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U.S. Food and Drug Administration Approves KALYDECO™ (ivacaftor) for Use in Eight Additional Mutations that Cause Cystic Fibrosis

-KALYDECO is the first medicine to treat the underlying cause of CF for people with specific mutations in the CFTR gene-

-KALYDECO facilitates increased chloride transport by potentiating the channel-open probability (or gating) of the CFTR protein-

-The eight additional mutations are present in approximately 150 people ages six and older in the United States-

BOSTON--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced the U.S. Food and Drug Administration (FDA) approved a supplemental New Drug Application (sNDA) for KALYDECO™ (ivacaftor) for people with cystic fibrosis (CF) ages 6 and older who have one of eight additional mutations in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene. KALYDECO was first approved in January 2012 for people with CF ages 6 and older who have at least one copy of the G551D mutation. With the approval of the sNDA, KALYDECO is now approved for use in people with CF with the following nine mutations: G551D, G178R, S549N, S549R, G551S, G1244E, S1251N, S1255P and G1349D. In the United States, approximately 150 people ages 6 and older have one of the additional eight mutations for which KALYDECO is now approved.

CF is caused by defective or missing CFTR proteins that result from mutations in the *CFTR* gene. The defective function or absence of CFTR proteins in people with CF results in poor flow of salt and water into and out of the cell in a number of organs, including the lungs. Ivacaftor facilitates increased chloride transport by potentiating the channel-open probability (or gating) of the CFTR protein.

"We believe that KALYDECO has the potential to help more people with CF, and today's approval is an important step toward that goal," said Robert Kauffman, M.D. Ph.D., Senior Vice President and Co-Chief Medical Officer at Vertex. "As we progress over the coming year, we look forward to data from multiple other ongoing studies that are designed to evaluate whether additional people with CF may benefit from KALYDECO."

KALYDECO was granted Breakthrough Therapy designation by the U.S. FDA in late 2012. The sNDA approval is based on previously announced data from a Phase 3, two-part, randomized, double-blind, placebo-controlled, cross-over study of 39 people with CF who had one of the following mutations: G178R, S549N, S549R, G551S, G1244E, S1251N, S1255P, G1349D or G970R. The study showed statistically significant improvements in lung function (FEV_1) for people in the overall study population who received ivacaftor, and the safety profile was similar to prior Phase 3 studies in people with the G551D mutation. Based on data from four patients with the G970R mutation enrolled in the study, the efficacy of KALYDECO in patients with the G970R mutation could not be established to support approval in the U.S. Vertex estimates that approximately 10 people with CF have the G970R mutation worldwide, including two people in the United States.

Data from the study noted above were also used to support regulatory submissions in Europe, Canada and Australia for approval of KALYDECO in additional people with CF ages 6 and older. In Europe and Australia, approximately 250 people with CF have these additional mutations.

Vertex today reaffirmed its 2014 net revenue guidance for KALYDECO as provided on January 29, 2014.

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 that aims to help the CFTR protein function more normally once it reaches the cell surface, to help hydrate and clear mucus from the airways. KALYDECO (150mg, q12h) was first approved by the U.S. Food and Drug Administration in January 2012 for use in people with CF ages 6 and older who have at least one copy of the G551D mutation and in February 2014 for use in people with CF ages 6 and older who have the following additional CFTR mutations: G178R, S549N, S549R, G551S, G1244E, S1251N, S1255P and G1349D.

KALYDECO was approved by the European Medicines Agency in July 2012, by Health Canada in November 2012 and by the Therapeutic Goods Administration in Australia in July 2013 for use in people with CF ages 6 and older who have at least one copy of the G551D mutation in the *CFTR* gene.

Vertex retains worldwide rights to develop and commercialize KALYDECO.

About Cystic Fibrosis

Cystic fibrosis is a rare, life-threatening genetic disease affecting approximately 75,000 people in North America, Europe and Australia. Today, the median predicted age of survival for a person with CF is between 34 and 47 years, but the median age of death remains in the mid-20s.

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 more than 1,900 known mutations in the *CFTR* gene. Some of these mutations, which can be determined by a genetic, or genotyping test, lead to CF by creating non-working or too few CFTR protein at the cell surface. The defective function or absence of CFTR proteins in people with CF results in poor flow of salt and water into and 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.

Collaborative History with Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT)

Vertex initiated its CF research program in 1998 as part of a collaboration with CFFT, the nonprofit drug discovery and development affiliate of the Cystic Fibrosis Foundation. This collaboration was expanded to support the accelerated discovery and development of Vertex's CFTR modulators.

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. Vertex scientists and our collaborators are working on new medicines to cure or significantly advance the treatment of cystic fibrosis, hepatitis C, rheumatoid arthritis and other life-threatening diseases. In addition to our clinical development programs, Vertex has more than a dozen ongoing preclinical 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 four 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.

INDICATION AND IMPORTANT SAFETY INFORMATION FOR KALYDECO™ (ivacaftor)

Ivacaftor (150 mg tablets) is indicated for the treatment of cystic fibrosis (CF) in patients age 6 years and older who have a *G551D* mutation in the *CFTR* gene.

In the United States only, ivacaftor is also indicated for the treatment of CF in patients age 6 and older who have one of the following mutations in the CFTR gene: *G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N or S549R*.

Ivacaftor is not effective in patients with CF with 2 copies of the *F508del* mutation (*F508del/F508del*) in the *CFTR* gene. The safety and efficacy of ivacaftor in children with CF younger than 6 years of age have not been established.

Elevated liver enzymes (transaminases; ALT and AST) have been reported in patients receiving ivacaftor. It is recommended that ALT and AST be assessed prior to initiating ivacaftor, every 3 months during the first year of treatment, and annually thereafter. Patients who develop increased transaminase levels should be closely monitored until the abnormalities resolve. Dosing should be interrupted in patients with ALT or AST of greater than 5 times the upper limit of normal. Following resolution of transaminase elevations, consider the benefits and risks of resuming ivacaftor dosing.

Use of ivacaftor with medicines that are strong CYP3A inducers, such as the antibiotics rifampin and rifabutin; seizure medications (phenobarbital, carbamazepine, or phenytoin); and the herbal supplement St. John's Wort, substantially decreases exposure of ivacaftor and may diminish effectiveness. Therefore, co-administration is not recommended.

The dose of ivacaftor must be adjusted when used concomitantly with strong and moderate CYP3A inhibitors or when used in patients with moderate or severe hepatic disease.

Ivacaftor can cause serious adverse reactions including abdominal pain and high liver enzymes in the blood. The most common

side effects associated with ivacaftor include headache; upper respiratory tract infection (the common cold), including sore throat, nasal or sinus congestion, and runny nose; stomach (abdominal) pain; diarrhea; rash; and dizziness. These are not all the possible side effects of ivacaftor. A list of the adverse reactions can be found in the product labeling for each country where ivacaftor is approved. Patients should tell their healthcare providers about any side effect that bothers them or does not go away.

Please see KALYDECO U.S. Prescribing Information, EU Summary of Product Characteristics, Canadian Product Monograph, Australian Consumer Medicine Information and Product Information, Swiss Prescribing Information and Patient Information, and the New Zealand Datasheet and Consumer Medicine Information.

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, Dr. Kauffman's statements in the third paragraph of the press release and statements regarding Vertex's expectations regarding 2014 KALYDECO net revenues. 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 2014 KALYDECO net revenues may be incorrect (including because one or more of the company's assumptions underlying its revenue 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.

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