May 31, 2016

U.S. FDA Accepts for Priority Review Supplemental New Drug Application for the Use of ORKAMBI® (lumacaftor/ivacaftor) in Children with Cystic Fibrosis Ages 6 to 11 who have Two Copies of the F508del Mutation

-Approximately 2,400 children ages 6 to 11 have two copies of the F508del mutation in the U.S.-

-Target review date of September 30, 2016 set for the FDA's decision on the application-

BOSTON--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq:VRTX) today announced that the U.S. Food and Drug Administration (FDA) has accepted for review a supplemental New Drug Application (sNDA) for the use of ORKAMBI® (lumacaftor/ivacaftor) in people with cystic fibrosis (CF) ages 6 to 11 who have two copies of the *F508del* mutation. The FDA granted Vertex's request for Priority Review of this sNDA, and a target review date of September 30, 2016 was set under the Prescription Drug User Fee Act (PDUFA).

"As complications related to CF can occur early in life, we believe it is important to begin treatment as early as possible and this supplemental New Drug Application for approval of ORKAMBI in children as young as six is an important step in that direction," said Jeffrey Chodakewitz, M.D., Executive Vice President and Chief Medical Officer at Vertex. "This submission demonstrates Vertex's continued progress toward our goal of developing medicines for all people with CF."

The sNDA is based on data from an open label Phase 3 clinical safety study of ORKAMBI. Data from this study will be presented at the 39th European Cystic Fibrosis Society conference being held June 8 to 11 in Basel, Switzerland.

To support potential approval in the European Union, a six-month Phase 3 efficacy study of children ages 6 to 11 is ongoing. Vertex recently completed enrollment in this study and, pending data from the study, plans to submit a Marketing Authorization Application (MAA) variation in the European Union in the first half of 2017 for children ages 6 to 11 who have two copies of the *F508del* mutation. The primary endpoint of this efficacy study is the absolute change in lung clearance index (LCI). There are approximately 3,400 children ages 6 to 11 who have two copies of the *F508del* mutation in the European Union.

About CF and ORKAMBI

Cystic fibrosis is a rare genetic disease that is caused by defective or missing cystic fibrosis transmembrane conductance regulator (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 with fat-containing food.

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

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. It is not known if ORKAMBI is safe and effective in children under 12 years of age.

Patients should not take ORKAMBI if they are taking certain medicines or herbal supplements, such as: the antibiotics rifampin or rifabutin; the seizure medicines phenobarbital, carbamazepine, or phenytoin; the sedatives/anti-anxiety medicines triazolam or midazolam; the immunosuppressant medicines everolimus, sirolimus, or tacrolimus; or St. John's wort.

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). 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. It is unknown if ORKAMBI passes into breast milk.

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 such as ketoconazole, itraconazole, posaconazole or voriconazole; or antibiotics such as telithromycin, clarithromycin, or erythromycin.

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.

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, amber-colored urine; or confusion.

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.

An increase in blood pressure has been seen in some patients treated with ORKAMBI. The patient's doctor should monitor their blood pressure during treatment with ORKAMBI.

Abnormality of the eye lens (cataract) has been noted in some children and adolescents receiving ivacaftor, a component of ORKAMBI. For children and adolescents, 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.

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 born today with CF in the United States is 39 years, but the median age of death is 29 years.

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

Vertex initiated its CF research program in 1998 as part of collaboration with CFFT, the nonprofit drug discovery and development affiliate of the Cystic Fibrosis Foundation. KALYDECO (ivacaftor) and ORKAMBI (lumacaftor/ivacaftor) 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 six 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, including, without limitation, Dr. Chodakewitz's statements in the second paragraph of the press release, the target review date of September 30, 2016 and the expected timing for submission of an MAA variation in Europe for children ages 6 to 11 who have two copies of the F508del mutation. While Vertex 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, that regulatory authorities may not approve, or approve on a timely basis, the sNDA, that the data from the Phase 3 safety study may not be sufficient to support approval of the sNDA, 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, 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 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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