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Interim Data from Phase 2 Combination Study of VX-809 and KALYDECO™ (ivacaftor) Showed Significant Improvements in Lung Function (FEV₁) in People with Cystic Fibrosis Who Have Two Copies of the F508del Mutation

- *Interim analysis showed 46% of patients experienced at least 5% absolute improvement in lung function (FEV₁) from baseline; 30% of patients experienced at least 10% absolute improvement -*
- *Vertex plans to start a pivotal study of VX-809 and KALYDECO to treat the underlying cause of CF in adults with two copies of the F508del mutation, pending final data and discussions with regulatory agencies -*

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) announced today an interim analysis of data from an ongoing Phase 2 study of VX-809 and KALYDECO™ (ivacaftor) that showed significant improvement in lung function (FEV₁) among adults with cystic fibrosis (CF) who have two copies (homozygous) of the most common mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene, F508del. A planned interim analysis was conducted after approximately half of the study patients had completed 56 days of treatment. Today's results are based on data from 37 homozygous F508del patients who completed treatment in the 56-day study and 11 patients with one or two copies of the F508del mutation who received placebo. There was a statistically significant improvement in lung function (absolute change in percent predicted FEV₁) across the combined treatment groups relative to baseline compared to placebo (p=0.002). Of those who received VX-809 and KALYDECO (250mg, q12h), approximately 46 percent (17/37) experienced an absolute improvement from baseline to Day 56 in lung function of 5 percentage points or more, and approximately 30 percent (11/37) experienced an absolute improvement from baseline to Day 56 of 10 percentage points or more. None of the patients treated with placebo (0/11) achieved a 5-percentage point or more improvement from baseline to Day 56 in lung function. Most adverse events were mild or moderate in severity and comparable between treatment and placebo groups.

The study is ongoing and complete data, including statistical analyses for all patient groups, will be available in mid-2012. Vertex plans to start a pivotal study of VX-809 and KALYDECO in people with two copies of the F508del mutation, pending final study results and discussions with regulatory agencies. Evaluation of patients with one copy (heterozygous, n=21) of the F508del mutation is ongoing, but at the time of this interim analysis not enough patients had completed the study to make any conclusions. These complete data will be included in the final study analysis and will be used to determine next steps for the development of VX-809 and KALYDECO in heterozygous F508del patients. Vertex will host a conference call for investors and media today, May 7, 2012 at 8:30 a.m. ET to discuss this interim data analysis.

Cystic fibrosis is a rare, life threatening genetic disease affecting approximately 30,000 people in the United States and 70,000 people worldwide. Nearly half of those with CF are estimated to have two copies of the F508del mutation.

"For the past 14 years, our teams have focused on learning about the underlying cause of cystic fibrosis so we can develop new medicines to help as many patients as possible. Today we believe we're one step closer to this goal," said Chris Wright, M.D., Ph.D., Vertex's Senior Vice President, Global Medicines Development and Medical Affairs. "People with two copies of the F508del mutation have one of the most severe forms of cystic fibrosis. In these patients, the combination of VX-809 and KALYDECO led to significant improvements in lung function that exceeded our expectations. We look forward to beginning discussions with regulatory agencies later this year when we have full data from the study, with the goal of moving forward with a pivotal study as quickly as possible."

"Lung function is the single most important marker of disease progression for people with cystic fibrosis, and improvement in lung function is the goal of every new CF therapy," said Michael P. Boyle, M.D, FCCP, Associate Professor of Medicine, Director of the Johns Hopkins Adult Cystic Fibrosis Center, and lead investigator for this study. "While we still eagerly await the results from the remainder of the trial, we are definitely encouraged that this interim analysis showed a significant improvement in lung function in people with two copies of the F508del mutation who received VX-809 and KALYDECO."

Interim Results

Data from the first part of this study were announced in 2011. The interim data announced today are from the second part of the ongoing Phase 2 randomized, double-blind, placebo-controlled study. This part of the study enrolled 108 people with CF ages 18 and older with one or two copies of the F508del mutation who were divided into five treatment groups of approximately 20 patients each. Three groups of homozygous patients were randomized to receive VX-809 alone (200mg, 400mg or 600mg) for 28 days and then in combination with KALYDECO (250mg) for an additional 28 days. One group of heterozygous patients is receiving VX-809 alone (600mg) for 28 days and then in combination with KALYDECO (250mg) for an additional 28 days. The placebo group includes both homozygous and heterozygous patients.

Lung function: Progressive lung disease is a major source of illness and is the leading cause of death in people with CF. Typically people with CF lose 1 percent to 2 percent of their lung function (FEV₁) each year.

Improvements in lung function (absolute change in percent predicted FEV₁) were observed in all combination treatment dose groups in homozygous patients. The percent of patients who experienced absolute improvement from baseline in lung function was as follows:

Treatment Group	Absolute Improvement from Baseline in Lung Function (FEV ₁) (Baseline — Day 56)	
	≥ 5 percentage points	≥ 10 percentage points
VX-809 alone (200mg, 400mg or 600mg) for 28 days followed by KALYDECO (250mg, q12h) + VX-809 (200mg, 400mg, 600mg dose groups combined) for 28 days	46% (17/37)	30% (11/37)
Placebo	0 (0/11)	0 (0/11)

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 biomarker of improved CFTR function in the skin.

One of the two primary endpoints in this study is change in sweat chloride from Day 28 to Day 56. Reductions in sweat chloride were observed between Day 28 and Day 56 in homozygous patients treated with VX-809 and KALYDECO. At the time of this interim analysis, these reductions were not statistically significant.

