July 2, 2015

FDA Approves ORKAMBI™ (lumacaftor/ivacaftor), the First Medicine to Treat the Underlying Cause of Cystic Fibrosis for People Ages 12 and Older with Two Copies of the F508del Mutation

-Approximately 8,500 people in the U.S. are ages 12 and older and have two copies of the F508del mutation, the most common genetic form of the disease-

BOSTON--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that the U.S. Food and Drug Administration (FDA) approved ORKAMBI™ (lumacaftor/ivacaftor), the first medicine to treat the underlying cause of cystic fibrosis (CF) in people ages 12 and older with two copies of the *F508del* mutation. It is only indicated for these patients, who can be identified with a genetic test.

Cystic fibrosis is a rare, life-threatening genetic disease. People with two copies of the *F508del* mutation represent the largest group of people with CF. Of the 30,000 people in the United States with CF, approximately 8,500 ages 12 and older have two copies of the *F508del* mutation. ORKAMBI will be available for shipment to specialty pharmacies in the United States within days.

"Today is a remarkable day for science, medicine and the CF community," said Jeffrey Leiden, M.D., Ph.D., Vertex's Chairman, President and Chief Executive Officer. "More than 15 years ago, our scientists set out to discover and develop medicines to treat the underlying cause of cystic fibrosis. Today, the approval of ORKAMBI represents a fundamental change in the treatment of the most common form of CF, marking significant progress for us and for the entire CF community. While we celebrate this important step forward, we also recognize that two out of three patients in the U.S. still do not have a medicine to treat the underlying cause of their disease. We share their urgency and are committed to continuing our significant investment in research and development to discover new medicines for them and to improve upon what we offer patients today."

Vertex will host an investor conference call on Thursday, July 2, at 2:15 p.m. ET. to provide more information on the approval of ORKAMBI.

The approval of ORKAMBI was based on data from two Phase 3 studies (TRAFFIC and TRANSPORT) that enrolled more than 1,100 people with CF ages 12 and older with two copies of the *F508del* mutation. Patients treated with ORKAMBI experienced statistically significant improvements in lung function. Patients also experienced reductions in pulmonary exacerbations and improvements in body mass index (BMI). The most common adverse events included shortness of breath and/or chest tightness, upper respiratory tract infection (common cold) and gastrointestinal symptoms (including nausea, diarrhea, or gas).

Vertex continues to invest in CF research and development with the goal of treating the vast majority of people with the disease and enhancing the benefit for those we treat. Multiple Phase 2 and Phase 3 clinical studies are in progress and Vertex has an ongoing research program focused on discovering new CF medicines.

"In 1998, Vertex and the CF Foundation embarked on a scientific challenge that many believed would be impossible - to discover medicines that treat the cause of CF," said Robert J. Beall, Ph.D., President and CEO of the Cystic Fibrosis Foundation. "Today's approval is a milestone for the CF community. We congratulate Vertex for their success in developing new CF medicines and are pleased with their continuing commitment to help all eligible patients get access to these medicines."

Helping Patients Access ORKAMBI

The people who work at Vertex understand that medicines can only help patients who can get them. The Vertex Guidance & Patient Support (Vertex GPS™) program provides a dedicated team of Vertex employees who help eligible patients who have been prescribed our medicines within their labeled indications understand their insurance benefits and the resources that are available to help them.

Vertex also offers a co-pay assistance program for patients with commercial insurance coverage and a free medicine program for qualifying patients who are uninsured and who meet certain income and other eligibility criteria. More information is available by visiting www.VertexGPS.com or by calling 1-877-752-5933.

About CF and ORKAMBI

Cystic fibrosis is a rare genetic disease that is caused by defective or missing cystic fibrosis transmembrane conductance regulatory (CFTR) proteins resulting from mutations in the CFTR gene. The defective or missing proteins result in poor flow of salt and water into or out of the cell in a number of organs, including the lungs. In people with two copies of the *F508del* mutation, the CFTR protein is not processed and trafficked normally within the cell, resulting in little to no CFTR protein at the cell surface. Patients with two copies of the *F508del* mutation are easily identified by a simple genetic test.

ORKAMBI is a combination of lumacaftor, which is designed to increase the amount of mature protein at the cell surface by targeting the processing and trafficking defect of the *F508del* CFTR protein, and ivacaftor, which is designed to enhance the function of the CFTR protein once it reaches the cell surface. ORKAMBI is taken every 12 hours - once in the morning and once in the evening.

INDICATION AND IMPORTANT SAFETY INFORMATION FOR ORKAMBI™ (lumacaftor/ivacaftor) TABLETS

ORKAMBI is a combination of lumacaftor and ivacaftor indicated for the treatment of cystic fibrosis (CF) in patients age 12 years and older who are homozygous for the *F508del* mutation in the *CFTR* gene. The efficacy and safety of ORKAMBI have not been established in patients with CF other than those homozygous for the *F508del* mutation.

Worsening of liver function, including hepatic encephalopathy, in patients with advanced liver disease has been reported in some patients with CF while receiving ORKAMBI. ORKAMBI should be used with caution in patients with advanced liver disease and only if the benefits are expected to outweigh the risks. If ORKAMBI is used in these patients, the patients should be closely monitored and the dose reduced.

