Gilead's Once-Daily Single Tablet Regimen Stribild™ Maintains High Viral Suppression Through Two Years of Therapy Among Treatment-Naïve HIV Patients

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-- Pivotal Data from Two Phase 3 Studies Highlight Stribild's Sustained Efficacy, Safety and Tolerability Profile --

GLASGOW, England--(BUSINESS WIRE)--Nov. 15, 2012-- Gilead Sciences (Nasdaq:GILD) today announced two-year (96-week) results from two pivotal Phase 3 studies (Studies 102 and 103) evaluating the company's newest single tablet HIV regimen, Stribild™ (elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg), among treatment-naïve patients with HIV-1 infection. Data show that Stribild was non-inferior after two years of treatment to two standard of care HIV regimens, Atripla® (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) in Study 102 and a protease-based regimen of ritonavir-boosted atazanavir plus Truvada® (emtricitabine and tenofovir disoproxil fumarate) in Study 103. These results were presented today in an oral session at the 11th International Congress on Drug Therapy in HIV Infection (HIV11) in Glasgow, United Kingdom.

"In these studies, Stribild demonstrated a robust clinical profile, including sustained efficacy, safety and resistance results over two years of treatment," said Jürgen Rockstroh, MD, Professor of Medicine, University of Bonn, Germany and a lead investigator for Study 103. "Stribild was also associated with a lower incidence of certain central nervous system side effects compared to Atripla, and had a favorable triglycerides profile versus the atazanavir-based regimen."

Stribild combines four compounds in one daily tablet: elvitegravir, an integrase inhibitor; cobicistat, a pharmacoenhancing agent; emtricitabine and tenofovir disoproxil fumarate. The regimen was approved by the U.S. Food and Drug Administration (FDA) on August 27, 2012 for use by treatment-naïve HIV-positive adults based on 48-week results from Studies 102 and 103. A marketing application for Stribild is currently under review in the European Union.

Study 102 found that at 96 weeks of treatment, 84 percent of Stribild patients (n=293/348) and 82 percent of Atripla patients (n=287/352) achieved HIV RNA (viral load) < 50 copies/mL, based on the FDA snapshot algorithm (95 percent CI for the difference: -2.9 to +8.3 percent for Stribild vs. Atripla; predefined criterion for non-inferiority was a lower bound of a two sided 95 percent CI of -12 percent).

Similarly, results from Study 103 show that 83 percent of Stribild patients (n=294/353) and 82 percent of patients receiving the atazanavir-based regimen (n=292/355) achieved HIV RNA < 50 copies/mL, based on the FDA snapshot algorithm (95 percent CI for the difference: -4.5 to +6.7 percent for Stribild vs. the atazanavir-based regimen; predefined criterion for non-inferiority was a lower bound of a two sided 95 percent CI of -12 percent).

In both Studies 102 and 103, rates of discontinuation due to adverse events were similar across all treatment groups (5 percent for Stribild in each study, 7 percent for Atripla and 6 percent for the atazanavir-based regimen). The most common adverse events occurring in at least 10 percent of Stribild patients in Study 102 were diarrhea, nausea, upper respiratory infection, headache, abnormal dreams, fatigue, depression and insomnia; in Study 103, they were diarrhea, nausea, upper respiratory infection, headache, nasopharyngitis, depression, back pain and fatigue. In Study 102, there were consistently higher reports at each study visit through 96 weeks of abnormal dreams and dizziness in the Atripla arm, with 14 percent and 4 percent of patients experiencing abnormal dreams and dizziness, respectively, on the Atripla arm vs. 8 percent and 1 percent, respectively on the Stribild arm at 96 weeks. Similarly, in Study 103, reports of diarrhea were consistently higher through 96 weeks of treatment on the atazanavir-based arm compared to Stribild, with 4 percent of Stribild patients vs. 9 percent of patients on an atazanavir-based regimen experiencing this problem at 96 weeks.

