Gilead Sciences Announces Preliminary Results from Phase III Study of Investigational Anti-HIV Agent Tenofovir DF

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Primary Efficacy Endpoint Achieved in Pivotal Study

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Gilead Sciences, Inc. (Nasdaq: GILD) today announced that 24-week data from Study 907 were unblinded and show that treatment of HIV-infected patients with once-daily tenofovir disoproxil fumarate 300 mg (tenofovir DF) is associated with a statistically significant HIV RNA decrease in mean DAVG24 of -0.61 log10 copies/mL compared to -0.03 log10 copies/mL in the placebo group ($p<0.0001$). These preliminary results, which meet the study's primary efficacy endpoint, are from an ongoing 48-week pivotal Phase III clinical trial designed to investigate the safety and efficacy of tenofovir DF when used to intensify a stable background antiretroviral regimen in 552 treatment-experienced patients. Gilead expects to present these data in detail at scientific conferences later this year.

"It is promising to see an investigational agent that offers this level of antiviral effect along with a favorable safety profile in heavily treatment-experienced patients," said clinical investigator Kathleen Squires, M.D., Associate Professor of Medicine, Keck School of Medicine, University of Southern California. "Combined with results from an earlier long-term clinical study, these data suggest that tenofovir DF 300 mg has the potential to offer a much needed new treatment option that has the added benefit of being administered as a simple, one pill, once daily dose."

Study 907 Design
The 48-week study enrolled 552 treatment-experienced patients who had HIV RNA levels of 400-10,000 copies/mL and were receiving stable antiretroviral therapy for at least eight weeks prior to entering the study. Patients were randomized (2:1) to receive tenofovir DF (one pill dosed once daily) or placebo in addition to their existing antiretroviral therapy. After 24 weeks of blinded, placebo-controlled dosing, patients assigned to tenofovir DF or placebo were allowed to receive tenofovir DF for the remainder of the 48-week study period. This multi-center study included sites in Australia, Europe and North America.

At baseline, patients had a mean HIV RNA level of 3.36 log10 copies/mL and a mean CD4 cell count of 427 cells/mm3. Prior to enrollment, patients had received antiretroviral therapy for a mean duration of 5.4 years. Approximately half of all study participants ($n=253$) were randomly assigned to a virology sub-study of this clinical trial. Baseline genotypic analysis of HIV isolates from these patients revealed that 94 percent of patients had evidence of nucleoside reverse transcriptase inhibitor resistance mutations, 58 percent had protease inhibitor resistance mutations and 48 percent had non-nucleoside reverse transcriptase inhibitor resistance mutations. The level of viral resistance seen in this cohort is consistent with the extensive prior treatment experience of this patient population.

Anti-HIV Activity
In addition to DAVG24, a measurement of the average post-baseline change in HIV RNA over 24 weeks, other secondary analyses were performed to measure antiviral activity in Study 907. The mean absolute change in HIV RNA at 24 weeks compared to baseline was -0.59 log10 copies/mL for the tenofovir DF group compared with a -0.01 log10 change in the placebo group ($p<0.0001$). Additionally, 45 percent (155/346) of patients treated with tenofovir DF achieved HIV RNA reductions below 400 copies/mL at 24 weeks compared to 13 percent (23/172) in the placebo group ($p<0.0001$), as determined by the Roche Amplicor® Monitor™ Ultrasensitive Test. Reduction in HIV RNA to less than 50 copies/mL was achieved by 22 percent (76/346) of patients in the tenofovir DF group compared to one percent (2/172) in the placebo group ($p<0.0001$). The DAVG24 for CD4 cells was an increase of 12.6 cells/mm3 in the tenofovir DF group compared with a decrease of 10.6 cells/mm3 in the placebo group ($p=0.0008$).

"These are the toughest patients to treat. After years of anti-HIV therapy, most patients have greater difficulty adhering to and tolerating multi-drug regimens, and as seen in this patient population, these factors often result in viral resistance to currently available drugs," said Dr. Squires. "So, I am impressed that nearly half the patients receiving tenofovir DF 300 mg in this study achieved viral suppression below 400 copies/mL. Not only did patients achieve significant viral load reduction, but the very low drug discontinuation rate clearly indicates to me that tenofovir DF was easy to use and well tolerated in this study."

