June 28, 2012

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

- Mean absolute improvement in lung function of 6.1 percentage points within group (p < 0.001) and 8.6 percentage points compared to placebo (p < 0.001) in homozygous patients receiving combination treatment (Day 28 to 56) with highest study dose of VX-809 (600mg) -

- Adverse events were similar between treatment and placebo groups; most events were mild to moderate -

- Pivotal program to evaluate VX-809 (600mg) in combination with KALYDECO (250mg) planned to start in early 2013, pending discussions with regulatory agencies -

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) announced today final data from a Phase 2 study of VX-809 and KALYDECO™ (ivacaftor) that showed statistically significant improvements in lung functi 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. The study randomized homozygous F508del patients to three treatment groups that evaluated increasing doses of VX-809 (200mg, 400mg or 600mg; QD) alone for 28 days, followed by VX-809 in combination with KALYDECO (250mg; q12h) from Day 28 to 56. When patients received the two medicines in combination (Day 28 to 56), there was a statistically significant improvement in lung function (percent predicted forced expiratory volume in one second, FEV_1) in each of the homozygous treatment groups compared to placebo. The greatest improvements in lung function were observed in patients who received 600mg of VX-809, the highest dose evaluated in this study, in combination with KALYDECO. These data support Vertex's plans to initiate a pivotal program in early 2013, which is expected to evaluate VX-809 (600mg) in combination with KALYDECO (250mg) in homozygous patients, pending discussions with regulatory agencies. Most adverse events observed during the 56-day study were mild to moderate in severity across all treatment groups and similar between treatment and placebo groups.

The study also included an exploratory treatment group that looked at a subset of heterozygous patients who have one copy of the F508del mutation and a second mutation that is not expected to respond to KALYDECO dosed as monotherapy. This group of patients received VX-809 (600mg) and KALYDECO on the same dosing schedule as homozygous patients. Heterozygous patients who were treated with the combination experienced a mean absolute improvement in lung function compared to placebo from Day 28 to 56. Based on these data, Vertex plans to conduct additional clinical studies of VX-809 and KALYDECO in heterozygous patients.

"We are focused on developing additional medicines to treat the underlying cause of cystic fibrosis, and these data represent exciting progress toward that goal," said Chris Wright, M.D., Ph.D., Vertex's Senior Vice President, Global Medicines Development and Medical Affairs. "The data announced today show that the addition of KALYDECO to VX-809 resulted in improvements in lung function and support our plans to start a pivotal program in people with cystic fibrosis who have two copies of the most common *CFTR* mutation in early 2013."

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 commented, "I am particularly encouraged with these results given the significant improvements in lung function when cystic fibrosis patients with two copies of the F508del mutation went from receiving VX-809 alone to combination treatment with KALYDECO and look forward to the start of the pivotal program."

Vertex will host a conference call for investors and media today, June 28, 2012 at 8:00 a.m. ET, to discuss these data. Full data from this study will be submitted for presentation at an upcoming medical meeting.

Study Results

This is a Phase 2 randomized, double-blind, placebo-controlled study. Data from the first part of this study (Cohort 1) were announced in 2011 and an interim analysis of the second part (Cohort 2) was announced in May 2012. Today's announcement includes final data from the second part of this study that enrolled 109 people with CF ages 18 and older with one or two copies of the F508del mutation. Patients 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 received VX-809 alone (600mg) for 28 days and then in combination with KALYDECO (250mg) for an additional 28 days. The placebo group included both homozygous and heterozygous patients.

LUNG FUNCTION: PATTERN OF RESPONSE

Progressive lung disease is a major source of illness and is the primary cause of death in people with CF. Typically, people with CF lose 1 percent to 2 percent of their lung function (FEV_1) each year.

During the first 28 days of the study, there was a decline in lung function in the majority of patients in both the treatment and placebo groups. In contrast, from Day 28 to 56, when the treatment groups received the combination of VX-809 and KALYDECO, there was a mean absolute improvement in lung function in each of the treatment groups, while lung function continued to decline for the placebo group.

HOMOZYGOUS PATIENTS RECEIVING VX-809 -- 600mg

Lung Function: Homozygous patients treated with the highest dose of VX-809 (600mg) in combination with KALYDECO from Day 28 to 56 experienced a mean absolute improvement in lung function of 8.6 percentage points compared to placebo ($p < 0.001$) and a mean absolute improvement of 6.1 percentage points within group ($p < 0.001$). Fifty-five percent of these patients experienced an absolute improvement in lung function of 5 percentage points or more compared to 9.5 percent of those treated with placebo. Twenty-five percent experienced an absolute improvement of 10 percentage points or more compared to 0 percent of those treated with placebo.

