Gilead Announces Full 24-Week Phase 2 Results for Once-Daily Single Tablet HIV Regimen Containing Novel Prodrug Tenofovir Alafenamide (TAF)

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-- TAF-Based Regimen Now in Phase 3 Development --

ATLANTA--(BUSINESS WIRE)--Mar. 5, 2013-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced detailed 24-week results from a Phase 2 study (Study 102) evaluating a once-daily single tablet regimen containing tenofovir alafenamide (TAF) for the treatment of HIV-1 infection. A regimen of TAF 10 mg/elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg was found to be similar to Stribild® (elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) based on the percentage of patients with HIV RNA levels less than 50 copies/mL at 24 weeks of treatment. These findings were presented today in a latebreaker session (Abstract #99LB) at the 20th Conference on Retroviruses and Opportunistic Infections (CROI 2013) taking place in Atlanta.

"Given that HIV is now a chronic disease that can be managed with life-long therapy, there remains a need for new treatment options that are well tolerated," said Andrew Zolopa, MD, Professor of Medicine, Infectious Diseases, Stanford University School of Medicine and an investigator for Study 102. "In this study, a TAF-based single tablet regimen achieved comparable viral suppression to Stribild while demonstrating improvement in renal and bone safety indicators."

In Study 102, HIV-positive treatment-naïve adult patients were randomized (2:1) to receive the investigational TAF-based regimen or Stribild. At 24 weeks, 87 percent (n=97/112) of patients taking TAF and 90 percent (n=52/58) of patients taking Stribild achieved HIV RNA (viral load) less than 50 copies/mL, based on the FDA snapshot algorithm (95 percent CI for the difference: -15.7 percent to 5.9 percent for TAF vs. Stribild; p=0.36). There were no statistically significant differences in the frequency and nature of Grades 3-4 laboratory abnormalities, and the frequency and nature of adverse events were similar between the two arms. Both regimens were generally well tolerated.

"We are pleased with these positive Phase 2 data, which we believe demonstrate that TAF-based single tablet regimens have the potential to play an important role in HIV therapy," said Norbert W. Bischofberger, PhD, Gilead's Executive Vice President, Research and Development and Chief Scientific Officer. "Our Phase 3 program for TAF is enrolling rapidly, and we look forward to sharing initial results from the first pivotal study in 2014."

In January 2013, Gilead announced the initiation of two Phase 3 trials, Studies 104 and 111, which are examining TAF/elvitegravir/cobicistat/emtricitabine compared to Stribild among HIV patients new to therapy.

Topline results from Study 102 were announced in October 2012.

About Study 102

Study 102 is a randomized, double-blind 48-week clinical trial evaluating the efficacy and safety of a once-daily single tablet regimen containing TAF 10 mg/elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg (n=112) compared to Stribild (elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) (n=58) among HIV-1 infected treatment-naïve adults with HIV RNA levels greater than or equal to 5,000 copies/mL and CD4 cell counts greater than 50 cells/mm^3. Bone mineral density was assessed in all patients by DEXA scans at baseline and at 24 weeks of treatment. The primary endpoint of the study is the percentage of patients with HIV RNA levels less than 50 copies/mL at week 24, per the FDA snapshot algorithm. Secondary endpoints include the proportion of patients who achieve viral load of less than 50 copies/mL at week 48, and changes in HIV-1 RNA and in CD4 cell count from baseline to weeks 24 and 48.

At baseline, patients receiving the TAF-based regimen had a median HIV RNA of 4.55 $\log_{10}$ copies/mL and median CD4 cell count of 385 cells/mm^3. Patients receiving Stribild had a median HIV RNA of 4.58 $\log_{10}$ copies/mL and median CD4 cell count of 397 cells/mm^3.

At week 24, mean CD4 cell count increases from baseline were 163 cells/mm^3 in the TAF arm and 177 cells/mm^3 for Stribild (p=0.76).

Both regimens were generally well tolerated, and discontinuations due to adverse events were similar in both treatment arms (3.6 percent for TAF vs. 0 percent for Stribild).

