February 26, 2013

Vertex Announces Initiation of Pivotal Phase 3 Program of VX-809 in Combination with Ivacaftor for the Treatment of People with Cystic Fibrosis Who Have Two Copies of the F508del Mutation

-Global studies to evaluate two different doses of VX-809 in combination with ivacaftor-

- 24-week safety and efficacy data and submission of New Drug Application expected in 2014-

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced the initiation of a global pivotal Phase 3 development program for fixed-dose combinations of VX-809 (lumacaftor) and ivacaftor in people with cystic fibrosis (CF) who have two copies (homozygous) of the F508del mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene. Vertex plans to conduct two 24-week Phase 3 studies to support approval of the combination of VX-809 and ivacaftor in people with CF ages 12 and older. The studies, TRAFFIC and TRANSPORT, will each include two treatment groups that will evaluate VX-809 (600mg QD or 400mg q12h) in combination with ivacaftor (250mg q12h) compared to a placebo group. Vertex expects to obtain 24-week safety and efficacy data from both studies and to submit 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), pending study results.

Vertex also plans to conduct a pharmacokinetics and safety study to evaluate VX-809 in combination with ivacaftor in children with CF ages 6 to 11 who have two copies of the F508del mutation. The company expects to use the data from this study for subsequent registration in children ages 6 to 11 in the United States and is continuing discussions with European regulatory agencies for patients in this age group.

Vertex will host a conference call for investors and media today, February 26, 2013 at 5:15 p.m. EST, to discuss the company's Phase 3 development plan.

"This Phase 3 development program is a significant advance in our efforts to develop new medicines that treat the underlying cause of cystic fibrosis for people with the most common type of the disease," said Robert Kauffman, M.D., Ph.D., Senior Vice President and Chief Medical Officer at Vertex. "Importantly, these studies will evaluate two doses of VX-809 in combination with ivacaftor for 24 weeks, and pending data, enable submissions to U.S. and European regulatory authorities. People with CF are in urgent need of new treatments, and we are committed to advancing this combination through Phase 3 development as quickly as possible."

Cystic fibrosis is a rare, life-shortening genetic disease for which there is no cure. Approximately 70,000 people worldwide have CF, including 30,000 in the United States and 35,000 in Europe. Globally, nearly half of those with CF have two copies of the F508del mutation.

About the Phase 3 TRAFFIC and TRANSPORT Studies

Vertex plans to conduct two 24-week, randomized, double-blind, placebo-controlled Phase 3 studies of VX-809 in combination with ivacaftor. TRAFFIC and TRANSPORT will each enroll approximately 500 people with CF ages 12 and older who have two copies of the F508del mutation in the *CFTR* gene, for a total of 1,000 patients. The studies have the same design and together will be conducted at approximately 200 clinical trial sites in North America, Europe and Australia.

The primary endpoint of each study is relative improvement in lung function (percent predicted FEV_1) through 24 weeks of treatment, compared to placebo. Safety and tolerability will also be assessed through 24 weeks. Key secondary endpoints through 24 weeks include absolute improvement in FEV_1, change in body mass index (BMI) or weight gain, number of pulmonary exacerbations and improvements in patient-reported outcomes as measured by the CF Questionnaire Revised (CFQ-R), among others.

Each study will include two combination treatment groups and one placebo group. The treatment groups will evaluate two regimens of VX-809 (600mg QD or 400mg q12h) in combination with ivacaftor (250mg q12h). Fixed-dose tablets that contain both VX-809 and ivacaftor, or placebo, will be used in both studies. Vertex plans to follow the initial 24-week treatment period

with a separate rollover double-blind extension study where all eligible patients, including those who received placebo, will receive one of the combination regimens for up to an additional 96 weeks. The design of the studies is as follows:

Treatment Group	24-Week Dosing Regimen
Group 1 (n=167)	VX-809 (600mg QD) + ivacaftor (250mg q12h)
Group 2 (n=167)	VX-809 (400mg q12h) + ivacaftor (250mg q12h)
Group 3 (n=167)	Placebo + Placebo

About the Study in Patients Ages 6 to 11

Vertex also plans to conduct a study of VX-809 in combination with ivacaftor in children with CF ages 6 to 11 who have two copies of the F508del mutation. The study will evaluate the pharmacokinetics and safety of the combination for up to 24 weeks. Vertex expects to use the data from this study, along with data from TRAFFIC and TRANSPORT, for registration of the combination in the United States in children ages 6 to 11, following registration in patients ages 12 and older. In Europe, the company is in discussions with regulatory agencies regarding patients in this age group.

