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New England Journal of Medicine Publishes Data from Phase 3 STRIVE Study of KALYDECOTM (ivacaftor) in People Ages 12 and Older with a Specific Type of Cystic Fibrosis

- Study shows that treating CF by targeting the underlying cause of the disease leads to significant clinical benefits among people with the G551D mutation -

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq:VRTX) today announced that the *New England Journal of Medicine (NEJM)* published data from a Phase 3 study of KALYDECO™ (ivacaftor, VX-770), a medicine in development that targets the defective protein that causes cystic fibrosis (CF). In this study, called STRIVE, people with CF ages 12 and older with at least one copy of the G551D mutation who were treated with KALYDECO (kuh-LYE-deh-koh) experienced significant improvements in lung function and other measures of disease. Improvements in lung function (forced expiratory volume in one second, FEV_1) were seen as early as week two and were sustained throughout the 48-week study.

The most commonly reported adverse events were respiratory in nature and comparable across treatment groups. Data from STRIVE will be published along with an accompanying editorial in the November 3, 2011 issue of *NEJM*. Data from a second pivotal Phase 3 study, ENVISION, which evaluated KALYDECO in children with CF ages 6 to 11 years who had at least one copy of the G551D mutation, will be presented at the North American CF Conference, November 3-5, 2011 in Anaheim, Calif.

"I've been involved in cystic fibrosis care and research for 30 years and have seen great progress in managing CF symptoms," said Bonnie Ramsey, M.D., lead author of the STRIVE study and Associate Director of the Cystic Fibrosis Clinic at Seattle Children's Hospital. "These data are historic because they are the first to show that targeting the underlying cause of the disease can improve outcomes for patients."

The results from STRIVE showed a mean absolute improvement in lung function of 10.6 percentage points through week 24 (primary study endpoint) among those treated with KALYDECO compared to placebo. The changes in lung function through week 24 represented a 16.9 percent relative mean improvement in lung function from baseline compared to placebo. Through week 48, the mean absolute improvement in lung function for those treated with KALYDECO was 10.5 percentage points compared to placebo and the relative mean improvement was 16.8 percent from baseline compared to placebo. Phase 3 results and product labeling for currently available CF medicines generally describe relative improvements in lung function. Adverse events that occurred more frequently among those treated with KALYDECO compared to placebo were headache, upper respiratory tract infections, nasal congestion, rash, dizziness and bacteria in the sputum. Events that were more common among those in the placebo group than in the KALYDECO group were pulmonary exacerbation, cough, hemoptysis (bloody cough) and decreased pulmonary function.

"The discovery of the CF gene more than two decades ago gave us hope that we'd one day be able to develop medicines that would treat more than just the symptoms of this disease," said Peter Mueller, Ph.D., Chief Scientific Officer and Executive Vice President of Global Research and Development at Vertex. "We now have a potential new medicine that targets the cause of the disease and has shown an ability to help some people with CF breathe better."

"KALYDECO represents an entirely new approach to treating CF and provides exciting evidence of the progress that has been made in the fight against the disease," said Robert J. Beall, Ph.D., President and CEO of the CF Foundation.

CF is a life-threatening genetic disease that is caused by defective or missing cystic fibrosis transmembrane conductance regulator (CFTR) proteins resulting from mutations in the *CFTR* gene. The absence of functional CFTR proteins results in poor flow of salt and water across cell membranes 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. Currently available medicines have led to improved treatment and outcomes for people living with CF by treating the symptoms and some of the complications of the disease.

In some people, CFTR proteins are present at the cell surface but do not function properly. This dysfunction is known as a gating defect, the most common of which is the G551D mutation. Approximately 4 percent of those with CF, or about 1,200 people in the United States and 1,000 people in Europe, are believed to have the G551D mutation. KALYDECO is designed to

keep the CFTR channels at the cell surface open longer to improve the transport of chloride ions across the cell membrane in people who have gating mutations. If approved, KALYDECO will be first treatment to target the underlying cause of CF.

In October 2011, Vertex submitted 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 KALYDECO, Vertex's CFTR potentiator. Vertex requested Priority Review from the FDA and has received agreement from the EMA for accelerated assessment of KALYDECO in Europe.

Summary of Key Data from STRIVE

Improvements across all key disease measures, including lung function, respiratory symptoms and weight gain were demonstrated among patients treated with KALYDECO compared to those who received placebo in the STRIVE study. There also was a reduction in pulmonary exacerbations among people who were treated with KALYDECO.

Lung Function: Progressive lung disease is a major source of illness and is the leading cause of death in people with CF. The primary endpoint of STRIVE was mean absolute improvement from baseline in lung function (FEV_1) and is reported in the *NEJM* publication.

Baseline lung function in STRIVE was 63.5 percent predicted for patients in the KALYDECO treatment group and 63.7 percent predicted among those in the placebo control group. Results of the STRIVE study showed that people treated with KALYDECO experienced rapid, significant and sustained improvements in lung function throughout the 48 week study.

Sweat Chloride: Elevated sweat chloride levels are a diagnostic hallmark in CF and are the result of CFTR protein dysfunction. Although not a clinically validated endpoint, a reduction in sweat chloride is considered to be a marker of improved CFTR function. The amount of chloride in the sweat is measured using a standard test. People with CF typically have elevated sweat chloride levels in excess of 60 mmol/L, while normal values are less than 40 mmol/L.

