

Data Evaluating Long-Term Therapy with Hepsera for Hepatitis B "e" Antigen-Negative Chronic Hepatitis B Published in the New England Journal of Medicine

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FOSTER CITY, Calif.--(BUSINESS WIRE)--June 29, 2005--Gilead Sciences, Inc. (Nasdaq:GILD) today announced that data through 144 weeks supporting the efficacy and tolerability of its oral antiviral drug Hepsera(R) (adefovir dipivoxil) in patients chronically infected with hepatitis B "e" antigen-negative (HBeAg-negative) chronic hepatitis B were published in the June 30th edition of the New England Journal of Medicine (NEJM). Continued viral suppression and changes in laboratory markers of liver function were evaluated through three years.

"The sustained efficacy and tolerability we have observed among patients receiving continuous therapy in this study indicates that Hepsera is a valuable long-term treatment option for patients with HBeAg-negative chronic hepatitis B," said Stephanos Hadziyannis, MD, Department of Medicine, Henry Dunant Hospital, Athens, Greece, a lead investigator for the study and lead author of the paper. "There is a great need for treatments with proven long-term effectiveness among patients with this form of the disease, which often requires indefinite therapy and which has an increasing prevalence around the world."

Study 438 is a multi-center, randomized, double-blind, placebo-controlled study evaluating the efficacy, tolerability and safety of Hepsera. One-hundred eighty-five (185) patients were randomized in a 2:1 ratio to receive Hepsera or placebo orally once daily for 48 weeks. Hepsera patients on therapy at week 48 were randomized again to either receive an additional 48 weeks of Hepsera ("adefovir-adefovir," n=80) or switch to placebo ("adefovir-placebo," n=40). Patients who initially received placebo were switched to Hepsera ("placebo-adefovir," n=60). Long-term efficacy and safety (144 weeks) was evaluated in patients treated with Hepsera between weeks 48 and 96 of the study.

These data through 144 weeks further describe the profile seen at 48 weeks, which was published in the NEJM on February 27, 2003. Among patients in the adefovir-adefovir group, 71 percent achieved undetectable levels of serum HBV DNA (less than 1000 copies/mL, Roche Amplicor Monitor(TM) PCR assay) at week 96, compared with 76 percent in the placebo-adefovir group. In patients who switched to placebo at week 48, HBV DNA levels increased compared to those continuing on Hepsera, with only 8 percent in patients of the adefovir-placebo group remaining with undetectable levels at week 96 (p less than 0.001). Among patients treated with Hepsera, 79 percent had undetectable levels of serum HBV DNA at week 144.

Treatment with Hepsera also resulted in changes in laboratory markers of liver function, as measured by serum levels of alanine aminotransferase (ALT). The proportion of patients with ALT levels above the upper limit of normal at baseline whose ALT levels returned to normal at 96 weeks was 73 percent in the adefovir-adefovir group and 80 percent in the placebo-adefovir group. In patients who switched to placebo at week 48, ALT levels increased, compared to those who continued Hepsera, with only 32 percent in the adefovir-placebo group remaining normal at week 96 (p less than 0.001). Sixty-nine percent of patients in the adefovir-adefovir group exhibited normalized ALT levels at week 144. Hepatitis B surface ("s") antigen seroconversion was observed in two patients, one in the adefovir-adefovir group and the other in the placebo-adefovir group.

The safety profile of Hepsera over 96 and 144 weeks was consistent with that reported over 48 weeks, which was similar to placebo. The most common adverse reactions reported through 96 weeks were headache, abdominal pain and pharyngitis. Three patients in the adefovir-adefovir group had a confirmed increase in serum creatinine of greater than or equal to 0.5 mg/dL from baseline by week 144. All cases resolved, one while continuing Hepsera therapy and two with discontinuation of Hepsera therapy. Thirteen adefovir-placebo patients (32.5 percent) experienced significant elevations in ALT levels (greater than or equal to 10 times the upper limit of normal), most of which (10/13) occurred within 12 weeks of discontinuing therapy.

Two mutations (rtN236T and rtA181V) in the viral polymerase have been associated with resistance to Hepsera. In patients treated with Hepsera in this study, viral resistance emerged in six patients in the adefovir-adefovir group in the second year of the study. The emergence of rtN236T was associated with a rebound in HBV DNA and ALT levels. Two of the three patients with the rtA181V mutation experienced a rebound in HBV DNA levels.

About Hepsera

Hepsera, a nucleotide analogue for the treatment of chronic hepatitis B, works by inhibiting HBV DNA polymerase, an enzyme involved in the replication of the virus in the body.

In the United States, Hepsera is indicated 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.

The adverse reactions considered at least possibly related to treatment reported in 3 percent or greater of patients in the first 48 weeks in Hepsera pivotal clinical studies were asthenia, 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 up to a maximum of 109 weeks. Changes in serum creatinine were observed very commonly in patients pre- and post-transplantation with 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, post-treatment exacerbations of hepatitis, and the occurrence of lactic acidosis and severe hepatomegaly with steatosis. Dosing instructions for patients with underlying renal impairment and for patients co-infected with HIV are also provided in the package insert, which is available for download online at www.hepsera.com.

About Chronic Hepatitis B

Chronic hepatitis B is a serious disease that can lead to potentially fatal complications such as cirrhosis and liver cancer. More than 400 million people are estimated to be chronically infected with HBV worldwide, with approximately 1.25 million people infected in the United States alone. HBeAg-negative hepatitis B accounts for approximately 14 to 33 percent of chronic hepatitis B cases worldwide.

About Gilead

Gilead Sciences is a biopharmaceutical company that discovers, develops and commercializes innovative therapeutics in areas of unmet medical need. The company's mission is to advance the care of patients suffering from life-threatening diseases worldwide. Headquartered in Foster City, California, Gilead has operations in North America, 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. These risks and uncertainties could cause actual results to differ materially from those referred to in the forward-looking statements. Risks are described in detail in the Gilead Annual Report on Form 10-K for the year ended December 31, 2004 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 registered 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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