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Interim Phase 2 Data Showed a Combination of VX-770 and VX-809 Improved Function of the Defective Protein that Causes Cystic Fibrosis in People With the Most Common Form of the Disease

-13.17 mmol/L reduction in sweat chloride in one arm supports further evaluation of a combination approach to treating the root cause of cystic fibrosis-

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced interim results from the first part of a Phase 2 study designed to evaluate multiple combination regimens of VX-770 and VX-809, Vertex's lead medicines in development that aim to treat the defective protein that causes cystic fibrosis (CF). That protein, known as the cystic fibrosis transmembrane conductance regulator (CFTR), is responsible for regulating the flow of chloride across the cell surface to help hydrate and clear mucus from the airways. The first part of the study enrolled and randomized 62 people with two copies of the most common mutation in the CF gene, known as the F508del mutation. In people with the F508del mutation, the CFTR protein does not reach the cell surface in normal amounts, resulting in a buildup of mucus and other complications that can lead to lung damage. VX-809, known as a CFTR corrector, is designed to help the protein reach the cell surface, while VX-770, known as a CFTR potentiator, aims to help the protein function more normally once it reaches the cell surface. VX-770 and VX-809 were advanced into development with support from Cystic Fibrosis Foundation Therapeutics, Inc., the nonprofit affiliate of the Cystic Fibrosis Foundation. Vertex retains worldwide rights to develop and commercialize these potential medicines.

The first part of the study met its two primary endpoints: (1) safety and tolerability of the combination regimen and (2) the effect of the combination of VX-770 and VX-809 on CFTR function as measured by sweat chloride, a key measure of the function of the CFTR protein. There were no serious adverse events reported, and the adverse event profile during the combination-dosing portion of the study (Day 14 to Day 21) was similar to that during the VX-809 monotherapy-dosing portion (Day 0 to 14). In the arm that evaluated VX-809 (200 mg) followed by dosing of VX-770 (250 mg) in combination with VX-809, a statistically significant reduction in sweat chloride of -13.17 mmol/L ($p<0.001$) was observed from baseline (Day 0) through Day 21. In this arm, a -9.10 mmol/L ($p<0.001$) reduction was observed after VX-770 (250 mg) was added to VX-809 (200 mg) for seven days (Day 14 to 21). Vertex intends to initiate the second part of this study in the fourth quarter of 2011 after the completion of further analyses of data from Part 1.

The most commonly reported adverse events were respiratory in nature and occurred in approximately half of people across all arms of the study. One person receiving VX-809 in the monotherapy portion of the study discontinued treatment due to an increase in respiratory symptoms during the first 7 days of the study.

"These data open the door to the possibility of treating people with the most common form of cystic fibrosis by using two medicines together that target the defective protein that causes the disease," said Peter Mueller, Ph.D., Chief Scientific Officer and Executive Vice President of Global Research and Development at Vertex. "We look forward to beginning the second part of this study later this year, which may help us begin to further explore the hypothesis that enhanced CFTR function may result in meaningful clinical benefits for people with cystic fibrosis."

"The CF Foundation's mission is to support the development of new medicines for cystic fibrosis that improve the quality of life for those with the disease," said Robert J. Beall, Ph.D., president and CEO of the Cystic Fibrosis Foundation. "These data, while early, provide important new information about the potential to address the basic defect found among people with the most common form of CF."

About the Phase 2 Study

The results announced today are from Part 1 of a multiple-part, randomized, double-blind, placebo-controlled Phase 2 trial that will inform future clinical studies that combine a CFTR potentiator and corrector. The first part of the study enrolled 62 people with CF aged 18 years or older who had two copies of the F508del mutation in the *CFTR* gene. The primary goals of the trial were to evaluate the safety and tolerability and the effect on CFTR function of the combination of VX-770 and VX-809 as measured by sweat chloride.

There were three treatment arms in Part 1 of the study that evaluated VX-809 (200 mg) or placebo alone for 14 days, followed

by VX-809 (200 mg) in combination with VX-770 (150 mg or 250 mg) or placebo for seven days.

Interim Results

Safety: In Part 1 of this study, no serious adverse events were reported, and the adverse event profile observed during the 14-day portion of the study in which VX-809 was dosed as monotherapy was similar to the profile observed during the subsequent 7-day portion in which VX-809 and VX-770 were dosed in combination. Safety was a primary endpoint of the study, and these interim safety results support further clinical evaluations of CFTR potentiator and corrector regimens.

Sweat Chloride: A co-primary endpoint of the study was the effect on CFTR function as measured by sweat chloride during the combination-dosing portion of the study (Day 14 to Day 21). Elevated sweat chloride levels are a diagnostic hallmark that occur in all people with CF and result directly from defective CFTR activity in epithelial cells in the sweat duct. 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 values in people who do not have CF are less than 40 mmol/L. Reduction in sweat chloride is considered to be a marker of improved CFTR function.