The frequency of adverse events was similar in both treatment arms, and more than 90 percent of adverse events were Grades 1-2. The most common adverse events occurring in at least 5 percent of TAF patients were nausea (18 percent for TAF vs. 12 percent for Stribild), diarrhea (12 percent in both study arms), fatigue (12 percent for TAF vs. 9 percent for Stribild), headache (10 percent in both arms), upper respiratory tract infection (7 percent for TAF vs. 12 percent for Stribild) and flatulence (5 percent for TAF vs. 3 percent for Stribild). There were no treatment-related serious adverse events in either treatment arm.

There was a similarly low incidence of laboratory abnormalities (Grades 3-4) in both arms of the study. Grades 3-4 laboratory abnormalities occurring in at least 5 percent of patients in either treatment arm were LDL (low-density lipoprotein or "bad" cholesterol), neutropenia and elevated creatine phosphokinase. No proximal renal tubulopathy cases and no discontinuations due to renal events occurred in either treatment arm.

Median changes from baseline in total cholesterol, HDL (high-density lipoprotein or "good" cholesterol) and LDL at 24 weeks were, respectively, +31, +6 and +17 mg/dL for TAF and +15, +2 and +4 mg/dL for Stribild (total cholesterol, $p<0.001$; HDL, $p=0.007$; LDL, $p=0.001$). The median change in total cholesterol/HDL ratio at week 24 was 0.1 in both arms ($p=0.47$). The median change in triglycerides was +24 mg/dL for TAF and +21 mg/dL for Stribild ($p=0.48$).

Additionally, at 24 weeks of treatment there were numeric differences in renal laboratory abnormalities favoring the TAF-based regimen. The median change in serum creatinine from baseline to week 24 was 0.07 mg/dL for the TAF-based regimen compared to 0.12 mg/dL for Stribild ($p=0.02$). The median change in the estimated glomerular filtration rate (eGFR) from baseline to week 24 was -4.9 mL/min compared to -11.8 mL/min for the TAF and Stribild arms, respectively ($p=0.04$). The mean percentage decrease in bone mineral density from baseline to week 24 for the TAF-based regimen compared to Stribild was -0.8 vs. -2.5 ($p=0.002$) for the lumbar spine and -0.3 vs. -2.0 ($p<0.001$) for the hip.

The study is ongoing. After week 48, patients will continue to take their blinded study drug until treatment assignments have been unblinded, at which point all will be given the option to participate in an open-label rollover extension and receive the TAF-based single tablet regimen.

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

About Tenofovir Alafenamide

Tenofovir alafenamide (TAF) is a nucleotide reverse transcriptase inhibitor (NtRTI). It is a novel prodrug of tenofovir. Phase 1b dose-ranging studies identified a dose of TAF that is ten times lower than Viread and provides greater antiviral efficacy. The smaller milligram dose of TAF may enable the development of new fixed-dose combinations and single tablet regimens for HIV therapy that are not feasible with Viread.

About Elvitegravir

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 the U.S. Food and Drug Administration (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.

About Cobicistat

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.

TAF/elvitegravir/cobicistat/emtricitabine and elvitegravir and cobicistat as single agents are investigational products and their safety and efficacy have not yet been established.

Indication and Important Safety Information for 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 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.

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 should not be coadministered with products containing any of the same active components; with products containing lamivudine; with adefovir dipivoxil; or with products containing ritonavir.
- **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, diarrhea, abnormal dreams, headache and fatigue.

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 H8IV 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 risks related to the possibility of unfavorable results from other clinical trials involving the single tablet regimen containing TAF, including Phase 3 studies. In addition, Gilead may also be unable to enroll patients in the Phase 3 studies or obtain trial results in the timelines currently anticipated and may need to modify or delay the clinical trials or to perform additional trials. In addition, Gilead may make a strategic decision to discontinue development of the single table regiment containing TAF if, for example, Gilead believes commercialization will be difficult relative to other opportunities in its pipeline. Further, Gilead may be unable to obtain approvals from regulatory authorities for elvitegravir and/or cobicistat, alone or in combination with other products. If marketing approval is granted for any of these products, there may be significant limitations on their use. As a result, these product candidates as standalone agents or as part of single tablet regimens may never be successfully commercialized. 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 Annual Report on Form 10-K for the year ended December 31, 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 and Viread is available at www.gilead.com.

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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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