Gilead Sciences Presents 48-Week Viral Resistance Data From Phase II Study of Investigational Anti-HIV Agent, Tenofovir DF

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Data Presented at 5th International Conference on Drug Therapy in HIV Infection

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Gilead Sciences, Inc. (Nasdaq: GILD) today announced 48-week data characterizing the viral resistance profile of tenofovir disoproxil fumarate (tenofovir DF), the company's investigational, once-daily agent for the treatment of HIV infection. These data are from a prospective virology sub-study of a 48-week Phase II clinical trial (Study 902), where tenofovir DF or placebo was added to patients' background antiretroviral regimens. The data indicate that the addition of tenofovir DF resulted in a significant reduction in HIV RNA in treatment-experienced patients with common viral mutations associated with thymidine analog (AZT/d4T) and/or 3TC drug resistance. Additionally, patients treated with tenofovir DF for 48 weeks did not develop viral mutations that led to virological failure.

These data were presented for the first time by Michael Miller, Ph.D., Director of Clinical Virology, Gilead Sciences, in a poster session (Poster #326) at the 5th International Conference on Drug Therapy in HIV Infection in Glasgow, Scotland. Safety and efficacy results from Study 902 also will be presented at the conference by Robert Schooley, MD, Professor and Division Head, Department of Infectious Diseases, University of Colorado on Tuesday, October 24. Dr. Schooley previously reported the safety and efficacy data in September at the 40th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in Toronto, Canada.

"As physicians evaluate potential antiretroviral treatment regimens for their patients, a compound's resistance profile can be an important factor," said Dr. Schooley, an investigator for Study 902. "The 48-week virology data from Study 902 are encouraging because treatment with tenofovir DF does not appear to result in the development of clinically relevant resistance mutations and the drug remains active even in the presence of viral mutations that decrease the activity of other antiretrovirals."

Study Design and Results
Study 902 is a 48-week, double-blind, dose-ranging Phase II clinical trial that enrolled 189 patients who were on a stable antiretroviral regimen for at least eight weeks prior to entering the study. Prior to enrollment, patients had received a mean of 4.6 years of antiretroviral therapy. Patients were randomized to receive one of three doses of tenofovir DF (300 mg, 150 mg or 75 mg) or placebo in addition to their existing antiretroviral treatment regimen. At week 24, all patients receiving placebo were switched to treatment with tenofovir DF 300 mg.

The mean reduction in HIV RNA from baseline for patients receiving the 300 mg dose of tenofovir DF for 48 weeks of treatment was 0.62 log10 copies/mL (n=43). Patients in the 150 mg and 75 mg tenofovir DF arms had mean reductions in viral load of 0.58 log10 copies/mL (n=35) and 0.40 log10 (n=42), respectively. In addition, patients who had received placebo for the first 24 weeks of the study and switched to the 300 mg dose for the second 24 weeks had a mean reduction in HIV RNA of 0.56 log10 at 48 weeks (n=19). Through 48 weeks, there was no difference in the incidence of grade 3 or 4 laboratory abnormalities or clinical adverse events among the three dosage arms of tenofovir DF and the discontinuation rate in the study was similar across all treatment arms. After the 48-week blinded study concluded, 135 patients rolled over into an extension phase, receiving treatment with tenofovir DF 300 mg once daily. As of October 12, 113 of these patients remain on study for a median of 89 weeks.

Virology Sub-Study and Resistance Profile
The virology sub-study of Study 902 was conducted to evaluate the clinical effects of pre-existing nucleoside resistance mutations and the potential development of resistance mutations associated with tenofovir DF therapy.

Baseline genotypic analysis was conducted in 184 patients. This analysis showed that 94 percent of patients had nucleoside-associated reverse transcriptase resistance mutations; 74 percent of patients had thymidine analog (AZT/d4T) mutations, 66 percent had the 3TC-associated M184V mutation and 47 percent had both. For all patients with available samples and sufficient viral load for analysis, post-baseline genotypic analyses were conducted at weeks 24 (n=159) and 48 (n=110).

In Study 902, the response to treatment with 300 mg of tenofovir DF was independent of baseline genotype. Patients expressing

thymidine analog (AZT/d4T), 3TC or both types of resistance mutations showed statistically significant HIV RNA reductions relative to placebo-treated patients at 24 weeks. The antiviral response was durable through 48 weeks of treatment, with no evidence of viral rebound.

Four patients whose regimens contained various doses of tenofovir DF developed the K65R mutation, a reverse transcriptase mutation previously selected by tenofovir in vitro. All four patients were also taking either ddI (n=3) or abacavir (n=1), both of which have been associated with the development of the K65R mutation. There was no evidence of viral rebound in these patients. Additional mutations developed during the study that can be attributed to patients' background regimens. The development of these mutations was not associated with viral rebound and the activity of tenofovir DF was maintained.

"Resistance to currently available antiretrovirals continues to be an obstacle in the effective long-term treatment of HIV infection. As a result, favorable resistance and safety profiles and a convenient dosing schedule to increase compliance have become among the most important attributes considered when evaluating the potential value of investigational treatments to patients and their physicians," said John C. Martin, Ph.D., President and Chief Executive Officer, Gilead Sciences. "We believe that tenofovir DF will provide an important new option that meets these criteria for HIV-treating physicians."

These 48-week virology data from Study 902 are complemented by in vitro studies that have demonstrated that tenofovir shows activity against all common strains of nucleoside-resistant HIV-1, including thymidine analog (AZT/d4T), 3TC or both types of mutations. Based on the growing body of virology data, tenofovir DF appears to achieve significant and durable HIV RNA reductions among antiretroviral-experienced patients who have these common mutations. Additional phenotypic analyses of patient samples from Study 902 are underway, the results of which will be presented at a future scientific conference.

Ongoing Tenofovir DF Phase III Program

To further evaluate the safety and efficacy of tenofovir DF 300 mg in combination with other antiretroviral agents for the treatment of HIV infection, Gilead initiated Phase III clinical testing with Study 907 in November 1999 and completed enrollment in this study in June 2000. Conducted in the United States, Europe and Australia, Study 907 is an intensification study in antiretroviral treatment-experienced patients.

Gilead recently initiated a second Phase III trial, Study 903, to evaluate tenofovir DF as a potential therapy for treatment-naive patients with HIV infection. This 48-week trial is designed to compare a treatment regimen of tenofovir DF, lamivudine (3TC) and efavirenz to a treatment regimen of stavudine (d4T), lamivudine and efavirenz in a blinded fashion in patients who have not previously received antiretroviral treatment. Study 903 is currently enrolling patients in the United States, Europe and South America.

Patients and physicians who would like more information about enrollment in Study 903 may call the AIDS Clinical Trials Information System (ACTIS) at 1-800-TRIALS-A or Gilead Sciences Medical Information at 1-800-GILEAD-5 (1-800-445-3235) or 1-650-574-3000 from outside the United States.

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, 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 the safety, efficacy and resistance data observed in Gilead's Phase II clinical trials and preclinical testing may not be observed in Gilead's more reliable Phase III clinical trials and risks related to regulatory approval of 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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