Gilead's Boosting Agent Cobicistat for HIV Therapy as Effective as Ritonavir in Pivotal Phase 3 Study

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WASHINGTON--(BUSINESS WIRE)--Jul. 24, 2012-- Gilead Sciences, Inc. (Nasdaq:GILD) today announced full clinical trial results from a pivotal Phase 3 study evaluating cobicistat, a pharmacoenhancing or "boosting" agent for HIV therapy, compared to ritonavir, which is currently the only agent used to boost certain antiretroviral treatment regimens. The study found that an HIV regimen containing a cobicistat-boosted protease inhibitor was non-inferior to a regimen containing a ritonavir-boosted protease inhibitor at 48 weeks of therapy. The findings will be presented today in an oral session (abstract #TUAB0103) at the 19th International AIDS Conference (AIDS 2012) taking place in Washington, D.C.

"These data demonstrate that cobicistat may be an effective option for boosting the potency of HIV regimens that are based on protease inhibitors," said Joel Gallant, MD, MPH, Professor of Medicine and Epidemiology at Johns Hopkins University, and principal investigator of the study.

In the trial (Study 114), treatment-naïve adult patients received either cobicistat or ritonavir for 48 weeks. All patients also received atazanavir (a protease inhibitor) plus Truvada® (emtricitabine and tenofovir disoproxil fumarate). At 48 weeks, the study found that 85 percent of patients on the cobicistat-containing regimen compared to 87 percent of patients on the ritonavir-containing regimen achieved HIV RNA (viral load) levels less than 50 copies/mL, based on the U.S. Food and Drug Administration (FDA) snapshot algorithm (95 percent CI for the difference: -7.4 percent to +3.0 percent; predefined criterion for non-inferiority was a lower bound of a two-sided 95 percent CI of -12 percent). Twenty-five patients (7 percent) discontinued treatment due to adverse events in each arm of the study.

"We believe that cobicistat has a central role to play in boosting protease-based HIV therapies," said Norbert Bischofberger, PhD, Executive Vice President, Research and Development and Chief Scientific Officer, Gilead Sciences. "In addition to our marketing application for cobicistat that is currently under FDA review, we are partnering with other pharmaceutical companies to develop two new fixed-dose combinations that combine cobicistat with some of today's most prescribed protease inhibitors."

In June 2011, Gilead entered into an agreement with Janssen R&D Ireland for the development of a fixed-dose combination of cobicistat and the protease inhibitor darunavir. In October 2011, Gilead also announced an agreement with Bristol-Myers Squibb to develop a fixed-dose combination of cobicistat and atazanavir.

Gilead submitted a New Drug Application to FDA for cobicistat on June 28, 2012. On May 23, 2012, the company's Marketing Authorisation Application for the product was validated for review by the European Medicines Agency (EMA). Cobicistat is also a component of the Quad, a complete single tablet regimen for HIV combining cobicistat with elvitegravir, emtricitabine and tenofovir disoproxil fumarate. The Quad is currently under U.S. and European regulatory review.

Gilead announced topline results for Study 114 on December 5, 2011.

About Study 114

Study 114 is a randomized, double-blind Phase 3 clinical trial comparing the efficacy and safety of cobicistat-boosted atazanavir versus ritonavir-boosted atazanavir, each administered with Truvada, over a 192-week period at more than 200 study sites in North America, South America, Europe and Asia Pacific. Eligible participants were HIV-infected treatment-naïve adults with HIV RNA levels greater than or equal to 5,000 copies/mL. Trial participants were randomized (1:1) to receive a once-daily regimen of cobicistat 150 mg, atazanavir 300 mg and Truvada (n=344) or ritonavir 100 mg, atazanavir 300 mg and Truvada (n=348).

The primary endpoint of the study is the proportion of patients achieving HIV RNA levels of less than 50 copies/mL at 48 weeks of treatment, as determined by the FDA-defined snapshot analysis. Secondary objectives evaluated the efficacy, safety and tolerability of the treatment regimens through 96 weeks of treatment.