Phase 2 Data Supporting Phase 3 Trial Design

The Phase 3 studies announced today are supported by data from a Phase 2 study of VX-809 in combination with ivacaftor. The two combination dosing regimens selected for evaluation in Phase 3 were evaluated in Cohorts 2 and 3 of the Phase 2 study.

Cohort 2: As previously reported, the once-daily (QD) 600mg dose of VX-809 in combination with ivacaftor (250mg q12h) was evaluated in 21 patients in the second part (Cohort 2) of the Phase 2 study and resulted in statistically significant improvements in lung function (within group and versus placebo) during the combination dosing period, as noted below:

Cohort 2

Mean Absolute and Relative Changes in Percent Predicted FEV_1		Day 0 — 28; VX-809 Alone	Day 28 — 56; VX-809 + ivacaftor	Day 0 - 56
VX-809 (600mg QD) + ivacaftor (250mg q12h)	*Within-Group*			
	Absolute	-2.9 (p=0.07)	+6.1 (p < 0.001)	+3.4 (p=0.03)
	Relative	-3.5 (p=0.13)	+9.7 (p < 0.001)	+5.3 (p=0.02)
	Versus Placebo			
	Absolute	-2.0 (p=0.36)	+8.6 (p < 0.001)	+6.7 (p=0.002)
	Relative	-3.9 (p=0.21)	+12.8 (p < 0.001)	+9.2 (p=0.004)

Cohort 3: Vertex also evaluated a 400mg twice-daily (q12h) dosing regimen of VX-809 in combination with ivacaftor in a third cohort of patients in the Phase 2 study. Cohort 3 evaluated 11 patients who received VX-809 (400mg q12h) for 28 days followed by VX-809 (400mg q12h) in combination with ivacaftor (250mg q12h) for 28 days. This cohort was designed to evaluate safety and pharmacokinetics of the 400mg q12h dose of VX-809 to support inclusion of this dose in the Phase 3 program. Cohort 3 also included the randomization of four patients to placebo to allow for a blinded safety assessment. Three patients completed treatment in the placebo group. A pharmacokinetic model suggested that 400mg dosing every 12 hours (q12h) of VX-809 would provide a higher total exposure (AUC; area under the curve) compared to 600mg QD dosing, and data from Cohort 3 were consistent with this model.

Safety results from the 400mg (q12h) dose group were similar to that of the 600mg (QD) dose group. In both dose groups, VX-809 was generally well-tolerated alone and in combination with ivacaftor. The most common adverse events in both groups were respiratory in nature. In Cohort 3, one patient in the treatment group discontinued treatment because of a pulmonary adverse event.

Together, these pharmacokinetic and safety data support inclusion of VX-809 400mg (q12h) in combination with ivacaftor 250mg (q12h) in the Phase 3 program to evaluate the effect that higher exposures of VX-809 have on efficacy and safety.

The pattern of lung function response observed in Cohort 3 was similar to that observed in the 600mg QD dose group in Cohort 2, with a decline in FEV_1 during the VX-809 monotherapy dosing period followed by a statistically significant increase in FEV_1 during the VX-809 and ivacaftor combination dosing period. The within-group mean absolute improvement in FEV_1 observed during the combination-dosing period in Cohort 3 was 6.6 percentage points, compared to 6.1 percentage points for the 600mg QD dose group in Cohort 2.

