February 23, 2011

Phase 3 Study of VX-770 Showed Profound and Sustained Improvements in Lung Function (FEV1) and Other Measures of Disease Among People With a Specific Type of Cystic Fibrosis

- Relative mean improvement in lung function of approximately 17% from baseline compared to placebo achieved by people treated with VX-770; mean absolute improvement from baseline of approximately 10.5% compared to placebo; both measures through 24 and 48 weeks -

- Significant improvements in all key secondary endpoints for VX-770; patients were 55% less likely to experience a pulmonary exacerbation, had significant reductions in sweat chloride and, on average, gained nearly 7 pounds -

- Discontinuations due to adverse events were less frequent among people treated with VX-770 -

- Data support Vertex plan to submit U.S. and European regulatory applications for approval in the second half of 2011 -

CAMBRIDGE, Mass., Feb 23, 2011 (BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced positive results from the Phase 3 STRIVE study of VX-770, an oral medicine in development that targets the defective protein that causes cystic fibrosis (CF). STRIVE was designed to evaluate people with a mutation in the CF gene known as G551D. In this study, profound improvements in lung function (forced expiratory volume in one second, or FEV_1) were observed through week 24, and sustained through week 48, among those who received VX-770 (n=83) compared to those treated with placebo (n=78). Significant improvements in all key secondary endpoints were also observed through week 48 among those who received VX-770.

The primary endpoint of the study was mean absolute change from baseline compared to placebo in percent predicted FEV_1 (lung function) through week 24. Data from the study showed a mean absolute improvement in lung function from baseline compared to placebo through week 24 of 10.6 percent among those treated with VX-770. Mean absolute improvement in lung function among those treated with VX-770 was 10.5 percent through week 48.

Highly statistically significant improvements in key secondary endpoints in this study were also reported through week 48. Compared to those treated with placebo, people who received VX-770 were 55 percent less likely to experience a pulmonary exacerbation (periods of worsening in signs and symptoms of the disease requiring treatment with antibiotics) and, on average, gained nearly seven pounds (3.1 kilograms) through 48 weeks. There was a significant reduction in the amount of salt in the sweat (sweat chloride) among people treated with VX-770 in this study. Increased sweat chloride is a diagnostic hallmark of CF. Sweat chloride is a marker of CFTR protein dysfunction, which is the underlying molecular mechanism responsible for CF. People who received VX-770 also reported having fewer respiratory symptoms.

Adverse events that were 5 percent greater among those treated with VX-770 compared to placebo were headache, upper respiratory tract infections, nasal congestion, rash, dizziness and bacteria in the sputum. The most commonly reported serious adverse events included pulmonary exacerbation (13 percent in the VX-770 group compared to 33 percent in the placebo group) and hemoptysis (or bloody cough; 1 percent in the VX-770 group and 5 percent in the placebo group). Discontinuations through 48 weeks due to adverse events were less frequent in the VX-770 treatment group compared to placebo (1 percent compared to 5 percent).

"Treating the underlying cause of cystic fibrosis with VX-770 led to clinical improvements that were far beyond our expectations, providing support for an entirely new approach to the treatment of this disease," said Peter Mueller, Ph.D., Executive Vice President, Global Research and Development, and Chief Scientific Officer for Vertex. "All primary and key secondary outcome measures in this study supported VX-770 over placebo. Patients' lung function improved, they gained weight, experienced fewer respiratory symptoms and felt substantially better. Due to the significance of these data and the great need for new, more effective medicines, we will work with regulatory agencies to determine the fastest way to get VX-770 approved for people with this specific type of CF."

"The results from STRIVE are highly encouraging for the CF community and provide scientific evidence supporting our long-standing belief that targeting the underlying defect of CF may have a profound effect on the disease," said Robert J. Beall, Ph.D., president and CEO of the Cystic Fibrosis Foundation. "We have much more to do to eliminate this disease, but these data are extremely exciting, especially for people with the G551D mutation and their families. They also offer significant hope that a similar approach to treatment may help others living with CF."

All patients who completed 48 weeks of treatment in STRIVE (n=144), including those in the placebo group, were eligible to receive VX-770 as part of an extension study called PERSIST. All patients (n=77) who completed dosing in the VX-770 arm and all but one patient (n=67) in the placebo arm chose to enroll in the extension study and receive VX-770 for up to an additional 96 weeks or until VX-770 is approved.

STRIVE is one of three studies in the VX-770 registration program. Vertex plans to submit data from STRIVE for presentation at an upcoming medical meeting. The registration program for VX-770 also includes two other studies, the Phase 2 DISCOVER study and Phase 3 ENVISION study. Data from DISCOVER were also reported today. Data from ENVISION are expected in mid-2011. Vertex plans to submit regulatory applications for approval in the United States and Europe in the second half of 2011.

