**Gilead Sciences Announces Statistically Significant Antiviral Activity Against Hepatitis B Virus**

September 16, 1996 4:19 PM ET

*GS 840 data from Phase I/II human clinical study to be presented today at 36th ICAAC conference*

**Foster City, CA -- September 16, 1996**

Gilead Sciences, Inc. (NASDAQ:GILD) announced today Phase I/II data demonstrating that during treatment, GS 840 (adefovir dipivoxil) was well tolerated and resulted in significant and sustained antiviral activity against hepatitis B virus (HBV). After four weeks of once daily dosing in patients with chronic HBV infection, viral load decreased 97 percent from baseline in treated patients compared with a seven percent increase in patients who received inactive placebo.

These data will be presented today at the 36th Interscience Conference on Antimicrobial Agents and Chemotherapy in New Orleans by clinical investigator Dr. Richard Gilson of the University College London Medical School in the United Kingdom.

Phase I/II Data Summary - A total of 20 patients with chronic hepatitis B virus infection were enrolled in this double-blind, placebo-controlled, Phase I/II study at three clinical centers in the United Kingdom. Neither the treating physicians nor the patients knew if a patient was receiving active drug or inactive placebo. A total of 15 patients received treatment with GS 840 (one 125 mg tablet) and 5 received placebo once per day for 28 days. Antiviral activity was determined by monitoring the viral load levels of hepatitis B virus using the Digene Hybrid Capture System assay to quantify HBV DNA before, during and after the treatment period.

The mean time since HBV diagnosis was four years and 25% of patients had previously failed HBV treatment with interferon-alpha. The majority of patients enrolled in the study (65%) also tested positive for human immunodeficiency virus (HIV), the causative agent of AIDS.

During four weeks of treatment, GS 840 resulted in a statistically significant ($p=0.001$) mean decline in HBV DNA levels of 97 percent (1.8 log) from baseline, compared with an increase of 7 percent (0.02 log) from baseline, in the placebo group. All treated patients experienced a >90 percent decrease in HBV DNA versus none of patients on placebo. Levels of HBV DNA returned to baseline between one and six weeks after the 28 days of GS 840 dosing, underscoring the antiviral effect of drug treatment. In addition, during the first eight weeks, one marker of hepatitis infection (HBe antigen) became transiently undetectable in one patient.

GS 840 treatment was well tolerated with only mild to moderate clinical events, which included moderate nausea in two patients. The principal drug-related serum chemistry changes were transient hepatic transaminase elevations (AST or ALT >300 U/L). These elevations in liver enzymes were observed in three patients while receiving treatment and in four patients after dosing. Similar transaminase elevations have been observed during or after treatment with other anti-HBV therapies in association with a response to HBV and eradication of chronic infection or seroconversion.

Several features support that the elevations observed in the GS 840 study were related to an immunological response. Specifically, patients with transaminase elevations during dosing also had more sustained reductions in HBV DNA. Additionally, the elevations during dosing were observed only in HIV negative patients and not in HIV positive patients. HIV positive patients may have been less able to generate an immunologic response to the viral infection.

To date, more than 180 patients have received GS 840 at 120 mg per day or higher doses in clinical studies. These patients have received GS 840 as once daily dosing for up to 14 months without any signs of cumulative toxicities.

GS 840 is an oral prodrug from a new class of antiviral compounds known as nucleotides, potent inhibitors of viral replication. GS 840 inhibits HBV DNA polymerase, an essential enzyme used by the hepatitis B virus in its replication cycle. GS 840 has also demonstrated activity against other viral polymerases, giving it broad-spectrum antiviral activity against HIV and herpesviruses as well. Clinical studies have previously demonstrated that GS 840 has an approximate oral bioavailability of 40%.

GS 840 Ongoing Studies - Based upon these data, Gilead plans studies to evaluate the longer-term effects of GS 840 treatment, monitoring for safety and efficacy in patients with chronic HBV infection. Patients enrolled in the Phase I/II study reported on

today will be eligible to receive up to six months of maintenance treatment with GS 840. In addition, Gilead plans to commence longer-term dosing in a multinational, Phase II program of GS 840 for the treatment of chronic HBV infection.

GS 840 is also under investigation in an ongoing Phase II/III study in the United States for the potential treatment of HIV in combination with other approved antiretroviral therapies, including protease inhibitors. This study began in June 1996 and is designed to enroll 400 patients at multiple clinical centers.

Nucleotide analogues such as GS 840 are characterized by their ability to inhibit viral replication for long periods of time in a variety of cells and potentially to form protective reservoirs of active drug in cells. These characteristics allow for infrequent dosing, potential prophylactic use and may confer advantages over earlier generations of antiviral drugs, known as nucleosides.

HBV Infection Background - It is estimated that 5% of the world's population is infected with hepatitis B. Many of these people die from liver disease associated with the virus, although most individuals recover quickly from an acute illness. Those who do not may develop chronic hepatitis, which can lead to cirrhosis or cancer of the liver. Hepatitis B virus is contagious and can be spread through direct contact with infected blood, blood products or other bodily fluids.

In addition to GS 840 for the potential treatment of HBV infection, Gilead is developing a portfolio of nucleotide analogues for viral disease. These include Gilead's first product, VISTIDE® (cidofovir injection), which was granted marketing clearance by the U.S. Food and Drug Administration in June 1996 for the treatment of cytomegalovirus (CMV) retinitis in patients with AIDS. The Company also has product candidates in human testing for the potential treatment of diseases caused by CMV, HIV, herpes simplex virus and human papillomavirus.

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. Gilead common stock is traded on The Nasdaq Stock Market under the symbol GILD.