Results of Two Pivotal Studies of Gilead's Hepsera Published in the New England Journal of Medicine

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FOSTER CITY, Calif., Feb 27, 2003 (BUSINESS WIRE) --

Treatment Reduces Signs of Disease Progression in Patients with Chronic Hepatitis B

Gilead Sciences (Nasdaq:GILD) today announced the publication of results from two studies evaluating the safety and efficacy of Hepsera(TM) (adefovir dipivoxil 10 mg), Gilead's once-daily oral antiviral for the treatment of chronic hepatitis B, in the February 27 edition of the New England Journal of Medicine (NEJM). In both studies (437 and 438), Hepsera significantly reduced liver damage and improved liver function compared to placebo. Results from these studies show that Hepsera provides effective and well-tolerated long-term therapy for patients with chronic hepatitis B.

Chronic hepatitis B is a serious disease caused by the hepatitis B virus (HBV), which attacks the liver. Chronic hepatitis B infection can lead to potentially fatal complications such as cirrhosis and liver cancer, and is one of the leading causes of death worldwide. Over 400 million people are chronically infected with HBV worldwide. Approximately 1.25 million people are chronically infected with HBV in the United States alone.

"Hepatitis B infection is a challenging disease to manage," said Patrick Marcellin, MD, head of the Claude Bernard Research Center on Viral Hepatitis, Service d'Hepatologie and INSERM Unit 481, Hopital Beaujon, Assistance Publique Hopitaux de Paris, Clichy and Professor, Universite Paris VII, France, an investigator in both studies and lead author on one of the papers. "Until recently, available drugs were limited either by tolerability issues or by loss of effectiveness due to viral resistance, as early as six months on therapy. In these studies, Hepsera slowed or even reversed signs of disease progression after a year in most patients, with good tolerability and no incidence of viral resistance."

In September 2002, the U.S. Food and Drug Administration approved Hepsera for the treatment of chronic hepatitis B in adults with evidence of active viral replication and either evidence of persistent elevations in serum aminotransferases (ALT or AST) or histologically active disease. In March 2002, Gilead submitted a Marketing Authorisation Application for Hepsera for the treatment of chronic hepatitis B to the European Medicines Evaluation Agency (EMEA). In November 2002, the European Union's Committee for Proprietary Medicinal Products (CPMP), the scientific committee of the EMEA, recommended granting Marketing Authorisation for Hepsera for the treatment of chronic hepatitis B in all 15 member states of the European Union. On the basis of the CPMP's recommendation, the European Commission will consider granting final Marketing Authorisation, which is anticipated to occur by mid-2003.

Results in Hepatitis B "e" Antigen-positive (HBeAg-positive) Patients

The first Hepsera study (Study 437) published in this edition of NEJM was a randomized, double-blind, placebo-controlled trial involving 515 patients with "e" antigen-positive chronic hepatitis B. The "e" antigen (HBeAg) is a viral protein found in the blood of many HBV-infected persons. At 48 weeks, twice as many patients who received Hepsera had decreased liver inflammation and damage -- the primary endpoint of the study -- compared with patients taking placebo, according to liver biopsy results (53 percent vs. 25 percent, respectively, p less than 0.001). Three times as many Hepsera patients showed improvements in liver function, as measured by a reduction to normal levels of the liver enzyme alanine aminotransferase (ALT), as compared to placebo (48 percent vs. 16 percent, respectively, p less than 0.001). In addition, as reported in the NEJM, patients in the Hepsera arm had a median reduction in HBV DNA from baseline of 3.52 log10 copies/mL, compared to a reduction of 0.55 log10 copies/mL in patients receiving placebo (p less than 0.001). Twenty-one percent of Hepsera patients had undetectable levels of HBV DNA in their blood (less than 400 copies/mL) compared with none of the placebo patients (p less than 0.001). Additionally, no Hepsera-associated resistance mutations were observed during the study period.

Various measures of treatment response continued to improve among patients who took Hepsera daily beyond 48 weeks. According to Kaplan-Meier estimates based on interim data, 75 percent of Hepsera patients had normalized ALT levels and 46 percent had undetectable levels of HBV DNA.

