



U.S. Food and Drug Administration Approves Gilead's Single Tablet Regimen Genvoya® (Elvitegravir, Cobicistat, Emtricitabine and Tenofovir Alafenamide) for Treatment of HIV-1 Infection

– Gilead's First TAF-based Regimen Demonstrates High Efficacy with Improved Renal and Bone Parameters Compared to TDF-based Regimens –

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FOSTER CITY, Calif.--(BUSINESS WIRE)--Gilead Sciences, Inc. (NASDAQ:GILD) announced today that the U.S. Food and Drug Administration (FDA) has approved Genvoya® (elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/tenofovir alafenamide 10 mg or E/C/F/TAF) for the treatment of HIV-1 infection. Genvoya is the first TAF-based regimen to receive FDA approval.

Genvoya is indicated as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients 12 years of age and older who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically-suppressed (HIV-1 RNA levels less than 50 copies per mL) on a stable antiretroviral regimen for at least six months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Genvoya. No dosage adjustment of Genvoya is required in patients with estimated creatinine clearance greater than or equal to 30 mL per minute.

Genvoya has a boxed warning in its product label regarding the risks of lactic acidosis/severe hepatomegaly with steatosis, and post treatment acute exacerbation of hepatitis B. Further important safety information, adverse drug reactions and drug interactions are listed below.

Photos and multimedia gallery available at www.GileadHIVMedia.com.

TAF is a novel targeted prodrug of tenofovir that has demonstrated high antiviral efficacy similar to and at a dose less than one-tenth that of Gilead's Viread® (tenofovir disoproxil fumarate, TDF), as well as improvement in surrogate laboratory markers of renal and bone safety as compared to TDF in clinical trials in combination with other antiretroviral agents. Data show that because TAF enters cells, including HIV-infected cells, more efficiently than TDF, it can be given at a lower dose and there is 91 percent less tenofovir in the bloodstream.

"As the HIV patient population ages there is an increased risk for development of age- and treatment-related comorbidities, including low bone mineral density and renal impairment. This is due to the combination of HIV infection, antiretroviral treatments and the natural aging process," said David Wohl, MD, Associate Professor of Medicine, Division of Infectious Diseases, University of North Carolina at Chapel Hill and lead author of the Genvoya efficacy analysis. "Given its demonstrated efficacy and safety profile, Genvoya represents an important new treatment option for a range of patients who are either new to therapy or who choose to switch treatments."

Genvoya was studied in a Phase 3 HIV clinical program in more than 3,500 patients across 21 countries, including treatment-naïve, virologically suppressed, renally impaired and adolescent patients. The approval is supported by 48-week data from two Phase 3 double-blind studies (Studies 104 and 111) among 1,733 treatment-naïve patients in which the regimen met its primary objective of non-inferiority compared to Stribild® (elvitegravir 150 mg, cobicistat 150 mg, emtricitabine 200 mg and tenofovir disoproxil fumarate 300 mg or E/C/F/TDF). In the combined analysis of the studies, 92.4 percent of Genvoya patients and 90.4 percent of Stribild patients had HIV-1 RNA levels less than 50 copies/mL at Week 48. Tests of certain renal and bone laboratory parameters also favored Genvoya over Stribild.

Additionally, the approval is supported by a Phase 3 study (Study 109) evaluating Genvoya among virologically suppressed patients who switched from TDF-based regimens. The study enrolled 1,436 subjects and 1,196 had reached the 48-week time point at the time of filing. Among those patients, Genvoya was found to be statistically non-inferior to the TDF-based regimens based on the percentages of patients with HIV-1 RNA levels less than 50 copies/mL at Week 48. Patients receiving Genvoya also demonstrated improvements in certain bone and renal laboratory parameters compared to those treated with the TDF-based regimens. Finally, data from Phase 3 studies evaluating Genvoya among adolescents and patients with mild-to-moderate renal impairment supported the approval.

"While exceptional progress has been made in the field of HIV, there is still a need for new treatment options that may help improve the health of people as they grow older with the disease," said John C. Martin, PhD, Chairman and Chief Executive Officer, Gilead Sciences. "For more than 25 years, Gilead has been committed to changing the trajectory of HIV management and we are now pleased to introduce Genvoya, the first in a portfolio of TAF-based products that have the potential to advance the long-term treatment of HIV."

Two other TAF-based regimens are currently under evaluation by the FDA. The first is an investigational, fixed-dose combination of emtricitabine 200 mg and tenofovir alafenamide 25 or 10 mg (F/TAF) for use in combination with other antiretroviral agents. The second is an investigational, once-daily single tablet regimen that combines emtricitabine 200 mg, tenofovir alafenamide 25 mg and rilpivirine 25 mg (R/F/TAF). Emtricitabine and tenofovir alafenamide are from Gilead and rilpivirine is from Janssen Sciences Ireland UC, one of the Janssen Pharmaceutical Companies of Johnson & Johnson.

F/TAF and R/F/TAF are investigational products and have not been determined to be safe or efficacious.

Genvoya does not cure HIV infection or AIDS.

