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Preliminary Phase IIa Data for VX-702 Demonstrate Tolerability and Reduction in C-Reactive Protein in Cardiovascular Patients

-First demonstration of CRP reduction in cardiovascular patients using an oral cytokine inhibitor-

Rome, Italy October 18, 2004 -- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) announced today the presentation at a medical conference of preliminary results from a Phase IIa clinical trial of VX-702, an investigational oral p38 MAP kinase inhibitor, in the treatment of patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI) such as stent placement. The results, presented at the European Society of Cardiology's Acute Cardiac Care Symposium in Rome, indicate that VX-702 met pre-established safety and pharmacokinetic objectives. In addition, VX-702 significantly reduced serum levels of the inflammatory biomarker C-reactive protein (CRP) in patients undergoing PCI, and CRP remained significantly lowered out to four weeks beyond the five-day dosing period. This is the first demonstration of CRP reduction in cardiovascular patients using an oral cytokine inhibitor, and the results suggest that VX-702 may suppress inflammatory processes that play a role in the onset and progression of cardiovascular events.

Inflammation is increasingly recognized as an important contributing factor in the development of coronary artery disease. CRP is a marker of inflammation measured in the blood. Patients with established cardiovascular disease who have elevated CRP have significantly higher rates of cardiovascular events, such as acute myocardial infarction (heart attack), unstable angina (chest pain) and stroke, as well as hospitalization and death, compared to patients with normal CRP levels. The VX-702 clinical results suggest that the inflammation associated with ACS may be mediated by the p38 MAP kinase pathway.

"Vascular inflammation is thought to play an essential role in the pathophysiology of a variety of cardiovascular events. A sudden activation of inflammatory processes may cause plaque instability and rupture, leading to unstable angina, myocardial infarction and stroke," said Robbert De Winter, M.D., Director, Catheterization Laboratory, Academic Medical Center, Amsterdam and Principal Investigator for the Study. Based on the results presented today, VX-702 has the potential to inhibit these processes and may represent a novel approach to the treatment of patients with coronary artery disease."

Study Results: Safety and Clinical Activity

The Phase IIa, double-blind, randomized, placebo-controlled dose-escalation study was designed to evaluate the safety, tolerability and pharmacokinetics of VX-702 in 45 unstable angina patients with elevated CRP levels undergoing PCI. The study also included an evaluation of the drug's anti-inflammatory activity, as assessed by measurement of CRP levels. In the study, patients were treated with VX-702 once daily for a five-day period just prior to and following the PCI (two doses before and three doses after PCI). Study evaluation included post-treatment follow-up at four weeks post-PCI.

Preliminary safety results indicated that there were no clinically significant differences between treatment and placebo groups with respect to adverse events, including bleeding and arrhythmias as well as overall clinical event rates. In addition, the incidence of liver enzyme abnormalities was similar in patients receiving VX-702 or placebo.

Assessment of the laboratory data demonstrated a potent and sustained anti-inflammatory effect as measured by CRP levels at multiple timepoints during the study. Relative to placebo treatment, statistically significant dose-dependent inhibition of CRP following treatment with VX-702 was observed within 24 hours of the first dose ($p<0.05$; Jonckheere-Terpstra test across all of the treatment groups of the change from baseline in CRP levels), and 24 hours ($p<0.005$), 48 hours ($p<0.001$) and four weeks post-PCI ($p<0.05$). Moreover, at 48 hours post-procedure, median CRP levels had decreased from baseline in a highly statistically significant, dose-dependent manner in all VX-702 treatment groups: 5 mg (-37%); 10 mg (-67%); 20 mg (-71%) and 40 mg (-63%) ($p<0.001$). By contrast, in patients in the placebo group, CRP increased (+98%) from baseline at 48 hours post-procedure.

"The results reported today strongly support further development of VX-702 in acute coronary syndromes," said John Alam, M.D., Senior Vice President of Drug Evaluation and Approval at Vertex. Beyond ACS, Vertex continues to evaluate the clinical and commercial potential of VX-702 in additional indications. The results from the current study indicate that the doses we are considering for these other indications are associated with potent anti-inflammatory activity."

About ACS

Patients diagnosed with acute coronary syndrome are defined as having one or more of the following conditions: unstable angina, non ST-elevated myocardial infarction (NSTEMI) or acute myocardial infarction (AMI). According to the American Heart Association, in the U.S alone there are nearly 1.9 million cases of ACS each year, resulting in 500,000 deaths. The current standard of care for ACS includes treatment with antiplatelet agents, anticoagulants, nitroglycerin, beta-blockers and gpIIb/IIIa antagonists. Patients may also undergo an interventional procedure to relieve artery blockage. Despite the available treatments and procedures, ACS patients remain at risk for heart attack, stroke and death. Therapeutic interventions that block the inflammatory process have the potential to provide an important clinical benefit to patients with ACS.

About VX-702 and p38 MAP kinase

VX-702 is an orally administered small molecule inhibitor of p38 MAP kinase discovered by scientists at Vertex Pharmaceuticals. p38 MAP kinase regulates the production of proinflammatory cytokines such as tumor necrosis factor alpha (TNF-alpha), interleukin-1 beta (IL-1 beta) and interleukin-6 (IL-6), which are known to play roles in acute inflammation characteristic of ACS as well as in chronic inflammatory diseases such as rheumatoid arthritis. Vertex is targeting the p38 MAP kinase molecular mechanism to develop breakthrough treatments for a variety of inflammatory diseases representing significant unmet medical need.

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 partners. Vertex's product pipeline is principally focused on viral diseases, inflammation, autoimmune diseases and cancer. Vertex co-promotes the new HIV protease inhibitor, Lexiva(R), with GlaxoSmithKline.

This press release may contain forward-looking statements, including statements that (i) VX-702 may suppress inflammatory processes that play a role in the onset and progression of cardiovascular events; (ii) VX-702 represents a novel approach to inhibit inflammatory processes in patients with heart disease; (iii) inflammation associated with ACS may be mediated by the p38 pathway; (iv) the results of the Phase IIa study support further development of VX-702 in ACS and other indications; and (v) the p38 MAP kinase molecular mechanism may be a promising target for the development of breakthrough treatments for a variety of diseases. 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 preliminary clinical results from the Phase IIa clinical study may not reflect final results, that additional analyses being conducted or planned may not support the Phase IIa positive results, that clinical trials for VX-702 may not proceed as planned due to technical, scientific, supply or patient enrollment issues, that future nonclinical and clinical studies may not yield results confirming the value of VX-702, and other risks listed under Risk Factors in Vertex's form 10-K filed with the Securities and Exchange Commission on March 15, 2004.

Lexiva(R) is a registered trademark of the GlaxoSmithKline group of companies.

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