144-Week Data from Gilead's Study 934 Comparing Truvada(R) to Combivir(R) Both in Combination with Sustiva(R) Presented At International AIDS Society Meeting in Sydney

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SYDNEY, Australia--(BUSINESS WIRE)--July 23, 2007--Gilead Sciences, Inc. (Nasdaq:GILD) today announced the presentation of 144-week data from an ongoing clinical trial, Study 934, comparing a once-daily regimen of Truvada(R) (emtricitabine and tenofovir disoproxil fumarate) and Sustiva(R) (efavirenz) to a twice-daily regimen of Combivir(R) (lamivudine/zidovudine) with Sustiva once daily in treatment-naive adults with HIV. Data were presented by Jose Arribas, MD, of the University Hospital La Paz, Madrid, Spain at the 4th International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention taking place July 22-25 in Sydney, Australia (Poster #WEPEB029).

Study 934 is an ongoing Phase III, open-label clinical trial in the United States and Europe. Truvada is a fixed-dose once-daily tablet containing Gilead's Viread(R) (tenofovir disoproxil fumarate) and Emtriva(R) (emtricitabine). At study initiation, patients received Viread and Emtriva with Sustiva. At week 96, which coincided with commercial availability of Truvada in the United States, all patients receiving Viread, Emtriva and Sustiva were switched to receive a simplified regimen of Truvada and Sustiva. Truvada is currently the most commonly prescribed nucleoside backbone for combination HIV therapy in the United States.

Truvada and Sustiva are also available in the United States as the fixed-dose product Atripla(TM) (efavirenz 600 mg/ emtricitabine 200 mg/ tenofovir disoproxil fumarate 300 mg), through a U.S. joint venture between Bristol-Myers Squibb Company and Gilead Sciences. Atripla was approved in the United States on July 12, 2006.

"These data demonstrate the safety and efficacy profile of the components of Atripla over three years," commented Dr. Arribas. "As the treatment landscape for HIV improves and patients live longer, the importance of a proven and durable first-line regimen with simple dosing is critical."

Study 934 Results

Study 934 is a Phase III, open-label, non-inferiority study that enrolled 517 HIV-infected patients in the United States and Europe. Two patients were protocol violations and six never received drug, resulting in an intent to treat population of 509 patients. The study's primary endpoint was at 48 weeks and the study has continued through 144 weeks. Twenty-two patients with baseline non-nucleoside reverse transcriptase inhibitor (NNRTI) mutations and 31 patients who completed week 48 and week 96 of the study with HIV RNA (viral load) less than 400 copies/mL but did not consent to participate after week 96 were excluded from the week 144 efficacy population. Participants were originally randomized to receive Viread 300 mg, Emtriva 200 mg and Sustiva 600 mg, all dosed once daily, or Combivir twice daily and Sustiva 600 mg once daily. At study entry, patients were treatment-naive, had HIV RNA greater than 10,000 copies/mL and any CD4 cell count. At week 96, patients receiving Viread, Emtriva and Sustiva were switched to a regimen of Truvada/Sustiva.

After 144 weeks of treatment, 71 percent of Truvada/Sustiva patients compared to 58 percent of Combivir/Sustiva patients achieved and maintained viral load less than 400 copies/mL using the Time to Loss of Virologic Response algorithm (TLOVR) (n=456, p=0.004; 95% CI, +4.2% to +21.6%). Sixty-four percent of patients in the Truvada/Sustiva arm compared to 56 percent of patients in the Combivir/Sustiva arm achieved and maintained viral load less than 50 copies/mL using TLOVR (n=458, p=0.08; 95% CI, -0.8% to +17%). The mean increase from baseline in CD4 cell counts at week 144 was 312 and 271 cells/mm(3) in the Truvada/Sustiva and Combivir/Sustiva arms, respectively (p=0.09).

Genotypic resistance analyses were performed on patients without pre-existing baseline NNRTI resistance mutations who either had confirmed plasma HIV RNA greater than 400 copies/mL or discontinued study drug early. Through 144 weeks, no patients in either arm of the study developed the K65R mutation, which is associated with reduced susceptibility to Viread. Fewer Truvada/Sustiva patients developed the M184V/I mutation, which is associated with

resistance to Emtriva and to the lamivudine component of Combivir (2 vs. 10 patients; p=0.02).

After 144 weeks of treatment, a significantly greater percentage of patients in the Combivir/Sustiva group experienced adverse events that resulted in discontinuation of study medications compared to the Truvada/Sustiva arm (11 vs. 5 percent, respectively; p=0.01). The most common cause of discontinuation in the Combivir/Sustiva arm was anemia/hemoglobin decrease (14 vs. 0 patients in the Truvada/Sustiva arm), and in the Truvada/Sustiva arm was rash (4 patients vs. 1 patient in the Combivir/Sustiva arm).