Patient Assistance Programs

Gilead's U.S. Advancing Access® program provides assistance to patients in the United States who are uninsured, underinsured or who need financial assistance to pay for their medications, including Genvoya.

The program offers support services for patients and providers, including:

- Access to counselors who can help patients and their providers with insurance-related needs, including identifying coverage options.
- The Advancing Access Copay Coupon Program, which provides co-pay assistance for eligible patients with private insurance who need assistance paying for out-of-pocket medication costs.
- The Advancing Access Patient Assistance Program and Truvada Medication Assistance Program, which will provide Gilead medications at no charge for eligible patients with no other insurance options.

Additionally, Gilead is working closely with the ADAP Crisis Task Force, as the company has done for each of its other HIV medications, to provide discounts to state AIDS Drug Assistance Programs (ADAPs) that will help ensure access to Genvoya for patients who receive medications through these programs.

Information about how to apply for any of these forms of assistance can be found at www.GileadAdvancingAccess.com or by calling 1-800-226-2056 between 9:00 a.m. and 8:00 p.m. (Eastern).

Important U.S. Safety Information for Genvoya

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 in combination with other antiretrovirals.**
- **Genvoya is not approved for the treatment of chronic hepatitis B virus (HBV) infection and the safety and efficacy of Genvoya have not been established in patients coinfecting with HIV-1 and HBV. Severe acute exacerbations of hepatitis B have been reported in patients who are coinfecting with HIV-1 and HBV and have discontinued products containing emtricitabine and/or tenofovir disoproxil fumarate, and may occur with Genvoya. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who are coinfecting with HIV-1 and HBV and discontinue Genvoya. 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 Genvoya. Do not use with alfuzosin, carbamazepine, phenobarbital, phenytoin, rifampin, dihydroergotamine, ergotamine, methylergonovine, cisapride, lovastatin, simvastatin, pimozide, sildenafil for pulmonary arterial hypertension, triazolam, oral midazolam, or St. John's wort.

Warnings and precautions

- **Other antiretroviral products:** Do not coadminister with other antiretroviral products, including products containing any of the same active components, tenofovir disoproxil fumarate, lamivudine, ritonavir, or adefovir dipivoxil.
- **Drug interactions:** See Contraindications and Drug Interactions sections. Consider the potential for drug interactions prior to and during Genvoya therapy and monitor for adverse reactions.
- **Fat redistribution** or 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.
- **New onset or worsening renal impairment:** Cases of acute renal failure and Fanconi syndrome have been reported with the use of tenofovir prodrugs. In clinical trials of Genvoya, there have been no cases of Fanconi syndrome or proximal renal tubulopathy (PRT). Do not initiate Genvoya in patients with CrCl <30 mL/min. Patients with impaired renal function and/or taking nephrotoxic agents (including NSAIDs) are at increased risk of renal-related adverse reactions. Discontinue Genvoya in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome.

Renal monitoring: In all patients, monitor estimated creatinine clearance (CrCl), urine glucose, and urine protein prior to initiating and during therapy. In patients with chronic kidney disease, additionally monitor serum phosphorus. If serum creatinine increases >0.4 mg/dL from baseline, closely monitor for renal safety.

- **Bone mineral density (BMD) and mineralization:** Decreases in BMD have been reported with the use of tenofovir prodrugs. Consider monitoring BMD in patients with a history of pathologic fracture or risk factors for bone loss. Mineralization defects, including osteomalacia associated with PRT, have been reported with the use of TDF-containing products.

Adverse reactions

- **Common adverse reactions** (incidence ≥5%; all grades) in clinical studies were nausea (10%), diarrhea (7%), headache (6%), and fatigue (5%).

Drug interactions

- **Prescribing information:** Consult the full prescribing information for Genvoya for more information on Contraindications, Warnings, and potentially significant drug interactions, including clinical comments.

- **Metabolism:** Genvoya can increase the concentration of drugs metabolized by CYP3A, CYP2D6, P-gp, BCRP, OATP1B1 or OATP1B3. Drugs that inhibit CYP3A, P-gp, or BCRP can increase the concentrations of components of Genvoya. Drugs that induce CYP3A or P-gp can decrease the concentrations of components of Genvoya.
- **Drugs affecting renal function:** Coadministration of Genvoya 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.

Dosage and administration

- **Dosage:** Patients 12 years and older (≥ 35 kg): 1 tablet taken orally once daily with food.
- **Renal impairment:** Not recommended in patients with CrCl < 30 mL/min.
- **Hepatic impairment:** Not recommended in patients with severe hepatic impairment.
- **Testing prior to initiation:** Test patients for HBV infection.

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 has 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

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. Gilead has operations in more than 30 countries worldwide, with headquarters in Foster City, California.

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 physicians may not see the benefits of prescribing Genvoya. In addition, marketing authorizations for F/TAF and R/F/TAF may not be approved by the FDA or other regulatory authorities, and any marketing approvals, if granted, may have 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, 2015, 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, including **BOXED WARNING**, for Genvoya is available at www.gilead.com.*

*U.S. Full Prescribing Information, including **BOXED WARNING**, for Stribild, Truvada and Viread are 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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