A statistically significant reduction in sweat chloride was observed in patients treated with VX-809 alone (baseline — Day 28).

Safety: A co-primary endpoint in this study is safety. Safety results reported today include data from all patients who had started treatment prior to this interim analysis. VX-809 was generally well tolerated alone and in combination with KALYDECO. The most common adverse events were pulmonary in nature. Most adverse events were mild or moderate in severity and comparable between treatment and placebo groups. The rate of serious adverse events was similar between treatment and placebo groups.

Cystic fibrosis is caused by defective or missing CFTR proteins resulting from mutations in the *CFTR* gene. Located at the surface of cells, CFTR proteins act as channels to regulate the flow of salt and water into and out of the cells. In people with the F508del mutation in the *CFTR* gene, little to no CFTR protein reaches the cell surface. As a result, thick, sticky mucus builds up and blocks the passages in many organs, leading to a variety of symptoms. In particular, mucus builds up and clogs the airways in the lungs, causing chronic lung infections and progressive lung damage. VX-809, known as a CFTR corrector, is believed to help CFTR proteins reach the cell surface. KALYDECO, known as a CFTR potentiator, keeps the CFTR protein channels open longer to increase the flow of salt and water into and out of the cell.

VX-809 and KALYDECO were discovered as part of collaboration with Cystic Fibrosis Foundation Therapeutics, Inc., the nonprofit drug discovery and development affiliate of the Cystic Fibrosis Foundation.

Conference Call for Media and Investors

Vertex will host a conference call and webcast today, May 7, 2012 at 8:30 a.m. ET to discuss this interim data analysis. The conference call will be webcast live and a link to the webcast may be accessed from the 'Events & Presentations' page of the Vertex website at www.vrtx.com.

To listen to the live call on the telephone, dial 1-866-501-1537 (United States and Canada) or 1-720-545-0001 (International). To ensure a timely connection, it is recommended that users register at least 15 minutes prior to the scheduled webcast.

The conference ID number for the live call and replay is 78832581.

The call will be available for replay via telephone commencing May 7, 2012 at 11:30 a.m. ET running through 5:00 p.m. ET on May 14, 2012. The replay phone number for the United States and Canada is 1-855-859-2056. The international replay number is 1-404-537-3406.

Following the live webcast, an archived version will be available on Vertex's website until 5:00 p.m. ET on May 21, 2012. Vertex is also providing a podcast MP3 file available for download on the Vertex website at www.vrtx.com.

About Cystic Fibrosis

Cystic fibrosis is a rare, 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 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 proteins at the cell surface. The absence of working CFTR proteins results in poor flow of salt and water into and out of the cell in a number of organs, including the lungs.

In people with the most common mutation in the *CFTR* gene, F508del, little to no CFTR protein reaches the cell surface. Globally, nearly half (46 percent) of people with CF have two copies of the F508del mutation and one-third (33 percent) have one copy of the F508del mutation.

About KALYDECO

KALYDECO™ (ivacaftor) is the first treatment to target the underlying cause of CF. KALYDECO (150mg, q12h) was approved by the U.S. Food and Drug Administration (FDA) in January 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. In October 2011, Vertex submitted a marketing authorization application to the European Medicines Agency (EMA) for KALYDECO and has received agreement from the EMA for accelerated assessment in Europe. The EMA regulatory review is ongoing.

Indication and Important Safety Information

KALYDECO (150mg, q12h) is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients age 6 years and older who have a certain mutation in their *CFTR* gene called the G551D mutation.

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.

It is not known if KALYDECO is safe and effective in children under 6 years of age.

KALYDECO should not be used with certain medicines, including the antibiotics rifampin and rifabutin; seizure medications (phenobarbital, carbamazepine, or phenytoin); and the herbal supplement St. John's Wort.

KALYDECO can cause serious side effects. High liver enzymes in the blood have occurred in patients taking KALYDECO as well as those receiving placebo. Regular assessment is recommended.

The most common side effects associated with KALYDECO include headache; upper respiratory tract infection (common cold) including sore throat, nasal or sinus congestion, and runny nose; stomach (abdominal) pain; diarrhea; rash; nausea; and dizziness.

These are not all the possible side effects of KALYDECO. Patients should tell their healthcare providers about any side effect that bothers them or doesn't go away.

Please see full Prescribing Information for KALYDECO at www.KALYDECO.com.

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 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, MA, 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 *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, including Dr. Wright's and Dr. Boyle's statements in the fourth and fifth paragraphs of this press release, and statements regarding (i) Vertex's plan to start a pivotal study of VX-809 and KALYDECO in people with two copies of the F508del mutation, pending final data and discussions with regulatory agencies, (ii) the expected availability of complete data from the study in mid-2012 and (iii) the expectation that the final data that will become available in mid-2012 will be used to determine next steps for the development of VX-809 and KALYDECO in heterozygous F508del patients. 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 final outcomes of this clinical trial or future clinical trials of VX-809 and KALYDECO may be less favorable than the interim analysis reported today, or may not be favorable at all, that final data from heterozygous patients may not be favorable or may be less favorable than the data from homozygous patients, that final data and/or discussions with regulatory agencies regarding the scope and design of future clinical trials may result in additional clinical trials needing to be conducted before Vertex can initiate the first pivotal clinical trials evaluating VX-809 in combination with KALYDECO 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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