December 19, 2012

NHS in England Funds KALYDECO™ (ivacaftor), the First Medicine to Treat the Underlying Cause of Cystic Fibrosis, for People with a Specific Genetic Mutation (G551D)

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) announced today that a decision has been made by the National Health Service (NHS) in England to fund KALYDECO™ (ivacaftor), the first medicine treat the underlying cause of cystic fibrosis (CF), for people ages 6 and older who have at least one copy of the G551D mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene. Cystic fibrosis is a rare genetic disease for which there is no cure. It is caused by a defective or missing CFTR protein resulting from mutations in the *CFTR* gene. In people with the G551D mutation, ivacaftor helps the defective CFTR protein function more normally. In England, several hundred of the nearly 8,000 people with CF are believed to have at least one copy of the G551D mutation.

Today's announcement concludes a comprehensive and robust clinical and economic evaluation of the medicine by the NHS in England. Vertex has agreed to a patient access scheme with the NHS, the details of which remain confidential. Vertex will make ivacaftor available to eligible people with CF as quickly as possible and anticipates reimbursement to begin in the second quarter of 2013.

"We are pleased to have been able to work with the NHS to receive a decision to fund ivacaftor so quickly," said Simon Bedson, General Manager of Vertex Europe. "We will be working with the NHS to help them to implement this decision as quickly as possible to ensure that people with cystic fibrosis who are eligible for ivacaftor can access it without delay."

"Ivacaftor changes the way we treat cystic fibrosis because now, for the first time, we are able to target the underlying cause of the disease in those with the G551D mutation, instead of just the symptoms and complications," said Jane Davies, M.D., Royal Brompton Hospital and Imperial College, London.

Health technology appraisals are ongoing with the relevant authorities in Wales, Scotland and Northern Ireland. Vertex's goal is to help all eligible people with cystic fibrosis in the UK gain access to this medicine as soon as possible.

Ivacaftor was discovered as part of a collaboration with Cystic Fibrosis Foundation Therapeutics, Inc., the non-profit drug discovery and development affiliate of the Cystic Fibrosis Foundation.

About Ivacaftor

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, ivacaftor 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. Ivacaftor (150mg, q12h) was first approved by the U.S. Food and Drug Administration in January 2012, by the European Medicines Agency in July 2012 and by Health Canada in November 2012 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 ivacaftor. A Marketing Authorization application is under review by the Therapeutic Goods Administration (TGA) of Australia.

Indication and Important Safety Information

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 CF patients with two 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.

High 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. Moderate transaminase elevations are common in subjects with CF. Overall, the incidence and clinical features of transaminase elevations in clinical trials was similar between subjects in the ivacaftor and placebo treatment groups. In the subset of patients with a medical history of elevated transaminases, increased ALT or AST have been reported more frequently in patients receiving ivacaftor compared to placebo.

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 concomitantly used 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 full product labeling for each country where ivacaftor is approved. Patients should tell their healthcare providers about any side effect that bothers them or doesn't 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, and the KALYDECO Canadian Product Monograph at www.vrtx.ca.

About Cystic Fibrosis

Cystic fibrosis is a rare, life-shortening 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 nearly 3,000 in Australia. Today, the median predicted age of survival for a person with CF is approximately 37 years in the United States, about 40 years in Europe and 48 years in Canada, but the median age of death remains in the mid-20s.

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 non-profit drug discovery and development affiliate of the Cystic Fibrosis Foundation in the U.S. 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, (i) the statement that implementation of this national reimbursement decision in England for ivacaftor is anticipated to start in the second quarter of 2013 and (ii) the statements by Mr. Bedson and Dr. Davies in the third and fourth paragraphs of this press release. 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 the 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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