Gilead Sciences Announces Discovery of Orally Active Influenza Inhibitors

September 17, 1996 4:22 PM ET

Preclinical Data Presented at 36th ICAAC Demonstrate Potent Activity Against Multiple Strains of Flu Virus

Foster City, CA -- September 17, 1996

Gilead Sciences, Inc. (NASDAQ:GILD) announced today the discovery of an orally active, highly potent compound that inhibits the replication of influenza virus. In a preclinical model, GS 4104 was given orally to mice and demonstrated antiviral activity against multiple strains of influenza, increased survival and decreased levels of the virus in lung tissue, without any reported toxicities. Based upon these data, Gilead is completing additional preclinical studies required to commence human clinical testing of GS 4104.

These data will be presented today at the 36th Interscience Conference on Chemotherapy and Antimicrobial Agents (ICAAC) in New Orleans by Choung U. Kim, Ph.D., Director of Medicinal Chemistry at Gilead Sciences.

"Treatment of influenza is an unmet medical need, and an orally administered agent that is active against different strains of influenza would represent an important option for both treatment and prophylaxis of influenza infections," said Norbert W. Bischofberger, Ph.D., Vice President of Research at Gilead Sciences.

GS 4104 - Data Summary and Discovery

In preclinical studies, GS 4104 demonstrated 100% survival in mice when given as prophylaxis before exposure or when given as treatment after exposure to influenza virus. In contrast, survival rates in the control groups were 13% and 15%, respectively. GS 4104 was administered as an oral formulation twice per day for five days at a daily dose of 10 mg/kg. In additional studies, no toxicities were observed in rats after 14 days of GS 4104 dosing at levels more than 100 times the anticipated human dose. The oral bioavailability, or amount of GS 4104 delivered systemically after oral dosing, ranged from 30% to 100% in three different preclinical models.

Gilead's GS 4104 emerged as the lead compound from a class of new chemical entities known as carbocyclic compounds, which work by inhibiting the influenza neuraminidase enzyme in a highly selective manner. These unique compounds have lipophilic properties that allow for potentially high oral bioavailability. In addition, these compounds interact with the neuraminidase enzyme at previously unexploited regions of the active site.

Neuraminidase is essential to the replication cycle of influenza. This enzyme promotes the release of new viral particles produced by infected cells. Inhibition of neuraminidase therefore blocks the ability of influenza to spread from cell to cell. The neuraminidase enzyme is consistently required in the replication of a variety of different influenza types and strains. GS 4104 provides broad-spectrum activity against multiple strains of the virus, including influenza A and B.

Gilead believes that an orally active, highly potent, systemic influenza treatment may have advantages over other neuraminidase inhibitors in development, which must be administered intranasally or inhaled. Administration of one such neuraminidase inhibitor being developed by another company has reduced clinical symptoms associated with influenza infection in early human studies, thus validating the importance of this target.

Gilead researchers discovered GS 4104 and related inhibitors of neuraminidase using a combination of structure-based drug design, computer modeling and the company's expertise in antiviral chemistry. GS 4104 is the result of more than five years of influenza research at Gilead and is the lead candidate selected from hundreds of potential compounds.

Influenza Background

An estimated 70 million to 120 million people in North America, Western Europe and Japan are infected with influenza each year. People over 65 can be especially susceptible to influenza infections, and between 80 and 90 percent of all flu-related deaths occur in elderly patients. In periods of flu epidemics, which occur approximately every 10 years, highly virulent strains of the virus are responsible for significant morbidity and mortality. The worst known influenza pandemic occurred in 1918 and was estimated to

have caused 700 million cases of flu and 20 million deaths worldwide.

The development of effective therapeutics has been challenging for medical researchers due to the seasonal variance and infectious nature of influenza. Historically, treatment options have had limited efficacy, low oral bioavailability, adverse side effects and rapid development of resistance.

Gilead Sciences is a leader in the discovery and development of a new class of human therapeutics based on nucleotides, the building blocks of DNA and RNA. The Company's research and development efforts encompass three interrelated programs: small molecule antivirals, cardiovascular therapeutics and genetic code blockers for cancer and other diseases. Gilead's expertise in each of these areas has also resulted in the discovery of non-nucleotide product candidates that expand the Company's technology platforms, including the discovery of novel inhibitors of HIV protease for the treatment of HIV and the neuraminidase inhibitor for viral influenza. Gilead common stock is traded on The Nasdaq Stock Market under the symbol GILD.

A fact sheet and background information regarding influenza are available from Gilead Corporate Communications at 415-573-4858.