Gilead Sciences Announces Results From Phase III Study of Adefovir Dipivoxil In Precore Mutant Chronic Hepatitis B Virus Infection

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Primary Efficacy Endpoint Achieved in Second Pivotal Study

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Gilead Sciences, Inc. (Nasdaq: GILD) today announced preliminary data from a Phase III clinical trial (Study 438) evaluating the safety and efficacy of adefovir dipivoxil 10 mg once daily as monotherapy compared to placebo in patients infected with precore mutant chronic hepatitis B virus (HBV). Precore mutant HBV is a strain of the HBV virus with a mutation in the viral genome that destroys the ability of the virus to produce the hallmark "e" antigen. Results from this intent-to-treat analysis demonstrate that treatment with adefovir dipivoxil 10 mg once daily for 48 weeks is associated with improvements in liver histology in 64 percent of patients who received the drug compared to 33 percent of patients who received placebo (p=0.0002). Change in liver histology is an important marker of disease progression in patients with chronic HBV infection, and the primary endpoint in this study. Gilead expects to present these data in detail at scientific conferences in 2002.

"These are the most encouraging results reported to date on the safety and efficacy of antiviral therapy in patients infected with precore mutant HBV in controlled studies," said Professor Stephanos Hadziyannis, MD, Department of Internal Medicine, Ipprokration General Hospital, Athens, Greece. "Together with results of previous clinical studies, these data demonstrate that adefovir dipivoxil 10 mg once daily may provide a promising treatment option for patients with either "e" antigen-negative or "e" antigen-positive chronic HBV infection, as well as those who may be resistant to other antiviral treatments."

Study 438 Design
Study 438 is an ongoing international, multicenter, double-blind, placebo-controlled Phase III clinical trial that enrolled 185 patients with precore mutant HBV, or hepatitis B "e" (HBe) antigen-negative virus (HBe antibody-positive, HBV DNA-positive), and compensated liver function. This study is being conducted in Australia, Canada, France, Greece, Israel, Italy and Southeast Asia. Patients were randomized (2:1) to receive adefovir dipivoxil 10 mg once daily (n=123) or placebo (n=62) for 48 weeks. To further evaluate the long-term safety and resistance profiles of adefovir dipivoxil in this patient population, patients are continuing on Study 438 for an additional 48 weeks of treatment. Following the first 48 weeks of treatment, patients who had received adefovir dipivoxil have been re-randomized (2:1) to receive either adefovir dipivoxil 10 mg or placebo for a second year. Patients who initially received placebo are receiving adefovir dipivoxil 10 mg for the second 48 weeks of the study.

Liver biopsies were obtained for 91 percent of patients prior to study initiation and at 48 weeks. At baseline, patients had a median serum HBV DNA level of 7.08 log10 copies/mL and a median ALT level of 98 IU/L.

Efficacy of Adefovir Dipivoxil 10 mg
After 48 weeks, 64 percent of patients treated with adefovir dipivoxil 10 mg exhibited significant improvements in liver histology, compared with 33 percent of patients receiving placebo (p=0.0002). Improvement in liver histology is defined as a reduction from baseline of two points or more in the Knodell necro-inflammatory score and no concurrent worsening in the fibrosis score.

In addition to meeting the primary endpoint, the study's secondary efficacy endpoints were achieved as well, including change in HBV viral load, as measured by the Roche Amplicor® Monitor™ Test (PCR). Treatment with adefovir dipivoxil 10 mg resulted in a median reduction in HBV DNA from baseline of 3.91 log10 copies/mL, compared with a median reduction in the placebo group of 1.35 log10 copies/mL (p<0.0001). This equates to a 99.99 percent reduction in circulating virus in patients on treatment. In addition, results at 48 weeks demonstrated that patients treated with adefovir dipivoxil 10 mg achieved a median ALT reduction of 55 IU/L, compared to a median ALT level reduction in the placebo group of 38 IU/L (p=0.01). Seventy-two percent of patients treated with adefovir dipivoxil 10 mg achieved normalization of ALT levels, compared to 29 percent of patients receiving placebo (p<0.0001). Patients with precore mutant HBV infection (HBe antigen-negative virus) are unable to achieve HBe antigen seroconversion because their hepatitis B virus has mutated and does not express the hepatitis B "e" antigen.

"Patients infected with the precore mutant HBV strain often experience poor clinical outcomes and may exhibit more advanced liver disease," said Professor Hadziyannis. "The worldwide prevalence of precore mutant HBV is a significant public health concern, calling for new treatments with improved safety and efficacy to help maintain the health of these chronically ill patients."