The frequency of Grade 3-4 adverse events and laboratory abnormalities was also comparable between study regimens. However, in Study 102, patients taking Stribild experienced lower rates of neuropsychiatric side effects (Grades 1-4) through 96 weeks compared to Atripla patients, including abnormal dreams (15 percent for Stribild vs. 28 percent for Atripla), dizziness (8 percent vs. 25 percent) and insomnia (11 percent vs. 16 percent). Patients taking Stribild also experienced lower increases in total cholesterol and LDL (low-density lipoprotein or "bad" cholesterol) compared to Atripla, and in Study 103, experienced significantly smaller increases in triglycerides compared to those taking the atazanavir-based regimen. Additionally, through week 96, reports of Grade 3-4 hyperbilirubinemia were lower in the Stribild arm compared to the atazanavir-based arm (0.6 percent

vs. 65 percent).

In September 2012, Stribild was added to U.S. Department of Health and Human Services (DHHS) guidelines as an “alternative” treatment regimen for patients new to HIV therapy. Atripla and ritonavir-boosted atazanavir plus Truvada are both listed as “preferred” first-line regimens in the guidelines. Stribild has a Boxed Warning of lactic acidosis/severe hepatomegaly with steatosis and post treatment acute exacerbation of hepatitis B; see below for important safety information.

Gilead recently initiated WAVES, a Phase 3b study evaluating Stribild compared to ritonavir-boosted atazanavir plus Truvada among more than 500 HIV-positive treatment-naïve women. Additional studies examining the efficacy and safety of switching treatment-experienced virologically suppressed patients to Stribild are also underway.

Study 102

Study 102 is a randomized (1:1), double-blind Phase 3 clinical trial comparing the efficacy, safety and tolerability of Stribild (elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) (n=348) versus Atripla (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) (n=352) among HIV-infected treatment-naïve adults with HIV RNA levels greater than or equal to 5,000 copies/mL. The primary endpoint of the study is the proportion of patients achieving HIV RNA levels < 50 copies/mL at 48 weeks of treatment, per the FDA snapshot algorithm. Secondary objectives will evaluate the efficacy, safety and tolerability of the treatment regimens through 192 weeks of treatment.

At baseline, patients in the Stribild arm had a median HIV RNA of 4.75 $\log_{10}$ copies/mL and mean CD4 cell count of 391 cells/mm^3. Patients in the Atripla arm had a median HIV RNA of 4.78 $\log_{10}$ copies/mL and mean CD4 cell count of 382 cells/mm^3. Across both arms, 33 percent of patients had HIV RNA > 100,000 copies/mL, and 13 percent of patients had CD4 counts ≤ 200 cells/mm^3.

At 96 weeks, mean increases in CD4 cell counts were 295 cells/mm^3 for Stribild patients and 273 cells/mm^3 for Atripla patients (p=0.19). Virologic failure rates were 6 percent for Stribild compared to 8 percent for Atripla.

Five percent of Stribild patients and 7 percent of Atripla patients discontinued treatment due to adverse events. The most common adverse events leading to treatment discontinuation among patients taking Stribild were renal events, depression and fatigue. Between 48 and 96 weeks of treatment, two Stribild patients discontinued due to serum creatinine increase without features of proximal renal tubulopathy, and both patients improved after treatment discontinuation.

Median changes from baseline in total cholesterol, HDL (high-density lipoprotein or “good” cholesterol) and LDL at 96 weeks were, respectively, +9, +6 and +9 mg/dL for Stribild and +18, +8 and +16 mg/dL for Atripla (total cholesterol, p<0.001; HDL, p=0.008; LDL, p=0.011). The median change in triglycerides was +4 mg/dL for Stribild and +8 mg/dL for Atripla (p=0.41).

Study 103

Study 103 is a randomized (1:1), double-blind Phase 3 clinical trial comparing the efficacy, safety and tolerability of Stribild (elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) (n=353) versus atazanavir 300 mg boosted by ritonavir 100 mg plus Truvada (emtricitabine and tenofovir disoproxil fumarate) (n=355) among HIV-infected treatment-naïve adults with baseline HIV RNA levels > 5,000 copies/mL. The primary endpoint of the study is the proportion of patients achieving HIV RNA levels < 50 copies/mL at 48 weeks of treatment, per the FDA snapshot algorithm. Secondary objectives will evaluate the efficacy, safety and tolerability of the treatment regimens through 192 weeks of treatment.

