European Commission Approves KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) in Combination With Ivacaftor to Treat Cystic Fibrosis in People Ages 12 Years and Older

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– For the first time, up to 10,000 people in Europe ages 12 years and older with one F508del mutation and one minimal function mutation will be eligible for a medicine that treats the underlying cause of cystic fibrosis –

– People 12 years of age and older who have two F508del mutations will also be eligible for the new triple combination regimen –

LONDON--(BUSINESS WIRE)--Aug. 21, 2020-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that the European Commission (EC) has granted marketing authorization for KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) in a combination regimen with ivacaftor to treat people with cystic fibrosis (CF) ages 12 years and older with one *F508del* mutation and one minimal function mutation (F/MF), or two *F508del* mutations (F/F) in the *cystic fibrosis transmembrane conductance regulator* (*CFTR*) gene.

For the first time, up to 10,000 people in Europe ages 12 years and older with CF who have one *F508del* mutation and one minimal function mutation will be eligible for a CFTR modulator that treats the underlying cause of the disease. Approval of the triple combination regimen also expands the number of treatment options available to people ages 12 years and older with CF who have two copies of the *F508del* mutation, the most common CF-causing mutation worldwide.

"Today is a significant day for those with CF, their families and Vertex, and one that brings us one step closer towards our ultimate goal of discovering and developing treatments for all patients with CF," said Reshma Kewalramani, M.D., Chief Executive Officer and President, Vertex. "I would like to thank our dedicated scientists, as well as study investigators and people with CF who participated in our clinical trials to enable this innovative medicine to be approved in Europe today. Without their commitment, this milestone would not have been possible."

As a result of long-term reimbursement agreements in England, Denmark and the Republic of Ireland, and provisions for access in health care systems such as Germany, eligible patients in these countries will have access to the triple combination regimen in the upcoming weeks. Vertex is committed to working closely with national health authorities and governments in all other countries in Europe to secure access for eligible patients as quickly as possible.

Marketing authorization was based on the results of two global Phase 3 studies, which showed statistically significant and clinically meaningful improvements in lung function (primary endpoint) and all key secondary endpoints, in people with CF ages 12 years and older with one *F508del* mutation and one minimal function mutation or two *F508del* mutations in the *CFTR* gene. The triple combination regimen was generally well tolerated in both studies.

"The triple combination regimen has been shown to have a major impact on several outcome measures in people with CF," said Professor Harry Heijerman, Professor and Head of the Department of Pulmonology at University Medical Center Utrecht, Netherlands. "The clinical data showed significant improvements in lung function and other important measures, such as sweat chloride levels and quality of life as measured by the CFQ-R respiratory domain score, in patients treated with the triple combination therapy. I now look forward to seeing the impact of the medicine in clinical practice."

About Cystic Fibrosis

Cystic Fibrosis (CF) is a rare, life-shortening genetic disease affecting approximately 75,000 people worldwide. 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.

About KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) in a Combination Regimen With ivacaftor

KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) in a combination regimen with ivacaftor 150 mg was developed for the treatment of cystic fibrosis (CF) in patients ages 12 years and older with one *F508del* mutation and one minimal function mutation (F/MF) or two *F508del* mutations (F/F) in the *cystic fibrosis transmembrane conductance regulator* (*CFTR*) gene. KAFTRIO® is designed to increase the quantity and function of the F508del-CFTR protein at the cell surface. The EU submission for KAFTRIO® was supported by positive results of two global Phase 3 studies in people ages 12 years and older with CF: a 24-week Phase 3 study in 403 people with one *F508del* mutation and one minimal function mutation (F/MF) and a four-week Phase 3 study in 107 people with two *F508del* mutations (F/F).

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 genetic and cell 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, UK. 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 10 consecutive years on Science magazine's Top Employers list and top five on the 2019 Best Employers for Diversity list by Forbes.

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 Professor Harry Heijerman in this press release, statements regarding the eligible patient population in Europe, our expectations regarding the timing of access to the triple combination regimen across countries in Europe, and our plans to secure access to our medicine for additional patients in Europe. 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 factors that could cause actual events or results to differ materially from those indicated 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, risks related to commercializing medicines in Europe, and other risks listed under Risk Factors in Vertex's annual report and subsequent quarterly reports filed with the Securities and Exchange Commission and available through the company's website at www.vrtx.com. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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