Gilead Initiates Phase III Clinical Program Evaluating Single-Tablet, Once-Daily "Quad" Regimen for HIV

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FOSTER CITY, Calif., Apr 12, 2010 (BUSINESS WIRE) --Gilead Sciences, Inc. (Nasdaq:GILD) today announced that it has dosed the first patient in the Phase III clinical program evaluating its investigational fixed-dose, single-tablet "Quad" regimen of elvitegravir, cobicistat (formerly GS 9350), emtricitabine and tenofovir disoproxil fumarate. The Phase III clinical program for the Quad includes two studies (Studies 102 and 103) that will evaluate the Quad regimen versus a standard of care among HIV-1 infected antiretroviral treatment-naïve adults.

"We are pleased to announce that the Quad Phase III clinical program is underway," said Norbert Bischofberger, PhD, Executive Vice President, Research and Development and Chief Scientific Officer, Gilead Sciences. "Efficacy and safety results from the Phase II study suggest that the Quad may represent an important new option for patients with HIV. We look forward to further defining the clinical profile of the Quad in a larger number of patients in the Phase III trials."

Gilead is also examining cobicistat as a stand-alone boosting agent for other antiretrovirals, in particular protease inhibitors. Later this quarter, Gilead plans to initiate a Phase III clinical trial evaluating the efficacy, safety and tolerability of cobicistat-boosted atazanavir compared to ritonavir-boosted atazanavir, each in combination with Truvada$^{(R)}$ (emtricitabine and tenofovir disoproxil fumarate).

Study Design

Study 102 is a randomized, double-blind clinical trial that will compare the efficacy, safety and tolerability of the Quad versus Atripla$^{(R)}$ (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) over a 96-week period at 130 study sites in the United States and Puerto Rico. Eligible participants will be HIV-infected treatment-naïve adults with HIV RNA levels greater than or equal to 5,000 copies/mL. Approximately 700 trial participants will be randomized (1:1) to receive a once-daily tablet containing elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg (n=350) or Atripla (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) (n=350).

Study 103 is a randomized, double-blind clinical trial that will compare the efficacy, safety and tolerability of the Quad versus ritonavir-boosted atazanavir and Truvadaover a 96-week period at more than 200 study sites in North America, South America, Europe and Asia Pacific. Eligible participants will be HIV-infected treatment-naïve adults with HIV RNA levels greater than or equal to 5,000 copies/mL. Approximately 700 trial participants will be randomized (1:1) to receive a once-daily tablet containing elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg (n=350) or ritonavir 100 mg and atazanavir 300 mg and emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg (n=350).

The primary endpoint of both trials will be the proportion of patients achieving HIV RNA levels of less than 50 copies/mL at 48 weeks of treatment. Secondary objectives will evaluate the efficacy, safety and tolerability of the treatment regimens through 96 weeks of treatment.

After week 96, subjects will continue to take their blinded study drug until treatment assignments have been unblinded, at which point all subjects will be given the option to participate in an open-label rollover extension and receive the Quad single-tablet regimen.

About Elvitegravir

Elvitegravir is an HIV integrase inhibitor. Unlike other classes of antiretroviral agents, 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 Cobicistat

Cobicistat is Gilead's proprietary potent mechanism-based inhibitor of cytochrome P450 3A (CYP3A), an enzyme that metabolizes drugs in the body. In addition to studying the agent as part of an integrase-based fixed-dose regimen, Gilead is also examining cobicistat's potential stand-alone role in boosting commercially available HIV protease inhibitors, which are used in many HIV treatment regimens.

The fixed-dose single-tablet "Quad" regimen, elvitegravir and cobicistat are investigational products and have not yet been determined safe or efficacious in humans.

Important Product Safety Information About Truvada and Atripla

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 including Viread (tenofovir disoproxil fumarate), a component of Atripla and Truvada. Atripla and Truvada are not approved for the treatment of chronic hepatitis B virus (HBV) infection and their safety and efficacy have not been established in patients co-infected with HBV and HIV-1. Severe acute exacerbations of hepatitis B have been reported in patients co-infected with HIV-1 and HBV who have discontinued Atripla or Truvada.Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who are co-infected with HBV and HIV-1 and discontinue Atripla or Truvada. If appropriate, initiation of anti-hepatitis B treatment may be warranted.

It is important for patients to be aware that anti-HIV medicines including **Atripla and Truvada** do not cure HIV infection or AIDS and do not reduce the risk of transmitting HIV to others.