Mean Absolute Changes in Lung Function (percent predicted FEV_1)

	Day 0 to 28	**Day 28 to 56**
Placebo within group	-0.9 (p=0.54)	-2.5 (p=0.08)
VX-809 alone (600mg; QD) for 28 days followed by the addition of **KALYDECO** (250mg, q12h) for 28 days **within group**	-2.9 (p=0.07)	+6.1 ($p < 0.001$)
VX-809 alone (600mg; QD) for 28 days followed by the addition of **KALYDECO** (250mg, q12h) for 28 days **compared to placebo**	-2.0 (p=0.36)	+8.6 ($p < 0.001$)

Response Analysis

	Day 0 to 28		**Day 28 to 56**	
	Placebo	VX-809 (600mg) monotherapy	Placebo	VX-809 (600mg) and KALYDECO (250mg)
≥ 5 percentage point absolute improvement FEV_1	13.0% (3/23)	10.0% (2/20)	9.5% (2/21)	55.0% (11/20)
≥ 10 percentage point absolute improvement FEV_1	4.3% (1/23)	5.0% (1/20)	0.0% (0/21)	25.0% (5/20)

From Day 0 to 56, patients receiving VX-809 (600mg) and KALYDECO experienced a mean absolute improvement in lung function of 6.7 percentage points compared to placebo (p=0.002) and a 3.4 percentage point improvement within group (p=0.03). Patients treated with placebo experienced a mean absolute decline in lung function of 3.3 percentage points (p=0.03) over the same time period.

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 was change in sweat chloride from Day 28 to 56 compared to placebo. There was no decrease in sweat chloride among those receiving placebo from Day 0 to 28 or from Day 28 to 56. In homozygous patients treated with 600mg of VX-809 alone for 28 days, there was a statistically significant mean decrease in sweat chloride of 6.4 mmol/L compared to placebo (p=0.01). An additional mean decrease in sweat chloride of 3.7 mmol/L compared to placebo was observed with combination treatment between Day 28 and 56, which was not statistically significant.

HOMOZYGOUS PATIENTS RECEIVING VX-809 -- 400mg, 200mg

Lung function: During the combination treatment period (Day 28 to 56), there were statistically significant mean absolute improvements in lung function compared to placebo in both the 200mg and 400mg VX-809 treatment groups. These improvements were smaller than those seen during the combination treatment period in the VX-809 600mg group.

Sweat chloride: A statistically significant reduction in sweat chloride was observed from Day 0 to 28 in homozygous patients treated with VX-809 (200mg, 400mg) alone compared to placebo. Additional reductions in sweat chloride were observed between Day 28 and 56, but were not statistically significant.

HETEROZYGOUS PATIENTS RECEIVING VX-809 -- 600mg

Lung function: In heterozygous patients who received 600mg of VX-809 in combination with KALYDECO, there was a mean absolute improvement in lung function from Day 28 to 56 compared to placebo. This improvement in lung function was smaller than the improvement seen in homozygous patients receiving 600mg of VX-809 in combination with KALYDECO. Based on these data, Vertex plans to conduct additional clinical studies of VX-809 and KALYDECO in heterozygous patients.

SAFETY DATA FOR ALL PATIENTS

Safety: A co-primary endpoint in this study was safety. The final safety results are consistent with those announced at the time of the interim analysis and include data from all 109 patients enrolled in the study. As previously reported, 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 to moderate in severity and similar between treatment and placebo groups. The rate of serious adverse events was also similar between treatment and placebo groups.

VX-809 and KALYDECO were discovered as part of a 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, June 28, 2012 at 8:00 a.m. ET to discuss these data. 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 1-877-250-8889 (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 95886622.

The call will be available for replay via telephone commencing June 28, 2012 at 12:00 p.m. ET running through 5:00 p.m. ET on July 5, 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 July 11, 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.

CF is caused by defective or missing CFTR proteins 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 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. 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. Globally, nearly half (46 percent) of people with CF have two copies of the F508del mutation and an additional 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 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 May 2012, Vertex received a positive opinion by consensus from the European Committee for Medicinal Products for Human Use (CHMP) recommending approval. Vertex is also preparing to submit a regulatory filing in Australia in the third quarter of 2012.

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. Serious side effects that may or may not be related to KALYDECO but which occurred more frequently in patients treated with KALYDECO included stomach (abdominal) pain, high liver enzymes in the blood, and low blood sugar. 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 U.S. 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, without limitation, Dr. Wright's statements in the third paragraph of this press release, Dr. Boyle's statements in the fourth paragraph of this press release and statements regarding (i) Vertex's plan to start a pivotal program to evaluate VX-809 (600mg) in combination with KALYDECO (250mg) in early 2013, pending discussions with regulatory agencies, and (ii) Vertex's plan to conduct additional clinical studies of VX-809 and KALYDECO in heterozygous 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 outcomes of future clinical trials of VX-809 and KALYDECO may be less favorable than the data reported today, or may not be favorable at all, that the initiation of pivotal clinical trials evaluating VX-809 in combination with KALYDECO may be delayed or prevented as a result of discussions with regulatory agencies or other factors 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 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.

(VRTX-GEN)

Vertex Pharmaceuticals Incorporated
Media:
Zach Barber, 617-444-6992
mediainfo@vrtx.com
or
Megan Goulart, 617-444-6992
mediainfo@vrtx.com
or
Dawn Kalmar, 617-444-6992
mediainfo@vrtx.com
or
Investors:
Michael Partridge, 617-444-6108

Source: Vertex Pharmaceuticals Incorporated

News Provided by Acquire Media