At baseline, patients in the Stribild arm had a median HIV RNA of 4.88 $\log_{10}$ copies/mL and mean CD4 cell count of 364 cells/mm^3. Patients in the atazanavir-based arm had a median HIV RNA of 4.86 $\log_{10}$ copies/mL and mean CD4 cell count of 375 cells/mm^3. Across both arms, 41 percent of patients had HIV RNA > 100,000 copies/mL and 13 percent had CD4 counts ≤ to 200 cells/mm^3.

At 96 weeks, patients in both arms experienced similar increases in CD4 cell counts (mean increase of 256 cells/mm^3 for Stribild and 261 cells/ mm^3 for the atazanavir-based regimen). The virologic failure rate was 7 percent for both treatment regimens. Five

percent of Stribild patients and 6 percent of patients on the atazanavir-based regimen discontinued treatment due to adverse events. The most common adverse events leading to treatment discontinuation among patients taking Stribild were renal events, diarrhea, pyrexia, nausea, vomiting and fatigue. Between 48 and 96 weeks of treatment, one Stribild patient and one patient in the atazanavir-based regimen discontinued due to serum creatinine increase without features of proximal renal tubulopathy, and both patients improved after treatment discontinuation.

Ocular icterus (associated with elevated bilirubin levels) was less common among Stribild patients (less than 1 percent) compared to patients taking the atazanavir-based regimen (14 percent).

Median changes from baseline in total cholesterol, HDL and LDL at 96 weeks, were, respectively, +14, +6 and +14 mg/dL for Stribild, and +8, +5 and +11 mg/dL for the atazanavir-based regimen (total cholesterol, p=0.046; HDL, p=0.24; LDL, p=0.32). The median change in triglycerides was +5 mg/dL for Stribild and +16 mg/dL for the atazanavir-based regimen (p=0.012).

Studies 102 and 103 are ongoing in a blinded fashion. After week 192, patients 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 Stribild. Additional information about the study can be found at www.clinicaltrials.gov.

About Stribild

Stribild contains four Gilead compounds in a complete once-daily, single tablet regimen: elvitegravir 150 mg; cobicistat 150 mg; emtricitabine 200 mg; and tenofovir disoproxil fumarate 300 mg. Stribild is indicated in the United States as a complete regimen for the treatment of HIV-1 infection in adults who are antiretroviral treatment-naïve. A Marketing Authorisation Application (MAA) for the regimen was validated for review by the European Medicines Agency (EMA) on December 20, 2011. Stribild does not cure HIV-1 infection.

Elvitegravir is a member of the integrase inhibitor class of antiretroviral compounds. 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. Gilead submitted a New Drug Application (NDA) to FDA for elvitegravir as a standalone agent on June 27, 2012, and the agency has set a target action date under the Prescription Drug User Fee Act (PDUFA) of April 27, 2013. An MAA for elvitegravir in the EU was validated for review by EMA on June 18, 2012.

Cobicistat is Gilead's proprietary potent mechanism-based inhibitor of cytochrome P450 3A (CYP3A), an enzyme that metabolizes drugs in the body. Unlike ritonavir, cobicistat acts only as a pharmacoenhancing or "boosting" agent and has no antiviral activity. Gilead submitted an NDA to FDA for cobicistat as a standalone agent on June 28, 2012, and a PDUFA date of April 28, 2013 has been set. An MAA for cobicistat in the EU was validated for review by EMA on May 22, 2012.

Elvitegravir and cobicistat as standalone agents are investigational products and their safety and efficacy have not yet been established.

Important Safety Information about Stribild

BOXED WARNING: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT ACUTE EXACERBATION OF HEPATITIS B

- **Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including tenofovir disoproxil fumarate ("tenofovir DF"), a component of Stribild, in combination with other antiretrovirals.**
- **Stribild is not approved for the treatment of chronic hepatitis B virus (HBV) infection and the safety and efficacy of Stribild have not been established in patients coinfected with HBV and HIV-1. Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HBV and HIV-1 and have discontinued Emtriva or Viread, which are components of Stribild. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who are coinfected with HIV-1 and HBV and discontinue Stribild. If appropriate, initiation of anti-hepatitis B therapy may be warranted.**

Contraindications

- **Coadministration:** Do not use with drugs highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events. Do not use with drugs that strongly induce CYP3A as this may lead to a loss of virologic response and possible resistance to Stribild. Use with the following drugs is contraindicated: alfuzosin, rifampin, dihydroergotamine, ergotamine, methylergonovine, cisapride, lovastatin, simvastatin, pimozide, sildenafil for pulmonary arterial hypertension, triazolam, oral midazolam, and St. John's wort.

