Viread Demonstrates Anti-HIV Potency Similar to the Protease Inhibitor Ritonavir in Short-Term Study of Treatment-Naive Patients

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SEATTLE, Feb 25, 2002 (BUSINESS WIRE) --

Results from Aaron Diamond AIDS Research Center Study Presented at 9th Conference on Retroviruses and Opportunistic Infections

Gilead Sciences' (Nasdaq:GILD) novel treatment for patients infected with HIV, Viread(TM) (tenofovir disoproxil fumarate) or tenofovir DF, demonstrates anti-HIV activity in treatment-naive patients, according to new data presented today. Antiretroviral-naive patients experienced a mean decrease of 1.5 log10 copies/mL in HIV RNA when treated with Viread 300 mg once daily as monotherapy for 21 days, an antiviral effect similar to the potent protease inhibitor ritonavir. Reduction in HIV RNA, or viral load, and viral dynamics studies are important indicators of antiviral efficacy.

These data were described in an oral presentation (#3) given by Michael Louie, MD, Aaron Diamond AIDS Research Center, The Rockefeller University, New York, NY, at the 9th Conference on Retroviruses and Opportunistic Infections in Seattle, Washington.

"Studies of early changes in plasma HIV-1 RNA levels may provide a reliable comparative analysis of the potency of antiretroviral agents. The results of this study suggest that tenofovir DF has potency comparable to that of a protease inhibitor when used as monotherapy in patients infected with HIV who have not been previously treated with antiretrovirals," commented Martin Markowitz, MD, Clinical Director and Staff Investigator, Aaron Diamond AIDS Research Center and lead investigator for the study.

Study 917 Design and Results

Inherent potency can be determined through viral dynamics, which measures the initial phase of HIV-1 RNA decay caused by an antiretroviral agent or drug regimen. Comparisons of initial viral decay rates are useful in determining the relative antiviral efficacy of one drug versus another.

Study 917 was a 21-day open-label study designed to assess the anti-HIV activity of Viread as monotherapy in antiretroviral-naive patients infected with HIV. In this study, 10 chronically HIV-infected patients (nine males, one female) with an average age of 34 years were hospitalized for initiation of Viread 300 mg once daily as monotherapy. Patients' HIV RNA levels were monitored every six hours for the first 72 hours. After discharge, patients were seen daily until day 10 and then on days 12, 14 and 21.

At study enrollment, patients had a mean HIV RNA level of 4.3 log10 copies/mL (range: 3.7 to 5.1). After three weeks, patients treated with Viread monotherapy experienced a mean reduction in HIV RNA of 1.5 log10 copies/mL (range: 0.6 to 2.7). The mean initial decay rate for Viread was -0.39 per day (range: -0.24 to -0.59). Previously determined mean initial decay rates were -0.99 per day for a highly active antiretroviral therapy (HAART) regimen containing Kaletra(R) (lopinavir/ritonavir), Sustiva(R) (efavirenz), Viread and Epivir(R) (lamivudine) and -0.34 per day for ritonavir monotherapy. By comparison to these previously determined rates, data from this study indicate that the relative efficacy of Viread is 15 percent higher than ritonavir monotherapy and is 39 percent that of the potent four-drug HAART regimen, as detailed above.

"Results from this Aaron Diamond study confirm earlier data demonstrating that Viread is a potent inhibitor of viral replication in treatment-naive patients," said John C. Martin, PhD, President and CEO, Gilead Sciences. "Together with a safety profile comparable to placebo and single-tablet, once-daily dosing, these data are further evidence that Viread may provide physicians and patients with a new antiretroviral option applicable for any regimen."

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.

HIV Resistance Profile

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

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.

About HIV/AIDS

More than 900,000 Americans and 560,000 Europeans are infected with HIV, the virus that causes acquired immunodeficiency syndrome (AIDS). Each year, approximately 560,000 U.S. and European patients receive anti-HIV treatment regimens. Treatment with antiretroviral agents is crucial to control viral load and delay the emergence of the debilitating AIDS-defining events. Over years of treatment with existing agents, however, multiple factors can lead to the development of viral mutations that render patients' HIV resistant to currently available medications.

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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