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# Vertex Reports Investigational p38 MAP Kinase Inhibitor, VX-702, Meets Primary Objectives in Phase II Clinical Study in Rheumatoid Arthritis

--Vertex to Advance Clinical Program; Company Expects to Initiate Combination Study of VX-702 and Methotrexate by Mid-2006--

Cambridge, MA, March 8, 2006- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that its investigational p38 MAP kinase inhibitor, VX-702, has met its primary objectives in a 12-week Phase II clinical study involving 315 patients. A preliminary analysis indicates that VX-702 was well-tolerated through 12 weeks of dosing, and demonstrated statistically significant clinical effects on signs and symptoms of rheumatoid arthritis (RA), as determined by ACR20 criteria, as well as several other widely used clinical measures. The Company continues to conduct a full analysis of safety, pharmacokinetics and efficacy data from the study. Vertex anticipates that results from the study will be presented at a medical conference later in 2006. The preliminary results from this study support Vertex's plans to advance its clinical program and to initiate by mid-2006 clinical studies of VX-702 in combination with methotrexate, a commonly used therapy for RA. VX-702, dosed as one tablet, once a day, is one of the lead agents in a new class of investigational oral anti-cytokine therapies.

"Demonstration of clear effects on the signs and symptoms of RA, in conjunction with good tolerability with three months of treatment, represents a major achievement for the VX-702 clinical program," commented John Alam, M.D., Executive Vice President, Medicines Development and Chief Medical Officer at Vertex. "The preliminary data announced today provide strong support for our plans to move forward in clinical development and evaluate VX-702 in combination with methotrexate in RA patients."

## **VeRA: Clinical Study Design and Results**

The VeRA study is a randomized, double-blind, 12-week, Phase II clinical study that enrolled 315 patients with moderate to severe RA. A total of 278 patients completed 12 weeks of treatment. The study was conducted at more than 40 centers in Eastern and Central Europe. Patients received either 5 mg or 10 mg VX-702 once daily, or placebo. In addition, patients could receive certain disease-modifying anti-rheumatic drugs (DMARDs), but could not receive methotrexate or anti-TNF therapies. At the end of 12 weeks, patients completed dosing with VX-702 and were evaluated for improvement in clinical signs and symptoms according to American College of Rheumatology (ACR) criteria.

Effects on Signs and Symptoms of Rheumatoid Arthritis: VX-702 treatment led to a dose-dependent, statistically significant increase in week 12 ACR20 response rates, the primary endpoint of the study. Thirty percent of patients receiving placebo, 38% of those receiving 5 mg VX-702 and 40% of those receiving 10 mg VX-702 achieved an ACR20 response at week 12 (p=0.04; Jonckheere-Terpstra test for increasing dose-response). In addition, 32% of placebo patients, 41% of 5 mg VX-702-treated patients and 44% of 10 mg VX-702-treated patients achieved a EULAR (moderate or good) response (p=0.01). Dose-dependent, statistically significant effects were also seen on tender joint counts (p=0.007), swollen joint counts (p=0.003), disease activity score (DAS28; p=0.02) and morning stiffness (p=0.03). Analyses of additional clinical measures and biomarkers are ongoing.

Safety and Tolerability: A preliminary analysis of study data indicates that VX-702 was well-tolerated. Premature discontinuations for adverse events were low across the study arms: placebo (2%), 5 mg (3%) and 10 mg (5%). No clinically significant effects were seen on laboratory parameters, including liver function tests. The most common adverse events that led to treatment discontinuation in patients receiving VX-702 were seen in two patients each and were: gastroenteritis, nausea/vomiting, rash, and renal impairment (increased serum creatinine levels to 1.2 to 1.5 times upper limit of normal). Based on preliminary analysis, the most common adverse events were generally mild or moderate and were: infection (5% of placebo patients and 10% of VX-702 patients), GI disorders (6% placebo and 8% VX-702), and skin disorders (0% placebo and 9% VX-702).

