Vertex Announces UK MHRA Approval of ALYFTREK® (Deutivacaftor/Tezacaftor/Vanzacaftor), a Once-Daily Next-in-Class CFTR Modulator for the Treatment of Cystic Fibrosis

March 7, 2025

- Deutivacaftor/tezacaftor/vanzacaftor approved for people with cystic fibrosis 6 years and older with at least one responsive mutation in the CFTR gene, including additional mutations not previously approved with other CFTR modulator therapies -

- In head-to-head clinical trials, deutivacaftor/tezacaftor/vanzacaftor was non-inferior on ppFEV$_1$ and further decreased sweat chloride compared to ivacaftor/tezacaftor/elexacaftor in combination with ivacaftor -

LONDON--(BUSINESS WIRE)--Mar. 7, 2025-- Vertex Pharmaceuticals (Nasdaq: VRTX) announced today that the United Kingdom (UK) Medicines and Healthcare products Regulatory Agency (MHRA) has granted approval for ALYFTREK® (deutivacaftor/tezacaftor/vanzacaftor), a once-daily next-in-class triple combination cystic fibrosis transmembrane conductance regulator (CFTR) modulator treatment for people living with cystic fibrosis (CF) ages 6 years and older who have at least one *F508del* mutation or another responsive mutation in the *CFTR* gene.

“For more than 20 years we have been focused on discovering medicines that treat the underlying cause of the disease with the goal of helping people live longer and better lives. The approval of ALYFTREK, our fifth CFTR modulator regimen, represents another significant milestone in that journey for people with CF in the UK,” said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex.

“The deutivacaftor/tezacaftor/vanzacaftor Phase 3 trial results showed that it is possible to further improve CFTR protein function with this once-a-day, more flexible and less burdensome regimen,” said Professor Alex Horsley, Professor of Respiratory Medicine at the University of Manchester, UK. “Children and adults taking the new triple combination therapy were more likely to have carrier levels of sweat chloride compared to those on the ivacaftor/tezacaftor/elexacaftor regimen, which we hope will translate to reduced risk of developing CF-related complications in the long term.”

Vertex is working with the National Institute for Health and Care Excellence (NICE) and the NHS to ensure eligible patients can access this new therapy, which treats the underlying cause of CF, as soon as possible.

This medicine was approved for patients ages 6 years and older by the U.S. FDA in December 2024 and Marketing Authorization Applications are ongoing with the European Medicines Agency (EMA) and the regulatory authorities in Canada, Switzerland, Australia and New Zealand in the same age group.

About Cystic Fibrosis

Cystic fibrosis (CF) is a rare, life-shortening genetic disease affecting more than 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 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 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). 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.

ALYFTREK® (deutivacaftor/tezacaftor/vanzacaftor) is approved in the UK for the treatment of CF in patients aged 6 years and older who have at least one *F508del* mutation or another responsive mutation in the *CFTR* gene.

For complete product information, please see the Summary of Product Characteristics that can be found 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 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.

Vertex 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, the statements by Carmen Bozic, M.D., and Professor Alex Horsley, in this press release, and statements regarding expectations for and the anticipated benefits of ALYFTREK, Vertex’s work with NICE and the NHS to ensure eligible patients can access this new therapy as soon as possible, and the status of the Marketing Authorization Applications for ALYFTREK with global regulatory authorities. While we believe 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 development programs may not support registration or further development of its compounds due to safety, efficacy, and other reasons, and other risks listed under the heading “Risk Factors” in Vertex's most recent annual report and subsequent quarterly reports 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. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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