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Supplemental New Drug Application for Use of KALYDECO® (ivacaftor) in People with Cystic Fibrosis Ages 2 and Older who have One of 23 Residual Function Mutations Accepted for Priority Review by U.S. FDA

-More than 1,500 people with CF are ages two and older and have one of these 23 residual function mutations in the U.S.-

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 KALYDECO® (ivacaftor) in people with cystic fibrosis (CF) ages 2 and older who have one of 23 residual function mutations. The FDA granted Vertex's request for Priority Review of this sNDA, and a target review date of February 6, 2016 was set under the Prescription Drug User Fee Act (PDUFA) for the FDA's decision on the sNDA. The submission was based on preclinical and clinical data showing the effect of ivacaftor on CFTR function in certain residual function mutations.

"Given the severity of cystic fibrosis, we are committed to getting KALYDECO to more people as quickly as possible," said Jeffrey Chodakewitz, M.D., Executive Vice President and Chief Medical Officer at Vertex. "Based on the established safety profile of KALYDECO and our increasing understanding of the biology of these specific residual function mutations and their response to ivacaftor, we believe that people with these mutations would benefit from treatment with this medicine."

The sNDA was based on preclinical data for ivacaftor in the 23 residual function mutations, the established clinical profile of KALYDECO and on previously reported data from an exploratory Phase 2a study in 24 people with residual function mutations. In 19 of the 24 patients enrolled in this study, 8 of the 23 mutations proposed in the sNDA were represented.

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 (chloride) and water into and out of the cell in a number of organs, including the lungs. Chloride transport is a marker of the function of the CFTR protein at the cell surface. KALYDECO is currently approved to treat people with CF ages 2 and older who have one of 10 mutations in the *CFTR* gene (*G551D*, *G1244E*, *G1349D*, *G178R*, *G551S*, *S1251N*, *S1255P*, *S549N*, *S549R or R117H*). As with the mutations for which KALYDECO is currently approved, the 23 residual function mutations in the sNDA are known to have some CFTR protein at the cell surface and have shown *in vitro* increases in chloride transport in response to ivacaftor in cells expressing the CFTR form produced by each mutation, characteristics associated with clinical response to KALYDECO. Similar to the *R117H* mutation for which KALYDECO was previously approved, these 23 mutations result in a moderate loss of CFTR chloride transport, and people with these mutations generally have progressive lung function decline and other complications of CF.

There are more than 1,500 people ages 2 and older with CF in the United States who have one of the 23 residual function mutations included in the sNDA. The 23 residual function mutations included in the sNDA are: *2789+5G- > A, 3849+10kbC- > T, 3272-26A- > G, 711+3A- > G, E56K, P67L, R74W, D110E, D110H, R117C, L206W, R347H, R352Q, A455E, D579G, E831X, S945L, S977F, F1052V, R1070W, F1074L, D1152H,* and *D1270N*.

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 one of the following mutations in their CF gene: *G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R, or R117H.*

KALYDECO is not for use in people with CF due to other mutations in the CF gene. KALYDECO is not effective in patients with CF with two copies of the *F508del* mutation (*F508del/F508del*) in the CF gene. It is not known if KALYDECO is safe and effective in children under 2 years of age.

IMPORTANT SAFETY INFORMATION

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 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. A patient 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. 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.

Please click here to see the full Prescribing Information for KALYDECO (ivacaftor).

About KALYDECO® (ivacaftor)

KALYDECO (ivacaftor) is the first medicine to treat the underlying cause of CF in people with specific mutations in the cystic fibrosis transmembrane conductance regulator (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 approved in the U.S., Europe, Canada, Australia and New Zealand to treat people with CF who have specific genetic mutations in the CFTR gene.

Vertex retains worldwide rights to develop and commercialize KALYDECO.

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 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. KALYDECO 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 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, including, without limitation, Dr. Chodakewitz's statements in the second paragraph of the press release and the target review date of February 6, 2016. 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 preclinical data, the established clinical profile and the data from the exploratory Phase 2a study may not be sufficient to support approval, 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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