Gilead Announces Primary Endpoint Met in Phase III Study of Adefovir Dipivoxil 10 mg in Patients with Lamivudine-Resistant Chronic Hepatitis B Infection

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Gilead Sciences, Inc. (Nasdaq: GILD) today announced preliminary results from a Phase III clinical trial (Study 461) evaluating the efficacy and safety of adefovir dipivoxil 10 mg once daily in patients with lamivudine-resistant chronic hepatitis B virus (HBV) infection and compensated liver disease. In a planned interim analysis, patients receiving adefovir dipivoxil 10 mg monotherapy (n=20) and patients receiving adefovir dipivoxil 10 mg in combination with lamivudine 100 mg daily (n=20) exhibited a time-weighted average decrease in serum HBV DNA from baseline (DAVG16) of 2.46 log10 copies/mL and 2.45 log10 copies/mL, respectively, compared to a decrease in time-weighted average serum HBV DNA of 0.07 log10 copies/mL ($p<0.001$) for patients receiving lamivudine monotherapy (n=19). There was no difference in the frequency of adverse events across treatment groups. These data are expected to be presented at a scientific conference during 2002.

"With the development of new treatment options for patients with chronic HBV infection, physicians continue to refine strategies that will improve patient outcomes," said Marion Peters, M.D., Professor of Medicine and Chief of Hepatology Research, University of California, San Francisco Medical Center. "These early data suggest a potential medical approach to the treatment of lamivudine-resistant HBV, showing that adefovir dipivoxil 10 mg monotherapy reduces viral load in patients who have developed resistance to lamivudine. The findings from this controlled trial will confirm the previously announced results of open-label trials documenting the antiviral activity of adefovir dipivoxil in lamivudine-resistant patients. These findings will be especially important because nearly one-third of patients treated with lamivudine develop resistance to that drug within a year, and as many as 67 percent become resistant after four years."

Study 461 Design

Study 461 is an ongoing 48-week randomized, double-blind, placebo-controlled multicenter study that enrolled 59 patients at sites in the United States, Europe, Australia and Canada. Study participants exhibited chronic HBV infection with compensated liver disease (evidence of cellular liver damage with adequate overall liver function). These patients were treated with lamivudine monotherapy for their HBV infection prior to study entry and had developed the YMDD mutation in the hepatitis B viral polymerase associated with lamivudine-resistance. At baseline, patients had a median serum HBV DNA of 8.1 log10 copies/mL.

Patients were randomized (1:1:1) to three study groups receiving 1) adefovir dipivoxil 10 mg in combination with placebo, 2) adefovir dipivoxil 10 mg in combination with lamivudine 100 mg or 3) lamivudine 100 mg in combination with placebo. The primary endpoint for the study is the time-weighted average change from baseline in serum HBV DNA up to 16 weeks of treatment (DAVG16). Secondary endpoints will evaluate the time-weighted average change from baseline in serum HBV DNA up to week 48 (DAVG48) and the change from baseline in serum levels of HBV DNA at 16 and 48 weeks in each treatment arm. Additionally, the study will evaluate the proportion of patients whose ALT levels (an enzyme marker that indicates liver disease) have returned to normal after 48 weeks of treatment.

Week 16 Primary Efficacy and Safety Results

Through week 16, patients who received either adefovir dipivoxil 10 mg monotherapy or adefovir dipivoxil 10 mg in combination with lamivudine 100 mg exhibited statistically significant reductions in median time-weighted change in serum HBV DNA from baseline (DAVG16) of 2.46 and 2.45 log10 copies/mL, respectively, compared to a reduction of 0.07 log10 copies/mL in patients receiving lamivudine monotherapy ($p<0.001$). At week 16, the median decrease from baseline in serum HBV DNA was 2.86 log10 copies/mL and 2.87 log10 copies/mL in patients receiving adefovir dipivoxil 10 mg monotherapy and adefovir dipivoxil 10 mg in combination with lamivudine 100 mg, respectively, compared to a median change of 0.00 log10 copies/mL for patients receiving lamivudine monotherapy ($p<0.001$).

No patient withdrew from this study during treatment. The most common adverse events reported were asthenia, abdominal pain and pharyngitis, and the frequency and type of adverse events were similar among all treatment arms. No patients receiving adefovir dipivoxil 10 mg 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, both laboratory markers of renal function, as confirmed by two consecutive laboratory assessments.

"These data add to a growing body of evidence suggesting that adefovir dipivoxil 10 mg may be a potential new therapy for people with both wild-type and lamivudine-resistant chronic HBV infection," said John C. Martin, Ph.D., President and CEO of Gilead Sciences. "We believe that adefovir dipivoxil 10 mg holds great promise for the many patients with chronic HBV infection who currently have few reliable treatment options."

About Adefovir Dipivoxil 10 mg
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 HBV in the body. The investigational drug is dosed as one 10 mg tablet taken once daily.

Gilead initiated two pivotal Phase III studies to determine the safety and efficacy of adefovir dipivoxil 10 mg. Study 437 is a Phase III clinical trial evaluating the safety and efficacy of adefovir dipivoxil once daily as monotherapy compared to placebo in HBe antigen-positive patients with chronic HBV infection and compensated liver function. Preliminary results were released on June 22, 2001.

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" antigen-negative virus (HBe antibody-positive, HBV DNA-positive), and compensated liver function. This two-year study is being conducted in Australia, Canada, France, Greece, Israel, Italy and Southeast Asia. Preliminary results were released on September 19, 2001. To further evaluate the long-term safety and resistance profiles of adefovir dipivoxil 10 mg in this patient population, patients are continuing on Study 438 for an additional 48 weeks of treatment.

Data from these studies will comprise the core of the regulatory filing packages in both the United States and Europe. The company anticipates filing U.S. and European regulatory packages during the first half of 2002. Adefovir dipivoxil is an investigational compound and has not yet been determined safe or efficacious in humans for its ultimate intended use.

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 infection include cirrhosis (scarring of the liver), 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 percent and 80 percent of chronic HBV-infected 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, development, manufacturing or sales and marketing facilities 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 16 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.