January 29, 2004

Vertex Researchers Publish Structure of FLT-3 Kinase in Molecular Cell

-Potential Mechanism Underlying Various Types of Leukemia Described-

Cambridge, MA, January 29, 2004 -- Researchers from Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) have published the first crystal structure of Flt-3, a member of the receptor tyrosine kinase family that is implicated in the development and progression of leukemia. This research was published in the January 30th issue of the scientific journal Molecular Cell. The study provides direct insight into the mechanism by which mutated forms of the Flt-3 receptor can activate themselves and trigger uncontrolled proliferation of immature blood cells, a common feature of several types of leukemia. Based on an analysis of the crystal structure, Vertex scientists hypothesize that specific mutations cause Flt-3's juxtamembrane domain to adopt a conformation that enables the receptor to phosphorylate itself, resulting in uncontrolled cellular proliferation.

"Several research groups have already demonstrated that a mutated form of Flt-3 can activate itself, and our analysis of the crystal structure suggests how this can occur," commented James Griffith, Staff Investigator at Vertex and lead author of the study. "Given the genetic and structural homology among the receptor tyrosine kinase family, and the overactivation of these receptor kinases in many tumor types, we may speculate that the mechanism we have identified may have broad implications for the development of small molecule cancer therapies."

Flt-3 is primarily expressed in immature hematopoietic cells, which are responsible for generating blood cells, and is essential for the normal function of stem cells and the immune system. Growth and proliferation of blood cells is, in part, accomplished through the controlled stimulation of receptor tyrosine kinases, such as Flt-3, which propagate a growth signal to other proteins in a biological pathway. Mutations in Flt-3 are most common in acute myeloid leukemia (AML), and they are associated with a poor prognosis of disease. Exploring the mechanism by which these Flt-3 mutations cause uncontrolled proliferation through their overactive state may provide insights for the design and development of new small molecule drugs.

"The findings of this study are very intriguing, and we believe they may open a window of opportunity for the design of new drugs that address the mechanism of mutated FLT-3, in leukemia patients, as well other cancer types where tyrosine kinases use the same mechanism," said Peter Mueller, Ph.D., Chief Scientific Officer of Vertex.

About Leukemia and FLT-3
Flt-3 is expressed in high levels in a wide range of leukemias, including 70-100% of acute myelogenous leukemia (AML), lymphoblastic leukemia (ALL), and myelogenous leukemia (CML). Furthermore, activating Flt-3 mutations are present in up to 40% of AML patients. The mutated form of this tyrosine kinase is believed to promote uncontrolled growth of abnormal immature blood cells that crowd out the normal cells, leading to deadly forms of leukemia. According to the American Cancer Society, in 2003, 30,600 patients were diagnosed in the United States with leukemia, more than a third of whom have AML. The American Cancer Society estimates that AML resulted in 7800 deaths in the United States in 2003.

The authors of the Molecular Cell paper, titled "The Structural Basis for Autoinhibition of FLT-3 by the Juxtamembrane Domain," are James Griffith, James Black, Carlos Faerman, Lora Swenson, Michael Wynn, Fan Lu, Judith Lippke, and Kumkum Saxena, all of Vertex.

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(TM), with GlaxoSmithKline.

Vertex Safe Harbor Statement
This press release may contain forward-looking statements, including statements that the research findings for Flt-3 may have broad implications for the development of small molecule cancer therapies, and that insights into the Flt-3 mechanism may provide an opportunity to design novel anti-cancer therapies. 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 those risks listed under Risk Factors in Vertex's form 10-K filed with the Securities and Exchange Commission on March 31, 2003.

Vertex Contacts:
Lynne Brum, VP, Corporate Communications and Financial Planning, (617) 444-6614
Michael Partridge, Director, Corporate Communications, (617) 444-6108