U.S. FDA Approves Gilead's Once-Daily Single Tablet HIV-1 Regimen Complera® for Patients Switching from a Stable Regimen

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-- European Commission Also Approves Expanded Indication for Regimen, Marketed as Eviplera® in the European Union --

FOSTER CITY, Calif.--(BUSINESS WIRE)--Dec. 13, 2013-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced that the U.S. Food and Drug Administration (FDA) has approved the single tablet HIV-1 regimen Complera® (emtricitabine/rilpivirine/tenofovir disoproxil fumarate) for use in certain virologically-suppressed (HIV RNA <50 copies/mL) adult patients on a stable antiretroviral regimen in order to replace their current antiretroviral treatment regimen. Complera was first approved in 2011 for patients new to therapy and is now one of the most widely-prescribed HIV regimens in the United States.

"Complera is an effective single-pill therapy with a demonstrated safety profile, and has rapidly become an important option for appropriate HIV patients who are initiating antiretroviral treatment," said Calvin J. Cohen, MD, M.Sc., Research Director, Community Research Initiative of New England and an investigator on clinical trials of Complera. "The data supporting today's approval demonstrate Complera has the potential to help a broader range of HIV-infected patients who have achieved virologic control on another regimen."

Complera combines a complete course of three antiretroviral medications into a single, once-daily tablet. The product contains Gilead's Truvada®, which itself is a fixed-dose combination of two HIV medicines, and Janssen R&D Ireland's rilpivirine (marketed as Edurant®). Patients switching to Complera should have no history of virologic failure, have suppressed viral load for at least six months, be on their first or second antiretroviral regimen, and have no current or past history of resistance to Complera components. The efficacy of Complera was established in patients who were virologically suppressed (HIV RNA <50 copies/mL) on a stable ritonavir-boosted protease inhibitor-containing regimen.

Today's approval is supported by clinical data from the Phase 3 SPIRIT (Study 106) clinical trial. In this randomized, open-label study, virologically suppressed patients who were taking multi-tablet HIV therapy containing a ritonavir-boosted protease inhibitor (PI) either switched to Complera or remained on their PI-based regimen. The study found that, after 48 weeks of treatment with Complera, 89 percent (n=283/317) of switch patients had viral load less than 50 copies/mL, compared to 90 percent (143/159) of patients who remained on a PI-regimen for 24 weeks. Complera was well tolerated in SPIRIT and there were few treatment discontinuations due to adverse events. The most common side effects in previous clinical studies of Complera were headache, depressive disorders and insomnia (2 percent for all). No new adverse reactions were identified in SPIRIT, but the frequency of adverse reactions increased from 2 percent to 2.4 percent. Complera has a labeled Boxed Warning on the risks of lactic acidosis/severe hepatotoxicity with steatosis and acute exacerbation of hepatitis B; see below for Important Safety Information.

Marketed as Eviplera® (emtricitabine/rilpivirine/tenofovir disoproxil (as fumarate)) in the European Union, the regimen also was recently granted European regulatory approval for any HIV-infected adult patients without known mutations associated with resistance to the non-nucleoside reverse transcriptase inhibitor (NNRTI) class, tenofovir or emtricitabine, and with a viral load ≤ 100,000 HIV-1 RNA copies/mL.

Important Safety Information about Complera

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 COMPLERA, in combination with other antiretrovirals.

COMPLERA is not approved for the treatment of chronic hepatitis B virus (HBV) infection and the safety and efficacy of COMPLERA 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, which are components of COMPLERA. 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 COMPLERA. If appropriate, initiation of anti-hepatitis B therapy may be warranted.

CONTRAINDICATIONS

- **Coadministration:** COMPLERA should not be coadministered with drugs that induce CYP3A or increase gastric pH as this may lead to loss of virologic response and possible resistance to COMPLERA. Use of the following drugs with COMPLERA is contraindicated: carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine, proton pump inhibitors (e.g., esomeprazole, lansoprazole, dexlansoprazole, omeprazole, pantoprazole, rabeprazole), systemic dexamethasone (>1 dose) 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. In all patients, assess estimated creatinine clearance (CrCl) prior to initiating and during therapy. In patients at risk for renal dysfunction, additionally monitor serum phosphorus, urine glucose, and urine protein. Do not administer COMPLERA in patients with CrCl <50 mL/min. Avoid concurrent or recent use with a nephrotoxic agent. Cases of acute renal failure, some requiring hospitalization and renal replacement therapy, have been reported after initiation of high dose or multiple NSAIDs in patients with risk factors for renal dysfunction; consider alternatives to NSAIDs in these patients. Persistent or worsening bone pain, pain in extremities, fractures and/or muscular pain or weakness may be manifestations of proximal renal tubulopathy and should prompt an evaluation of renal function.

