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U.S. Food and Drug Administration Approves KALYDECO® (ivacaftor) for Use in People with Cystic Fibrosis Ages 6 and Older Who Have the R117H Mutation

--Approximately 500 people with cystic fibrosis ages 6 and older have the R117H mutation in the United States--

BOSTON--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that the U.S. Food and Drug Administration (FDA) approved a supplemental new drug application (sNDA) for the use of KALYDECO® (ivacaftor) in people with cystic fibrosis (CF) ages 6 and older who have the R117H mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene. Today's approval follows a recommendation by the FDA's Pulmonary-Allergy Drugs Advisory Committee (PADAC) to approve the medicine in this group of people with CF. KALYDECO is now approved for use in the U.S. in people ages 6 and older with CF with one of the following ten mutations: R117H, G551D, G178R, S549N, S549R, G551S, G1244E, S1251N, S1255P or G1349D. The approval is based on previously announced data from a Phase 3 study of ivacaftor that enrolled 69 people with CF ages 6 and older who had the R117H mutation.

"Today's approval marks an important milestone for people with the R117H mutation who will now have a medicine to treat the underlying cause of their disease for the first time," said Jeffrey Chodakewitz, M.D., Executive Vice President and Chief Medical Officer at Vertex. "We are now one step closer to reaching our goal of providing new medicines to many more people living with cystic fibrosis."

Cystic fibrosis is caused by a defective or missing CFTR protein resulting from mutations in the *CFTR* gene. In people with the R117H mutation, the CFTR protein reaches the cell surface but does not function properly. Approximately 500 people with CF ages 6 and older have this mutation in the United States. With the approval, KALYDECO is now approved to treat more than 3,100 people ages 6 and older in North America, Europe and Australia who have specific mutations in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene.

In July, Vertex submitted a Marketing Authorization Application (MAA) variation to the European Medicines Agency for the approval of KALYDECO for people with the R117H mutation.

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 more often 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, Switzerland, Australia and New Zealand to treat people with CF ages 6 and older with specific genetic mutations in the *CFTR* gene. Only in the United States is KALYDECO approved to treat people with CF who have the R117H mutation.

Vertex retains worldwide rights to develop and commercialize KALYDECO.

INDICATION AND IMPORTANT SAFETY INFORMATION FOR KALYDECO® (ivacaftor)

Ivacaftor (150 mg tablets) is a cystic fibrosis transmembrane conductance regulatory (CFTR) potentiator indicated for the treatment of cystic fibrosis (CF) in patients age 6 years and older who have a *G551D* mutation in the *CFTR* gene.

In the United States (U.S.) and Europe, ivacaftor is also indicated for the treatment of CF in patients age 6 and older who have one of the following mutations in the *CFTR* gene: *G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N,* or *S549R*. In Canada, ivacaftor is indicated for these same mutations and additionally for *G970R*. Additionally, in the U.S. ivacaftor is indicated for the treatment of CF in patients age 6 and older who have an *R117H* mutation in the *CFTR* gene.

Ivacaftor is not effective in patients with CF with 2 copies of the *F508del* mutation (*F508del/F508del*) in the *CFTR* gene. The safety and efficacy of ivacaftor in children with CF younger than 6 years of age have not been established.

Elevated liver enzymes (transaminases; ALT and AST) have been reported in patients receiving ivacaftor. It is recommended that ALT and AST be assessed prior to initiating ivacaftor, every 3 months during the first year of treatment, and annually thereafter. Patients who develop increased transaminase levels should be closely monitored until the abnormalities resolve. Dosing should be interrupted in patients with ALT or AST of greater than 5 times the upper limit of normal. Following resolution of transaminase elevations, consider the benefits and risks of resuming ivacaftor dosing.

Use of ivacaftor with medicines that are strong CYP3A inducers, such as the antibiotics rifampin and rifabutin; seizure medications (phenobarbital, carbamazepine, or phenytoin); and the herbal supplement St. John's Wort, substantially decreases exposure of ivacaftor and may diminish effectiveness. Therefore, co-administration is not recommended. The dose of ivacaftor must be adjusted when used concomitantly with strong and moderate CYP3A inhibitors or when used in patients with moderate or severe hepatic disease.

Cases of non-congenital lens opacities/cataracts have been reported in pediatric patients up to 12 years of age treated with ivacaftor. Baseline and follow-up ophthalmological examinations are recommended in pediatric patients initiating ivacaftor treatment.

Ivacaftor can cause serious adverse reactions including abdominal pain and high liver enzymes in the blood. The most common side effects associated with ivacaftor include headache; upper respiratory tract infection (the common cold), including sore throat, nasal or sinus congestion, and runny nose; stomach (abdominal) pain; diarrhea; rash; and dizziness. These are not all the possible side effects of ivacaftor. A list of the adverse reactions can be found in the product labeling for each country where ivacaftor is approved. Patients should tell their healthcare providers about any side effect that bothers them or does not go away.

Please see KALYDECO (ivacaftor) U.S. Prescribing Information, EU Summary of Product Characteristics, Canadian Product Monograph, Australian Consumer Medicine Information and Product Information, Swiss Prescribing Information and Patient Information, and the New Zealand Datasheet and Consumer Medicine Information.

About Cystic Fibrosis

Cystic fibrosis is a rare, life-threatening genetic disease affecting approximately 75,000 people in North America, Europe and Australia. Today, the median predicted age of survival for a person with CF is between 34 and 47 years, but the median age of death remains in the mid-20s.

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 more than 1,900 known mutations in the *CFTR* gene. Some of these mutations, which can be determined by a genetic, or genotyping test, lead to CF by creating non-working or too few CFTR protein at the cell surface. The defective function or absence of CFTR proteins in people with CF results in poor flow of salt and water into and 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.

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. This collaboration was expanded to support the accelerated discovery and development of Vertex's CFTR modulators.

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. 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 regulatory authorities may not approve, or approve on a timely basis, the company's drug candidates 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.

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