Data From Study of Gilead's Adefovir Dipivoxil in Hepatitis B Patients With Lamivudine-Resistant Virus Presented At International Medical Meeting

April 19, 2002 8:38 AM ET

MADRID, Spain, Apr 19, 2002 (BW HeathWire) --

Additional Virology Data Presented at 37th Meeting of European Association for the Study of the Liver

Gilead Sciences (Nasdaq:GILD) today announced results from a clinical trial (Study 461) of its novel, once-daily, oral antiviral agent adefovir dipivoxil 10 mg that is being developed for the treatment of chronic hepatitis B. These results demonstrate that treatment with adefovir dipivoxil as monotherapy or in combination with lamivudine was associated with significant reductions in both serum hepatitis B virus (HBV) DNA and alanine transaminase (ALT, a measure of liver damage) levels through 16 weeks in patients infected with lamivudine-resistant HBV. Treatment with lamivudine monotherapy in these patients was not associated with statistically significant reductions in HBV DNA or ALT levels.

The data were discussed (#646) in an oral presentation at the 37th Annual Meeting of the European Association for the Study of the Liver (EASL) in Madrid, Spain by Marion Peters, MD, Principal Investigator and Chief of Hepatology Research, University of California, San Francisco Medical Center. This presentation is one of more than 20 abstracts on adefovir dipivoxil scheduled for presentation at EASL describing the anti-HBV activity, safety and resistance profile of adefovir dipivoxil in a variety of chronic hepatitis B patient populations. Preliminary data from Study 461 previously were announced in November 2001.

Adefovir dipivoxil belongs to a class of drugs called nucleotide analogues which are designed to work by blocking HBV DNA polymerase, an enzyme involved in the replication of the virus in the body. Gilead recently filed a New Drug Application (NDA) for adefovir dipivoxil with the U.S. Food and Drug Administration (FDA) and a Marketing Authorisation Application (MAA) with the European Medicines Evaluation Agency (EMEA). Gilead has requested a priority, or six month, review in the United States, and anticipates receiving an opinion from the Committee for Propriety Medicinal Products (CPMP) in Europe in the first half of 2003.

"These data indicate that adefovir dipivoxil, whether used alone or in combination with lamivudine, is active against HBV resistance mutations that develop in nearly one third of patients within one year of beginning treatment with lamivudine," said Dr. Peters. "The growing database from controlled clinical trials, including data presented earlier at this conference, suggest that treatment with adefovir dipivoxil significantly lowers serum HBV DNA and normalizes ALT levels. These results indicate that treatment with adefovir dipivoxil monotherapy may be a potential new therapeutic option for patients with chronic hepatitis B."

```
About Study 461
```

Study 461 is an ongoing 48-week, randomized, double-blind, placebo-controlled, multicenter study of 59 patients in the United States, Europe, Australia and Canada. Participants had chronic hepatitis B with compensated liver disease and had received treatment with lamivudine monotherapy prior to enrollment. YMDD mutations in the HBV DNA polymerase, associated with lamivudine resistance, were present in all patients upon entry into the study.

Patients were randomized to receive either adefovir dipivoxil 10 mg (n=20), a combination of adefovir dipivoxil 10 mg with lamivudine 100 mg (n=20) or lamivudine 100 mg (n=19). After 16 weeks, patients in both the adefovir dipivoxil monotherapy and combination adefovir dipivoxil and lamivudine groups achieved similar, significant median reductions in serum HBV DNA levels from baseline (2.86 log10 copies/mL vs. 2.87 log10 copies/mL, p less than 0.0001). In comparison, serum HBV DNA levels remained the same (no decrease, or change of 0.00 log10 copies/mL) in patients treated with lamivudine 100 mg monotherapy (p less than 0.001 vs. both the adefovir dipivoxil monotherapy and adefovir dipivoxil plus lamivudine treatment arms). In addition, ALT levels normalized in 42 percent of patients receiving combination adefovir dipivoxil and lamivudine (p=0.008) and in 32 percent of patients treated with adefovir dipivoxil monotherapy (p=0.04) compared to six percent of patients receiving lamivudine monotherapy. Serum HBV DNA and ALT levels both are markers of disease severity. The most common adverse events reported were asthenia, abdominal pain and pharyngitis, and the nature, severity and frequency of adverse events were similar among all treatment arms. Additional data from this study will be analyzed following 48 weeks of treatment.

```
Study 461 Resistance Data
```

Preliminary virology analyses from the first 32 weeks of Study 461 also were discussed in an oral presentation at the conference (#568) by Shelly Xiong, PhD, Gilead. At the end of the 32 weeks of treatment, 32 percent of patients who received adefovir dipivoxil monotherapy (n=20) lost the YMDD resistance mutation (a hallmark of lamivudine resistance) and reverted to wild-type HBV. No patients receiving lamivudine lost the YMDD resistance mutation.

"Gilead is dedicated to advancing therapeutics for life-threatening diseases worldwide by seeking solutions to complex treatment issues, such as resistance, faced by physicians and their patients," said John C. Martin, PhD, President and CEO, Gilead. "The breadth of adefovir dipivoxil data presented this week at EASL underscores the potential this drug may have to address the urgent, unmet medical needs of patients suffering from chronic hepatitis B."

Chronic Hepatitis B

Worldwide, there are approximately 350 million chronic carriers of hepatitis B, of which approximately one million die each year from complications of the disease, making chronic hepatitis B one of the 10 most common causes of death. Complications of chronic hepatitis B include cirrhosis (scarring of the liver), liver failure and primary liver cancer (hepatocellular carcinoma). Between one-quarter and one-third of people with chronic hepatitis B are expected to develop progressive liver disease. Patients infected with the precore mutant strain of hepatitis B may be predisposed to more severe and progressive liver injury. Precore mutant hepatitis B infects up to approximately 50 percent of the 350 million chronic hepatitis B carriers worldwide and is most prevalent in countries of the Mediterranean and Southeast Asia, where between 30-80 percent of chronic hepatitis B patients are estimated to be infected with this strain.

Early Access Program Initiated

In March 2002, Gilead announced the initiation of an early access program in the United States to provide adefovir dipivoxil to chronic hepatitis B patients with lamivudine-resistant HBV. A similar program opened in France in July 2001 and has enrolled 300 patients to date, and additional programs in Canada, Australia and in other countries in Europe will open in the coming months as appropriate regulatory approvals are obtained.

For more information regarding the adefovir dipivoxil early access program, or to request program registration materials, physicians may call 1-800-GILEAD-5 or 1-650-574-3000.

Gilead Sciences

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 five marketed products and focuses its research and clinical programs on anti-infectives, including antivirals, antifungals and antibacterials. 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. Such risks and uncertainties include the risk that further data from ongoing and future clinical trials may not be as favorable as current data and other risks related to regulatory review and approval of adefovir dipivoxil in the United States and Europe. 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, 2001 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.

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 or 1-650-574-3000.

CONTACT: Gilead Sciences
Sheryl Meredith, 650/522-5505 (Investors)
Amy Flood, 650/522-5643 (Media)