Gilead's Single Tablet HIV Regimen Stribild® Demonstrates Durable Viral Suppression Through Three Years of Therapy

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-- Long-Term Data In Treatment-Naïve Patients Highlight Stribild's Sustained Efficacy, Safety and Tolerability Profile --

BRUSSELS--(BUSINESS WIRE)--Oct. 16, 2013-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced three-year (144-week) efficacy and safety results from two pivotal Phase 3 studies (Studies 102 and 103) evaluating the once-daily single tablet 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 after three years of treatment, Stribild demonstrated comparable efficacy 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 inhibitor-based regimen of ritonavir-boosted atazanavir plus Truvada® (emtricitabine and tenofovir disoproxil fumarate) in Study 103. These data are being presented this week at the 14th European AIDS Clinical Society Conference (EACS) in Brussels, Belgium.

"HIV has become a chronic disease that can be managed with life-long therapy, increasing the need for convenient, once-daily treatment options that offer long-term efficacy and tolerability," said Jürgen Rockstroh, MD, Professor of Medicine, University of Bonn, Germany. "In these large-scale clinical trials, Stribild demonstrated high and durable viral suppression and a favorable safety profile over three years of therapy. These results support Stribild as an important single-tablet treatment option for people starting antiretroviral therapy."

Study 102 found that, at 144 weeks of treatment, 80 percent of Stribild patients (n=279/348) compared to 75 percent of patients receiving Atripla (n=265/352) achieved HIV RNA (viral load) less than 50 copies/mL based on the FDA snapshot algorithm (95 percent CI for the difference: -1.3 to 11.1 percent for Stribild vs. Atripla).

Similarly, in Study 103, 78 percent of Stribild patients (n=274/353) versus 75 percent of patients taking a protease inhibitor-based regimen of ritonavir-boosted atazanavir plus Truvada (n=265/355) achieved HIV RNA less than 50 copies/mL (95 percent CI for the difference: -3.2 to 9.4 percent for Stribild vs. the atazanavir-based regimen).

In both studies, rates of discontinuation due to adverse events were similar across all treatment groups (6 percent for Stribild in each study, 8 percent for Atripla and 9 percent for the atazanavir-based regimen).

In Study 102, the most common adverse events occurring in at least 10 percent of Stribild patients were diarrhea, nausea and upper respiratory tract infection, and for Atripla, they were abnormal dreams, dizziness and diarrhea. Stribild was associated with numerically lower rates of certain neuropsychiatric side effects compared to Atripla through 144 weeks, including abnormal dreams (16 percent for Stribild vs. 29 percent for Atripla), dizziness (8 percent vs. 26 percent) and insomnia (12 percent vs. 17 percent). The frequency of laboratory abnormalities was comparable between study regimens. Patients taking Stribild also experienced significantly lower increases in total cholesterol and LDL (low-density lipoprotein, or "bad" cholesterol) compared to patients taking Atripla.

In Study 103, Grade 3-4 laboratory abnormalities were generally similar for both treatment regimens, with the exception of hyperbilirubinemia, the rate of which was lower among patients taking Stribild compared to those taking the atazanavir-based regimen through 144 weeks of treatment (2 percent vs. 69 percent). In addition, patients taking Stribild in Study 103 experienced a lower change from baseline in spine bone mineral density compared to atazanavir patients (-1.43 percent vs. -3.68 percent , p=0.018), and a similar median change from baseline in hip bone mineral density (-2.83 percent for Stribild and -3.77 percent for the atazanavir-based regimen, p=0.23).

Stribild has a Boxed Warning on the risks of lactic acidosis/severe hepatomegaly with steatosis and post treatment acute exacerbation of hepatitis B; see below for important safety information.

Stribild was approved by the U.S. Food and Drug Administration in August 2012 and by the European Commission in May 2013.

Study 102

Study 102 is a randomized (1:1), double-blind Phase 3 clinical trial comparing the efficacy, safety and tolerability of Stribild (n=348) versus Atripla (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 less than 50 copies/mL at 48 weeks of treatment, per the FDA snapshot algorithm. Secondary objectives are to 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. Thirty-four percent of Stribild patients and 33 percent of Atripla patients had HIV RNA greater than 100,000 copies/mL. Twelve percent of Stribild patients and 14 percent of Atripla patients had CD4 counts less than or equal to 200 cells/mm^3.

Mean increases in CD4 cell counts were 321 cells/mm^3 for Stribild patients and 300 cells/mm^3 for Atripla patients at 144 weeks. Virologic failure rates were seven percent for Stribild and 10 percent for Atripla based on a component of the FDA snapshot analysis.

Through 144 weeks, six percent of Stribild patients and eight percent of Atripla patients discontinued treatment due to adverse events. Adverse events leading to treatment discontinuation among patients taking Stribild were renal events (2.3 percent), depression (0.3 percent) and fatigue (0.3 percent), and among patients taking Atripla, they were depression (1.4 percent), rash events and drug hypersensitivity (1.4 percent), fatigue (0.6 percent), abnormal dreams (0.6 percent), insomnia (0.6 percent) and anxiety (0.6 percent).

The frequency of Grade 3-4 adverse events and laboratory abnormalities was comparable between study regimens. Median changes from baseline in total cholesterol and LDL at 144 weeks were significantly smaller for Stribild compared to Atripla and were, respectively, +14 and +13 mg/dL for Stribild and +22 and +19 mg/dL for Atripla (total cholesterol, p=0.007; LDL, p=0.007). Median changes from baseline in HDL (high-density lipoprotein or “good” cholesterol) and triglycerides were similar for both treatment arms and were, respectively, +7 mg/dL and +9 mg/dL for Stribild and +9 mg/dL and +5 mg/dL for Atripla (HDL, p=0.021; triglycerides, p=0.72).

