Health Canada Grants Market Authorization for KALYDECO® (ivacaftor) in Children Ages 12 to <24 months with Certain Mutations in the CFTR Gene

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-KALYDECO is the first and only approved medicine in Canada to treat the underlying cause of cystic fibrosis in these young patients-

BOSTON--(BUSINESS WIRE)--Jan. 28, 2019-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that Health Canada has granted Market Authorization for KALYDECO® (ivacaftor) to include use in children with cystic fibrosis (CF) ages 12 to <24 months who have one of the following mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N or S549R.

“We believe it is important to treat the underlying cause of cystic fibrosis as early as possible, and are pleased that parents and physicians now have a medicine to treat the underlying cause of CF in indicated patients as young as one year of age,” said Reshma Kewalramani, M.D., Executive Vice President and Chief Medical Officer at Vertex. “We look forward to working with the Canadian health officials and provinces to achieve rapid access to KALYDECO for this small, but important group of young children.”

The label update is based on data from the ongoing Phase 3 open-label safety study (ARRIVAL) of children with CF aged 12 to <24 months who have a gating mutation in the CFTR gene. The study demonstrated a safety profile consistent with that observed in previous Phase 3 studies of older children and adults, and improvements in sweat chloride, a key secondary efficacy endpoint.

KALYDECO was previously approved for expanded use in patients aged 12 to <24 months by the U.S. Food and Drug Administration (FDA) in August of 2018 and by the European Commission in November of the same year.

About Cystic Fibrosis

Cystic fibrosis is a rare, life-threatening genetic disease affecting approximately 75,000 people in North America, Europe and Australia, including 4,200 people in Canada.

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 the ARRIVAL Study

The ARRIVAL study is an ongoing Phase 3 open-label safety study 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).

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.

U.S. 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 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 U.S. 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'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® (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, as amended, including the statements by Dr. Kewalramani in the second paragraph. While the company believes the forward-looking statements contained in this press release are accurate, 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 the other risks listed under Risk Factors in Vertex's annual report and quarterly reports filed with the Securities and Exchange Commission and available through Vertex'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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