Vertex Receives CHMP Positive Opinion for ALYFTREK®, a New Once-Daily CFTR Modulator for the Treatment of Cystic Fibrosis

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- ALYFTREK®(deutivacaftor/tezacaftor/vanzacaftor) recommended for people with CF ages 6 years and older with at least one non-class I mutation in the CFTR gene -

- In head-to-head clinical trials, deutivacaftor/tezacaftor/vanzacaftor was non-inferior on ppFEV$_1$ and superior compared to KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) at reducing sweat chloride -

LONDON--(BUSINESS WIRE)--Vertex Pharmaceuticals (Nasdaq: VRTX) today announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion for ALYFTREK®(deutivacaftor/tezacaftor/vanzacaftor)for the treatment of people with cystic fibrosis (CF) ages 6 years and older who have at least one non-class I mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene.

"Our goal has always been to serially innovate to help people with cystic fibrosis live healthier and longer lives. If approved, this new medicine would be indicated for people with CF ages 6 years and older with at least one non-class I mutation, meaning more patients would be eligible for a medicine that gets them closer to normal levels of sweat chloride," said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer, Vertex.

"CFTR modulators have already revolutionized the way we treat CF and I am encouraged that, if approved, this medicine could advance CF treatment even further," said Professor Marcus A. Mall, M.D., Professor and Chair of the Department of Pediatric Respiratory Medicine, Immunology and Critical Care Medicine and Cystic Fibrosis Center at Charité - Universitätsmedizin Berlin. "The results we saw from the two deutivacaftor/tezacaftor/vanzacaftor Phase 3 clinical trials were motivating as they showed non-inferiority in ppFEV$_1$ and superior improvement of sweat chloride levels compared to ivacaftor/tezacaftor/elexacaftor in combination with ivacaftor."

ALYFTREK® is currently licensed in the U.S. and UK and is under regulatory review in Canada, Switzerland, Australia and New Zealand.

About Cystic Fibrosis

Cystic fibrosis (CF) is a rare, life-shortening genetic disease affecting more than 109,000 people, including 94,000 people in North America, Europe and Australia. 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 car 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 68,000 people with CF across more than 60 countries on six continents. This represents 2/3 of the diagnosed people with CF eligible for CFTR modulator therapy.

Diagnosis of CF is often made by genetic testing and is confirmed by testing sweat chloride (SwCl), which measures CFTR protein dysfunction. The diagnostic threshold for CF is SwCl ≥60 mmol/L, while levels between 30-59 indicate CF is possible and more testing may be needed to make the diagnosis of CF. A SwCl level of <30 mmol/L is seen in people who carry one copy of a *CFTR* gene mutation but do not have any manifestation of disease (carriers). At a population level, higher levels of SwCl are associated with more severe disease. Restoring CFTR function leads to lower levels of SwCl. SwCl levels below 60 mmol/L are associated with improved outcomes such as better and more stable lung function, fewer pulmonary exacerbations, better quality of life and improved survival. Restoring SwCl levels below 30 mmol/L has long been the ultimate treatment goal for Vertex, as levels below 30 mmol/L are considered normal and are typical of CF carriers who do not have disease.

About ALYFTREK® (deutivacaftor/tezacaftor/vanzacaftor)

In people with CF, mutations in the *CFTR* gene lead to decreased quantity and/or function of the CFTR protein channel at the cell surface. Vanzacaftor and tezacaftor are designed to increase the amount of CFTR protein at the cell surface by facilitating the processing and trafficking of the CFTR protein. Deutivacaftor is a potentiator designed to increase the channel open probability of the CFTR protein delivered to the cell surface to improve the flow of salt and water across the cell membrane.

About Vertex

Vertex is a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious diseases and conditions. The company has approved therapies for cystic fibrosis, sickle cell disease, transfusion-dependent beta thalassemia and acute pain, and it continues to advance clinical and research programs in these areas. 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 neuropathic pain, APOL1-mediated kidney disease, IgA nephropathy, primary membranous nephropathy, autosomal dominant polycystic kidney disease, type 1 diabetes and myotonic dystrophy type 1.

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 15 consecutive years on Science magazine's Top Employers list and one of Fortune’s 100 Best Companies to Work For.

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 Carmen Bozic, M.D., and Professor Marcus A. Mall, M.D., in this press release, statements regarding the expected eligible patient population for ALYFTREK, if approved, and statements regarding the potential benefits of ALYFTREK. 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 regulatory authorities in the EU may not approve ALYFTREK on a timely basis or at all, and other risks listed under the heading “Risk Factors” in Vertex's annual report and in subsequent filings filed with the Securities and Exchange Commission and available through the company's website at www.vrtx.com and www.sec.gov. You should not place undue reliance on these statements. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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