Vertex's medicines in development for CF were discovered as part of a collaboration with Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT) to discover and develop novel CFTR modulators. CFFT is the nonprofit drug discovery and development affiliate of the Cystic Fibrosis Foundation. Vertex retains worldwide rights to develop and commercialize these potential medicines.

Summary of Key Data from STRIVE

In the STRIVE study, 161 people were enrolled and received at least one dose of either VX-770 as a single 150 mg tablet or placebo twice daily. The study was designed to evaluate VX-770 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).

Preliminary Efficacy Results

Lung Function: Absolute and relative changes in lung function are being reported in today's announcement. The primary endpoint of STRIVE was mean absolute improvement from baseline. Phase 3 results and product labeling for currently available CF medicines generally describe relative improvements in lung function.

Baseline lung function in STRIVE was 63.5 percent predicted for patients in the VX-770 treatment group and 63.7 percent predicted among those in the placebo control group. Results of the STRIVE study showed that people treated with VX-770 achieved a mean absolute improvement from baseline compared to placebo of 10.6 percent through 24 weeks ($p<0.0001$). Mean absolute improvement in lung function achieved by people who received VX-770 was sustained through 48 weeks (10.5 percent; $p<0.0001$).

In addition, people treated with VX-770 experienced a 16.9 percent relative mean improvement in lung function from baseline compared to placebo ($p<0.0001$) through week 24, which was sustained through week 48 (16.8 percent; $p<0.0001$).

Additional secondary endpoints were measured to observe the effect of VX-770 through week 48. These secondary endpoints included:

Pulmonary Exacerbations: People treated with VX-770 in STRIVE were 55 percent less likely to experience a pulmonary exacerbation compared to those treated with placebo through week 48. Through 48 weeks, 67 percent of people treated with VX-770 were exacerbation free compared to 41 percent of people treated with placebo.

Weight: Many people with CF have a hard time gaining and maintaining weight due to factors such as nutrition, chronic infection and inflammation. In the STRIVE study, those who received VX-770 experienced an average weight gain of approximately 6.8 lbs (3.1 kilograms) at 48 weeks compared to baseline. Those in the placebo group gained approximately 0.9 lbs (0.4 kilograms).

Sweat Chloride: 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 normal values are less than 40 mmol/L. Reduction in sweat chloride is considered to be a marker of improved CFTR function.

In STRIVE, the baseline sweat chloride level for both treatment groups was approximately 100 mmol/L. Statistically significant

decreases in measurements of sweat chloride were observed among those treated with VX-770 but not those treated with placebo. Through week 48, mean sweat chloride levels for patients treated with VX-770 were below 60 mmol/L.

Patient Reported Outcomes: The Cystic Fibrosis Questionnaire — Revised (CFQ-R) is a validated patient reported outcome tool that was used in this study to measure the impact of VX-770 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 this study, statistically significant and clinically meaningful improvements in respiratory symptoms (a secondary endpoint of the study) were reported among patients who received VX-770.

DISCOVER Data

Vertex also announced today the results of the Phase 2 DISCOVER study, which was primarily designed to provide additional safety data for VX-770 and is part of the registration program. DISCOVER enrolled 140 people who had two copies of the F508del mutation, which prevents the CFTR protein from moving to its proper location at the cell surface. The majority of people with CF have at least one copy of the F508del mutation.

The primary endpoints of DISCOVER were safety and absolute change from baseline in lung function through 16 weeks. Adverse events were similar between the treatment groups. Adverse events that occurred more frequently (≥5 percent) in the VX-770 treatment group compared to placebo were cough, nausea, rash and contact dermatitis. None of these events were serious or led to discontinuation of VX-770. Data from the DISCOVER study will be submitted for presentation at an upcoming medical meeting.

Mean baseline lung function (FEV_1) was 79.7 percent predicted for people who received VX-770 compared to 74.8 percent predicted for patients in the placebo group. Results of the DISCOVER study showed that people treated with VX-770 achieved a mean absolute improvement from baseline compared to placebo of 1.6 percent through 16 weeks ($p=0.25$). The improvement was not statistically significant and was not considered clinically meaningful. Data from the study also showed a mean relative improvement in lung function from baseline compared to placebo of 2 percent through week 16. A mean reduction in sweat chloride of 2.9 mmol/L compared to placebo through 16 weeks was observed among those treated with VX-770. This improvement was statistically significant but small ($p<0.04$).

"Based on the results of DISCOVER, we continue to believe the combination of a potentiator and corrector may be the best approach to treating people with two copies of the F508del mutation," said Robert Kauffman, M.D., Ph.D., Senior Vice President and Chief Medical Officer for Vertex. "Data are anticipated later this year from the first study to evaluate the combination of VX-770 and VX-809 in this group of people with cystic fibrosis."