In STRIVE, the baseline sweat chloride level for both treatment groups was approximately 100 mmol/L. People who received KALYDECO experienced a significant and rapid reduction in the amount of salt in their sweat (sweat chloride concentration). As early as two weeks after dosing initiation, patients treated with KALYDECO experienced an average reduction in sweat chloride of approximately 45 mmol/L. The decreases in sweat chloride among these patients were maintained through week 48, at which time the mean sweat chloride level was 50.4 mmol/L. The mean absolute improvement in sweat chloride for those treated with KALYDECO was 48.1 mmol/L through week 48, compared to placebo ($p < 0.0001$). Those treated with the placebo maintained mean baseline sweat chloride levels of approximately 100 mmol/L through 48 weeks.

Weight: Many people with CF have a hard time gaining and maintaining weight due to factors such as reduced pulmonary function, nutrition, chronic infection and inflammation. In STRIVE, people treated with KALYDECO gained weight throughout the study and by week 48 weighed, on average, 3.1kg (6.9 lbs) more than at the start of the study. Those in the placebo group gained 0.4kg (0.9 lbs) by week 48.

Pulmonary Exacerbation: Pulmonary exacerbations are periods of worsening in signs and symptoms of the disease requiring treatment with antibiotics. At week 48, 67 percent of those treated with KALYDECO were free from pulmonary exacerbations, as compared with 41 percent in the placebo group. In STRIVE, people treated with KALYDECO were 55 percent less likely to experience a pulmonary exacerbation compared to those treated with placebo.

Patient-Reported Outcomes: The Cystic Fibrosis Questionnaire — Revised (CFQ-R) is a validated patient-reported outcome tool that was used in the STRIVE study to measure the impact of KALYDECO on overall health, daily life, perceived well-being and symptoms. One aspect of the CFQ-R, referred to as the respiratory domain, addresses patient reported symptoms including things such as coughing, congestion, wheezing and other respiratory symptoms. In STRIVE, statistically significant and clinically meaningful improvements in respiratory symptoms (a secondary endpoint of the study) were reported among those treated with KALYDECO, as compared to those receiving placebo.

Safety: The incidence of adverse events through week 48 was similar between groups. Adverse events that occurred more frequently among those treated with KALYDECO compared to placebo were headache, upper respiratory tract infections, nasal congestion, rash, dizziness and bacteria in the sputum; none of which were considered serious or led to discontinuation. The most commonly reported serious adverse events included pulmonary exacerbation (13 percent in the KALYDECO group compared to 33 percent in the placebo group), hemoptysis (or bloody cough; 1 percent in the KALYDECO group and 5 percent in the placebo group) and hypoglycemia (2 percent in the KALYDECO group and zero in the placebo group). Discontinuations through 48 weeks due to adverse events were less frequent in the KALYDECO treatment group compared to placebo (1 percent compared to 3.8 percent).

About STRIVE

STRIVE evaluated 161 patients 12 years or older who received at least one dose of either KALYDECO as a single 150 mg tablet (n=83) or placebo (n=78) twice daily. The study was designed to evaluate KALYDECO in people with at least one copy of the G551D CFTR mutation. The primary endpoint of the study was mean absolute change from baseline in predicted FEV_1 (lung function) through week 24. Lung function was assessed using a standard test that measures the amount of air a person can exhale in one second (forced expiratory volume in one second, or FEV_1).

About KALYDECO

KALYDECO (ivacaftor, VX-770) is Vertex's lead medicine in development for the treatment of people with cystic fibrosis who have the G551D CFTR mutation. Known as a CFTR potentiator, KALYDECO is an oral medicine that aims to help CFTR protein function more normally once it reaches the cell surface, to help hydrate and clear mucus from the airways. Vertex retains worldwide rights to develop and commercialize KALYDECO. The brand name KALYDECO has been approved by the EMA and provisionally approved by the FDA for use in connection with VX-770, but VX-770 itself has not received marketing authorization or NDA approval from any regulatory authorities.

Expanded Access Programs for KALYDECO

An expanded access program for KALYDECO is currently open at participating clinical trial sites in the United States. This program is designed to provide KALYDECO to people ages 6 and older who have at least one copy of the G551D mutation, are in critical medical need and may benefit from treatment prior to potential FDA approval in the United States.

Vertex is working toward implementing additional expanded access programs in other countries, with a goal of opening programs for eligible patients by the end of 2011.

For more information, please call Vertex Medical Information at 1-877-634-VRTX (8789).

About Cystic Fibrosis

CF is a life-threatening genetic disease affecting approximately 30,000 people in the United States and 70,000 people worldwide. Today, the median predicted age of survival for a person with CF is approximately 38 years. According to the 2010 Cystic Fibrosis Foundation Patient Registry Annual Data Report, approximately 4 percent of the total CF patient population in the United States have at least one copy of the G551D mutation.

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 KALYDECO and other CFTR modulators.

About the Cystic Fibrosis Foundation

The Cystic Fibrosis Foundation is the world's leader in the search for a cure for cystic fibrosis. The Foundation funds more CF research than any other organization and nearly every CF drug available today was made possible because of Foundation support. Based in Bethesda, Md., the Foundation also supports and accredits a national care center network that has been recognized by the National Institutes of Health as a model of care for a chronic disease. The CF Foundation is a donor-supported nonprofit organization. For more information, visit www.cff.org.

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, epilepsy 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 1,900 employees around the world, and *Science* magazine named Vertex number one on its 2011 list of 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, as amended, including statements regarding (i) Vertex's potential new medicine that targets the cause of the disease and has demonstrated the ability to help patients breathe better; (ii) the potential that KALYDECO will be approved; and (iii) the possibility that additional expanded access programs will be implemented with the goal of opening programs to eligible patients by the end of 2011. 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 KALYDECO; that future outcomes from clinical trials of KALYDECO may not be favorable; that future scientific, clinical, competitive or other market factors may adversely affect the potential for KALYDECO 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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