Safety Results
Through the 24-week, placebo-controlled portion of the trial, the incidence of grade 3 and 4 laboratory abnormalities and clinical adverse events was similar between the placebo and tenofovir DF arms. Additionally, drug discontinuation at 24 weeks was six percent in both the placebo and tenofovir DF arms of the study. Following the 24-week phase of the study, 170 patients who received placebo rolled over to receive treatment with tenofovir DF.

"These data confirm results observed in an earlier 48-week clinical trial of tenofovir DF, and further support the important role we believe this compound will play in the HIV treatment landscape," said John C. Martin, Ph.D., President and CEO of Gilead Sciences. "Based on our growing safety and efficacy database, which now includes more than 1,200 patients who have received tenofovir DF 300 mg, we are confident in our ability to complete regulatory filings in the United States and Europe by mid-year. Now a near-term goal, the registration of this compound will mark a key corporate milestone for Gilead, and most importantly, may offer hope for the many individuals in need of new treatment options."

Tenofovir DF in Treatment-Naïve Patients
To evaluate the potential role of tenofovir DF in treatment-naïve patients, Gilead initiated a Phase III clinical trial (Study 903) in June 2000. This trial is designed to compare the safety and tolerability of two treatment regimens, tenofovir DF, efavirenz and lamivudine (3TC) versus stavudine (d4T), efavirenz and lamivudine. This randomized, double-blind, multi-center, active-controlled trial was fully enrolled in January 2001 with 601 treatment-naíve patients.

Tenofovir DF for HIV/AIDS
Tenofovir DF is an investigational reverse transcriptase inhibitor in Phase III development for the potential treatment of HIV infection. Tenofovir DF is a single pill taken once daily and belongs to a class of drugs called nucleotide analogues. These drugs work by blocking reverse transcriptase, an enzyme crucial to HIV replication. Gilead's preclinical studies have shown that tenofovir DF is eliminated by the kidney, is not metabolized by the liver and is not associated with cytochrome p450 interactions.

Early Access Program Initiated
In January, Gilead announced the initiation of a limited expanded access program to provide tenofovir DF to people with advanced HIV infection in the United States and five countries in the European Union. Regulatory review has been concluded and programs are open for registration in the United States and France. Early access programs will be initiated in Germany, Italy, Spain and the United Kingdom as regulatory approvals are obtained.

For more information regarding the tenofovir DF early access program or to request registration materials, physicians in the United States may call 1-800-GILEAD-5 and those within Europe may call 33-1-44-90-34-46.

Conference Call
Gilead will host a conference call today, February 20, 2001, at 8:30 a.m. (Eastern) to discuss these results. The dial-in numbers for the call are 888-740-8120 (domestic) and 212-231-6036 (international). A replay of this call will be available from 1:00 p.m. February 20, 2001, until 1:00 p.m. February 23, 2001. The replay dial-in numbers are 800-633-8284 (domestic) and 858-812-6440 (international). The password is 18034385.

Gilead Sciences
Gilead Sciences, Inc., 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. Gilead 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; Cambridge, UK, and Dublin, Ireland, and sales and marketing organizations 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, including statements relating to the efficacy, safety and resistance profile of tenofovir DF and the ability to complete regulatory filings by mid-year and achieve marketing approval for tenofovir DF. These statement 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, when available, the 48-week data we obtain from this study and data from other trials may not show the same efficacy, safety and resistance profile that was observed in these preliminary 24-week data, and the risk that unexpected results of ongoing clinical trials and unexpected requests from the FDA for additional data regarding tenofovir DF may delay our ability to file for and obtain marketing approval for tenofovir DF. 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, 1999 and in Gilead's Quarterly Reports on Form 10-Q, all of which are on file with the U.S. Securities and Exchange Commission.

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For more information on Gilead Sciences, please visit the company's Web site at www.gilead.com or call the Gilead Corporate Communications Department at 1-800-GILEAD-5 (1-800-445-3235).