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

September 25, 2020

-Approval provides opportunity to treat the underlying cause of CF earlier than ever before-

-Safety data from a cohort of the Phase 3 ARRIVAL study support treatment with KALYDECO in children ages four to <6 months with eligible mutations-

BOSTON--(BUSINESS WIRE)--Sep. 25, 2020-- 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 four months to less than six months old 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. and EU for the treatment of CF in patients ages six months and older.

"Since the initial approval of KALYDECO more than eight years ago, we have continued to advance our clinical development program with the goal of treating the underlying cause of cystic fibrosis as early in life as possible," said Reshma Kewalramani, M.D., Chief Executive Officer and President, Vertex. "Today's approval is a testament to our relentless efforts, alongside the clinical and scientific community, to reach all people with CF who may benefit from our medicines."

This FDA approval is based on data from a cohort in the 24-week Phase 3 open-label safety cohort (ARRIVAL) consisting of 6 children with CF ages four months to less than six months who have one of 10 mutations in the *CFTR* gene (*G551D*, *G178R*, *S549N*, *S549R*, *G551S*, *G1244E*, *S1251N*, *S1255P*, *G1349D* or *R117H*). This cohort demonstrated a safety profile similar to that observed in older children and adults.

"Initiating therapy that treats the underlying cause of cystic fibrosis as early as four months of age may have 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.

KALYDECO was first approved in 2012 in the U.S. and is now available in more than 40 countries. 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 worldwide. CF is a progressive, multi-system disease that affects the lungs, liver, GI tract, sinuses, sweat glands, pancreas and reproductive tract. CF is caused by a defective and/or missing CFTR protein resulting from certain mutations in the *CFTR* gene. Children must inherit two defective *CFTR* genes — one from each parent — to have CF. While there are many different types of *CFTR* mutations that can cause the disease, the vast majority of all people with CF have at least one *F508del* mutation. These mutations, which can be determined by a genetic test, or genotyping test, lead to CF by creating non-working and/or too few CFTR proteins at the cell surface. The defective function and/or absence of CFTR protein results in poor flow of salt and water into and out of the cells 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 early 30s.

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 4 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 4 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; 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 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 diseases. The company has multiple approved medicines that treat the underlying cause of cystic fibrosis (CF) — a rare, life-threatening genetic disease — and has several ongoing clinical and research programs in CF. Beyond CF, Vertex has a robust pipeline of investigational small molecule medicines in other serious diseases where it has deep insight into causal human biology, including pain, alpha-1 antitrypsin deficiency and APOL1-mediated kidney diseases. In addition, Vertex has a rapidly expanding pipeline of genetic and cell therapies for diseases such as sickle cell disease, beta thalassemia, Duchenne muscular dystrophy and type 1 diabetes mellitus.

Founded in 1989 in Cambridge, Mass., Vertex's global headquarters is now located in Boston's Innovation District and its international headquarters is in London, UK. Additionally, the company has research and development sites and commercial offices in North America, Europe, Australia and Latin America. Vertex is consistently recognized as one of the industry's top places to work, including 10 consecutive years on Science magazine's Top Employers list and top five on the 2019 Best Employers for Diversity list by Forbes. For company updates and to learn more about Vertex's history of innovation, visit www.vrtx.com or follow us on Facebook, Twitter, LinkedIn, YouTube and Instagram.

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 quotes by Dr. Kewalramani and Dr. Rosenfeld. 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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