

Gilead Begins Second Pivotal Phase III Trial of Once Daily Oral Hepatitis B Drug, Adefovir Dipivoxil 10 mg

January 11, 2000 2:39 PM ET

Study Targets Patient Population with Precore Mutant Strain of Hepatitis B Virus

Foster City, CA -- January 11, 2000

Gilead Sciences, Inc. (Nasdaq: GILD) announced today that it has initiated a second pivotal Phase III clinical trial of its investigational agent adefovir dipivoxil 10 mg for the potential treatment of chronic hepatitis B virus (HBV) infection. The study, designed to enroll a total of 180 patients at 32 sites in Australia, Canada, France, Greece, Israel, Italy and Southeast Asia, will evaluate patients diagnosed with precore mutant chronic HBV infection and compensated liver disease.

Recent advances in diagnostic technology have helped reveal the emergence of the precore mutant strain of HBV. This strain has evolved without the hallmark HBV "e" antigen, allowing it to escape detection by certain commonly used diagnostic assays. The precore mutant virus has been associated with chronic HBV infection that may affect patients more intensely. Researchers also are concerned that this HBV strain may predispose patients to severe and progressive liver injury. Precore mutant HBV infects up to 30 percent of the 350 million chronic HBV carriers worldwide and is most prevalent in countries of the Mediterranean and Southeast Asia, where 40 to 80 percent of chronic HBV patients are infected with this strain.

"We are pleased to begin the second pivotal trial in our Phase III program to evaluate adefovir dipivoxil 10 mg in patients with precore mutant hepatitis B infection," said John C. Martin, Ph.D., President and Chief Executive Officer. "With the growth of this patient group worldwide, this trial will help provide additional insight into this increasingly prevalent form of chronic hepatitis B infection."

Study Design

The Phase III clinical trial (Study 438) is a randomized, double-blind, placebo-controlled trial that will evaluate the efficacy and safety of adefovir dipivoxil 10 mg compared to placebo (2:1). The primary endpoint of the study is improvement in liver histology after one year of treatment. Study 438 also will evaluate the efficacy of adefovir dipivoxil compared to placebo in suppressing HBV DNA replication.

Patients completing the first year of Study 438 who receive adefovir dipivoxil 10 mg will be further randomized to receive either 10 mg adefovir dipivoxil or placebo (2:1) for a second year. Patients who receive placebo during the first year of the study will receive adefovir dipivoxil 10 mg for the second year. All patients will be followed for six months after the end of the doing period, at which time the data will be further analyzed.

Ongoing HBV Clinical Trials

In 1998, Gilead successfully completed a hepatitis B Phase II clinical program (Studies 412/413) in which multiple doses of adefovir dipivoxil were shown to have significant anti-HBV activity. Based on these positive results, Gilead initiated its hepatitis B Phase III clinical program in March 1999, and is currently completing enrollment in the first clinical trial (Study 437), having accrued more than 470 of the 500-patient enrollment target. Study 437 is a randomized, double-blind, placebo-controlled trial being conducted at 79 sites in Australia, Europe, North America and Southeast Asia that will evaluate the safety and efficacy of adefovir dipivoxil at two active doses (10 mg and 30 mg) given once daily in HBV "e" antigen positive patients.

In response to the growing importance of lamivudine-resistant HBV, especially in liver transplant patients, Gilead is conducting an open-label clinical trial (Study 435) to evaluate the efficacy and safety of adefovir dipivoxil in this population. In vitro and early in vivo data have indicated that adefovir dipivoxil is active against all clinically relevant HBV strains including lamivudine-resistant HBV. HBV resistance to lamivudine has been reported to occur in 14 to 30 percent of patients with chronic HBV infection who have been treated for one year and becomes even more common after 24 months of therapy.

Gilead Sciences

Gilead Sciences, headquartered in Foster City, CA, is an independent biopharmaceutical company that seeks to provide

accelerated solutions for patients and the people who care for them. The Company discovers, develops, manufactures and commercializes proprietary therapeutics for challenging infectious diseases (viral, fungal and bacterial infections) and cancer. Gilead maintains research, development or manufacturing facilities in Foster City, CA, Boulder, CO, San Dimas, CA, and Cambridge, UK, and sales and marketing organizations in the United States, Europe and Australia. For more information about Gilead, visit the Company's Web site at www.gilead.com.