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Health Canada Approves KALYDECO™ (ivacaftor), the First Medicine to Treat the Underlying Cause of Cystic Fibrosis in People with a Specific Genetic Mutation (G551D)

-- Approximately 100 people in Canada have the G551D mutation in the CFTR gene --

-- First medicine resulting from 1989 co-discovery of CF gene by researchers in Canada and the U.S. --

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) announced today that Health Canada has approved KALYDECO™ (ivacaftor), the first medicine to 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, KALYDECO (kuh-LYE-deh-koh) helps the defective or missing CFTR protein function more normally. Approximately 100 people in Canada with CF are believed to have this mutation.

"KALYDECO is an important step toward our ultimate goal of developing new medicines that target the underlying cause of cystic fibrosis for more people with this life-shortening disease," said Peter Mueller, Ph.D., Chief Scientific Officer and Executive Vice President of Global Research and Development at Vertex. "We are working closely with federal, provincial and territorial governments and private health insurers to bring KALYDECO to all eligible Canadians with cystic fibrosis who have the G551D mutation."

"KALYDECO is a fundamental shift in the way cystic fibrosis is treated because it addresses the underlying cause of the disease, not just its symptoms," said Felix Ratjen, M.D., Division Chief, Respiratory Medicine, The Hospital for Sick Children, and KALYDECO investigator. "In clinical trials, KALYDECO helped people with the G551D mutation breathe more easily and gain weight."

The approval of KALYDECO was based on data from two global Phase 3 studies of people with CF who have at least one copy of the G551D mutation. Those who were treated with KALYDECO experienced significant and sustained improvements in lung function and weight gain compared to those who received placebo. In one study, people who took KALYDECO were also significantly less likely to experience pulmonary exacerbations, which are periods of worsening respiratory signs and symptoms that often require treatment with antibiotics and hospital visits.

The most common serious adverse events included abdominal pain, increased liver enzymes and low blood sugar, which occurred in less than 1 percent of patients. Adverse events commonly observed in those taking KALYDECO included headache, upper respiratory tract infection (common cold), stomach pain and diarrhea. Fewer people in the KALYDECO treatment groups discontinued treatment due to adverse events than in the placebo group. The majority of adverse events associated with KALYDECO were mild to moderate.

"Health Canada's approval of KALYDECO is a welcome first step to getting Canadian CF patients access to this important advance in treatment," said Ken Chan, Vice President, Advocacy, Research and Healthcare of Cystic Fibrosis Canada. "We are pleased that advances in CF research have led to the development of innovative, personalized new medicines such as KALYDECO. We look forward to working with Vertex and Canada's publicly-funded drug plans to provide patients with access to KALYDECO."

The gene that causes CF was identified in 1989 as a result of collaborative research led by Lap-Chee Tsui, Ph.D., and Jack Riordan, Ph.D., at The Hospital for Sick Children in Toronto and Francis Collins, M.D., Ph.D., at the University of Michigan.

KALYDECO 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 the Canadian Funding Process

Canadian approval and reimbursement of a new medicine is a multi-step process. Once a new medicine receives Notice of Compliance (NOC), or approval, from Health Canada, it goes through the Common Drug Review (CDR) process that conducts

a cost-benefit analysis. Each province and territory then conducts a review and makes its own reimbursement decision using the CDR recommendation as a guide.

About KALYDECO

KALYDECO™ (ivacaftor) is the first treatment to target 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 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 KALYDECO. KALYDECO is under review by the Therapeutic Goods Administration (TGA) of Australia. KALYDECO™ is a trademark of Vertex Pharmaceuticals Incorporated and has been authorized for use by Vertex Pharmaceuticals (Canada) Incorporated in Canada.

Indication and Important Safety Information

KALYDECO (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.

KALYDECO 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 KALYDECO 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 KALYDECO. It is recommended that ALT and AST be assessed prior to initiating KALYDECO, every three 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 five times the upper limit of normal. Following resolution of transaminase elevations, consider the benefits and risks of resuming KALYDECO 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 KALYDECO 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 KALYDECO compared to placebo.

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

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

KALYDECO can cause serious adverse reactions including abdominal pain and high liver enzymes in the blood. The most common side effects associated with KALYDECO 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 KALYDECO. A list of the adverse reactions can be found in the full product labeling for each country where KALYDECO is approved. Patients should tell their healthcare providers about any side effect that bothers them or doesn't go away.

For country-specific product information, 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 not enough CFTR protein at the cell surface. The absence of a 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.

Vertex's Ongoing CF Research and Development Program

Vertex is conducting additional studies to evaluate ivacaftor monotherapy in patients who may benefit from improved CFTR protein function, including children with CF as young as 2 years and people with CF who have the R117H mutation or gating mutations that were not evaluated in previous Phase 3 studies.

Vertex plans to initiate a pivotal program in early 2013 to evaluate a combination of VX-809, a CFTR corrector, and ivacaftor, a CFTR potentiator, in people with two copies of the F508del CFTR mutation, pending discussions with regulatory agencies. A Phase 2 study of VX-661, a second CFTR corrector, dosed in combination with ivacaftor for people with two copies of the F508del mutation is also ongoing, with final data expected in the first half of 2013.

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. 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.

Vertex's press releases are available at www.vrtx.com.

About Vertex in Canada

In 2009, Vertex established a research and development site in Laval, Quebec through the acquisition of Virochem Pharma Inc. Vertex employs approximately 50 researchers and support staff in Laval and has established Commercial and Medical teams in Canada, including an expansion to support the launch of KALYDECO.

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, statements regarding (i) the Canadian approval and reimbursement process and Vertex's plans to work closely with federal, provincial and territorial governments and private health insurers to bring KALYDECO to all eligible Canadians and (ii) Vertex's ongoing and planned clinical trials of ivacaftor alone and in combination with its CFTR corrector compounds, including its plans to initiate a pivotal program in early 2013 that is expected to evaluate VX-809 in combination with ivacaftor. While Vertex 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 the initiation of a pivotal program to evaluate VX-809 in combination with ivacaftor may be prevented or delayed 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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