Safety Profile
Through the first 48 weeks of Study 438, the discontinuation rate was the same between the treatment and placebo arms, with two percent of patients from the adefovir dipivoxil 10 mg and placebo groups discontinuing from study. No patients in the adefovir dipivoxil 10 mg and placebo groups had increases in serum creatinine of greater than or equal to 0.5 mg/dL from baseline or a serum phosphorus level less than 1.5 mg/dL, laboratory markers of renal function, as confirmed by two consecutive laboratory assessments. Additionally, the incidence of grade 3 and 4 laboratory abnormalities and clinical adverse events was similar between the treatment and placebo arms of this study.

Resistance Profile
Preliminary genotypic analyses from Study 438 show that after 48 weeks of treatment, no adefovir resistance mutations were observed. These data confirm Gilead's earlier clinical and in vitro studies, which demonstrated that treatment with adefovir dipivoxil does not lead to the development of resistance.

"These data confirm results observed in previous clinical trials of adefovir dipivoxil 10 mg and support the role we believe this antiviral drug will have in the treatment of chronic HBV infection," said John C. Martin, Ph.D., President and CEO of Gilead Sciences. "With the extensive safety and efficacy data for adefovir dipivoxil that we have accumulated, we are confident in our ability to complete regulatory filings in the United States and Europe during the first half of next year. More important, it is clear that this compound may offer a significant new treatment option for patients with chronic HBV for whom few effective options are currently available."

Adefovir Dipivoxil Phase III Program
These data along with results from Gilead's first pivotal Phase III trial, Study 437, will comprise the core of the regulatory filing packages in both the United States and Europe. Study 437 was a 48-week Phase III clinical trial evaluating the safety and efficacy of adefovir dipivoxil once daily as monotherapy compared to placebo in patients with chronic HBV infection who were HBe antigen-positive. Results from this study, which were released on June 22, 2001, met the study's primary and secondary endpoints.

Adefovir dipivoxil is an investigational compound and has not yet been determined safe or efficacious in humans for its ultimate intended use. Patients and physicians who would like more information about adefovir dipivoxil may contact Gilead Sciences Medical Information at 1-800-GILEAD-5 (1-800-445-3235) or 1-650-574-3000 from outside the United States.

Chronic Hepatitis B Infection
Worldwide, there are approximately 400 million chronic carriers of HBV, of which approximately one million die each year from complications of the disease, making chronic HBV one of the 10 most common causes of death. Complications of chronic HBV include cirrhosis, liver failure and primary liver cancer (hepatocellular carcinoma). Patients infected with the precore mutant strain of HBV may be predisposed to more severe and progressive liver injury. Precore mutant HBV infects up to approximately 50 percent of the 400 million chronic HBV carriers worldwide and is most prevalent in countries of the Mediterranean and Southeast Asia, where between 30-80 percent of chronic HBV patients are estimated to be infected with this strain.

Gilead Sciences
Gilead Sciences, Inc., headquartered in Foster City, CA, USA, is an independent biopharmaceutical company that seeks to provide accelerated solutions for patients and the people who care for them. Gilead discovers, develops, manufactures and commercializes proprietary therapeutics for challenging infectious diseases (viral, fungal, and bacterial infections) and cancer. Gilead maintains research facilities in Foster City, CA; Boulder, CO; San Dimas, CA; Cambridge, UK; and Dublin, Ireland; and sales and marketing organizations in the United States, Europe, and Australia.

This press release includes forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995, that are subject to risks, uncertainties, and other factors that could cause actual results to differ materially from those referred to in the forward-looking statements. Such risks and uncertainties include the risk that the resistance, safety and efficacy profile of adefovir dipivoxil 10 mg observed in this 48 week data may not be observed following longer periods of treatment, risks related to Gilead's ability to complete regulatory filings as anticipated, the risk that the FDA and other regulatory agencies could require longer-term safety and efficacy data prior to approval, and other risks related to regulatory approval of adefovir dipivoxil 10 mg. The reader is cautioned not to rely on these forward-looking statements. These and other risks are described in detail in the Gilead Annual Report on Form 10-K for the year ended December 31, 2000 and in Gilead's Quarterly Reports on Form 10-Q, all of which are on file with the U.S. Securities and Exchange Commission. All forward-looking statements are based on

information currently available to Gilead and Gilead assumes no obligation to update any such forward-looking statements.

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For more information on Gilead Sciences, please visit the company's Web site at www.gilead.com or call the Gilead Corporate Communications Department at 1-800-GILEAD-5 (1-800-445-3235).