/G and F/RF, are remarkable because they demonstrate additional benefit on top of standard of care and build further confidence for clinicians to treat people with CF who may have these mutations,” said Steven Rowe, M.D., Director, Gregory Fleming James Cystic Fibrosis Research Center, University of Alabama at Birmingham.

Study 445-104

The data published today are from a global Phase 3, randomized, double-blind, parallel-group study. All patients had a 4-week run-in period of either ivacaftor or tezacaftor/ivacaftor. Following the run-in, 258 patients were randomized to receive TRIKAFTA® or to remain on their prior regimen of ivacaftor or tezacaftor/ivacaftor for 8 weeks. Baseline was measured at the end of the run-in period, prior to the start of the 8-week treatment period. TRIKAFTA® improved the percent predicted forced expiratory volume in 1 second ($ppFEV_1$) by 3.7 percentage points (95% CI, 2.8 to 4.6; $P<0.001$) from baseline and by 3.5 percentage points (95% CI, 2.2 to 4.7; $P<0.001$) vs. active control and improved sweat chloride concentration by -22.3 mmol/liter (95% CI, -24.5 to -20.2; $P<0.001$) from baseline and by -23.1 mmol/liter (95% CI, -26.1 to -20.1; $P<0.001$) vs. active control. The change in the CFQ-R respiratory domain score was +10.3 points from baseline (95% CI, 8.0 to 12.7) and +8.7 points vs. active control (95% CI, 5.3 to 12.1). Subgroup analyses of patients with F/G and F/RF genotypes are also included in the manuscript. Safety data were consistent with those observed in previous Phase 3 studies with TRIKAFTA®.

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; 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 such as 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:

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. Carmen Bozic and Dr. Steven Rowe in this press release and statements regarding the potential benefits of TRIKAFTA® and our anticipated efforts to expand the indication for TRIKAFTA® globally. 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 data from the company's development programs, including its programs with its collaborators, 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 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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