Additional lung function results for Cohort 3 are provided below:

Cohort 3

Mean Absolute and Relative Changes in Percent Predicted FEV_1		**Day 0 — 28; VX-809 Alone**	**Day 28 — 56; VX-809 + ivacaftor**	**Day 0 - 56**
VX-809 (400mg q12h) + ivacaftor (250mg q12h)	*Within-Group*			
	Absolute	-4.3 (p=0.04)	+6.6 (p=0.01)	+1.9 (p=0.57)
	Relative	-6.3 (p=0.08)	+8.8 (p=0.01)	+2.5 (p=0.67)

Study in People with One Copy of the F508del Mutation

In addition to the Phase 3 studies in people with two copies of the F508del mutation, Vertex plans to conduct an 8-week exploratory Phase 2 study of VX-809 in combination with ivacaftor in people 12 and older with one copy (heterozygous) of the F508del mutation on one allele and a second mutation that is not expected to respond to either ivacaftor or VX-809 alone. This study is designed to provide additional safety and lung function data on the combination in heterozygous patients, and will evaluate the twice daily (q12h) combination of VX-809 (400mg) and ivacaftor (250mg).

VX-809 and ivacaftor were 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 Cystic Fibrosis and the Combination of VX-809 and Ivacaftor

Cystic fibrosis is a rare, life-shortening genetic disease affecting approximately 70,000 people worldwide, including 30,000 people in the United States and 35,000 in Europe. The median predicted age of survival for a person with CF born today is between 34 and 47 years, but the median age of death remains in the mid-20s. The most common cause of death among people with CF is lung disease, which results from recurring infections and chronic lung inflammation.

CF is caused by a defective or missing CFTR protein resulting from mutations in the cystic fibrosis transmembrane conductance regulator (*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 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.

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 protein reach the cell surface. Ivacaftor, known as a CFTR potentiator, keeps the CFTR protein channels on the cell surface open longer to increase the flow of salt and water into and out of the cell. Globally, nearly half of people with CF have two copies of the F508del mutation and an additional one-third have one copy of the F508del mutation.

As announced in January 2013, the FDA granted Breakthrough Therapy Designation to the combination regimen of VX-809 with ivacaftor for cystic fibrosis.

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, Dr. Kauffman's statements in the fourth paragraph of this press release and statements regarding (i) the clinical studies the company plans to conduct to evaluate VX-809 in combination with ivacaftor, (ii) the design of these studies, including the primary and secondary endpoints and the anticipated number of patients to be enrolled, (iii) the company's expectations regarding when data will be available from these clinical trials, (iv) the potential submission of the NDA and MAA for the combination therapy and (v) the expectation that the data from the study in children 6 to 11 will be used for subsequent registration in the United States and the plan to continue discussions with European regulatory agencies for this age group. While the Company believes the forward-looking statements contained in this press release are accurate, those statements are subject to risks and uncertainties that could cause actual outcomes to vary materially from the outcomes referenced in the forward-looking statements. These risks and uncertainties include, among other things, the risks that efforts to develop VX-809 in combination with ivacaftor may not be successful because the results of the clinical trials described in this press release may not support registration or for technical, scientific or other reasons, that clinical trials may not proceed as planned due to drug supply, patient enrollment or other issues, and that an adverse event profile for VX-809 in combination with ivacaftor could be revealed in further nonclinical or clinical studies 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.

Conference Call Information

Vertex will host a conference call and webcast today, February 26, 2013 at 5:15 p.m. ET to review the initiation of the Phase 3 pivotal program studying the combination regimen of VX-809 and ivacaftor for F508del homozygous patients. The conference call will be webcast live, and a link to the webcast may be accessed from the 'Vertex Events' page of Vertex's 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 15208263.

The call will be available for replay via telephone commencing February 26, 2013 at 8:00 p.m. ET running through 5:00 p.m. ET on March 5, 2013. 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 March 5, 2013. Vertex is also providing a podcast MP3 file available for download on the Vertex website at www.vrtx.com.

(VRTX — GEN)

Vertex Pharmaceuticals Incorporated
Media:
Megan Goulart, 617-341-6992
mediainfo@vrtx.com
or
Investors:
Michael Partridge, 617-341-6108
or
Kelly Lewis, 617-961-7530
or
Information for Patients and Healthcare Providers:
North America:
1-877-634-VRTX (8789)
medicalinfo@vrtx.com
or
Outside North America:
44 (0) 1923 437 672
EUmedicalinfo@vrtx.com

Source: Vertex Pharmaceuticals Incorporated