FDA Approves SYMDEKO® (tezacaftor/ivacaftor and ivacaftor) to Treat the Underlying Cause of CF in Children Ages 6-11 Years with Certain Mutations in the CFTR Gene

June 21, 2019

-SYMDEKO is now approved for patients 6 years of age and older with two copies of the F508del mutation or one copy of a responsive mutation-

-Vertex's third medicine approved to treat the underlying cause of CF in eligible patients in this age range-

BOSTON--(BUSINESS WIRE)--Jun. 21, 2019-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced the U.S. Food and Drug Administration (FDA) approved SYMDEKO® (tezacaftor/ivacaftor and ivacaftor) for use in children with cystic fibrosis ages 6 through 11 years who have two copies of the *F508del*-CFTR mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene that is responsive to SYMDEKO. It was previously approved by the FDA for use in patients with cystic fibrosis 12 years and older with two copies of the *F508del* mutation or one copy of a responsive mutation in the U.S. An additional dosage strength of SYMDEKO tablets is now available (tezacaftor 50 mg/ivacaftor 75 mg and ivacaftor 75 mg) in connection with this approval.

"Today's expanded approval of SYMDEKO in children ages 6 through 11 is an important step in our efforts to continue to bring treatment options to the youngest patients possible and importantly brings us closer to our goal of developing medicines for all people living with CF," said Reshma Kewalramani, M.D., Executive Vice President and Chief Medical Officer at Vertex.

Vertex completed a 24-week Phase 3 open-label, multicenter study to evaluate the pharmacokinetics, safety, and tolerability of tezacaftor/ivacaftor and ivacaftor in children ages 6 through 11 years in the U.S. and Canada. The regimen was generally well tolerated, and safety data were similar to what was observed in previous studies of patients aged 12 years and older. The full data from this study will be published later this year.

"We've seen the clinical impact of SYMDEKO in people with CF aged 12 years and above, and this approval marks a crucial milestone for patients ages 6 through 11 years who may benefit from CFTR modulation, enabling us to treat the basic defect in CF at an earlier stage of disease," said Seth Walker, M.D., University Hospitals of Cleveland, Cleveland Medical Center, Rainbow Babies and Children's Hospital. "SYMDEKO is an important treatment option for eligible people with CF who either never started or have discontinued another CFTR modulator."

SYMDEKO®/SYMKEVI® (tezacaftor/ivacaftor and ivacaftor) is already approved in the U.S., Canada, Switzerland, Australia and the EU for the treatment of CF in patients ages 12 years and older with certain mutations. Vertex plans to submit an application for the use in patients ages 6 through 11 years in the European Medicines Agency in the second half of 2019. For more information on SYMDEKO or patient assistance programs, visit SYMDEKO.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 SYMDEKO® (tezacaftor/ivacaftor and ivacaftor)
Some mutations result in CFTR protein that is not processed or folded normally within the cell, and that generally does not reach the cell surface. SYMDEKO is a combination of tezacaftor and ivacaftor. Tezacaftor is designed to address the trafficking and processing defect of the CFTR protein to enable it to reach the cell surface where ivacaftor can increase the amount of time the protein stays open.

U.S. INDICATION AND IMPORTANT SAFETY INFORMATION FOR SYMDEKO® (tezacaftor/ivacaftor and ivacaftor) tablets
SYMDEKO is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients aged 6 years and older who have two copies of the *F508del* mutation, or who have at least one mutation in the CF gene that is responsive to treatment with SYMDEKO. Patients should talk to their doctor to learn if they have an indicated CF gene mutation. It is not known if SYMDEKO is safe and effective in children under 6 years of age.

Patients should not take SYMDEKO if they take certain medicines or herbal supplements such as: the antibiotics rifampin or rifabutin; seizure medicines such as phenobarbital, carbamazepine, or phenytoin; St. John's wort.

Before taking SYMDEKO, patients should tell their doctor if they: have or have had liver problems; have kidney problems; are pregnant or plan to become pregnant because it is not known if SYMDEKO will harm an unborn baby; are breastfeeding or planning to breastfeed because it is not known if SYMDEKO passes into breast milk.

SYMDEKO may affect the way other medicines work, and other medicines may affect how SYMDEKO works. Therefore, the dose of SYMDEKO may need to be adjusted when taken with certain medicines. Patients should especially tell their doctor if they take antifungal medicines such as ketoconazole, itraconazole, posaconazole, voriconazole, or fluconazole; or antibiotics such as telithromycin, clarithromycin, or erythromycin.

SYMDEKO may cause dizziness in some people who take it. Patients should not drive a car, use machinery, or do anything that requires alertness until they know how SYMDEKO affects them.

Patients should avoid food or drink that contains grapefruit or Seville oranges while they are taking SYMDEKO.

SYMDEKO can cause serious side effects, including:

High liver enzymes in the blood, which have been reported in people treated with SYMDEKO or treated with ivacaftor alone. The patient's doctor will do blood tests to check their liver before they start SYMDEKO, every 3 months during the first year of taking SYMDEKO, and every year while taking SYMDEKO. 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 the skin or the white part of the eyes; loss of appetite; nausea or vomiting; dark, amber-colored urine.

Abnormality of the eye lens (cataract) in some children and adolescents treated with SYMDEKO or with ivacaftor alone. If the patient is a child or adolescent, their doctor should perform eye examinations before and during treatment with SYMDEKO to look for cataracts.

The most common side effects of SYMDEKO include headache, nausea, sinus congestion, and dizziness.

These are not all the possible side effects of SYMDEKO. **Please click here to see the fullU.S.Prescribing Information for SYMDEKO (tezacaftor/ivacaftor and ivacaftor) tablets.**

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'sInnovation 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™/SYMKEVI™ (tezacaftor/ivacaftor and ivacaftor), and VX-445 (elexacaftor) 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 quotes by Dr. Kewalramani in the second paragraph and Dr. Walker in the fourth paragraph and the statements regarding Vertex's plans to submit an application to the European Medicines Agency in the second half of 2019. 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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