Additional Important Information About Truvada

Truvada is a fixed-dose combination tablet containing 200 mg of emtricitabine (Emtriva) and 300 mg of tenofovir disoproxil fumarate (Viread). In the United States, Truvada is indicated in combination with other antiretroviral agents (such as non-nucleoside reverse transcriptase inhibitors or protease inhibitors) for the treatment of HIV-1 infection in adults.

Truvada should not be coadministered with Atripla, Emtriva, Viread or lamivudine-containing products, including Combivir(R) (lamivudine/zidovudine), Epivir(R) or Epivir-HBV(R) (lamivudine), Epzicom(R) (abacavir sulfate/lamivudine) or Trizivir(R) (abacavir sulfate/lamivudine/zidovudine). In treatment-experienced patients, the use of Truvada should be guided by laboratory testing and treatment history.

Emtricitabine and tenofovir are principally eliminated by the kidneys. Renal impairment, including cases of acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), has been reported in association with the use of Viread. It is recommended that creatinine clearance be calculated in all patients prior to initiating therapy with Truvada and as clinically appropriate during therapy. Routine monitoring of calculated creatinine clearance and serum phosphorous should be performed in patients at risk for renal impairment including patients who have previously experienced renal events while receiving Hepsera(R) (adefovir dipivoxil). Dosing interval adjustment and close monitoring of renal function are recommended in all patients with creatinine clearance 30-49 ml/min. Truvada should be avoided with concurrent or recent use of a nephrotoxic agent. Truvada should not be administered with Hepsera.

Coadministration of Truvada and didanosine should be undertaken with caution. Patients should be monitored closely for didanosine-associated adverse events and didanosine should be discontinued if these occur. Dose reduction of didanosine should be considered, if warranted. Patients on atazanavir and lopinavir/ritonavir plus Truvada should be monitored for Truvada-associated adverse events and Truvada should be discontinued if these occur. When co-administered with

Truvada, it is recommended that atazanavir be boosted with ritonavir 100 mg. Atazanavir without ritonavir should not be co-administered with Truvada.

Decreases in bone mineral density (BMD) at the lumbar spine and hip have been seen with the use of Viread. The effect on long-term bone health and future fracture risk is unknown. BMD monitoring should be considered in patients with a history of pathologic fractures or who are at risk for osteopenia. Cases of osteomalacia (associated with proximal renal tubulopathy and which may contribute to fractures) have been reported in association with the use of Viread.

Changes in body fat have been observed in patients taking anti-HIV medicines. Immune Reconstitution Syndrome has been reported in patients treated with combination therapy, including Viread and Emtriva, and may necessitate further evaluation and treatment.

Most common adverse reactions (incidence greater-than or equal to 10 percent) are diarrhea, nausea, fatigue, headache, dizziness, depression, insomnia, abnormal dreams, and rash.

The parent compound of Viread was discovered through a collaborative research effort between Dr. Antonin Holy, Institute for Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic (IOCB) in Prague and Dr. Erik DeClercq, Rega Institute for Medical Research, Katholic University in Leuven, Belgium. The inventors of Viread have agreed to waive their right to a royalty on sales of Viread and Truvada in the Gilead Access Program countries to ensure the product can be offered at a no-profit price in parts of the world where the epidemic has hit the hardest.

For complete prescribing information for Truvada, visit www.Truvada.com.

Additional Important Information About Atripla

In the United States, Atripla is indicated for use alone as a complete regimen or in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults.

Atripla contains the components of Truvada (emtricitabine and tenofovir disoproxil fumarate) and Sustiva (efavirenz), co-formulated as a single tablet. As such, the important safety information appearing in the above Truvada section also applies to Atripla, in addition to the following important product information.

As a fixed-dose regimen of Viread (tenofovir disoproxil fumarate), Emtriva (emtricitabine) and Sustiva (efavirenz), Atripla should not be coadministered with Viread, Emtriva, Truvada (emtricitabine and tenofovir disoproxil fumarate) or Sustiva. Due to similarities between Emtriva and lamivudine, Atripla should not be coadministered with drugs containing lamivudine, including Combivir(R) (lamivudine/zidovudine), Epivir(R) or Epivir-HBV(R) (lamivudine), Epzicom(R) (abacavir sulfate/lamivudine) or Trizivir(R) (abacavir sulfate/lamivudine/zidovudine).

