September 28, 2016

U.S. Food and Drug Administration Approves ORKAMBI® (lumacaftor/ivacaftor) for Use in Children with Cystic Fibrosis Ages 6 through 11 who have Two Copies of the F508del Mutation

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

- Vertex revises ORKAMBI revenue guidance for 2016 -

BOSTON--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that the U.S. Food and Drug Administration (FDA) approved ORKAMBI® (lumacaftor/ivacaftor) for use in children with cystic fibrosis (CF) ages 6 through 11 who have two copies of the *F508del* mutation. People with this mutation represent the largest population of those with CF, a rare, life-threatening disease. ORKAMBI is the first and only medicine to treat the underlying cause of CF for people with this mutation. It was previously approved by the FDA for use in people ages 12 and older with two copies of the *F508del* mutation. With today's approval, approximately 11,000 people with CF are eligible for treatment with ORKAMBI in the United States. ORKAMBI will be available for eligible children ages 6 through 11 in the United States as soon as possible. Vertex also today lowered its guidance for 2016 ORKAMBI revenues to a range of $950 million to $990 million.

"The ability to treat children as young as six who have the most common form of the disease is an important milestone as we pursue our goal to develop medicines for all people with CF," said Jeffrey Chodakewitz, M.D., Executive Vice President and Chief Medical Officer at Vertex. "We believe it is important to treat the underlying cause of the disease as early as possible in these patients."

The approval is based on data from a previously announced open-label Phase 3 clinical safety study of ORKAMBI presented at the 39th European Cystic Fibrosis Society Conference in June 2016. These data will be presented at the 30th Annual North American Cystic Fibrosis Conference October 27-29 in Orlando, Florida.

Vertex plans to submit a Marketing Authorization Application (MAA) variation in the European Union in the first half of 2017 for children ages 6 through 11 who have two copies of the F508del mutation. This application will be based on data from a Phase 3 efficacy study with a primary endpoint of absolute change in lung clearance index (LCI). These data are expected before the end of 2016.

ORKAMBI Financial Guidance

Vertex today revised its guidance for 2016 ORKAMBI revenues. The company now expects ORKAMBI revenues of $950 million to $990 million. Vertex's prior guidance was for total 2016 ORKAMBI revenues of $1.0 billion to $1.1 billion, and to date Vertex has reported ORKAMBI revenues of $223 million and $245 million for the first and second quarters of 2016, respectively. Vertex expects third quarter ORKAMBI revenues to be between $230 million and $235 million. The revised guidance primarily reflects the following:

- The slower than anticipated launch in Germany where fewer than 20 percent of the approximately 2,500 eligible patients have initiated treatment to date;
- That we are approaching peak penetration for ORKAMBI in the U.S. where there are approximately 8,500 eligible patients ages 12 and older; and
- Slower than expected refills for ORKAMBI during the summer months of July and August.

Today's approval in people ages 6 through 11 will drive growth in the U.S. in the fourth quarter of 2016. Growth for ORKAMBI in 2017 will be driven both by obtaining reimbursement approvals in key European and other countries and by continued growth among eligible patients ages 6 through 11 in the U.S.

About Cystic Fibrosis and ORKAMBI

Cystic fibrosis is a rare, life-threatening genetic disease affecting approximately 75,000 people in North

America, Europe and Australia.

CF is caused by defective or missing cystic fibrosis conductance regulator (CFTR) proteins 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.

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. In pediatric patients ages 6 through 11, two ORKAMBI tablets (each containing lumacaftor 100mg/ivacaftor 125mg) are taken orally 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 6 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 6 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; 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. Patients should tell their doctor if they are pregnant or plan to become pregnant (it is unknown if ORKAMBI will harm the unborn baby) or if they 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, patients 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. Patients 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 ORKAMBI and 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.

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

Vertex initiated its CF research program in 2000 as part of a collaboration with CFFT, the nonprofit drug discovery and development affiliate of the Cystic Fibrosis Foundation. ORKAMBI (lumacaftor/ivacaftor) was 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, the information provided in Dr. Chodakewitz's quote in the second paragraph of this press release and in the section captioned "ORKAMBI Financial Guidance" and statements regarding (i) Vertex's revenue guidance and expectations and (ii) plans to submit an MAA variation in the European Union for children ages 6 to 11 who have two copies of the F508del mutation and the timing of expected data from Vertex's Phase 3 efficacy study in this patient population. 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 the company's expectations regarding revenues may be incorrect (including because one or more of the company's assumptions underlying its expectations may not be realized), 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 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.

(VRTX-GEN)

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Source: Vertex Pharmaceuticals Incorporated