CHMP Grants Positive Opinion for KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) in Combination With KALYDECO® (ivacaftor) in People Ages 12 and Older With Cystic Fibrosis With the Most Common Genotypes

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– If granted Marketing Authorization, people ages 12 and older in Europe who have one F508del mutation and one minimal function mutation will for the first time be able to benefit from a medicine that treats the underlying cause of the disease –

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

LONDON--(BUSINESS WIRE)--Jun. 26, 2020-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion for KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) in a combination regimen with KALYDECO® (ivacaftor) 150 mg to treat people with cystic fibrosis (CF) ages 12 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. If approved, up to 10,000 people in Europe with CF ages 12 and older who have one *F508del* mutation and one minimal function mutation would be newly eligible for a medicine that targets the disease- causing protein defect. Additionally, people 12 years of age and older who have two *F508del* mutations and who are currently eligible for one of Vertex's other EMA-approved cystic fibrosis medicines would be eligible for the new triple combination regimen.

The CHMP positive opinion was based on the results of two global Phase 3 studies in people with CF: a 24-week placebo-controlled study in people ages 12 years and older with one *F508del* mutation and one minimal function mutation and a 4-week head-to-head study of the triple combination therapy in comparison to tezacaftor/ivacaftor in people ages 12 years and older with two *F508del* mutations. Both Phase 3 studies showed statistically significant and clinically meaningful improvements in lung function (percent predicted forced expiratory volume in one second; ppFEV1), which was the primary endpoint, and in all key secondary endpoints. In both studies, the ivacaftor/tezacaftor/elexacaftor plus ivacaftor combination regimen was generally well tolerated.

"The clinical data for ivacaftor/tezacaftor/elexacaftor plus ivacaftor in people with CF ages 12 years and older with an F/F or F/MF genotype are unprecedented. In addition to improvements in lung function, the data have shown improvements in multiple important outcome measures, including quality of life as measured by the CFQ-R respiratory domain score," said Professor Marcus A. Mall, M.D., Head of Department of Pediatric Pulmonology, Immunology and Critical Care Medicine at Charité University Medical Center Berlin. "Both the clinical and patient communities are excited that more people with CF will be able to benefit from CFTR modulators."

"We are delighted to have received this positive opinion from CHMP. If approved, this would be the first CFTR modulator for people with one *F508del* mutation and one minimal function mutation and would bring additional benefit to people with two *F508del* mutations," said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. "This milestone brings us one step closer to delivering this innovative CF medicine to those who are waiting, and toward our ultimate goal of providing a therapeutic option for every person with this rare and devastating disease."

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 KALYDECO® (ivacaftor)

KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) in a combination regimen with KALYDECO® (ivacaftor) is an investigational medicine

developed for the treatment of cystic fibrosis (CF) in patients ages 12 years and older who have at least one copy of the *F508del* mutation 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. Mall and Dr. Bozic in this press release, and statements regarding our expectations for the approval of KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) in a combination regimen with KALYDECO® (ivacaftor) in Europe, and our expectations regarding the eligible patient population 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 obtaining approval for and 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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