In Part 1 of this study, the baseline sweat chloride levels across the three arms were approximately 100 mmol/L. The within-group mean change in sweat chloride from baseline for each of the treatment groups was as follows:

Treatment Arm	**Within-Group Mean Change in Sweat Chloride From Baselines (Day 0 and Day 14)**	
	Day 0 — 14: VX-809 Alone	**Day 14 — 21: VX-809 in Combination with VX-770**
Arm 1 (n=20): VX-809 (200mg); VX-809 (200 mg) in combination with VX-770 (150 mg)	-4.21 mmol/L (p=0.008)	-2.24 mmol/L (p=0.163)
Arm 2 (n=21): VX-809 (200mg); VX-809 (200 mg) in combination with VX-770 (250 mg)		-9.10 mmol/L (p<0.001)
Arm 3 (n=21): VX-809 placebo; VX-809 placebo in combination with VX-770 placebo	-2.86 mmol/L (p=0.179)	+1.25 mmol/L (p=0.446)

A statistically significant reduction in sweat chloride of -9.10 mmol/L (p<0.001) was observed after VX-770 (250 mg) was added to VX-809 (200 mg) from Day 14 to Day 21. As compared to baseline (Day 0), people who received the combination regimen in this arm had a -13.17 mmol/L reduction in sweat chloride.

Eight of the 17 patients with evaluable data in Arm 2 had a reduction of sweat chloride that exceeded -15.0 mmol/L, while four of these 17 patients had a reduction of sweat chloride that exceeded -20.0 mmol/L. Four of the 21 patients in this arm did not have evaluable data in this arm and were not part of this responder analysis (n=17). Across the treatment arms, patients returned to baseline following the completion of dosing with VX-809 and VX-770.

Vertex intends to initiate the second part of this Phase 2 study in the fourth quarter of 2011 following the conclusion of additional analyses of data from the first part of the study. Similar to Part 1, the second part of the study will evaluate multiple doses of VX-770 and VX-809 in combination and will focus on the effect of the combination on sweat chloride measurements. Part 2 of the study is also expected to evaluate longer dosing periods for the VX-770 and VX-809 combinations.

About CFTR and CFTR Modulators

CF is caused by defective or missing CF transmembrane conductance regulator (CFTR) proteins, which result in poor ion flow across cell membranes, including in the lungs, causing the accumulation of abnormally thick, sticky mucus that leads to chronic lung infections and progressive lung damage. In people with the F508del mutation, which is the most common *CFTR* mutation, CFTR proteins do not reach the cell surface in normal amounts. As a CFTR corrector, VX-809 aims to increase CFTR function by increasing the movement of CFTR to the cell surface. Once these CFTR proteins are at the cell surface, VX-770, a CFTR potentiator, aims to further increase the function of the proteins by increasing their ability to transport ions across the cell membrane.

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 36 years. According to the *2008 Cystic Fibrosis Foundation Patient Registry Annual Data Report*, approximately 48 percent of the total CF patient population in the United States have two copies of the F508del mutation and an additional 39 percent of the total CF patient population have

one copy of the F508del mutation.

People interested in further information about clinical trials of VX-809 or VX-770 should visit **www.clinicaltrials.gov** or **http://www.cff.org/clinicaltrials**.

Collaborative History with Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT)

Vertex initiated its CF research program in 1998 as a part of a collaboration with CFFT, the non-profit drug discovery and development affiliate of the Cystic Fibrosis Foundation. From 2000 through 2006, Vertex and CFFT amended and expanded the collaboration four times to support the accelerated discovery and development of VX-770 and VX-809. In April 2011, Vertex and CFFT further expanded the collaboration to support development activities for VX-661, Vertex's second corrector to enter clinical development, and the discovery and development of next-generation correctors. As part of these collaborations, Vertex has received approximately $75 million from CFFT to support CF research and development efforts led by Vertex.

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, go to 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, 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.

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

Special Note Regarding Forward-Looking Statements

This press release contains forward-looking statements including statements regarding (i) the interim data from Part 1 of the clinical trial supporting further evaluation of a combination approach to treating the root cause of cystic fibrosis; (ii) the intention to initiate the second part of the clinical trial in the fourth quarter of 2011 after the completion of further analyses of data from Part 1; (iii) the possibility of treating people with the most common form of CF by using two medicines together that target the defective protein that causes the disease; (iv) the hypothesis that enhanced CFTR function may result in meaningful clinical benefits for people with CF; (v) Vertex's expectations regarding the design of Part 2 of the clinical trial; and (vi) VX-809 aiming to increase CFTR function by increasing the movement of CFTR to the cell surface. 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 risk that efforts to develop VX-809 in combination with VX-770 may not proceed due to technical, scientific, commercial, financial or other reasons, that clinical trials may not proceed as planned, that additional clinical trials involving VX-809 may not generate data indicating that VX-809 is a useful treatment for cystic fibrosis, that an adverse event profile for VX-809 or VX-770 could be revealed in further nonclinical or clinical studies that could put further development of VX-809 or VX-770 in jeopardy or adversely impact the therapeutic value of VX-809 and/or VX-770, 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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