May 17, 2017

FDA Approves KALYDECO® (ivacaftor) for More Than 900 People Ages 2 and Older with Cystic Fibrosis Who Have Certain Residual Function Mutations

- Precision medicine decision based on in vitro data and supported by more than five years of real-world clinical data that demonstrate KALYDECO's strong safety and efficacy profile for eligible patients -

- Vertex working with FDA to obtain rapid approval for more than 600 additional people who have mutations responsive to KALYDECO, including one of five "splice" mutations -

BOSTON--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that the U.S. Food and Drug Administration (FDA) has approved KALYDECO® (ivacaftor) for use in people with cystic fibrosis (CF) ages 2 and older who have one of 23 residual function mutations in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene. This precision medicine decision is based on analyses of *in vitro* data and is supported by more than five years of real-world clinical data that demonstrate KALYDECO's strong safety and efficacy profile. More than 900 people ages 2 and older in the U.S. have one of these mutations. Based on this approval, Vertex today increased its guidance for 2017 product revenues of KALYDECO to a range of $740 million to $770 million.

In addition to the mutations added to the label today, Vertex is continuing discussions with the FDA concerning the approval for additional people who have mutations responsive to KALYDECO, including one of five "splice" mutations. These five mutations were evaluated as part of the previously disclosed Phase 3 EXPAND study in which the KALYDECO monotherapy arm met its primary efficacy endpoint while being generally well tolerated. More than 600 people ages 2 and older in the U.S. have one of these mutations.

"Five years ago, KALYDECO became the first medicine to treat the underlying cause of CF. Since then, we have continued to invest in studies to improve the understanding of how this important medicine may benefit others with this serious and life-shortening disease," said Jeffrey Chodakewitz, M.D., Executive Vice President and Chief Medical Officer at Vertex. "We are encouraged by the FDA's willingness to explore innovative ways to make highly effective medicines like KALYDECO with a well-established safety profile available to more people who are in urgent need. We will continue to work closely with the FDA to bring KALYDECO to more people with responsive mutations who are still in need as rapidly as possible."

"CF treatment has advanced rapidly, but there is need for broader access to these important medicines and development of additional medicines remains urgent," said Patrick Flume, M.D., Director of the Medical University of South Carolina Cystic Fibrosis Center. "The use of *in vitro* data to support this approval is an important step forward in making medicines like KALYDECO available to more patients, especially those with rare mutations."

Based on clinical data from numerous prior studies and a demonstrated *in vitro* response employing a well-established, analytically validated method, KALYDECO is now approved to treat people with CF ages 2 and older who have one of 33 mutations in the *CFTR* gene.

CF is caused by defective or missing cystic fibrosis transmembrane conductance regulator (CFTR) proteins resulting from mutations in the *CFTR* gene. The defective or missing proteins result in poor flow of salt (chloride) and water into and out of the cell in a number of organs, including the lungs. Chloride transport is a marker of the function of the CFTR protein at the cell surface. As with the other mutations for which KALYDECO is approved, mutations covered under today's approval are known to have some CFTR protein at the cell surface and have shown *in vitro* increases in chloride transport in response to KALYDECO by at least 10 percent of normal over baseline. Similar to the *R117H* mutation for which KALYDECO was previously approved, these additional residual function mutations result in a moderate loss of CFTR chloride transport, and people with these mutations generally have progressive lung function decline and other complications of CF.

Pipeline Progress for Residual Function Mutations

On March 28, 2017, Vertex announced positive results from a Phase 3 study that evaluated tezacaftor/ivacaftor combination treatment in people who have one mutation that results in residual CFTR function and one *F508del* mutation. The study met its primary endpoint and the combination was generally well tolerated. Vertex plans to submit these data as part of a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) and a Marketing Authorization Application (MAA) to

the European Medicines Agency (EMA) for the tezacaftor/ivacaftor combination early in the third quarter of 2017.

About Cystic Fibrosis and KALYDECO® (ivacaftor)

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

CF is caused by a defective or missing 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, lead to CF by creating defective or too few CFTR proteins at the cell surface. The defective or missing CFTR protein results in poor flow of salt and water into or out of the cell in a number of organs, including 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 predicted age of survival for a person born today with CF is 41 years, but the median age of death is 27 years.

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. In adults and pediatric patients age 6 years and older one 150 mg tablet is taken orally every 12 hours with fat-containing food. Pediatric patients ages 2 to less than 6 years who weigh less than 14 kg take one 50 mg packet of oral granules mixed with 1 teaspoon (5 mL) of soft food or liquid administered orally every 12 hours with fat-containing food. Pediatric patients ages 2 to less than 6 years of age who weigh 14 kg or greater take one 75 mg packet of oral granules with 1 teaspoon (5 mL) of soft food or liquid administered orally every 12 hours 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.

KALYDECO® (ivacaftor) INDICATION AND IMPORTANT SAFETY INFORMATION

KALYDECO (ivacaftor) is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients age 2 years and older who have at least one mutation in the 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 2 years of age.

Patients should not take KALYDECO if they are taking 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 including:

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.

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) was discovered by Vertex as part of this collaboration.

About Vertex

Vertex is a global biotechnology company that aims to discover, develop and commercialize innovative medicines so people with serious diseases can lead better lives. In addition to our clinical development programs focused on cystic fibrosis, Vertex has more than a dozen ongoing research programs aimed at other serious and life-threatening diseases.

Founded in 1989 in Cambridge, Mass., Vertex today has research and development sites and commercial offices in the United States, Europe, Canada and Australia. For seven years in a row, *Science* magazine has named Vertex one of its Top Employers in the life sciences. For additional information and the latest updates from the company, please visit www.vrtx.com.

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 third and fourth paragraphs of the press release and statements regarding (i) the potential approval of KALYDECO for patients with "splice" mutations, (ii) Vertex's updated guidance for KALYDECO 2017 net product revenues and (iii) Vertex's plans to submit an NDA and MAA for tezacaftor/ivacaftor. 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 the company's expectations regarding its 2017 KALYDECO net product revenues may be incorrect (including because one or more of the company's assumptions underlying its expectations may not be realized), 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.

(VRTX-GEN)

View source version on businesswire.com: http://www.businesswire.com/news/home/20170517006271/en/

Vertex Pharmaceuticals Incorporated
Investors:
Michael Partridge, 617-341-6108
or
Eric Rojas, 617-961-7205
or
Zach Barber, 617-341-6470
or
Media: mediainfo@vrtx.com
or
North America:
David Whitrap, +1 617-961-5093
or
Europe & Australia:

Megan Goulart, +44 20 3204 5275

Source: Vertex Pharmaceuticals Incorporated