U.S. Food and Drug Administration Approves Gilead’s Second TAF-Based Single Tablet Regimen Odefsey® (Emtricitabine, Rilpivirine, Tenofovir Alafenamide) for the Treatment of HIV-1 Infection

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-- Odefsey is the Smallest Single Tablet HIV Regimen –

FOSTER CITY, Calif.--(BUSINESS WIRE)--Mar. 1, 2016-- Gilead Sciences, Inc. (NASDAQ:GILD) today announced that the U.S. Food and Drug Administration (FDA) has approved Odefsey® (emtricitabine 200 mg/rilpivirine 25 mg/tenofovir alafenamide 25 mg or R/F/TAF) for the treatment of HIV-1 infection in certain patients. Emtricitabine and tenofovir alafenamide are from Gilead Sciences and rilpivirine is from Janssen Sciences Ireland UC, one of the Janssen Pharmaceutical Companies of Johnson & Johnson (Janssen). Odefsey is Gilead’s second TAF-based regimen to receive FDA approval and represents the smallest pill of any single tablet regimen for the treatment of HIV.

Odefsey is indicated as a complete regimen for the treatment of HIV-1 infection in patients 12 years of age and older who have no antiretroviral treatment history and HIV-1 RNA levels less than or equal to 100,000 copies per mL. Odefsey is also indicated as replacement for a stable antiretroviral regimen in those who are virologically-suppressed (HIV-1 RNA less than 50 copies per mL) for at least six months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Odefsey. No dosage adjustment of Odefsey is required in patients with estimated creatinine clearance greater than or equal to 30 mL per minute.

Odefsey 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. See below for important safety information.


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). TAF has also demonstrated 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 much lower dose and there is 90 percent less tenofovir in the bloodstream.

“As people are living longer with HIV, there is an increasing need to develop new treatments that are tolerable and help address long-term health for patients,” said John C. Martin, PhD, Chairman and Chief Executive Officer, Gilead Sciences. “Odefsey’s safety, efficacy and tolerability profile offers a new treatment option to support the needs of a range of patients and represents Gilead’s commitment to innovation in the field of HIV.”

The approval is supported by a bioequivalence study demonstrating that Odefsey achieved similar drug levels of emtricitabine and TAF in the blood as Genvoya® (elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/tenofovir alafenamide 10 mg or E/C/F/TAF) and similar drug levels of rilpivirine as Edurant® (rilpivirine 25 mg). The safety, efficacy and tolerability of Odefsey is supported by clinical studies of rilpivirine-based therapy (administered as R+F/TDF or R/F/TDF) and F/TAF-based therapy (administered as E/C/F/TAF) in a range of patients with HIV, including treatment-naïve adults and adolescents, virologically suppressed adults who switched from PI-, NNRTI- and INSTI-based regimens and virologically suppressed adults with mild-to-moderate renal impairment.

The Odefsey approval is part of an ongoing development and commercialization agreement between Gilead and Janssen, first established in 2009. Under this agreement, Gilead is responsible for the manufacturing, registration, distribution and commercialization of the product in most countries, while Janssen will distribute it in approximately 17 markets and have co-detailing rights in several key markets, including the United States. The original agreement was established for the development and commercialization of Complera®, marketed as Eviplera® in the European Union, and expanded in 2014 to include Odefsey.
Odefsey does not cure HIV infection or AIDS.

**Patient Assistance Programs**

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

The program offers information and assistance for patients, including:

- Access to agents who can provide information related to coverage and insurance-related questions.
- 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 Odefsey 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](http://www.GileadAdvancingAccess.com) or by calling 1-800-226-2056 between 9:00 a.m. and 8:00 p.m. EST.

**Important U.S. Safety Information for Odefsey**

**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.
- Odefsey is not approved for the treatment of chronic hepatitis B virus (HBV) infection, and the safety and efficacy of Odefsey have not been established in patients coinfected with HIV-1 and HBV. Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HIV-1 and HBV and have discontinued products containing emtricitabine and/or tenofovir disoproxil fumarate (TDF), and may occur with discontinuation of Odefsey. 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 Odefsey. If appropriate, initiation of anti-hepatitis B therapy may be warranted.

**Contraindications**

- **Coadministration:** Do not use with drugs that induce CYP3A or increase gastric pH as this may lead to loss of efficacy and possible resistance to Odefsey or the NNRTI class. Do not use with carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, rifapentine, proton pump inhibitors (e.g., dextransoprazole, esomeprazole, lanzoprazole, omeprazole, pantoprazole, rabeprazole), systemic dexamethasone (>1 dose) and St. John’s wort.