Serious adverse reactions related to elevated transaminases have been reported in patients with CF receiving ORKAMBI and, in some instances, associated with concomitant elevations in total serum bilirubin. It is recommended that ALT, AST, and bilirubin be assessed prior to initiating ORKAMBI, every 3 months during the first year of treatment, and annually thereafter. For patients with a history of ALT, AST, or bilirubin elevations, more frequent monitoring should be considered. Patients who develop increased ALT, AST, or bilirubin should be closely monitored until the abnormalities resolve. Dosing should be interrupted in patients with ALT or AST greater than 5x upper limit of normal (ULN) when not associated with elevated bilirubin. Dosing should also be interrupted in patients with ALT or AST elevations greater than 3x ULN when associated with bilirubin elevations greater than 2x ULN. Following resolution of transaminase elevations, consider the benefits and risks of resuming dosing.

Respiratory events (e.g., chest discomfort, shortness of breath, and chest tightness) were observed more commonly in patients during initiation of ORKAMBI compared to those who received placebo. Clinical experience in patients with percent predicted FEV_1 < 40 is limited, and additional monitoring of these patients is recommended during initiation of therapy.

Co-administration of ORKAMBI with sensitive CYP3A substrates or CYP3A substrates with a narrow therapeutic index is not recommended as ORKAMBI may reduce their effectiveness.

ORKAMBI may substantially decrease hormonal contraceptive exposure, reducing their effectiveness and increasing the incidence of menstruation-associated adverse reactions. Hormonal contraceptives, including oral, injectable, transdermal, and implantable, should not be relied upon as an effective method of contraception when co-administered with ORKAMBI.

Co-administration with strong CYP3A inducers (e.g. rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin and St. John's wort) is not recommended as they may reduce the therapeutic effectiveness of ORKAMBI.

ORKAMBI has the potential to affect other drugs. For additional information regarding drug interactions, see full Prescribing Information.

Abnormalities of the eye lens (cataracts) have been reported in pediatric patients treated with ivacaftor, a component of ORKAMBI. Baseline and follow-up ophthalmological examinations are recommended in pediatric patients initiating treatment with ORKAMBI.

Serious adverse reactions that occurred more frequently in patients treated with ORKAMBI included pneumonia, blood in sputum, cough, increased muscle enzyme levels, and liver enzyme elevations. The most common adverse reactions associated with ORKAMBI include shortness of breath, sore throat, nausea, diarrhea, upper respiratory tract infection, fatigue, chest tightness, increased blood creatinine phosphokinase, rash, flatulence, runny nose, and influenza.

Please see full prescribing information for ORKAMBI available at www.ORKAMBI.com.

Global Regulatory Submissions for ORKAMBI

Outside of the U.S., Vertex has submitted ORKAMBI for regulatory approval in the European Union, Australia and Canada. A decision by the European Medicines Agency (EMA) is anticipated by the end of 2015. Reviews by Health Canada and Australia's Therapeutic Goods Administration (TGA) are also ongoing.

Investor Conference Call

Vertex will host an investor conference call and webcast on Thursday, July 2, at 2:15 p.m. ET. To listen to the live call on the telephone dial (866) 501-1537 (United States and Canada) or (720) 545-0001 (International). The conference ID number for the live call and replay is 76077705. In addition, the conference call will be webcast live, and a link to the webcast may be accessed through Vertex's website at www.vrtx.com in the "Investors" section under the "Events & Presentations" page.

The call will be available for replay via telephone and webcast. The replay phone number in the United States and Canada is (855) 859-2056. The international replay number is (404) 537-3406. The archived webcast will be available at www.vrtx.com.

About Cystic Fibrosis

Cystic fibrosis is a rare, life-threatening genetic disease affecting approximately 75,000 people in North America, Europe and Australia.

CF is caused by a defective or missing CFTR protein resulting from mutations in the *CFTR* gene. Children must inherit two defective *CFTR* genes — one from each parent — to have CF. There are approximately 2,000 known mutations in the *CFTR* gene. Some of these mutations, which can be determined by a genetic test, lead to CF by creating defective or too few CFTR proteins at the cell surface. The defective or missing CFTR protein results in poor flow of salt and water into or out of the cell in a number of organs, including 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 predicted age of survival for a person with CF is 41 years, but the median age of death is 27 years.

Collaborative History with Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT)

Vertex initiated its CF research program in 1998 as part of a collaboration with CFFT, the nonprofit drug discovery and development affiliate of the Cystic Fibrosis Foundation. Both of our approved CF medicines were discovered by Vertex as part of this collaboration.

About Vertex

Vertex is a global biotechnology company that aims to discover, develop and commercialize innovative medicines so people with serious diseases can lead better lives. In addition to our clinical development programs focused on cystic fibrosis, Vertex has more than a dozen ongoing research programs aimed at other serious and life-threatening diseases.

Founded in 1989 in Cambridge, Mass., Vertex today has research and development sites and commercial offices in the United States, Europe, Canada and Australia. For five years in a row, *Science* magazine has named Vertex one of its Top Employers in the life sciences. For additional information and the latest updates from the company, please visit www.vrtx.com.

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 the statements by Dr. Leiden in the third paragraph of this press release and statements regarding (i) the timing of the availability of ORKAMBI for shipment to specialty pharmacies in the United States; (ii) Vertex's commitment to continuing its significant investment in research and development programs in cystic fibrosis; and (iii) the anticipated timing of the completion of regulatory reviews in international markets. While the company believes the forward-looking statements contained in this press release are accurate, 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, risks related to commercializing ORKAMBI in the United States, obtaining approval and commercializing ORKAMBI in international markets, developing additional medicines to treat cystic fibrosis and the other risks listed under Risk Factors in Vertex's annual report and quarterly reports filed with the Securities and Exchange Commission and available through Vertex'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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