96-Week Data From Phase III Study Show Long-Term Efficacy With Reduced Risk of Lipid and Metabolic Changes for Viread Versus Stavudine in Treatment-Naive HIV Patients

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BOSTON, Feb 11, 2003 (BUSINESS WIRE) --

Data Presented at 10th Conference on Retroviruses and Opportunistic Infections

Gilead Sciences (Nasdaq: GILD) today presented 96-week data from a controlled clinical trial (Study 903) demonstrating that treatment-naive patients who received Viread(R) (tenofovir disoproxil fumarate) experienced substantially less lipodystrophy and lower elevations in fasting cholesterol and triglyceride levels, while achieving similar reductions in HIV viral load and increases in CD4 cell counts, compared to those who received stavudine (d4T).

Study 903 is an ongoing three-year, randomized, double-blind trial designed to compare the efficacy and safety of a treatment regimen of Viread, lamivudine (3TC) and efavirenz to a regimen of stavudine, lamivudine and efavirenz in 600 antiretroviral-naive patients with HIV infection. The 96-week data were presented today (Abstract #564b) at the 10th Conference on Retroviruses and Opportunistic Infections in Boston, Massachusetts.

"These data are impressive because efficacy remains strong in both arms at 96 weeks, but the Viread-containing arm has a side effect profile that has continued to improve compared to stavudine since the 48-week point," said Schlomo Staszewski, MD, University Hospital, J.W. Goethe-Universitat, Frankfurt, Germany and a lead investigator for the study. "The potential for long-term efficacy with reduced side effects compared to stavudine makes Viread an attractive antiretroviral for use in HIV therapy."

Study Results

The 96-week results presented today show that the Viread and stavudine arms reduced HIV RNA to less than 400 copies/mL in 82 and 78 percent of patients respectively, using the most conservative "missing equals failure" analysis. Seventy-eight and 74 percent of patients achieved HIV RNA less than 50 copies/mL. Excluding missing data, 96 and 93 percent of patients in the Viread and stavudine arms achieved HIV RNA less than 400 copies/mL and 92 and 88 percent of patients achieved HIV RNA less than 50 copies/mL. Patients in both arms of the study experienced substantial increases in mean CD4 cell counts, from the baseline mean of 276 to 537 cells/mm3 in the Viread arm and from the baseline mean of 283 to 549 cells/mm3 in the stavudine arm. Grade 3 and 4 adverse events and laboratory abnormalities were similar across treatment groups. Grade 3 and 4 adverse events were reported in less than two percent of patients and included rash, bacterial infection, depression, fever and pneumonia. There was a low discontinuation rate of approximately 15 percent in both arms.

Lipid levels (triglycerides and cholesterol) measured in the fasting state were significantly different between the Viread and stavudine treatment groups. Patients receiving Viread experienced a mean increase from baseline in triglycerides of 5 mg/dL, whereas patients in the stavudine group experienced an increase of 103 mg/dL (p less than 0.001). Increases in low-density lipoprotein cholesterol (LDL or "bad" cholesterol) were 82 percent higher for patients receiving stavudine, with an increase of 11 mg/dL in the Viread arm and an increase of 20 mg/dL in the stavudine arm (p less than 0.001). Significant differences also were noted in the impact of therapy on high-density lipoprotein cholesterol (HDL or "good" cholesterol), with patients in the Viread treatment group experiencing a mean increase of 9 mg/dL in "good" cholesterol, compared with an increase of 7 mg/dL in the stavudine arm (p=0.03). In addition, 10 percent of patients in the stavudine arm added a lipid-lowering drug during the study compared to two percent in the Viread arm.

Metabolic Changes

The 96-week data from this study further extend the evidence of Viread's favorable metabolic profile for treatment-naive patients observed at 48 weeks. Physician-reported lipodystrophy was observed in one percent of patients receiving Viread, compared with 12 percent of patients receiving stavudine (p less than 0.001). In a separate sub-study of 250 patients, whole-body DEXA scans showed significantly more limb fat in the Viread arm than the stavudine arm at 96 weeks. Loss of limb fat, or peripheral lipoatrophy, is a crucial component of lipodystrophy -- characterized as diverse changes in metabolism and body shape -- which has been associated with long-term administration of some anti-HIV medications.

Additionally, patients in the Viread arm experienced a favorable weight gain of 6.1 pounds from baseline versus 0.8 pounds in the stavudine arm (p=0.002). Weight gain is an important indicator of overall well being for HIV-infected patients.

Patients who received Viread had significantly fewer adverse events associated with mitochondrial toxicity, such as peripheral neuropathy, lactic acidosis and lipodystrophy. After 96 weeks of treatment, the relative risk of these toxicities was 5.5 fold greater (95 percent confidence interval: 3.0-10.3 fold) in the stavudine-containing arm compared with the Viread-containing arm.

"These results add to an expanding body of evidence suggesting that Viread can be broadly effective in suppressing HIV, and also may result in a lower rate of certain adverse side effects associated with other treatment regimens," said John C. Martin, PhD, President and Chief Executive Officer, Gilead Sciences. "As patients and physicians become more aware and justifiably concerned about the impact of cardiovascular problems and metabolic conditions such as lipodystrophy, these data support Viread as an increasingly important treatment option. Avoiding these potentially serious side effects helps ensure patients will be able to continue to benefit from therapy for long periods of time."

Study 903 Continues

Gilead designed Study 903 as a three-year trial to gather a wide variety of data on Viread's efficacy and safety profile in a controlled manner over time. Study 903 is being conducted in the United States, Europe and South America. Twenty-six percent of the study participants are women, and 36 percent are people of color. According to the U.S. Centers for Disease Control, women now account for 30 percent of new HIV infections in the United States, while nearly three-fourths of new HIV infections affect non-Caucasians.

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 85,000 patients have been prescribed Viread as part of combination therapy in the United States alone. 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 four 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.

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 these patients 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 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. 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. 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.

Viread is a registered trademark of Gilead Sciences, Inc.

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.

Note to Editors: In the figure "cells/mm3" mentioned in this release, the "3" should be read superscript.

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