- **Drug interactions:** Use COMPLERA with caution when given with drugs that may reduce the exposure of rilpivirine or when coadministered with a drug with known risk of Torsades de Pointes. Supratherapeutic doses of rilpivirine have been shown to prolong the QTc interval of the electrocardiogram (ECG) in healthy subjects.

- **Depressive disorders**: The incidence of depressive disorders (depressed mood, depression, dysphoria, major depression, mood altered, negative thoughts, suicide attempt, suicidal ideation) reported in clinical trials (N=686) was 9% (most were mild or moderate in severity); and Grades 3 and 4 depressive disorders (regardless of causality) was 1%. Suicidal ideation was reported in 4 subjects and suicide attempt was reported in 2 subjects. Patients with severe depressive symptoms should seek immediate medical evaluation and the risks of continued therapy should be determined.

- **Hepatotoxicity:** Hepatic adverse events have been reported, including cases of hepatic toxicity in patients without pre-existing hepatic disease or other identifiable risk factors. Patients with underlying hepatitis B or C, or those with marked elevations in liver-associated tests may be at increased risk. Appropriate laboratory testing and monitoring before and during therapy is recommended in patients with underlying hepatic disease or in patients with marked elevations in liver-associated tests prior to treatment initiation; consider testing and monitoring in patients without pre-existing hepatic dysfunction or other risk factors.

- **Bone effects:** Decreases in bone mineral density (BMD) and mineralization defects, including 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. In patients at risk of renal dysfunction who present with persistent or worsening bone or muscle symptoms, hypophosphatemia and osteomalacia secondary to proximal renal tubulopathy should be considered.

- **Other antiretrovirals:** COMPLERA is a complete regimen for the treatment of HIV-1 infection. Do not coadminister with other antiretrovirals including products containing any of the same active components, products containing lamivudine, or with adefovir dipivoxil.

- **Fat redistribution** and accumulation has been observed in patients receiving ARV therapy.

- **Immune reconstitution syndrome,** including the occurrence of autoimmune disorders with variable times to onset, has been reported.

ADVERSE REACTIONS

- **In adults with no ARV treatment history:** Common adverse reactions reported in clinical studies (incidence ≥2%, Grades 2-4) were depressive disorders (2%), insomnia (2%) and headache (2%).
- **In virologically suppressed adults:** No new types of adverse reactions to COMPLERA were identified in stable, virologically suppressed patients switching to COMPLERA; however, the frequency of adverse reactions increased by 20%.

DRUG INTERACTIONS

- **CYP3A inducers:** Drugs that induce CYP3A may decrease rilpivirine plasma concentrations which may lead to loss of virologic response and possible resistance to COMPLERA.
- **CYP3A inhibitors:** Drugs that inhibit CYP3A may increase rilpivirine plasma concentrations.
- **Drugs increasing gastric pH** may significantly decrease rilpivirine plasma concentrations and lead to loss of virologic response and possible resistance to COMPLERA.
    - Use of proton pump inhibitors with COMPLERA is contraindicated.
    - Antacids should be administered ≥2 hours before or ≥4 hours after COMPLERA.
    - H_2 receptor antagonists should be administered ≥12 hours before or ≥4 hours after COMPLERA.
- **Drugs affecting renal function**: Coadministration of COMPLERA with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of emtricitabine and tenofovir.
- **Prescribing information:** Consult the full Prescribing Information for COMPLERA for more information on potentially significant drug interactions, including clinical comments.

Pregnancy and Breastfeeding

- **Pregnancy Category B**: There are no adequate and well-controlled studies in pregnant women. Use during pregnancy only if potential benefits 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.

DOSAGE AND ADMINISTRATION

Adults: One tablet taken orally once daily with food.

Renal Impairment: Do not use in patients requiring dose adjustment or patients with estimated CrCl <50 mL/min.

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 and South 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 in the United States and European Union may not see advantages of switching virologically suppressed HIV patients to Complera/Eviplera and may therefore be reluctant to prescribe the product. 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, 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 Complera and Truvada, including **BOXED WARNING** for both products, *is available at www.Gilead.com.*

EU Summaries of Product Characteristics for Eviplera and Truvada are available at http://www.ema.europa.eu.

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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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