Gilead Presents Preliminary Clinical Data Demonstrating Activity of Adefovir Dipivoxil Against Lamivudine-Resistant Hepatitis B Virus

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Data Presented at 34th Annual Meeting of the European Association for the Study of the Liver

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Gilead Sciences, Inc. (Nasdaq: GILD) announced today the presentation of the first clinical data demonstrating that its investigational compound adefovir dipivoxil has potent antiviral activity in patients with chronic hepatitis B (HBV) infection who have failed antiviral therapy with lamivudine due to the development of resistance mutations. These in vivo data support earlier laboratory results indicating that adefovir remains active against lamivudine-resistant HBV.

"HBV resistance to lamivudine occurs in 14 to 30 percent of patients with chronic HBV who have been treated for one year and becomes even more common after 24 months of therapy," said clinical investigator Robert P. Perrillo, MD, Head, Section of Gastroenterology and Hepatology, Ochsner Clinic, New Orleans, LA, who conducted the adefovir dipivoxil study. "Lamivudine resistance can be potentially serious, especially for immunocompromised patients who have undergone liver transplantation, or for patients with advanced liver disease. In these preliminary observations, it is particularly encouraging that treatment with adefovir dipivoxil resulted in a rapid virologic response that has been sustainable for more than six months."

Dr. Perrillo will present these results during the 34th Annual Meeting of the European Association for the Study of the Liver (EASL) on April 9 in Naples, Italy.

Summary of Patient Cases
Three patients with progressive liver disease associated with lamivudine-resistant HBV had increasing levels of HBV DNA in their bloodstream despite therapy with lamivudine, and, in some cases, famciclovir, interferon-alpha or Hepatitis B immunoglobulin. As a result of chronic HBV infection, two of the patients had previously received liver transplants.

Treatment with adefovir dipivoxil at oral doses ranging from 10 mg to 30 mg once-daily resulted in rapid reductions in levels of HBV DNA from baseline by greater than 2.0 $\log_{10}$ (99 percent) in each patient. HBV DNA levels continue to decline during ongoing treatment with adefovir dipivoxil. Improvements in laboratory markers of liver disease including hepatic transaminase reductions also were associated with adefovir dipivoxil treatment. Adefovir dipivoxil therapy has been well tolerated for greater than six months without evidence of significant drug-related toxicity.

Based on these encouraging results, Gilead has initiated protocols to study the long-term safety and efficacy of treatment with adefovir dipivoxil in patients with chronic HBV who have failed prior lamivudine treatment due to the emergence of viral resistance.

Additional Presentations
Also on Friday, April 9, Gilead scientist Craig Gibbs, Ph.D. will present data that further define the potential role of adefovir dipivoxil in the treatment of chronic HBV. In one presentation, Dr. Gibbs will highlight the favorable *in vitro* activity of adefovir dipivoxil against all known clinically relevant lamivudine- and famciclovir-resistant HBV strains, including the common double mutant L528M+M552V. In another, he will present a mathematical model applied to evaluate the mechanism of rapid viral clearance observed during adefovir dipivoxil treatment in Phase II clinical trials.

Formulated as a pill taken once daily, adefovir dipivoxil is a nucleotide analogue from a class of antivirals shown to be long acting, potent inhibitors of viral replication with unique resistance profiles. A randomized, placebo-controlled Phase III study to enroll approximately 500 patients is ongoing to evaluate the long-term safety and efficacy of two dose levels of adefovir dipivoxil (10 mg and 30 mg) for the treatment of chronic HBV infection. The study is expected to involve more than 10 countries worldwide.

Antiviral Activity in HIV
Adefovir dipivoxil is the active ingredient in PREVEON®, which is being studied in multiple, late-stage clinical trials (60 mg once per day) for the potential treatment of HIV infection. The doses that have been studied for HIV are higher than those being evaluated for the treatment of chronic hepatitis B. During HIV clinical testing, the most common side effects reported with PREVEON (60 mg and 120 mg) have been dose-related gastrointestinal effects, including nausea and loss of appetite. Nephrotoxicity, including changes in serum creatinine and phosphate, is the most important drug-related toxicity. These changes generally occur after six months of treatment, are gradual in onset, asymptomatic, detectable by routine monitoring and resolvable upon dose reduction or withdrawal. Elevations in liver transaminases have been observed in some patients.

Gilead Sciences
Gilead Sciences is an independent biopharmaceutical company that seeks to provide accelerated treatment solutions for patients and the people who care for them. The company discovers, develops and commercializes proprietary therapeutics for important viral diseases, including a currently marketed product, VISTIDE® (cidofovir injection), for the treatment of CMV retinitis, a sight-threatening viral infection in patients with AIDS. In addition, the company is developing products to treat diseases caused by HIV, hepatitis B virus and influenza virus.

Editor's note: Patients seeking information about how to participate in the Phase III worldwide hepatitis B study may call 1-800-GILEAD-5 or refer to the Clinical Trial Locator on the Gilead Sciences Web site at www.gilead.com.