



FDA Approves KALYDECO® (ivacaftor) as First and Only Medicine to Treat the Underlying Cause of CF in Children Ages 12 to <24 Months with Certain Mutations in the CFTR Gene

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-Data from Phase 3 ARRIVAL study support treatment with KALYDECO in children ages 12 to <24 months -

BOSTON--(BUSINESS WIRE)--Aug. 15, 2018-- [Vertex Pharmaceuticals Incorporated](#) (Nasdaq: VRTX) today announced the U.S. Food and Drug Administration (FDA) approved KALYDECO® (ivacaftor) to include use in children with cystic fibrosis (CF) ages 12 to <24 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.

"Cystic fibrosis is a chronic, progressive disease that is present at birth, with symptoms often occurring in infancy," said Reshma Kewalramani, M.D., Executive Vice President and Chief Medical Officer at Vertex. "With today's approval, parents and physicians now have a medicine to treat the underlying cause of CF in patients as young as one year of age. We are excited about the progress of our portfolio and continue to support additional research on the potential benefit of early intervention with all of our medicines, with the goal of bringing a treatment to all people living with CF."

This FDA approval is based on data from the ongoing Phase 3 open-label safety study (ARRIVAL) of 25 children with CF aged 12 to <24 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 consistent with 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 due to adverse events. Two patients had elevated liver enzymes greater than eight times the upper limit of normal, but continued to receive KALYDECO after a dose interruption. The most common adverse events (≥30%) were cough (74%), pyrexia (37%), elevated aspartate aminotransferase (37%), elevated alanine aminotransferase (32%) and runny nose (32%). Four serious adverse events were observed in two patients.

Mean baseline sweat chloride for the children in this study was 104.1 mmol/L (n=14). Following 24 weeks of treatment with KALYDECO, the mean sweat chloride level was 33.8 mmol/L (n=14). In the 10 subjects with paired sweat chloride samples at baseline and week 24, there was a mean absolute change of -73.5 mmol/L. These data were presented at the 41st European Cystic Fibrosis Society (ECFS) Conference in June 2018 and published in *The Lancet Respiratory Medicine* (Volume 6, No 7, July 2018).

"I'm very excited about the approval of ivacaftor in children ages 12 to less than 24 months as this is the first regulatory approval of a CFTR modulator in this age group," said Margaret Rosenfeld, M.D., MPH, Seattle Children's Research Institute and Department of Pediatrics, University of Washington School of Medicine. "The premise of newborn screening for CF is to intervene very early in the course of disease with the goal of improving long term outcomes, so this is a significant milestone for parents and caregivers of young children with CF."

KALYDECO was already approved in the U.S. for the treatment of CF in patients ages 2 and older who have one of 38 ivacaftor-responsive mutations in the CFTR gene based on clinical and/or *in vitro* assay data. Vertex submitted a Marketing Authorization Application for a line extension (ages 12 to <24 months) to the European Medicines Agency with a decision anticipated in the first half of 2019.

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, and is taken with fat-containing food. It is also available as 50 mg and 75 mg granules in pediatric ages 12 months 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.

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 12 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 12 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 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 eight 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 fifth paragraphs of the press release and statements regarding the Marketing Authorization Application for a line extension submitted to the European Medicines Agency. 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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