Through 48 weeks, the discontinuation rates were similar between the treatment and placebo arms, with seven percent of patients receiving Hepsera and eight percent of patients receiving placebo discontinuing from the study. No patients in either the Hepsera

or 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 Hepsera and placebo arms.

Results in Hepatitis B "e" Antigen-negative (HBeAg-negative or precore mutant) Patients

The second randomized, double-blind, placebo-controlled Hepsera study (Study 438) published in this edition of NEJM involved 185 patients chronically infected with a mutant version of HBV lacking the hallmark hepatitis B "e" antigen - also known as "precore mutant" hepatitis B. Precore mutant hepatitis B is highly prevalent in Mediterranean countries and in Southeast Asia, where 50 to 80 percent of the infected population has HBeAg-negative disease. To date, this is the only one year, placebo-controlled clinical trial in hepatitis B "e" antigen-negative patients.

At week 48, significantly more patients treated with Hepsera showed reduced liver inflammation and damage (64 percent versus 33 percent, respectively, p less than 0.001) and normalized ALT levels (72 percent vs. 29 percent, respectively, p less than 0.001), compared with placebo-treated patients. Fifty-one percent of patients receiving Hepsera had undetectable levels of HBV DNA in their blood (less than 400 copies/mL), versus none of the patients receiving placebo (p less than 0.001). No Hepsera-associated resistance mutations were observed during the study period.

The incidence of grade 3 and 4 laboratory abnormalities and clinical adverse events was similar between the Hepsera and placebo arms. No patients in either the Hepsera or 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. The most common adverse events reported were headache, pharyngitis and abdominal pain.

"Precore mutant hepatitis B is associated with high rates of cirrhosis and frequently requires long-term therapy to keep disease progression in check," said Professor Stephanos Hadziyannis, MD, Department of Medicine, Henry Dunant Hospital, Athens, Greece, an investigator in Study 438 and lead author on one of the papers. "The efficacy and tolerability documented in this study after 48 weeks of therapy make Hepsera an important choice for long-term treatment of patients infected with this type of HBV."

About Hepsera

Hepsera, the first nucleotide analogue for chronic hepatitis B, is administered as a once daily 10 mg tablet and works by blocking HBV DNA polymerase, an enzyme involved in the replication of the virus in the body. Results from the clinical studies reported in the NEJM also have been presented at major medical meetings. In addition to Studies 437 and 438, Hepsera has been studied in patients who were treated with and developed resistance to lamivudine, including patients wait-listed for or who had received a liver transplant and patients co-infected with HIV.

The adverse reactions considered at least possibly related to treatment in the first 48 weeks were asthenia (weakness), headache, abdominal pain, nausea, flatulence, diarrhea and dyspepsia. With extended treatment, mild to moderate increases in serum creatinine were observed uncommonly in patients with chronic hepatitis B and compensated liver disease treated with Hepsera for a median of 49 weeks and a maximum of 109 weeks. Changes in serum creatinine were observed very commonly in patients with pre- and post-transplantation lamivudine-resistant liver disease and multiple risk factors for changes in renal function who were treated with Hepsera for up to 129 weeks, with a median time on treatment of 19 and 56 weeks, respectively. Clinical and laboratory evidence of exacerbations of hepatitis have occurred after discontinuation of treatment with antiviral therapies for hepatitis B, including Hepsera. Special warnings and precautions for use are included in the package insert regarding monitoring of renal function and post-treatment exacerbations of hepatitis, use in patients with underlying renal impairment or patients co-infected with HIV, and occurrence of nucleoside analogue-associated lactic acidosis and severe hepatomegaly with steatosis.

About Gilead

Gilead Sciences is a biopharmaceutical company that discovers, develops and commercializes therapeutics to advance the care of patients suffering from life-threatening diseases worldwide. The company has six marketed products and focuses its research and clinical programs on anti-infectives. Headquartered in Foster City, CA, Gilead has operations 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. These and other risks are described in detail in the Gilead Annual Report on Form 10-K for the year ended December 31, 2001 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.

Hepsera is a trademark of Gilead Sciences, Inc.

For more information on Gilead, please call the Gilead Public Affairs Department at 1-800-GILEAD-5 (1-800-445-3235) or visit www.gilead.com.

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