Gilead's Investigational Antiretroviral Elvitegravir Once Daily Non-Inferior to Raltegravir Twice Daily at 48 Weeks

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-- New Integrase Inhibitor Key Component of Gilead's Investigational "Quad" Single-Tablet Regimen --

ROME, Jul 20, 2011 (BUSINESS WIRE) -- Gilead Sciences, Inc. (Nasdaq:GILD) today announced Phase III clinical trial results from the pivotal Study 145 showing that its investigational antiretroviral elvitegravir, a novel oral integrase inhibitor being evaluated for the treatment of HIV-1 infection, was non-inferior to the integrase inhibitor raltegravir after 48 weeks of therapy in treatment-experienced patients. In the study, elvitegravir (150 mg or 85 mg) dosed once daily was compared to raltegravir (400 mg) dosed twice daily. Each integrase inhibitor was administered with a background regimen that included a ritonavir-boosted protease inhibitor (PI) and a second antiretroviral (ARV). These data are being presented today in a late-breaker session (LB# WELBB05) at the 6th International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention (IAS 2011) in Rome, Italy.

"Because many treatment-experienced HIV patients have developed resistance to currently available antiretrovirals, identifying novel therapeutic options from the integrase inhibitor class is critical," said Professor Jean-Michel Molina, MD, PhD, principal investigator, Hôpital Saint Louis in Paris and University of Paris 7. "These data suggest that elvitegravir may be an effective option for patients and may also have the potential for more convenient, once-daily dosing as part of combination HIV therapy."

At 48 weeks of treatment in Study 145, 59 percent of patients receiving ritonavir-boosted elvitegravir achieved and maintained HIV RNA levels (viral load) of less than 50 copies/mL, compared to 58 percent of patients receiving raltegravir, based on the Time to Loss of Virologic Response algorithm (TLOVR). Discontinuation rates due to adverse events, and safety and resistance profiles were comparable in both arms of the study.

"These data are an important component of the regulatory filings for elvitegravir as both a stand-alone product and as part of the Quad single-tablet regimen in the United States and Europe in 2012," said Norbert Bischofberger, PhD, Executive Vice President, Research and Development and Chief Scientific Officer, Gilead Sciences. "We believe elvitegravir, cobicistat and the Quad have the potential to be important new components of HIV therapy."

Gilead's investigational fixed-dose, single-tablet Quad regimen, which is currently in two Phase III studies, contains four Gilead compounds in a single pill: elvitegravir; cobicistat, an investigational pharmacoenhancing or "boosting" agent that increases blood levels of certain HIV medicines; Viread$^{(R)}$ (tenofovir disoproxil fumarate); and Emtriva$^{(R)}$ (emtricitabine). Phase III study results are expected in the third quarter of this year.

About the Elvitegravir Phase III Study

Study 145 is a double-blind, multicenter, randomized (1:1), active-controlled 96-week clinical trial evaluating the non-inferiority of ritonavir-boosted elvitegravir (n=351) versus raltegravir (n=351), each administered with a background regimen in HIV-infected treatment-experienced adults with HIV RNA (viral load) of greater than or equal to 1,000 copies/mL. Patients enrolled in the trial were required to have documented viral resistance and/or at least six months of treatment experience with two or more different classes of ARVs prior to screening.

Trial participants received either once-daily elvitegravir 150 mg or 85 mg or twice-daily raltegravir 400 mg. Patients' background regimens were based on the results of resistance testing and included a fully-active ritonavir-boosted PI, and a second investigator-selected agent that was permitted to be a nucleoside or nucleotide reverse transcriptase inhibitor (NRTI), etravirine, maraviroc or enfuvirtide. The most common background regimen was Viread and ritonavir-boosted darunavir in 24 percent of patients. Due to known pharmacokinetic interactions, patients randomized to elvitegravir whose background PI was either atazanavir or lopinavir received an 85 mg dose of elvitegravir.

At baseline, the mean HIV RNA for the intent-to-treat (ITT) population (702 patients) was 4.26 $\log_{10}$ copies/mL and the mean CD4 cell count was 262 cells/mm^3. Twenty-six percent of patients had HIV RNA greater than 100,000 copies/mL, and 45 percent of patients had CD4 cell counts less than or equal to 200 cells/mm^3. The percentage of patients with baseline resistance to two or more ARV classes was 62 percent. The mean age of the study population was 45, and 82 percent were male.

