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## FDA Approves KALYDECO® (ivacaftor) for More Than 600 People Ages 2 and Older With Cystic Fibrosis Who Have Certain Residual Function Mutations

BOSTON--(BUSINESS WIRE)-- [Vertex Pharmaceuticals Incorporated](#) (Nasdaq: VRTX) today announced that the U.S. Food and Drug Administration (FDA) has approved KALYDECO® (ivacaftor) for use in more than 600 people with cystic fibrosis (CF) ages 2 and older who have one of five residual function mutations that result in a splicing defect in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene. This approval was based on Phase 3 clinical data for KALYDECO in these mutations and follows the FDA's approval of KALYDECO in May 2017 for 23 other residual function mutations, which was based on analyses of *in vitro* data. Both approvals are supported by more than five years of real-world clinical experience that demonstrate KALYDECO's established safety and efficacy profile. Based on today's approval, Vertex increased its guidance for 2017 KALYDECO product revenues to a range of \$770 million to \$800 million. Vertex's guidance range for total CF product revenues in 2017 is now \$1.87 billion to \$2.1 billion, including ORKAMBI guidance of \$1.1 billion - \$1.3 billion.

"In the five years since KALYDECO became the first approved medicine to treat the underlying cause of cystic fibrosis, we have been relentless in our efforts to bring this important medicine to all who may benefit," said Jeffrey Chodakewitz, M.D., Executive Vice President and Chief Medical Officer at Vertex. "We will continue to pursue this goal until all people with CF have a medicine that treats their form of this serious and life-shortening disease."

CF 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 (sodium and chloride) and water into or out of cells in a number of organs, including the lungs. The five mutations covered under today's approval (2789+5G— > A, 3272-26A— > G, 3849+10kbC— > T, 711+3A— > G, and E831X) cause CF and result in a moderate loss of chloride transport. People who have these mutations generally experience progressive lung function decline and other complications of the disease. All five of these mutations were evaluated as part of the previously disclosed [Phase 3 EXPAND study](#) in which the KALYDECO monotherapy arm met its primary efficacy endpoint and was generally well tolerated.

KALYDECO is now approved in the U.S. to treat people with CF ages 2 and older who have one of 38 ivacaftor-responsive mutations in the *CFTR* gene.

### 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 is 41 years, but currently the median age of death is 29 years.

### About KALYDECO® (ivacaftor)

KALYDECO (ivacaftor) is the first medicine to treat the underlying cause of CF in people with specific mutations in the *CFTR* gene. Known as a *CFTR* potentiator, KALYDECO is an oral medicine designed to keep *CFTR* proteins at the cell surface open longer to improve the transport of salt and water across the cell membrane, which helps hydrate and clear mucus from the airways. KALYDECO is available as 150 mg tablets for adults and pediatric patients age 6 years and older, and is taken with fat-containing food. It is also available as 50 mg and 75 mg granules in pediatric patients ages 2 to less than 6 years and is administered with soft-food or liquid with fat-containing food.

People with CF who have specific mutations in the *CFTR* gene are currently benefiting from KALYDECO in 27 different

countries across North America, Europe and Australia.

## **KALYDECO® (ivacaftor) INDICATION AND IMPORTANT SAFETY INFORMATION**

KALYDECO (ivacaftor) is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients age 2 years and older who have at least one mutation in their CF gene that is responsive to KALYDECO. Patients should talk to their doctor to learn if they have an indicated CF gene mutation. It is not known if KALYDECO is safe and effective in children under 2 years of age.

**Patients should not take KALYDECO if they are taking certain medicines or herbal supplements such as:** the antibiotics rifampin or rifabutin; seizure medications such as phenobarbital, carbamazepine, or phenytoin; or St. John's wort.

**Before taking KALYDECO, patients should tell their doctor if they:** have liver or kidney problems; drink grapefruit juice, or eat grapefruit or Seville oranges; are pregnant or plan to become pregnant because it is not known if KALYDECO will harm an unborn baby; and are breastfeeding or planning to breastfeed because it is not known if KALYDECO passes into breast milk.

**KALYDECO may affect the way other medicines work, and other medicines may affect how KALYDECO works.** Therefore the dose of KALYDECO may need to be adjusted when taken with certain medications. Patients should especially tell their doctor if they take antifungal medications such as ketoconazole, itraconazole, posaconazole, voriconazole, or fluconazole; or antibiotics such as telithromycin, clarithromycin, or erythromycin.

KALYDECO can cause dizziness in some people who take it. Patients should not drive a car, use machinery, or do anything that needs them to be alert until they know how KALYDECO affects them. Patients should avoid food containing grapefruit or Seville oranges while taking KALYDECO.

**KALYDECO can cause serious side effects including:**

**High liver enzymes in the blood have been reported in patients receiving KALYDECO.** The patient's doctor will do blood tests to check their liver before starting KALYDECO, every 3 months during the first year of taking KALYDECO, and every year while taking KALYDECO. For patients who have had high liver enzymes in the past, the doctor may do blood tests to check the liver more often. Patients should call their 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 their skin or the white part of their eyes; loss of appetite; nausea or vomiting; or dark, amber-colored urine.

Abnormality of the eye lens (cataract) has been noted in some children and adolescents receiving KALYDECO. The patient's doctor should perform eye examinations prior to and during treatment with KALYDECO to look for cataracts. The most common side effects include headache; upper respiratory tract infection (common cold), which includes sore throat, nasal or sinus congestion, and runny nose; stomach (abdominal) pain; diarrhea; rash; nausea; and dizziness.

These are not all the possible side effects of KALYDECO.

Please [click here](#) to see the full Prescribing Information for KALYDECO.

### **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. KALYDECO (ivacaftor) was discovered by Vertex as part of this collaboration.

### **About Vertex**

Vertex is a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious and life-threatening diseases. In addition to clinical development programs in CF, Vertex has more than a dozen ongoing research programs focused on the underlying mechanisms of other serious diseases.

Founded in 1989 in Cambridge, Mass., Vertex's headquarters is now located in Boston's Innovation District. Today, the company has research and development sites and commercial offices in the United States, Europe, Canada and Australia. Vertex is consistently recognized as one of the industry's top places to work, including being named to *Science* magazine's Top Employers in the life sciences ranking for seven years in a row. For additional information and the latest updates from the company, please visit [www.vrtx.com](http://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 statements in the second paragraph of the press release and statements regarding guidance for 2017 KALYDECO and ORKAMBI net product revenues. 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 its 2017 KALYDECO and ORKAMBI net product 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](http://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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