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Vertex Receives U.S. Food and Drug Administration Approval of KALYDECO® (ivacaftor) for Children with Cystic Fibrosis Ages 2 to 5 who have Specific Mutations in the CFTR Gene

BOSTON--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that the U.S. Food and Drug Administration (FDA) approved KALYDECO® for use in children ages 2 to 5 with cystic fibrosis (CF) who have one of 10 mutations in the cystic fibrosis transmembrane conductance regulator (*CFTR)* gene (*G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R* and *R117H*). Prior to today's approval, KALYDECO was approved in the United States for people ages 6 and older with these mutations. There are approximately 300 children in the United States ages 2 to 5 who have one of these 10 mutations, including 150 who have the *R117H* mutation and 150 who have one of the other nine mutations that result in a gating defect in the CFTR protein. A new weight-based oral granule formulation of KALYDECO (50 mg and 75 mg) that can be mixed in soft foods or liquids was created to meet the needs of children in this age group who may be unable to swallow a tablet. The approval is based on previously announced results of an open-label Phase 3 24-week study that was designed to evaluate the safety and pharmacokinetics of weight-based dosing of ivacaftor (50 mg or 75 mg twice daily) in children ages 2 to 5. With today's approval, more than 3,400 people are currently eligible for treatment with KALYDECO in the United States, Canada, Europe and Australia. Cystic fibrosis is caused by a defective or missing CFTR protein resulting from mutations in the *CFTR* gene.

"Children with cystic fibrosis can begin to experience meaningful lung function decline and struggle to gain weight at a very young age, underscoring the importance of starting treatment early in life," said Jeffrey Chodakewitz, M.D., Executive Vice President and Chief Medical Officer at Vertex. "With today's approval, children as young as two years of age now have a medicine to treat the underlying cause of their CF, bringing us one step closer to our goal of helping the vast majority of people with this devastating disease."

In Europe, an MAA line extension for ivacaftor in children ages 2 to 5 with specific mutations in the *CFTR* gene has been validated by the European Medicines Agency (EMA) and is currently under review by the Committee for Medicinal Products for Human Use (CHMP).

INDICATION AND IMPORTANT SAFETY INFORMATION FOR KALYDECO® (ivacaftor)

Ivacaftor is a cystic fibrosis transmembrane conductance regulatory (CFTR) potentiator indicated for the treatment of cystic fibrosis (CF). In the U.S. (in patients age 2 years and older) and Europe (in patients age 6 years and older), ivacaftor is indicated for patients who have one of the following mutations in the *CFTR* gene: *G551D*, *G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N,* or *S549R.* In Canada (in patients 6 years and older), ivacaftor is indicated for patients with these same mutations and also for patients with the *G970R* mutation. Additionally, in the U.S. (in patients age 2 years and older) and Canada (in patients age 18 years and older) ivacaftor is indicated for the treatment of CF in patients who have an *R117H* mutation in the *CFTR* gene.

Ivacaftor is available as 150 mg tablets in countries where it is approved for patients age 6 years and older, and additionally in the U.S. as 50 mg and 75 mg oral granules for patients age 2 to less than 6 years.

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 2 years of age have not been studied. The use of ivacaftor in children under the age of 2 years is not recommended.

High liver enzymes (transaminases; ALT and AST) have been reported in patients with CF receiving ivacaftor. Transaminase elevations were more common in patients with a history of transaminase elevations or in patients who had abnormal transaminases at baseline. 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. For patients with a history of transaminase elevations, more frequent monitoring of liver function tests should be considered. 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 treated with ivacaftor. Baseline and follow-up ophthalmological examinations are recommended in pediatric patients initiating ivacaftor treatment.

Serious adverse reactions that occurred more frequently with ivacaftor included abdominal pain, increased liver enzymes, and low blood sugar (hypoglycemia). The most common side effects associated with ivacaftor include headache; upper respiratory tract infection (common cold), including 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 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 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. 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. In 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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