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Health Canada Approves PrORKAMBI® (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 1,500 people in Canada 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 Health Canada has approved PrORKAMBI® (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 approximately 4,000 people in Canada with CF, approximately 1,500 of these people ages 12 and older have two copies of the *F508del* mutation.

"With Health Canada's approval of ORKAMBI, people in Canada living with the most common form of CF now have a treatment for the underlying cause of the disease," said Andy Partridge, Vertex Vice President and Head of the North American Commercial Organization.

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.

Vertex continues to invest in CF research and development, including at our Laval, Quebec facility, with the goal of developing treatments for the vast majority of people with the disease. Multiple Phase 2 and Phase 3 clinical studies are in progress.

"Like PrKALYDECO® (ivacaftor) before it, ORKAMBI treats the underlying defect in cystic fibrosis, but for a much larger part of the CF population. Health Canada's approval of ORKAMBI is the first step in getting this drug into the hands of the people who need it most, the indicated patients for whom Cystic Fibrosis Canada advocates each and every day," said Cystic Fibrosis Canada Chief Scientific Officer Dr. John Wallenburg. "We congratulate Vertex on the approval of ORKAMBI by Health Canada and look forward to working with Vertex and the provincial drug plans to ensure access to ORKAMBI for eligible CF patients across Canada."

About the Public Reimbursement Process in Canada

Health Canada approval is the first step in the process for securing funding through Canada's public drug programs for a new medicine. Once a new medicine receives Notice of Compliance (NOC), or approval from Health Canada, it enters the Canadian Agency for Drugs and Technologies (CADTH) Common Drug Review (CDR) process. Following its review, CADTH will send a recommendation to participating public drug programs. In Quebec, new medicines are reviewed by l'institut national d'excellence en santé et en services sociaux (INESSS). Participating jurisdictions may then proceed to reimbursement discussions with the manufacturer through the Pan-Canadian Pharmaceutical Alliance (pCPA). When an agreement has been reached between the manufacturer and the pCPA, each province and territory determines how the new medicine will be funded.

About CF and ORKAMBI

CysticÂ fibrosis is a rare genetic disease that is caused by defective or missing cystic fibrosis transmembrane conductance regulatory (CFTR) proteins resulting from mutations in theÂ CFTRÂ 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 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 recommended to be taken every 12 hours - once in the morning and once in the evening.

INDICATION AND IMPORTANT SAFETY INFORMATION FOR ^{Pr}ORKAMBI^{TM} (lumacaftor/ivacaftor)

ORKAMBI is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients age 12 years and older who have two copies of the *F508del* mutation (*F508del/F508del*) in their *CFTR* gene. ORKAMBI should only be used in these patients. The efficacy and safety of ORKAMBI have not been established in patients with CF other than those homozygous for the *F508del* mutation.

IMPORTANT SAFETY INFORMATION

Before taking ORKAMBI, patients should tell their doctor if they have or have had liver problems or have kidney problems: have had an organ transplant; are using birth control (hormonal contraceptives, including oral, injectable, transdermal or implantable forms) because hormonal contraceptives should not be used as a method of birth control when taking ORKAMBI; are pregnant or plan to become pregnant because it is unknown if ORKAMBI will harm the unborn baby; are breastfeeding or planning to breastfeed as it is unknown if ORKAMBI passes into breast milk.

ORKAMBI can cause serious side effects including: High liver enzymes in the blood, which can be a sign of liver injury, have been reported in patients receiving ORKAMBI. The patient's doctor will do blood tests to check their liver before they start ORKAMBI, every three months during the first year of taking ORKAMBI, and annually thereafter. The patient should call the doctor right away if they have any of the following symptoms of liver problems: pain or discomfort in the upper right stomach (abdominal) area; yellowing of the skin or the white part of the eyes; loss of appetite; nausea or vomiting; dark urine; confusion; or pale stools.

Respiratory events such as shortness of breath or chest tightness were observed in patients when starting ORKAMBI. If a patient has poor lung function, their doctor may monitor them more closely when starting ORKAMBI.

Increased blood pressure and decreased heart rate have been observed during treatment with ORKAMBI. Blood pressure should be monitored periodically in all patients during treatment. Caution should be observed in patients with pre-existing hypertension. Concomitant medications that result in an increase in blood pressure and/or a decrease in heart rate should be avoided to the extent possible during treatment with ORKAMBI.

ORKAMBI may affect the way other medicines work and other medicines may affect how ORKAMBI works. Therefore, the dose of ORKAMBI or other medicines may need to be adjusted when taken together. Patients should especially tell their doctor if they take: antifungal medicines, antibiotic medicines, anticonvulsant medicines, ranitidine, a medication used to treat peptic ulcers and gastroesophageal reflux disease, St. John's wort, benzodiazepines, antidepressants, anti-allergics, anti-inflammatories, immunosuppressants, cardiac glycosides, anticoagulants, glucocorticoids and proton pump inhibitors.

When taking ORKAMBI, a patient should tell their doctor if they stop ORKAMBI for more than 1 week as the doctor may need to change the dose of ORKAMBI or other medicines the patient is taking. It is unknown if ORKAMBI causes dizziness. A patient should not drive a car, use machinery, or do anything requiring alertness until the patient knows how ORKAMBI affects them.

Abnormality of the eye lens (cataract) has been noted in some children and adolescents receiving ivacaftor, a component of ORKAMBI. The patient's doctor should perform eye examinations prior to and during treatment with ORKAMBI to look for cataracts.

The most common side effects of ORKAMBI include: shortness of breath and/or chest tightness; upper respiratory tract infection (common cold), including sore throat, stuffy or runny nose; gastrointestinal symptoms including nausea, diarrhea, or gas; rash; fatigue; flu or flu-like symptoms; increase in muscle enzyme levels; and irregular, missed, or abnormal menstrual periods and heavier bleeding.

Please click here to see the full prescribing information for ORKAMBI.

Global Regulatory Submissions for ORKAMBI

ORKAMBI has received regulatory approval in the United States, the European Union and Canada. Vertex has also submitted ORKAMBI for regulatory approval in Australia and review by Australia's Therapeutic Goods Administration (TGA)

is ongoing.

About Cystic Fibrosis

Cystic fibrosis is a rare, life-threatening genetic disease affecting approximately 75,000 people inÂ North America,Â EuropeÂ andÂ Australia.

CF is caused by a defective or missing CFTR protein resulting from mutations in theÂ *CFTRÂ* gene. Children must inherit two defectiveÂ *CFTRÂ* genes — one from each parent — to have CF. There are approximately 2,000 known mutations in theÂ *CFTRÂ* 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 age of survival for Canadians with CF is currently estimated to be 51 years. Of the 40 people who died of CF in 2013 half were under the age of 35.

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 inÂ Cambridge, Mass., Vertex today has research and development sites and commercial offices inÂ the United States,Â Europe,Â CanadaÂ and Australia. For five years in a row,Â *Science*Â magazine has named Vertex one of its Top Employers in the life sciences. For additional information and the latest updates from the company, please visitÂ 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 quotes in the third and sixth paragraphs of this press release and statements regarding Vertex's ongoing research and development programs and the Canadian reimbursement process. 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 Canada 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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