Phase III Study of Viread Shows Favorable Lipid and Mitochondrial DNA Profile in Treatment-naive HIV Patients; Data Presented in Late-Breaker Session at 42nd ICAAC

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SAN DIEGO, Sep 27, 2002 (BUSINESS WIRE) -- Gilead Sciences (Nasdaq:GILD) today announced that new data from an ongoing Phase III clinical trial suggest that Viread(R) (tenofovir disoproxil fumarate) has favorable effects on serum lipid profiles and mitochondrial DNA content through 48 weeks when taken as part of combination therapy in antiretroviral-naive HIV patients. In addition, patients who received Viread had significantly fewer adverse events associated with mitochondrial toxicity compared to patients receiving stavudine. The data were presented today by Joel Gallant, MD of Johns Hopkins University, Baltimore, Maryland during Late Breaker I, Session 19 (Abstract #3983) at the 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in San Diego, California.

These data are from Study 903, an ongoing three-year, randomized, double-blind trial being conducted in the United States, Europe and South America. The study was designed to compare the efficacy and safety of a treatment regimen of Viread, lamivudine (3TC) and efavirenz to a regimen of stavudine, 3TC and efavirenz in 600 antiretroviral-naive patients with HIV infection. To maintain the blinded nature of the study, patients in the Viread arm receive one tablet, twice daily of stavudine placebo while patients in the stavudine arm receive one tablet, once daily of Viread placebo. Treatment assignments will remain blinded to patients and their physicians through 144 weeks. Results from the primary efficacy and safety endpoints of Study 903 were presented at the International AIDS Conference in Barcelona, Spain in July 2002.

"The results of this analysis are particularly significant because side effects thought to be caused by mitochondrial toxicity are an area of great concern for patients. They decrease quality of life, contribute to non-adherence and can have significant long-term health consequences," said Dr. Gallant, a lead investigator for the study. "Since we're now faced with the prospect of treating HIV-infected patients over decades rather than months or years, it's critical that we are able to construct highly effective initial treatment regimens that are well tolerated and less toxic."

Study Results

Data through 48 weeks of Study 903 demonstrated statistically significant differences in lipid changes for the Viread and stavudine treatment groups, as measured by changes in fasting levels of triglycerides and cholesterol. Patients receiving Viread (n=199) had a mean increase from baseline in triglycerides of 12 mg/dL, whereas patients in the stavudine arm (n=208) showed an increase of 84 mg/dL (p less than 0.0001). The increase in total fasting cholesterol levels was significantly lower for patients receiving Viread compared with those receiving stavudine (29 mg/dL vs. 57 mg/dL, p less than 0.0001). Notably, increases in low-density lipoprotein cholesterol (LDL, or "bad cholesterol") were 86 percent higher in the stavudine arm compared to Viread (28 mg/dL vs. 15 mg/dL, p less than 0.0001).

In addition, the incidence of nucleoside analogue-associated toxicities, such as peripheral neuropathy and lipodystrophy, was three percent in the Viread-containing arm, compared with 10 percent in the stavudine-containing arm (p less than 0.001) after 48 weeks of treatment.

To explore the effect of treatment on mitochondrial DNA and its potential association with adverse effects, Gilead is conducting a sub-study of 227 patients enrolled in Study 903. Mitochondrial DNA levels were assessed in peripheral blood mononuclear cells at baseline and week 48 for sub-study patients. Because infection with HIV appears to result in decreased mitochondrial DNA levels in untreated individuals, levels also were assessed for a control group of uninfected males (n=49). This analysis shows that patients treated with Viread (n=113) experienced a significant median increase from baseline of 82 copies/cell of mitochondrial DNA (p less than 0.001) compared to an increase in the stavudine group (n=114) of only 18 copies/cell. The increase in mitochondrial DNA observed in patients receiving Viread brings the median level in those patients to levels seen in the uninfected cohort.

In a separate sub-study of 257 patients, venous lactate levels at week 48 were assessed. Ninety-three percent of Viread patients (n=128) compared to 64 percent of stavudine patients (n=129) had levels within normal limits (less than 2.1 milimoles/liter, p less than 0.0001).

Lipid and Metabolic Abnormalities in HIV Treatment

In recent years, alarming lipid changes and other metabolic abnormalities have become commonplace in HIV-infected patients - including increases in total cholesterol, lipoatrophy (wasting of fat around the face, limbs and buttocks), lipodystrophy (large accumulations of fat in the gut, back and neck) and diabetes. A growing body of research suggests that while antiretrovirals inhibit HIV replication, they also may inhibit the replication of mitochondrial DNA. The resulting depletion in mitochondrial DNA may play a significant role in these and other side effects, including peripheral neuropathy.

"These data empower HIV-infected patients and their physicians with the choice of an antiretroviral therapy that may spare some of the undesirable long-term side effects that have been associated with certain current treatment regimens," commented John C. Martin, PhD, President and Chief Executive Officer, Gilead Sciences. "While the results are preliminary, Gilead intends to monitor both study groups for an additional two years to best evaluate how these data impact patients and the long-term success of therapy."

About Viread

Viread is the first nucleotide analogue reverse transcriptase inhibitor (NtRTI) approved for the treatment of HIV in the United States and Europe. Since approval, approximately 50,000 patients have been prescribed Viread as part of combination therapy. The U.S. Food and Drug Administration approved Viread for marketing in October 2001 and the European Commission granted approval in February 2002. In clinical trials and expanded access programs, approximately 10,000 patients have been treated with Viread alone or in combination with other antiretroviral products for periods up to three years. 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 for use 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.

Viread is approved in Europe for use in combination with other antiretroviral agents for the treatment of HIV infection in patients who are experiencing early virological failure.

Safety Profile

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. 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. In clinical practice, a number of adverse events, including renal impairment, nausea, rash and asthenia (weakness) have been reported. Renal impairment occurred most often in patients with underlying systemic or renal disease, or in patients taking concomitant nephrotoxic agents. 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.

About HIV/AIDS

More than 920,000 Americans and 560,000 Europeans are infected with HIV, the virus that causes AIDS. Each year, approximately 600,000 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.

About 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 six 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 these 48-week data will not be observed through longer treatment periods. 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 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.

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

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