Median increases from baseline to 144 weeks in serum creatinine were 0.14 mg/dL for Stribild and 0.01 mg/dL for Atripla. There were four cases of proximal renal tubulopathy among Stribild patients reported in the first 48 weeks and none between weeks 48 and 144 weeks. Between 96 and 144 weeks of treatment, one Stribild patient discontinued treatment due to an isolated rise in creatinine without features of proximal renal tubulopathy, and the patient improved after treatment discontinuation.

There were no cases of resistance observed with Stribild between weeks 96 and 144.

Study 103

Study 103 is a randomized (1:1), double-blind Phase 3 clinical trial comparing the efficacy, safety and tolerability of Stribild (n=353) versus atazanavir 300 mg boosted by ritonavir 100 mg plus Truvada (n=355) among HIV-infected treatment-naïve adults with baseline HIV RNA levels greater than 5,000 copies/mL. The primary endpoint of the study is the proportion of patients achieving HIV RNA levels less than 50 copies/mL at 48 weeks of treatment, per the FDA snapshot algorithm. Secondary objectives are to 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. Forty-two percent of Stribild patients and 40 percent of atazanavir patients had HIV RNA greater than 100,000 copies/mL. Fifteen percent of Stribild patients and 11 percent of atazanavir patients had CD4 counts less than or equal to 200 cells/mm^3.

Patients in the Stribild arm experienced a mean increase of 280 cells/mm^3 in CD4 cell count at 144 weeks and patients on the

atazanavir-based regimen had a mean increase of 293 cells/mm^3. Virologic failure rates were eight percent for Stribild and seven percent for the atazanavir-based regimen based on a component of the FDA snapshot analysis.

Through 144 weeks, six percent of Stribild patients and nine percent of patients on the atazanavir-based regimen discontinued treatment due to adverse events. Adverse events leading to treatment discontinuation among patients taking Stribild were renal events (1.4 percent), hepatitis C (0.6 percent), diarrhea (0.6 percent), pyrexia (0.6 percent), nausea (0.3 percent), vomiting (0.3 percent) and fatigue (0.3 percent). The most common adverse events leading to treatment discontinuation among patients taking the atazanavir-based regimen were renal events (2.3 percent), nausea (1.1 percent), ocular icterus (1.1 percent), vomiting (0.6 percent), fatigue (0.6 percent), jaundice (0.6 percent), dizziness (0.6 percent), drug eruption (0.6 percent), hepatitis C (0.3 percent), diarrhea (0.3 percent) and pyrexia (0.3 percent). The most common adverse events occurring in at least 10 percent of patients in either treatment arm were diarrhea, nausea and upper respiratory tract infection.

With the exception of hyperbilirubenemia among atazanavir patients, Grade 3-4 laboratory abnormalities were similar for both treatment regimens. Median changes from baseline in total cholesterol, HDL and LDL at 144 weeks were similar for Stribild and the atazanavir-based regimen and were, respectively, +20, +8 and +17 mg/dL for Stribild, and +16, +7 and +18 mg/dL for the atazanavir-based regimen (total cholesterol, p=0.30; HDL, p=0.39; LDL, p=0.98). The median change in triglycerides was +15 mg/dL for Stribild and +22 mg/dL for the atazanavir-based regimen (p=0.24).

Both regimens had comparable renal profiles, with median increases from baseline to 144 weeks in serum creatinine of 0.12 mg/dL for Stribild and 0.08 mg/dL for the atazanavir-based regimen. Through 144 weeks, no patients taking Stribild and three patients taking the atazanavir-based regimen discontinued treatment due to proximal renal tubulopathy. Between 96 and 144 weeks of treatment, two Stribild patients and one atazanavir patient discontinued treatment due to an isolated rise in creatinine without features of proximal renal tubulopathy.

There were two cases of resistance observed in both the Stribild and atazanavir-based arms between weeks 96 and 144.

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. 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. 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.

Cobicistat is Gilead's proprietary potent mechanism-based inhibitor of cytochrome P450 3A (CYP3A), an enzyme that metabolizes drugs in the body.

On September 25, 2013, cobicistat was approved by the European Commission under the tradename Tybost®. On September 20, 2013, the Committee for Medicinal Products for Human Use, the scientific committee of the European Medicines Agency, adopted a positive opinion on Gilead's Marketing Authorisation Application (MAA) for elvitegravir.

Elvitegravir as a standalone agent and cobicistat as a standalone agent in the United States are investigational products and their safety and efficacy have not been established.

IMPORTANT SAFETY INFORMATION

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 emtricitabine or tenofovir DF, 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 loss of efficacy 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 >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.
- **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 ≥5%; all grades) were nausea (16%), diarrhea (12%), abnormal dreams (9%), and headache (7%).

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.
- **Drugs affecting renal function:** Coadministration of Stribild with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of emtricitabine and tenofovir and the risk of adverse reactions.
- **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.
- **Testing prior to initiation:** Test patients for HBV infection and document baseline CrCl, urine glucose, and urine protein.

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 Stribild. In addition, 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 in the European Union may not approve our marketing application for elvitegravir, and the FDA may not approve marketing applications for elvitegravir and/or cobicistat. 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 June 30, 2013, 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, Atripla, and Truvada is available at www.gilead.com.

EU Summary of Product Characteristics for Stribild, 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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