Warnings and Precautions

- **New onset or worsening renal impairment:** Cases of acute renal failure and Fanconi syndrome have been reported with the use of tenofovir DF and Stribild. Monitor estimated creatinine clearance (CrCl), urine glucose, and urine protein in all patients prior to initiating and during therapy; additionally monitor serum phosphorus in patients with or at risk for renal impairment. Cobicistat may cause modest increases in serum creatinine and modest declines in CrCl without affecting renal glomerular function; patients with an increase in serum creatinine greater than 0.4 mg/dL from baseline should be closely monitored for renal safety. Do not initiate Stribild in patients with CrCl below 70 mL/min. Discontinue Stribild if CrCl declines below 50 mL/min. Avoid concurrent or recent use with a nephrotoxic agent.
- **Use with other antiretroviral products:** Stribild is a complete regimen for the treatment of HIV-1 infection. Do not coadminister with other antiretroviral products, including products containing any of the same active components; products containing lamivudine; products containing ritonavir; or with adefovir dipivoxil.
- **Decreases in bone mineral density (BMD)** and cases of osteomalacia have been seen in patients treated with tenofovir DF. Consider monitoring BMD in patients with a history of pathologic fracture or risk factors for bone loss.
- **Fat redistribution and accumulation** have been observed in patients receiving antiretroviral therapy.
- **Immune reconstitution syndrome,** including the occurrence of autoimmune disorders with variable time to onset, has been reported.

Adverse Reactions

- **Common adverse drug reactions** in clinical studies (incidence greater than or equal to 5%; all grades) were nausea (16%), diarrhea (12%), abnormal dreams (9%), headache (7%), and fatigue (5%)

Drug Interactions

- **CYP3A substrates:** Stribild can alter the concentration of drugs metabolized by CYP3A or CYP2D6. Do not use with drugs highly dependent on these factors for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening adverse events.
- **CYP3A inducers:** Drugs that induce CYP3A can decrease the concentrations of components of Stribild. Do not use with drugs that strongly induce CYP3A as this may lead to loss of virologic response and possible resistance to Stribild.
- **Antacids:** Separate Stribild and antacid administration by at least 2 hours.
- **Prescribing information:** Consult the full prescribing information for Stribild for more information on potentially significant drug interactions, including clinical comments.

Dosage and Administration

- **Adult dosage:** One tablet taken orally once daily with food.
- **Renal impairment:** Do not initiate in patients with CrCl below 70 mL/min. Discontinue in patients with CrCl below 50 mL/min.
- **Hepatic impairment:** Not recommended in patients with severe hepatic impairment.

Pregnancy and Breastfeeding

- **Pregnancy Category B:** There are no adequate and well-controlled studies in pregnant women. Use during pregnancy only if the potential benefit justifies the potential risk. An Antiretroviral Pregnancy Registry has been established.
- **Breastfeeding:** Emtricitabine and tenofovir have been detected in human milk. Because of both the potential for HIV transmission and the potential for serious adverse reactions in nursing infants, mothers should be instructed not to breastfeed.

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.

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 the risk that healthcare providers may not recognize the benefits of starting patients new to therapy on Stribild. As Stribild is used over longer periods of time by many patients with underlying health problems taking numerous other medicines, Gilead may find new issues such as safety, resistance or drug interaction issues, which may require it to provide additional warnings or contraindications on the label or narrow Stribild's approved indication, each of which could reduce the market acceptance of Stribild. In addition, regulatory authorities including the European Medicines Agency may not approve marketing applications for Stribild, elvitegravir and/or cobicistat in the timelines anticipated or at all. Further, even if marketing approval is granted for any of these products, there may be significant limitations on their use. 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 September 30, 2012, 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.

U.S. full prescribing information for Stribild is available at www.Stribild.com.
U.S. full prescribing information for Atripla is available at www.Atripla.com.
U.S. full prescribing information for Truvada is available at www.Truvada.com.
EU Summary of Product Characteristics for Atripla and Truvada is available at www.ema.europa.eu

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

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