Gilead Announces Data From Study of Viread in Patients Co-infected With HIV and HBV; Data Presented at 9th Conference on Retroviruses and Opportunistic Infections

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SEATTLE, Feb 27, 2002 (BUSINESS WIRE) -- Gilead Sciences (Nasdaq:GILD) today announced data from two studies evaluating its novel antiretroviral agent Viread(TM) (tenofovir disoproxil fumarate) in patients co-infected with HIV and chronic hepatitis B virus (HBV) infection. Viread, a one-tablet, once-daily antiretroviral agent, received marketing approval in October 2001 for the treatment of HIV infection in the United States and was approved earlier this month in Europe. Study results presented this morning show that treatment with Viread was associated with a significant reduction in serum HBV DNA levels compared to placebo through 24 weeks of treatment and through 12 weeks in a second open-label study, both in patients co-infected with HIV and HBV.

These data were reviewed in an oral presentation (#124) by David Cooper, MD, DSc, Professor of Medicine and Director of the National Centre in HIV Epidemiology and Clinical Research, University of New South Wales, Sydney, Australia at the 9th Conference on Retroviruses and Opportunistic Infections in Seattle. Additional data from an analysis of an open-label study of 10 HIV/HBV co-infected patients in France were presented in a poster session (#675-M) on Monday by Yves Benhamou, MD, Service d'Hepato-Gastroenterologie, Groupe Hospitalier Pitie-Salpetriere, Paris, France.

"Approximately 10 percent of HIV patients are co-infected with HBV, and treatment options that combat the hepatitis B virus are currently limited, with up to 50 percent of co-infected patients developing HBV resistance to lamivudine after two years," commented Dr. Cooper. "The results seen in these patients are important because they indicate that Viread, a potent antiviral for the treatment of HIV, is well tolerated and has significant activity against both wild-type and lamivudine-resistant HBV in co-infected patients."

About the Study

The anti-HBV activity of Viread was evaluated in patients co-infected with HIV and HBV who were enrolled in Gilead Study 907. Twelve patients received Viread and two received placebo for 24 weeks. At baseline, patients had a mean serum HBV DNA of 8.74 log10 copies/mL. Genotypic analyses at baseline revealed that the HBV polymerase in seven patients expressed mutations associated with lamivudine resistance.

Following 24 weeks of Viread treatment, the mean change in serum HBV DNA from baseline was a reduction of 4.81 log10 copies/mL for patients receiving Viread and an increase of 1.23 log10 copies/mL for patients on placebo (p=0.04). This equates to a 99.998 percent decrease in circulating HBV DNA for patients receiving Viread. Follow-up HBV genotyping revealed no new resistance mutations in the HBV polymerase of these patients. Viread was generally well tolerated in these co-infected patients.

Additional Data in Lamivudine-Resistant Patients

In a French early access protocol for Viread, 10 HIV/HBV co-infected patients taking lamivudine as part of their anti-HIV therapy also were given Viread 300 mg once daily. At the beginning of this open-label, non-comparative study, all patients had clinical evidence of HBV resistance to lamivudine.

At study entry, nine of 10 patients were hepatitis B "e" antigen positive and one was hepatitis B "e" antigen negative (presumed precore mutant strain). At baseline, patients had a median serum HBV DNA of 8.10 log10 copies/mL. The median decrease in HBV DNA (by Roche PCR) from baseline was 3.34 log10 copies/mL at week 12 (p less than 0.01), a 99.95 percent decrease in circulating HBV DNA. There were no significant changes in serum ALT levels from baseline, and no ALT flares occurred during treatment. In general, Viread was well tolerated. Viread treatment was discontinued in one patient whose serum creatinine increased by 1.70 mg/dL at week 12. This patient had pre-existing impaired renal function related to familial polycystic kidney disease.

About Viread

Viread is the first nucleotide analogue reverse transcriptase inhibitor (NtRTI) approved for the treatment of HIV in the United

States and Europe. The drug works by blocking reverse transcriptase, an enzyme involved in the replication of HIV. The approved dose of Viread for the treatment of HIV infection is 300 mg once daily taken orally with a meal.

In the United States, Viread is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection. This indication is based on analyses of plasma HIV-1 RNA levels and CD4 cell counts in a controlled study of Viread of 24 weeks duration and in a controlled, dose ranging study of Viread of 48 weeks duration. Both studies were conducted in treatment-experienced adults with evidence of HIV-1 viral replication despite ongoing antiretroviral therapy. Studies in antiretroviral-naive patients are ongoing; consequently, the risk-benefit ratio for this population has yet to be determined.