Extensive ambulatory and 12-lead electrocardiographic monitoring was also performed on patients throughout the study. No differences in ventricular ectopic (VE) activity or cardiac arrhythmias were observed between placebo and treated patients. On digital electrocardiograms, from baseline to end of treatment, a minimal (average approximately 1.5% or less for each group) dose-dependent increase in the Fridericia rate-corrected QT interval (QTcF) was seen in the VX-702 treatment groups. No patient experienced a clinically significant (60 msec, or approximately 15%) increase in QTcF at any time in the study.

#### **Clinical Plans**

By mid-2006, Vertex expects to initiate clinical studies of VX-702 in combination with methotrexate, including a three-month, dose-ranging Phase II study in more than 200 patients at centers in Eastern and Central Europe. Doses will be determined based on the final analysis of the VeRA study. Also in 2006, Vertex expects to file an investigational new drug (IND) application to conduct supporting clinical studies of VX-702 in the United States.

# About RA and p38 MAP Kinase

More than 2 million people in the U.S. and 5 million people worldwide suffer from RA, a chronic disease that causes pain, swelling and stiffness in the joints of hands, feet and wrists. In RA, the immune system attacks joint tissue, causing chronic inflammation and irreversible damage to cartilage, tendons and bones. The long-term prognosis for patients with RA is poor, and as a result, many patients face increased disability and premature death.

P38 MAP kinase inhibitors have the potential to be a powerful new class of oral anti-inflammatory medicines that reduce cytokine activity through a novel mechanism of action. P38 MAP kinase regulates the production of the inflammatory cytokines TNF-alpha, interleukin-1 (IL-1) beta, and IL-6, which have been implicated in a range of inflammatory diseases including RA. Vertex holds development and commercial rights in the United States and Europe for its p38 MAP kinase inhibitors. Kissei Pharmaceutical Co., Ltd. holds development and commercial rights in Japan and certain Asian countries for VX-702. In 2005, Kissei initiated clinical development of VX-702 in Japan.

### **About Vertex**

Vertex Pharmaceuticals Incorporated is a global biotechnology company committed to the discovery and development of breakthrough small molecule drugs for serious diseases. The Company's strategy is to commercialize its products both independently and in collaboration with major pharmaceutical companies. Vertex's product pipeline is principally focused on viral diseases, inflammation, autoimmune diseases and cancer. Vertex co-promotes the HIV protease inhibitor, Lexiva, with GlaxoSmithKline.

#### **Safe Harbor Statement**

This press release may contain forward-looking statements, including statements that (i) VX-702 is one of the lead agents in a new class of investigational oral anti-cytokine therapies; (ii) Vertex expects to advance its VX-702 clinical program and to initiate clinical studies of VX-702 in combination with methotrexate by mid-2006; (iii) in mid-2006, Vertex expects to initiate a three-month, dose-ranging study in more than 200 patients in Eastern and Central Europe; and (iv) in 2006, Vertex expects to file an investigational new drug (IND) application to conduct supporting clinical studies of VX-702 in the United States. While management makes its best efforts to be accurate in making forward-looking statements, such statements are subject to risks and uncertainties that could cause Vertex's actual results to vary materially. These risks and uncertainties include, among other things, the risks that full analysis of the data, including an ongoing detailed safety analysis, or further testing, will not reflect the interim results reported in this press release, or support any or all of the conclusions provided in this press release; clinical trials for VX-702 may not proceed as planned due to technical, scientific, or patient enrollment issues; expected regulatory filings or clinical trial starts may not occur or may be delayed due to adverse clinical or non-clinical trial developments or FDA action; and other risks listed under Risk Factors in Vertex's Form 10-K filed with the Securities and Exchange Commission on March 16, 2005.

Lexiva is a registered trademark of the GlaxoSmithKline group of companies.

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