**Warnings and precautions**

- **Skin and hypersensitivity reactions:** Severe skin and hypersensitivity reactions have been reported with the use of rilpivirine-containing regimens, including cases of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). In rilpivirine clinical trials, most rashes were Grades 1-2 and occurred in the first 4-6 weeks of treatment; Grades 2-4 rash occurred in 1% of subjects. Discontinue Odefsey immediately if severe skin or hypersensitivity reactions occur, including severe rash or rash accompanied by fever, blisters, mucosal involvement, conjunctivitis, facial edema, angioedema, hepatitis or eosinophilia. Monitor clinical status including laboratory parameters and
initiate appropriate therapy.

- **Loss of virologic response due to drug interactions**: See Contraindications and Drug Interactions sections. Consider the potential for drug interactions prior to and during Odefsey therapy and monitor for adverse reactions.

- **Prolongation of QTc interval**: Rilpivirine doses 3 and 12 times higher than the recommended dose can prolong the QTc interval. Consider alternatives to Odefsey in patients at higher risk for Torsade de Pointes or when coadministered with a drug with known risk of Torsade de Pointes.

- **Depressive disorders**: Evaluate patients with severe depressive symptoms to assess if symptoms are due to Odefsey and if the risks of continued treatment outweigh the benefits. In rilpivirine adult clinical trials (N=686), the incidence of depressive disorders was 9%, Grades 3-4 depressive disorders was 1%, discontinuation due to depressive disorders was 1%, and suicidal ideation and suicide attempt was reported in 4 and 2 subjects, respectively. In a rilpivirine adolescent clinical trial (N=36), the incidence of depressive disorders was 19%, Grades 3-4 depressive disorders was 6%, and suicidal ideation and suicide attempt were reported in 1 subject.

- **Hepatotoxicity**: Hepatic adverse events have been reported, including cases of hepatic toxicity, in patients without pre-existing hepatic disease or other identifiable risk factors. In patients with hepatic abnormalities (e.g., hepatitis, elevated liver-associated tests), order laboratory tests before starting treatment and monitor for hepatotoxicity during treatment; consider testing and monitoring in all patients.

- **Fat redistribution** or accumulation has 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 emtricitabine and tenofovir alafenamide with elvitegravir and cobicistat, there have been no cases of Fanconi syndrome or proximal renal tubulopathy (PRT). Do not initiate Odefsey in patients with estimated creatinine clearance (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 Odefsey in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome.

  *Renal monitoring*: In all patients, monitor CrCl, urine glucose, and urine protein prior to initiating and during therapy. In patients with chronic kidney disease, additionally monitor serum phosphorus.

- **Bone loss and mineralization defects**: Decreases in bone mineral density (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

- **Most common adverse reactions** with rilpivirine (incidence ≥2%, Grades 2-4) are depressive disorders (2%), insomnia (2%) and headache (2%); and with emtricitabine and tenofovir alafenamide (incidence ≥10%, all grades) is nausea (10%).

### Drug interactions

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

- **Metabolism**: Drugs that induce CYP3A or P-gp and drugs that increase gastric pH can decrease the concentrations of components of Odefsey. Drugs that inhibit CYP3A or P-gp can increase the concentrations of components of Odefsey.

- **QT prolonging drugs**: Consider alternatives to Odefsey in patients taking a drug with known risk of Torsade de Pointes.

- **Drugs affecting renal function**: Coadministration of Odefsey 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 a meal.
- **Renal impairment**: Not recommended in patients with CrCl <30 mL/min.
- **Testing prior to initiation**: Test patients for HBV infection and assess CrCl, urine glucose and urine protein.
- **Testing after initiation**: In virologically-suppressed patients, additional monitoring of HIV-1 RNA and regimen tolerability is recommended.

Pregnancy and lactation

- **Pregnancy**: There are insufficient data on the use of Odefsey during pregnancy. In animal studies, no adverse developmental effects were observed with the components of Odefsey. An Antiretroviral Pregnancy Registry has been established.
- **Lactation**: Women infected with HIV-1 should be instructed not to breastfeeding, due to the potential for HIV-1 transmission.

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 Odefsey. 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, 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 Odefsey is available at [www.gilead.com](http://www.gilead.com).

U.S. Full Prescribing Information, including **BOXED WARNING**, for Genvoya, Stribild, Complera, Truvada and Viread are available at [www.gilead.com](http://www.gilead.com).

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For more information on Gilead Sciences, please visit the company’s website at [www.gilead.com](http://www.gilead.com), follow Gilead on Twitter (@GileadSciences) or call Gilead Public Affairs at 1-800-GILEAD-5 or 1-650-574-3000.


Source: Gilead Sciences, Inc.