The effect of Viread on liver histology for people infected with chronic HBV has not been studied in a broad group of patients in a controlled clinical setting. Viread has not been determined safe or efficacious in humans for the treatment of HBV infection in patients co-infected with HIV and HBV.

HIV Resistance Profile

HIV resistance to Viread occurs in approximately three percent of patients and is slow to develop. Viread selects for the K65R mutation in HIV reverse transcriptase in vitro, and viruses expressing this mutation show a 3- to 4-fold reduced susceptibility to the drug. Zalcitabine, didanosine and abacavir can also select for this mutation. In clinical trials, three percent of patients developed the K65R mutation, which did not always result in treatment failure. The clinical significance of the K65R mutation for patients treated with Viread or other antiretroviral agents is not fully known at this time.

Safety Profile in HIV Infected Patients

More than 1,000 patients have been treated with Viread alone or in combination with other antiretroviral products for a period of 28 days to 143 weeks in Phase I, II and III clinical trials and in a compassionate access study (908). Assessment of adverse reactions is based on two studies (902 and 907) in which 653 treatment-experienced patients received treatment with Viread 300 mg (n=443) or placebo (n=210) for 24 weeks followed by extended treatment with the drug. In this analysis, adverse event rates in the Viread group were similar to those in the placebo-treated patients.

The most common adverse events in patients receiving Viread were mild to moderate gastrointestinal events, such as nausea, diarrhea, vomiting and flatulence. Laboratory abnormalities observed in clinical studies occurred with similar frequency in the Viread and placebo-treated groups. Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues alone or in combination with other antiretrovirals.

Ongoing Clinical Studies

Gilead is conducting Study 903 to further evaluate Viread in treatment-naive patients with HIV infection. This 96-week trial is designed to compare a treatment regimen of Viread, lamivudine (3TC) and efavirenz to a treatment regimen of stavudine (d4T), lamivudine (3TC) and efavirenz in a blinded fashion in patients in the United States, Europe and South America who have not previously received antiretroviral treatment. Enrollment in Study 903 was completed in January 2001 with 601 patients. In addition, Gilead has initiated a program to evaluate Viread in treatment-experienced pediatric patients.

HIV/HBV Co-infection

HIV and HBV co-infection occurs when a patient infected with one of the viruses contracts the other, resulting in a dual infection that is generally more difficult to treat. Co-infection is common because both HIV (the virus that causes acquired immunodeficiency syndrome, or AIDS) and HBV (the virus that causes chronic hepatitis B infection) are spread through similar means, such as infected blood or body fluids, sexual contact, injection drug use or transmission from mother to child during pregnancy.

HIV is currently estimated to infect more than 36 million people worldwide, and chronic hepatitis B infects approximately 350 million people worldwide. Approximately 10 percent of people with HIV also are carriers of chronic HBV.

Gilead HBV Development Program

Gilead's leading product candidate for the treatment of chronic HBV infection is adefovir dipivoxil 10 mg. Data from a study of adefovir dipivoxil 10 mg in patients co-infected with HIV and lamivudine-resistant HBV were discussed in an oral presentation

(#123) also given today by Dr. Benhamou. These data demonstrate significant sustained or increased reductions in HBV DNA in HIV/HBV co-infected patients with lamivudine-resistant HBV treated with adefovir dipivoxil 10 mg once daily up to 96 weeks. Forty-eight week data from this study were published in the Lancet in September 2001 (Lancet. 2001;358:718-723).

Gilead recently announced data from its two pivotal Phase III studies of adefovir dipivoxil in patients with chronic HBV infection. All primary and secondary endpoints were achieved and the safety profile of adefovir dipivoxil 10 mg was similar to placebo. Results from Study 437 were presented at the 52nd annual meeting of the American Association for the Study of Liver Diseases (AASLD) in November 2001. Data from Study 438, a second Phase III trial in patients with precore mutant HBV, were announced in September 2001 and will be presented at the 37th annual meeting of the European Association for the Study of Liver Disease in Madrid in April 2002.

Data from these studies will comprise the core of the regulatory filing packages in both the United States and Europe. Gilead anticipates completing these filings in 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.

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 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, including the risk that the safety and efficacy data observed in the studies described in this press release may not continue to be observed in broader patient groups or through longer periods of treatment. 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.

Note to Editors: Viread is a trademark of Gilead Sciences, Inc.

For full prescribing information on Viread, please call 1-800-GILEAD-5 (1-800-445-3235) or visit www.viread.com.

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