November 5, 2011

Phase 2 Data for Selective Oral JAK3 Inhibitor VX-509 Show Significant Improvements in Signs and Symptoms of Rheumatoid Arthritis

-Data to be presented at American College of Rheumatology Annual Meeting next week-

-Phase 2b study evaluating longer treatment duration for VX-509 planned for early 2012-

CHICAGO--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced the final results from a Phase 2a study of the investigational selective oral JAK3 inhibitor VX-509. The data showed substantial and statistically significant improvements in multiple measurements of rheumatoid arthritis (RA) activity. The 12-week study met its two primary endpoints, defined as a statistically significant improvement in the proportion of people who achieved at least a 20 percent improvement in the signs and symptoms of RA, also known as ACR_{20}, and a statistically significant improvement from baseline in Disease Activity Score 28 (DAS28). For the two highest dose groups of the study, statistically significant ACR_{20}, ACR_{50}, ACR_{70}, and DAS28 responses were also observed as compared to placebo, and more than one-third of people in these groups achieved clinical remission (DAS28 remission). Overall, the most frequently reported class of adverse event in the VX-509 and placebo arms was infections. The data from the study will be presented in a poster session on November 8 at the 2011 Annual Meeting for the American College of Rheumatology (ACR) in Chicago.

"People with RA experience frequent debilitating pain and discomfort in joints, which significantly impacts their lives and underscores the need for new RA medicines," said Roy Fleischmann, M.D., Clinical Professor of Medicine at the University of Texas Southwestern Medical Center and an investigator for the Phase 2 study of VX-509. "People in this study showed significant improvement in the signs and symptoms of RA after treatment with VX-509 — an encouraging step toward the future treatment of RA by selectively targeting an underlying mechanism of the disease."

Based on the Phase 2a data to be presented at ACR, a six-month Phase 2b study of VX-509 in RA is expected to begin in early 2012. This study, which will be run by Vertex, will evaluate once-daily (QD) and twice-daily (BID) doses of VX-509 in combination with methotrexate, a commonly prescribed disease-modifying antirheumatic drug (DMARD) for RA that is frequently used in combination with other RA medicines. The study is expected to enroll approximately 350 people with moderate to severe RA.

About the Phase 2a Study

This double-blind, randomized, placebo-controlled Phase 2a study of VX-509 enrolled 204 people with active moderate to severe RA. The study enrolled people who had an inadequate response to at least one currently available non-biologic (non-injectable) DMARD. The study evaluated four dose levels of VX-509, which was given twice daily (BID) for 12 weeks. Patients did not receive methotrexate during this study, but could have received it prior to the study. Approximately 40 clinical trial sites participated in the trial in the United States and Europe. Vertex reported top-line data from this study in September 2011.

Efficacy Data

The study met its two primary endpoints, which were the proportion of people who achieved an ACR_{20} response at week 12 and the change from baseline in DAS28 at week 12. Additional secondary endpoints were used to evaluate the clinical activity of VX-509, including ACR_{50} and ACR_{70} responses at week 12, DAS28 remission and EULAR response. The responses observed in the two highest dose groups for VX-509 indicated continuous and statistically significant improvements in the signs and symptoms of RA, with these effects being observed in some patients as early as the first week of the study. Efficacy results are provided below. ACR responses are based on an intent-to-treat analysis where patients who discontinued treatment prior to week 12 were counted as non-responders (failures) in the efficacy analyses, regardless of their response to treatment:

American College of Rheumatology Responses at Week 12:

VX-509 (n=163)	**ACR_{20}**	**ACR_{50}**	**ACR_{70}**

25 mg (n=41)	39% (*p=0.485*)	17% (*p=0.312*)	7% (*p=0.616*)
50 mg (n=41)	61% (*p=0.007*)	32% (*p=0.011*)	12% (*p=0.201*)
100 mg (n=40)	65% (*p=0.002*)	38% (*p=0.001*)	18% (*p=0.029*)
150 mg (n=41)	66% (*p=0.002*)	49% (*p<0.001*)	22% (*p=0.014*)
Placebo (n=41)	29%	7%	2%

Disease Activity Scores at Week 12:

VX-509	**DAS28 Improvement from Baseline**
25 mg	-1.75 (*p=0.155*)
50 mg	-2.60 (*p<0.001*)
100 mg	-2.70 (*p<0.001*)
150 mg	-3.06 (*p<0.001*)
Placebo	-1.25

DAS28 Remission:

The study also evaluated the proportion of patients in each treatment arm who experienced clinical remission, defined as a patient with a DAS28 score of less than 2.6 at week 12. In this study, 12 percent, 15 percent, 35 percent and 37 percent of people achieved DAS28 remission in the 25 mg, 50 mg, 100 mg and 150 mg treatment groups, respectively, compared to 7 percent of people in the placebo arm.