ENVISION Study

In addition to the STRIVE and DISCOVER studies, a third study known as ENVISION is evaluating VX-770 in children 6 to 11 years old with CF who have at least one copy of the G551D mutation. Data from the ENVISION study are anticipated in mid-2011.

Combination Study of VX-770 and VX-809

Vertex is conducting a Phase 2a clinical trial to evaluate multiple combination regimens of VX-770 and VX-809 in people with two copies of the F508del mutation. The first part of the study is designed to evaluate VX-809 (200 mg), or placebo dosed alone for 14 days and in combination with VX-770 (150 mg or 250 mg), or placebo, for seven days. Vertex expects to obtain data from Part One of the trial in the first half of 2011.

About the Cystic Fibrosis Transmembrane Conductance Regulator Protein (CFTR)

CF is caused by defective or missing CFTR proteins, which result in poor ion flow across cell membranes, including in the lung, and the accumulation of abnormally thick, sticky mucus that leads to chronic lung infections and progressive lung damage. In people with the G551D mutation, CFTR proteins are present on the cell surface but do not function normally. VX-770, known as a potentiator, aims to increase the function of defective CFTR proteins by increasing the gating activity, or ability to transport ions across the cell membrane, of CFTR once it reaches the cell surface. In people with the F508del mutation, CFTR proteins do not reach the cell surface in normal amounts. VX-809, known as a CFTR corrector, aims to increase CFTR function by increasing the amount of CFTR at the cell surface.

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 37 years. According to the *2008*

Cystic Fibrosis Foundation Patient Registry Annual Data Report, approximately 4 percent of the total CF patient population in the U.S. have at least one copy of the G551D mutation, 48 percent of the total CF patient population in the U.S. 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. Vertex and CFFT expanded the agreement in 2000 and again in 2004, and in March 2006 entered into a collaboration for the accelerated development of VX-770. In addition to the development collaboration for VX-770, in January 2006 Vertex and CFFT entered into an expanded research collaboration to develop novel corrector compounds. Vertex has received approximately $75 million from CFFT to support CF research and development efforts.

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.

About Vertex

Vertex creates new possibilities in medicine. Our team aims to discover, develop and commercialize 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.

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 statements regarding (i) Vertex's plan to submit U.S. and European regulatory applications for approval in the second half of 2011; (ii) the support provided by this study for an entirely new approach to treating cystic fibrosis; (iii) the plan to work with regulatory agencies to determine the fastest way to get VX-770 approved; (iv) the hope that a similar approach to treatment, targeting CFTR protein dysfunction caused by mutations other than the G551D mutation, may help others living with CF; (v) the planned presentation of data from STRIVE and DISCOVER at upcoming medical meetings; (vi) the expectation that data from ENVISION will be available in mid-2011; and (vii) our belief that a combination of a potentiator and corrector may be the best approach to treating people with two copies of the F508del mutation and the expectation that data from the ongoing Phase 2a combination study of VX-770 and VX-809 will be available in the first half of 2011. 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 Vertex could experience unforeseen delays, that future outcomes from ENVISION and from the various extension studies of VX-770 may not be favorable or may be less favorable than observed to date in STRIVE and other studies, that unexpected side effects may appear as VX-770 or VX-809 are more broadly dosed, that regulatory authorities may require more extensive data for VX-770 regulatory filings than currently expected; that future clinical, competitive and other factors may adversely affect the potential for VX-770; that the company may not be able to successfully develop VX-770 or combination therapies involving VX-770 and VX-809, 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.

Conference Call and Webcast

Vertex will host a conference call and webcast today, Wednesday, February 23, 2011 at 8:30 a.m. ET to review recent developments in cystic fibrosis. This call and webcast will be broadcast via the Internet at **www.vrtx.com**. It is suggested that webcast participants go to the web site at least 10 minutes in advance of the call to ensure that they can access the slides. The link to the webcast is available on the Events and Presentations button on the home page. To listen to the call on the

telephone, dial 866-501-1537 (U.S. and Canada) or 720-545-0001 (International). Vertex is also providing a podcast MP3 file available for download on the Vertex website at www.vrtx.com. The conference ID number is 46977282. The call will be available for replay via telephone commencing February 23, 2011 at 12:00 p.m. ET running through 5:00 p.m. ET on March 1, 2011. The replay phone number for the U.S. and Canada is 800-642-1687. The international replay number is 706-645-9291. The conference ID number is 46977282. Following the live webcast, an archived version will be available on Vertex's website until 5:00 p.m. ET on March 9, 2011.

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

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Source: Vertex Pharmaceuticals Incorporated