



FDA Approves KALYDECO® (ivacaftor) as First and Only CFTR Modulator to Treat Eligible Infants with CF as Early as Six Months of Age

April 30, 2019

-Opportunity to treat the underlying cause of CF earlier than ever before-

-Safety data from Phase 3 ARRIVAL study support treatment with KALYDECO in children ages six to <12 months with eligible mutations-

BOSTON--(BUSINESS WIRE)--Apr. 30, 2019-- [Vertex Pharmaceuticals Incorporated](#) (Nasdaq:VRTX) today announced the U.S. Food and Drug Administration (FDA) approved KALYDECO® (ivacaftor) for use in children with cystic fibrosis (CF) ages six months to less than 12 months who have at least one mutation in their cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to KALYDECO based on clinical and/or *in vitro* assay data. KALYDECO is already approved in the U.S., Canada and EU for the treatment of CF in patients ages 12 months and older.

"Today's approval for KALYDECO allows physicians to begin treating the underlying cause of CF in eligible infants as young as six months of age for the first time, with the potential to modify the course of the disease," said Margaret Rosenfeld, M.D., MPH, Seattle Children's Research Institute and Department of Pediatrics, University of Washington School of Medicine.

This FDA approval is based on data from a 24-week Phase 3 open-label safety cohort (ARRIVAL) of 11 children with CF aged six months to less than 12 months who have one of 10 mutations in the CFTR gene (*G551D*, *G178R*, *S549N*, *S549R*, *G551S*, *G1244E*, *S1251N*, *S1255P*, *G1349D* or *R117H*). The study demonstrated a safety profile similar to that observed in previous Phase 3 studies of older children and adults; most adverse events were mild or moderate in severity, and no patient discontinued therapy due to adverse events. The most common adverse events ($\geq 30\%$) were cough (64%), nasal congestion (36%) and rhinorrhea (36%). Three serious adverse events, all considered unrelated to study treatment by the investigators, were observed in three patients.

Mean baseline sweat chloride for the children in this cohort was 101.5 mmol/L (n=11). Following 24 weeks of treatment with KALYDECO, the mean sweat chloride level was 43.1 mmol/L (n=6). In the six subjects with paired sweat chloride samples at baseline and week 24, there was a mean absolute change of -58.6 mmol/L (95% CI; -75.9, -41.3).

Results of this study were presented at the 32nd Annual North American Cystic Fibrosis Conference in October 2018.

"The manifestations of CF are often present at birth, which underscores our relentless commitment to reach the youngest CF patients possible in our clinical trials," said Reshma Kewalramani, M.D., Executive Vice President and Chief Medical Officer at Vertex. "As an important outcome of these efforts, we are now able to treat infants with cystic fibrosis as early as six months of age with KALYDECO."

KALYDECO was first approved in 2012 in the U.S. and is now available in more than 40 countries with more than 5,000 patients on therapy. For more information on KALYDECO, prescribing information, or patient assistance programs, visit [Kalydeco.com](#) or [VertexGPS.com](#).

About Cystic Fibrosis

Cystic Fibrosis (CF) is a rare, life-shortening genetic disease affecting approximately 75,000 people in North America, Europe and Australia.

CF is caused by a defective or missing cystic fibrosis transmembrane conductance regulator (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, or genotyping test, lead to CF by creating non-working or too few CFTR proteins at the cell surface. The defective function or absence of CFTR protein 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 in many patients that eventually leads to death. The median age of death is in the mid-to-late 20s.

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. It is also available as 25 mg, 50 mg and 75 mg granules in pediatric patients ages 6 months to less than 6 years.

People with CF who have specific mutations in the *CFTR* gene are currently indicated for KALYDECO in different countries across North America, Europe and other International markets.

INDICATION AND IMPORTANT SAFETY INFORMATION FOR KALYDECO® (ivacaftor)

KALYDECO (ivacaftor) is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients age 6 months 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 6 months of age.

Patients should not take KALYDECO if they take 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.

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.**

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, Australia and Latin America. 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 nine years in a row.

For additional information and the latest updates from the company, please visit www.vrtx.com.

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), ORKAMBI® (lumacaftor/ivacaftor), SYMDEKO® (tezacaftor/ivacaftor and ivacaftor), VX-659 and VX-445 were discovered by Vertex as part of this collaboration.

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 and sixth paragraphs 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 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.

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