After 48 weeks of treatment, 59 percent of elvitegravir patients compared to 58 percent of raltegravir patients achieved and maintained a viral load of less than 50 copies/mL using the TLOVR algorithm (ITT population; non-inferiority p=0.001; 95% CI, -6.0% to +8.2%). Patients receiving elvitegravir experienced a similar mean increase in CD4 cell counts from baseline at week 48 compared to those receiving raltegravir (138 vs. 147 cells/mm^3, respectively).

Nine patients (3 percent) receiving elvitegravir and 15 patients (4 percent) receiving raltegravir discontinued treatment due to adverse events. The Grade 2-4 adverse events occurring in greater than or equal to 3 percent of patients in either treatment arm were diarrhea, upper respiratory tract infection, bronchitis, back pain, depression, sinusitis, arthralgia, nausea and urinary tract infection. The incidence of these adverse events was similar in both treatment arms, with the exception of diarrhea which occurred in 12 percent of patients in the elvitegravir arm and 7 percent of patients in the raltegravir arm. The Grade 3 or 4 serum laboratory abnormalities occurring in greater than 5 patients in either treatment arm were amylase, total bilirubin, cholesterol, triglycerides, hyperglycemia, GGT, neutrophils, creatine kinase, ALT and AST. The incidence of these laboratory abnormalities was similar in the elvitegravir-treated and the raltegravir-treated arms, with the exception of GGT (3 and 6 percent, respectively), ALT (2 and 5 percent, respectively) and AST (1 and 5 percent, respectively), which were higher in the raltegravir-treated arm.

Drug resistance rates were also similar in both study arms. In the elvitegravir arm, 16 of the 60 patients who experienced virologic failure exhibited integrase resistance, while 15 of the 72 patients who experienced virologic failure in the raltegravir arm exhibited integrase resistance.

On January 10, 2011, Gilead announced an amendment to the design of Study 145, extending the blinded, randomized period of the study from the originally planned 48 weeks to 96 weeks in order to obtain longer-term safety and efficacy data. Based on the achievement of the non-inferiority endpoint, patients will continue to receive the regimen to which they were randomized in a blinded fashion. Secondary endpoints include various additional measures of the efficacy, safety and tolerability of the two treatment regimens.

Additional information about the study can be found at http://www.clinicaltrials.gov.

Elvitegravir, cobicistat and the Quad are investigational products and have not yet been determined safe or efficacious in humans.

About Elvitegravir

Elvitegravir is an HIV integrase inhibitor. Unlike other classes of ARVs, integrase inhibitors interfere with HIV replication by blocking the ability of the virus to integrate into the genetic material of human cells. Elvitegravir was licensed by Gilead from Japan Tobacco Inc. (JT) in March 2005. Under the terms of Gilead's agreement with JT, Gilead has exclusive rights to develop and commercialize elvitegravir in all countries of the world, excluding Japan, where JT retains rights.

About Gilead Sciences

Gilead Sciences is a biopharmaceutical company that discovers, develops and commercializes innovative therapeutics in areas of unmet medical need. The company's mission is to advance the care of patients suffering from life-threatening diseases worldwide. Headquartered in Foster City, California, Gilead has operations in North America, Europe and Asia Pacific.

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, including the risk that Gilead will not complete the Phase III clinical studies of elvitegravir and the Quad in the currently anticipated timelines. In addition, Gilead may obtain unfavorable results from these studies, may need to modify or delay its studies or perform additional trials, and may fail to obtain approvals for these antiretroviral products from the regulatory authorities, and marketing approval, if granted, may have significant limitations on its use. As a result, elvitegravir or the Quad may never be successfully commercialized. Further, Gilead may make a strategic decision to discontinue development of elvitegravir or the Quad if, for example, it believes commercialization will be difficult relative to other opportunities in its pipeline. These risks, uncertainties and other factors could cause actual results to differ materially from those referred to in the forward-looking statements. The reader is cautioned not to rely on these forward-looking statements. These and other risks are described in detail in Gilead's Quarterly Report on Form 10-Q for the quarter ended March 31, 2011, as filed 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.

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