Atripla should not be taken with bepridil, cisapride, midazolam, pimozide, triazolam, or ergot derivatives due to a contraindication with efavirenz. Use of Atripla with voriconazole, St. John's wort (Hypericum perforatum) or St. John's wort-containing products is not recommended. Use of Atripla with atazanavir or atazanavir/ritonavir is not recommended.

Atripla should not be given to patients with creatinine clearance less than 50 ml/min.

Serious psychiatric adverse experiences, including severe depression (2.4 percent), suicidal ideation (0.7 percent), nonfatal suicide attempts (0.5 percent), aggressive behavior (0.4 percent), paranoid reactions (0.4 percent) and manic reactions (0.2 percent) have been reported in patients treated with efavirenz, a component of Atripla. In addition to efavirenz, factors identified in a clinical study that were associated with an increase in psychiatric symptoms included a history of injection drug use, psychiatric history and use of psychiatric medication. There have been occasional reports of death by suicide, delusions, and psychosis-like behavior, but it could not be determined if efavirenz was the cause. Patients with serious psychiatric adverse experiences should be evaluated immediately to determine whether the risks of continued therapy outweigh the benefits. Patients should tell their doctor if they have a history of mental illness or are using drugs or alcohol.

Fifty-three percent of patients in clinical studies have reported central nervous system symptoms including dizziness (28.1 percent), insomnia (16.3 percent), impaired concentration (8.3 percent), somnolence (7.0 percent), abnormal dreams (6.2 percent) and hallucinations (1.2 percent) when taking efavirenz compared to 25 percent of patients receiving control regimens. These symptoms usually begin during the first or second day of therapy and generally resolve after the first two to four weeks of therapy. After four weeks of therapy, the prevalence of central nervous system symptoms of at least moderate severity ranged from 5 to 9 percent in patients treated with regimens containing efavirenz. Nervous system symptoms are not predictive of the less frequent psychiatric symptoms.

Women should not become pregnant or breastfeed while taking Atripla. Serious birth defects have been seen in children of women treated with efavirenz during pregnancy. Women must use a reliable form of barrier contraception, such as a condom, for 12 weeks after discontinuation of Atripla even if they also use other methods of birth control.

Rash is a common side effect that usually goes away without any change in treatment. Rash may be a serious problem in some patients.

In patients with known or suspected history of hepatitis B or C and in patients treated with other medications associated with liver toxicity, monitoring of liver enzymes is recommended.

Atripla should be used with caution in patients with a history of seizures. Convulsions have been observed in patients receiving efavirenz, generally in the presence of a known medical history of seizures.

Invirase(R) (saquinavir) should not be used as the only protease inhibitor in combination with Atripla.

The most significant adverse events observed in patients treated with Sustiva are nervous system symptoms, psychiatric symptoms and rash. The most common adverse events (at least 5 percent) observed in clinical studies with Sustiva include fatigue, pain, dizziness, headache, insomnia, impaired concentration, nausea, vomiting, diarrhea, depression, rash and pruritus.

For complete prescribing information for Atripla, visit www.Atripla.com.

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 Australia.

Forward-Looking Statement

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 risks related to Gilead's ability to complete enrollment of the Phase III clinical trials for the Quad and to initiate the Phase III clinical trial of cobicistat in the timeline currently anticipated. In addition, we may face challenges in clinical trial protocol design, there may be unfavorable results of the ongoing or any further clinical trials of the Quad or cobicistat, and Gilead may need to modify or delay such clinical trials. Gilead may ultimately be unable to obtain the U.S. Food and Drug Administration and other regulatory body approvals, and as a result, the Quad or cobicistat may never be successfully commercialized. Further, Gilead may make a strategic decision to discontinue development of the Quad or cobicistat 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. Gilead directs readers to its Annual Report on Form 10-K for the year ended December 31, 2009. Gilead claims the protection of the Safe Harbor contained in the Private Securities Litigation Reform Act of 1995 for forward-looking statements. All forward-looking statements are based on information currently available to Gilead, and

Gilead assumes no obligation to update any such forward-looking statements.

U.S. full prescribing information for Truvada is available at www.Truvada.com.

U.S. full prescribing information for Atripla is available at www.Atripla.com.

U.S. full prescribing information for Viread is available at www.Viread.com.

U.S. full prescribing information for Emtriva is available at www.GileadHIV.com.

U.S. full prescribing information for Hepsera is available at www.Hepsera.com.

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For more information on Gilead Sciences, please visit the company's website at www.gilead.com or call Gilead Public Affairs at 1-800-GILEAD-5 or 1-650-574-3000.

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