Renal adverse events were uncommon at 144 weeks, consistent with study data at weeks 48 and 96. No patient discontinued study medication due to renal events.

After 144 weeks of treatment, patients in the Combivir/Sustiva arm experienced greater mean elevations from baseline in fasting total cholesterol levels (36 vs. 24 mg/dL in the Truvada/Sustiva arm; p=0.005) and greater mean increases from baseline in fasting triglycerides (36 vs. 4 mg/dL in the Truvada/Sustiva arm; p=0.047).

Loss of limb fat, a marker for lipodystrophy, was observed among patients receiving Combivir/Sustiva. Among 269 patients with available data, median total limb fat was significantly less in patients receiving Combivir/Sustiva compared to patients receiving Truvada/Sustiva (5.4 vs 7.9 kg; p less than 0.001) at week 144. Among patients with data available at 48 and 144 weeks, median total limb fat decreased significantly in the Combivir/Sustiva arm (from 6.0 kg to 4.9 kg; n=49, 38) and increased significantly in the Truvada/Sustiva arm (from 7.4 kg to 8.3 kg; n=51, 48).

Data from this analysis have not been reviewed by the U.S. Food and Drug Administration.

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. Truvada and Atripla 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. Severe acute exacerbations of hepatitis B have been reported in patients who have discontinued Viread or Emtriva, which are components of Truvada and Atripla. In some of these patients treated with Emtriva, the exacerbations of hepatitis B were associated with liver decompensation and liver failure. 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 HIV and HBV and discontinue Truvada or Atripla. If appropriate, initiation of anti-hepatitis B treatment may be warranted.

It is important for patients to be aware that anti-HIV medicines including Truvada and Atripla 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.

It is not recommended that Truvada be used as a component of a triple nucleoside regimen. Truvada should not be coadministered with Atripla, Emtriva, Viread or lamivudine-containing products, including Combivir (lamivudine/zidovudine), Epivir(R) or Epivir-HBV(R) (lamivudine), Epzicom(TM) (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, a component of Truvada. 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. 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.

No drug interaction studies have been conducted using Truvada. 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. 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 given 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. Cases of osteomalacia (associated with proximal renal tubulopathy) have been reported in association with the use of Viread.

Changes in body fat have been observed in patients taking anti-HIV medicines. The mechanism and long-term health effect of these conditions are unknown. Immune Reconstitution Syndrome has been reported in patients treated with combination therapy, including Viread and Emtriva.

Adverse events observed with Viread and Emtriva used in combination in Study 934 were generally consistent with those seen in other studies in treatment-experienced or treatment-naive patients receiving Viread and/or Emtriva. Treatment-emergent adverse events occurring in at least 3 percent of patients receiving Viread and Emtriva in Study 934 included dizziness (8%), diarrhea (7%), nausea (8%), fatigue (7%), sinusitis (4%), upper respiratory tract infections (3%), nasopharyngitis (3%), somnolence (3%), headache (5%), dizziness (8%), depression (4%), insomnia (4%), abnormal dreams (4%) and rash (5%).

Skin discoloration has been reported with higher frequency among Emtriva-treated patients. Skin discoloration, manifested by hyperpigmentation on the palms and/or soles was generally mild and asymptomatic. The mechanism and clinical significance are unknown.

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 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 (lamivudine/zidovudine), Epivir(R) or Epivir-HBV(R) (lamivudine), Epzicom(TM) (abacavir sulfate/lamivudine) or Trizivir(R) (abacavir sulfate/lamivudine/zidovudine).

Atripla should not be taken with Hismanal(R) (astemizole), Vascor(R) (bepridil), Propulsid(R) (cisapride), Versed(R) (midazolam), Orap(R) (pimozide), Halcion(R) (triazolam), ergot medicines (for example, Wigraine(R) and Cafergot(R)), or Vfend(R) (voriconazole) due to a contraindication with efavirenz. Use of Atripla with St. John's wort (Hypericum perforatum) or St. John's wort-containing products is not recommended. This list of medicines is not complete. Patients should discuss all prescription and non-prescription medicines, vitamin and herbal supplements, or other health preparations they are taking or plan to take with their healthcare provider.

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, 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 children.

Patients with liver disease may require the healthcare provider to check liver function or check drug levels in the blood.

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. Visit Gilead on the World Wide Web at www.gilead.com.

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

Full U.S. prescribing information for Truvada, Viread and Emtriva is available at www.gilead.com.

Full U.S. prescribing information for Sustiva is available at www.bms.com.

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