At baseline, patients in the cobicistat and ritonavir arms had a median HIV RNA of 4.78 $\log_{10}$ copies/mL and 4.84 $\log_{10}$ copies/mL and mean CD4 cell count of 353 cells/mm^3 and 351 cells/mm^3, respectively.

Mean increases in CD4 cell counts were 213 cells/mm^3 for cobicistat patients and 219 cells/mm^3 for ritonavir patients at 48 weeks (p=0.67). Virologic failure rates were low in both arms – 6 percent for patients receiving cobicistat and 4 percent for those receiving ritonavir. Drug resistance was also low – two patients developed an NRTI resistance mutation in the cobicistat arm, and none in the ritonavir arm.

Incidence of laboratory abnormalities (Grade 3-4) was similar in both arms of the study. Laboratory abnormalities (Grade 3-4) occurring in at least one percent of patients in either treatment arm included hyperbilirubinemia, creatine kinase, hematuria, ALT, AST, amylase, glycosuria, hyperglycemia, GGT and neutropenia. Only hyperbilirubinemia (65 percent in the cobicistat arm vs. 57 percent in the ritonavir arm, p=0.023) and creatine kinase (6 percent in both arms) occurred in more than 5 percent of patients in either arm.

The most common adverse events occurring in greater than or equal to 10 percent of patients in either treatment arm included jaundice (21 percent in the cobicistat arm vs. 16 percent in the ritonavir arm), ocular icterus (18 percent in both arms), nausea (18 percent vs. 16 percent), diarrhea (15 percent vs. 20 percent), headache (11 percent vs. 16 percent), nasopharyngitis (11 percent vs. 15 percent), hyperbilirubinemia (11 percent vs. 10 percent) and upper respiratory infection (10 percent vs. 8 percent).

The median increases in serum creatinine were 0.13 mg/dL for the cobicistat arm and 0.09 mg/dL for the ritonavir arm at 48 weeks (p<0.001). Discontinuation rates due to renal adverse events were low and comparable in both arms (1.7 percent in the cobicistat arm vs. 1.4 percent in the ritonavir arm).

Median changes from baseline to Week 48 in total cholesterol were +4 mg/dL and +10 mg/dL (p=0.081); median changes in low-density lipoprotein (LDL or "bad" cholesterol) were +5 mg/dL and +8 mg/dL (p=0.32); and median changes in triglycerides were +16 mg/dL and +24 mg/dL (p=0.63) for patients in the cobicistat and ritonavir arms, respectively. Median increases in high-density lipoprotein (HDL or "good" cholesterol) were similar in the cobicistat and ritonavir arms (+4 mg/dL vs. +3 mg/dL, p=0.69).

Study 114 is ongoing in a blinded fashion. Additional information about the study can be found at www.clinicaltrials.gov.

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 pharmacoenhancer and has no antiviral activity. Pharmacokinetic studies have demonstrated that cobicistat boosts the widely prescribed protease inhibitors atazanavir and darunavir.

About Quad

The Quad contains elvitegravir, cobicistat (a pharmacoenhancing or "boosting" agent that enables once-daily dosing of elvitegravir), and Truvada (emtricitabine and tenofovir disoproxil fumarate). In October 2011, Gilead submitted a New Drug Application to FDA for the Quad for the treatment of HIV. FDA has set a target action date for the Quad under the Prescription Drug User Fee Act (PDUFA) of August 27, 2012.

Cobicistat, elvitegravir and the Quad are investigational products and their safety and efficacy have not yet been established.

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 Gilead may fail to obtain approvals for cobicistat and Quad from regulatory authorities and any marketing approval, if granted, may have significant limitations on their use. As a result, cobicistat and Quad may never be successfully commercialized. In addition, Gilead may make a strategic decision

to discontinue development of cobicistat or Quad if, for example, it believes commercialization will be difficult relative to other opportunities in its pipeline. Further, Gilead may be unsuccessful in developing and commercializing fixed-dose combinations that combine cobicistat with other protease inhibitors, including darunavir and atazanavir. 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 March 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 Truvada is available at www.Truvada.com.

Truvada is a registered trademark of Gilead Sciences, Inc.

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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