EULAR Response:

The study also evaluated the proportion of patients in each treatment arm who experienced a good or moderate EULAR response. EULAR response is calculated as a measurement of the absolute value and improvement in a person's DAS28 score over time. EULAR responses were as follows:

VX-509	**Good or Moderate EULAR Response**
25 mg	59 percent of patients
50 mg	78 percent of patients**
100 mg	73 percent of patients*
150 mg	78 percent of patients**
Placebo	42 percent of patients

** p < 0.007 ** p ≤ 0.0001*

Safety Data

At least 80 percent of all people in each of the VX-509 treatment groups completed the 12-week treatment course, and 68 percent of people who received placebo completed treatment. Treatment discontinuations due to adverse events occurred in 5 percent of people in the placebo group compared to 0 percent, 2 percent, 18 percent and 12 percent of people in the 25 mg, 50 mg, 100 mg and 150 mg groups, respectively. Overall, the most frequently reported class of adverse event in the VX-509 and placebo arms was infections, which occurred in 17 percent of people who received placebo and in 17 percent of people who received VX-509. The most common individual adverse events were nausea (6 percent for the VX-509 groups; 0 percent for placebo), increased alanine aminotransferase (ALT) (4 percent for the VX-509 groups; 5 percent for placebo) and headache (4 percent for the VX-509 groups; 5 percent for placebo). Dose-related low-grade increases in high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol were observed in people who received VX-509.

Serious adverse events occurred in 2 percent of people in the placebo treatment group, compared to 0 percent, 2 percent 13 percent and 5 percent of people in the 25 mg, 50 mg, 100 mg and 150 mg VX-509 groups, respectively. The most common serious adverse events in the VX-509 treatment arms were infections, which occurred in 0 percent of people in the placebo treatment group, compared to 0 percent, 0 percent, 8 percent and 5 percent of people in the 25 mg, 50 mg, 100 mg and 150

mg VX-509 groups, respectively. There were no serious adverse events related to measurements in ALT.

As previously reported, in the 100 mg dose group of the study, one patient died of a hemorrhagic stroke, reported as unrelated to VX-509. Also in this dose group, one patient died of pneumonia. This patient received VX-509 and other medicines also associated with a potential increase in susceptibility to infections. As a result, a contribution of VX-509 to the severity of the pneumonia in this patient cannot be ruled out.

There were no meaningful declines observed in measures of hemoglobin or neutrophils among people who received VX-509 compared to those who received placebo. Two percent of all people who received VX-509 discontinued treatment due to lack of efficacy, compared to 15 percent in the placebo group.

About VX-509

VX-509 is an investigational oral medicine being developed by Vertex that is designed to selectively inhibit Janus kinase 3, or JAK3, which is an essential part of the underlying disease mechanisms that cause inflammation in diseases such as RA. JAK3 specific inhibition represents a new approach to the treatment of a range of autoimmune diseases where it is an essential component of the signaling cascade that contributes to the abnormal immune response, which results in chronic inflammation and, in the case of RA, irreversible damage to cartilage and bones. JAK3 is one of four JAK family kinases (JAK1, JAK2, JAK3 and Tyk2).

Based on *in vitro* data, VX-509 has demonstrated a high degree of potency for JAK3 and a high level of selectivity for inhibition of JAK3 compared to JAK1 and JAK2 dependent assays. VX-509 has been shown to be greater than 1000-fold more selective for JAK3 compared to non-JAK kinases and approximately 25- to 150-fold more selective for JAK3 compared to other JAK isotypes in cell-based assays. This high level of selectivity was confirmed in clinical studies where dose-related inhibition of a JAK3 dependent biomarker was observed while little to no effect was shown against a JAK2/JAK1 dependent biomarker.

