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Vertex Submits Supplemental New Drug Application (sNDA) to U.S. Food and Drug Administration for KALYDECO™ (ivacaftor) Monotherapy for People with Non-G551D Gating Mutations

-sNDA also includes long-term safety and efficacy data for KALYDECO from PERSIST open-label rollover study-

-Marketing Authorization Application (MAA) variation in Europe planned for October 2013-

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq:VRTX) today announced the submission of a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) for the approval of KALYDECO™ (ivacaftor) monotherapy for people with cystic fibrosis (CF) ages 6 and older who have at least one non-G551D gating mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene. KALYDECO is currently approved for people with CF ages 6 and older who have at least one copy of the G551D mutation. CF is caused by a defective CFTR protein that results from mutations in the *CFTR* gene. G551D is known as a gating mutation, and there are an additional nine known gating mutations. Gating mutations prevent the CFTR protein from opening or working (gating) properly at the cell surface. Worldwide, approximately 2,000 people with CF ages 6 and older have at least one copy of the G551D mutation, and approximately 400 people with CF ages 6 and older have at least one non-G551D gating mutation.

"Today's submission to the FDA is an important step toward our goal of helping more people with CF," said Robert Kauffman, M.D., Ph.D., Senior Vice President and Chief Medical Officer at Vertex. "The study in people with non-G551D gating mutations is the first of multiple ongoing efforts to expand the number of people who may benefit from ivacaftor, and we expect additional data from these ongoing studies beginning later this year."

The sNDA submission is based on previously announced data from a Phase 3 study of ivacaftor monotherapy that showed statistically significant improvements in lung function (FEV_1). The mean absolute treatment difference in percent predicted FEV_1 between treatment with ivacaftor and placebo was 10.7% ($p < 0.0001$) and the mean relative treatment difference in percent predicted FEV_1 was 14.2% ($p < 0.0001$) through the 8-week treatment period. The safety and tolerability results observed in this study were consistent with those observed in prior Phase 3 studies of ivacaftor monotherapy in people with CF who have the G551D mutation. The study in gating mutations is one of three ongoing Phase 3 label-expansion studies designed to evaluate whether additional people with CF may benefit from treatment with ivacaftor alone.

In addition to the sNDA submission, Vertex intends to submit a Marketing Authorization Application (MAA) variation in Europe in October 2013 for people with CF ages 6 and older who have at least one non-G551D gating mutation.

As part of the sNDA package, Vertex also submitted long-term data from the 96-week PERSIST open-label study of KALYDECO. PERSIST is an ongoing rollover study of people with cystic fibrosis ages 6 and older with a G551D mutation who took part in the 48-week Phase 3 STRIVE and ENVISON studies of KALYDECO. The data from PERSIST submitted as part of the sNDA included efficacy and safety results through 144 weeks of continuous treatment with KALYDECO.

The non-G551D gating data and the long-term PERSIST data will be presented at the 27th Annual North American Cystic Fibrosis Conference (NACFC) in Salt Lake City, Utah, October 17-19, 2013. Vertex expects the gating data to be presented as an oral presentation during Symposium III, "CFTR: Matching CFTR Mutations and Drugs," on October 19.

About KALYDECO

KALYDECO™ (ivacaftor) is the first medicine to treat the underlying cause of CF in people with the G551D mutation 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, 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.

INDICATION AND IMPORTANT SAFETY INFORMATION FOR KALYDECO™ (ivacaftor)

Ivacaftor (150mg 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.

Ivacaftor is not for use in people with CF due to other mutations in the CFTR gene. It is not effective in patients with CF with 2 copies of the *F508del* mutation (*F508del/F508del*) in the *CFTR* gene. The efficacy and safety of ivacaftor in children younger than 6 years of age have not been evaluated.

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 which may diminish effectiveness. Therefore, co-administration is not recommended.

The dose of ivacaftor must be adjusted when used concomitantly with potent and moderate CYP3A inhibitors. The dose of ivacaftor must be adjusted 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 full U.S. Prescribing Information for KALYDECO at www.KALYDECO.com, the EU Summary of Product Characteristics for KALYDECO at http://goo.gl/N3Tz4, the Canadian Product Monograph for KALYDECO at www.vrtx.ca and the Australian Consumer Medical Information and Product Information for KALYDECO at http://bit.ly/18wlMld.

About Cystic Fibrosis

Cystic fibrosis is a rare, life-threatening genetic disease affecting approximately 70,000 people worldwide, including 30,000 people in the United States, 35,000 in Europe, 4,000 in Canada and 3,000 in 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 1,800 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 absence of working CFTR protein 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 creates new possibilities in medicine. Our team discovers, develops and commercializes innovative therapies 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 hepatitis C, cystic fibrosis, rheumatoid arthritis and other life-threatening diseases.

Founded more than 20 years ago in Cambridge, Mass., we now have ongoing worldwide research programs and sites in the U.S., U.K. and Canada. Today, Vertex has more than 2,000 employees around the world, and for three years in a row, Science magazine has named Vertex one of its Top Employers in the life sciences.

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 second paragraph of this press release and statements regarding (i) Vertex's plan to submit a Marketing Authorization Application (MAA) variation in Europe and (ii) the data that will be presented at the NACFC conference. 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 Vertex could experience unforeseen delays in obtaining approval to market ivacaftor for people with non-G551D gating mutations 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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