About Rheumatoid Arthritis

RA is a chronic inflammatory disease that affects 1 percent to 2 percent of the world's population, including 1.5 million adults in the United States.[1,9] The disease causes destruction of joint cartilage and erosion of adjacent bone, resulting in deformity, loss of function, substantial disability and, for many, the need for joint replacement. Many people with RA suffer progressive disability over time,[2,3] pain,[4] work loss,[5] substantial health care costs,[6] and premature death.[7] Approximately 80 percent of people with RA become disabled within 20 years of diagnosis.[8]

The treatment of RA focuses on reducing symptoms and inhibiting progression of the disease. Nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids may reduce the symptoms of pain, swelling and stiffness, but they do not alter the natural course of the disease. Disease-modifying antirheumatic drugs (DMARDs) have shown effects in slowing the progression of joint damage and time to disability and thus altering the natural history of RA. While recently approved medicines are effective in a portion of patients, a significant number of people with RA do not respond adequately or become refractory to these medicines, creating a significant need for new approaches to RA treatment.

About Endpoints in RA: ACR and DAS Responses

The most common endpoints in RA clinical studies are ACR and DAS responses. ACR responses are defined as the proportion of patients in a trial who achieve at least a pre-specified percent improvement in the signs and symptoms of RA, as measured by tender and swollen joint counts and other criteria. For example, an ACR_{20} response reflects the proportion of people who had at least a 20 percent improvement in both tender and swollen joints in addition to improvements in other criteria such as C-reactive protein (CRP), Health Assessment Questionnaire (HAQ) disability scores and others. DAS responses, including DAS28, are derived from an assessment of multiple measurements of RA, including tender and swollen joints, C-reactive protein (CRP) and a patient's assessment of general health.

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 1,900 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 statements regarding (i) the plan to begin in early 2012 a six-month Phase 2b trial to evaluate VX-509 in approximately 350 people with RA; (ii) the potential to treat RA by selectively targeting an underlying mechanism of the disease; and (iii) the potential clinical trial design for the planned Phase 2b trial. While Vertex believes the forward-looking statements contained in this press release are accurate, these 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-509 may not proceed due to technical, scientific, commercial, financial or other reasons, that a safety profile for VX-509 could be established in further nonclinical studies or clinical trials that could put further development of VX-509 in jeopardy or adversely effect its therapeutic value, 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 Vertex's website at www.vrtx.com. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

References:

1. Linos A, Worthington JW, O'Fallon WM, Kurland LT. The epidemiology of rheumatoid arthritis in Rochester, Minnesota: a study of incidence, prevalence, and mortality. Am J Epidemiol. 1980;111:87-98.

2. Pincus T, Callahan LF, Sale WG, Brooks AL, Payne LE, Vaughn WK. Severe functional declines, work disability, and increased mortality in seventy-five rheumatoid arthritis patients studied over nine years. Arthritis Rheum. 1984;27:864-72.

3. Sherrer YS, Bloch DA, Mitchell DM, Young DY, Fries JF. The development of disability in rheumatoid arthritis. Arthritis Rheum. 1986;29:494-500.

4. Callahan LF, Brooks RH, Summey JA, Pincus T. Quantitative pain assessment for routine care of rheumatoid arthritis patients, using a pain scale based on activities of daily living and a visual analog pain scale. Arthritis Rheum. 1987;30:630-6.

5. Yelin E, Meenan R, Nevitt M, Epstein W. Work disability in rheumatoid arthritis: effects of disease, social, and work factors. Ann Intern Med. 1980;93:551-6.

6. Verstappen SM, Bijlsma JW, Verkleij H, Buskens E, Blaauw AA, ter Borg EJ,et al; Utrecht Rheumatoid Arthritis Cohort Study Group. Overview of work disability in rheumatoid arthritis patients as observed in cross-sectional and longitudinal surveys. Arthritis Rheum. 2004;51:488-97.

7. Pincus T, Brooks RH, Callahan LF. Prediction of long-term mortality in patients with rheumatoid arthritis according to simple questionnaire and joint count measures. Ann Intern Med. 1994;120:26-34.

8. Wong JB, Ramey DR, Singh G. Long-term morbidity, mortality, and economics of rheumatoid arthritis. Arthritis Rheum. 2001;44:2746-9.

9 Arthritis Rheum. 2010 Jun;62(6):1576-82. [Data source: Patient Cohort, Minnesota]

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