U.S. Food and Drug Administration Approves Descovy® for HIV Pre-Exposure Prophylaxis (PrEP)

October 3, 2019

- Descovy Demonstrated Non-inferior Efficacy and an Improved Bone and Renal Safety Profile Compared with Truvada® in People at Risk for Sexually Acquired HIV Infection in a Global Phase 3 Trial -

FOSTER CITY, Calif.--(BUSINESS WIRE)--Oct. 3, 2019-- Gilead Sciences, Inc. (NASDAQ: GILD) today announced that the U.S. Food and Drug Administration (FDA) approved a pre-exposure prophylaxis (PrEP) indication for Descovy (emtricitabine 200 mg and tenofovir alafenamide 25 mg tablets; F/TAF). Descovy for PrEP™ is indicated to reduce the risk of sexually acquired HIV-1 infection in adults and adolescents weighing at least 35 kg who are HIV-negative and at-risk for sexually acquired HIV, excluding individuals at-risk from receptive vaginal sex.

“Descovy for PrEP provides a new HIV prevention option that matches Truvada’s high efficacy with statistically significant improvements in renal and bone safety, which can be an important consideration as people at risk increasingly use PrEP for longer periods of time,” said Daniel O’Day, Chairman and Chief Executive Officer, Gilead Sciences. “This is a reflection of Gilead’s continued commitment to addressing the evolving needs of people living with or at risk for HIV and to driving innovation across the HIV care continuum.”

The FDA approved the supplemental New Drug Application (sNDA) for Descovy under a priority review designation. Descovy has a Boxed Warning in its U.S. product label regarding the risk of post treatment acute exacerbation of hepatitis B. The Descovy label also includes a Boxed Warning regarding the risk of drug resistance with PrEP use in undiagnosed early HIV-1 infection. The effectiveness of Descovy for PrEP in individuals at risk of HIV-1 from receptive vaginal sex has not been established; please see below for Important Safety Information.

The approval of a PrEP indication for Descovy, taken once daily with or without food in patients weighing at least 35 kg, is based on data from the DISCOVER trial, a multi-year global Phase 3 registrational clinical trial that evaluated the safety and efficacy of Descovy for PrEP compared with that of Truvada (emtricitabine 200 mg and tenofovir disoproxil fumarate 300 mg tablets; F/TDF) for PrEP® in reducing the risk of acquiring HIV-1 infection. Enrollment included more than 5,300 adult cisgender men who have sex with men or transgender women (TGW) who have sex with men.

The primary efficacy endpoint of DISCOVER was the incidence of documented HIV infection per 100 person-years after all participants had follow-up of at least 48 weeks and at least half had 96 weeks of follow-up. These data, which were presented in March at the 2019 Conference on Retroviruses and Opportunistic Infections (CROI), included 5,387 individuals who were randomized 1:1 to receive either Descovy or Truvada. Among the 2,694 participants (4,370 person-years (PY)) who were at risk of HIV-1 infection and received once-daily Descovy, seven HIV-1 infections (HIV-1 incidence 0.16/100 PY) were reported. Among the 2,693 participants (4,386 PY) who were at risk of HIV-1 infection and received Truvada, 15 HIV infections (0.34/100 PY) were reported.

Results from the DISCOVER trial demonstrated that Descovy achieved non-inferiority to Truvada in study participants who were at risk of HIV acquisition. Efficacy was strongly correlated to adherence to daily dosing.

Additionally, statistically significant advantages were observed with respect to all six pre-specified secondary endpoints for both renal and bone laboratory parameters in patients receiving Descovy compared to Truvada.

“Today, because of landmark biomedical and scientific research advances, there are unprecedented opportunities to significantly reduce new HIV infections,” said Edwin DeJesus, MD, FACP, FIDSA, Medical Director, Orlando Immunology Center. “Descovy for PrEP offers healthcare providers and appropriate people at risk for HIV an additional biomedical prevention option with a demonstrated improvement in bone and renal safety parameters as compared to Truvada.”

Descovy does not prevent other sexually transmitted infections or cure HIV infection or AIDS.

Gilead Patient Assistance Program

Gilead is committed to helping ensure access to its HIV medications to all who need them. Driven by this purpose, we offer the Gilead Advancing Access® program to help address affordability challenges and to help continue to ensure that cost is not a barrier to individuals in the United States who need Gilead medication.

Gilead’s longstanding patient support offerings in the United States include the co-pay coupon program for eligible commercially insured individuals; the Medication Assistance Program (MAP), which provides free medication for those who qualify based on financial need; and the Uninsured 24/7 portal, which provides access to MAP enrollment and free medication that can be accessed from a pharmacy within hours. In addition, the Advancing Access program offers a range of options to assist patients with obtaining information about insurance coverage and investigating insurance benefits for their Gilead medication.

Information about Gilead’s support programs is available on the Gilead Advancing Access website at www.gileadadvancingaccess.com.

About PrEP

PrEP is an HIV prevention strategy in which medicine is taken daily before an HIV-negative person may be exposed to the virus through sex to help reduce the risk of infection. According to the Centers for Disease Control and Prevention (CDC), PrEP is highly effective at reducing the risk of HIV infection in at-risk populations.

Prevention methods, including PrEP, and safer sex practices are essential tools in the effort to end the HIV epidemic. PrEP use received an “A” rating from the U.S. Preventive Services Task Force (USPSTF), signifying that PrEP has a high certainty of substantial preventive benefits for reducing the risk of HIV. In addition, PrEP is recommended by the CDC, the World Health Organization and other national healthcare organizations as part of a comprehensive prevention strategy for individuals at risk for HIV.

IMPORTANT U.S. SAFETY INFORMATION AND INDICATION FOR DESCOVY FOR PREP

INDICATION

DESCOVY for HIV-1 pre-exposure prophylaxis (PrEP) is indicated in at-risk adults and adolescents (≥35 kg) to reduce the risk of sexually acquired HIV-1 infection, excluding individuals at risk from receptive vaginal sex. HIV-1-negative status must be confirmed immediately prior to initiation.

Limitation of Use: DESCOVY FOR PrEP is not indicated in individuals at risk of HIV-1 from receptive vaginal sex because effectiveness in this population has not been evaluated.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: RISK OF DRUG RESISTANCE WITH USE OF DESCOVY FOR PrEP IN UNDIAGNOSED EARLY HIV-1 INFECTION and POST TREATMENT ACUTE EXACERBATION OF HEPATITIS B

- **DESCOVY FOR PrEP must be prescribed only to patients confirmed to be HIV negative immediately prior to initiation and at least every 3 months during use. Drug-resistant HIV-1 variants have been identified with use of emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) for HIV-1 PrEP following undetected acute HIV-1 infection. Do not initiate if signs or symptoms of acute HIV-1 infection are present unless HIV-negative status is confirmed**
- **Severe acute exacerbations of hepatitis B have been reported in patients infected with hepatitis B virus (HBV) who discontinued products containing FTC and/or TDF and may occur with discontinuation of DESCOVY. Closely monitor hepatic function with both clinical and laboratory follow-up for at least several months in patients with HBV who discontinue DESCOVY. If appropriate, anti-hepatitis B therapy may be warranted**

Contraindication

- DESCOVY FOR PrEP is contraindicated in patients with unknown or positive HIV status

Warnings and precautions

- **Comprehensive management to reduce risks:**
  - Use DESCOVY FOR PrEP to reduce the risk of HIV-1 infection as part of a comprehensive strategy that includes adherence to daily dosing and safer sex practices, including condoms, to reduce the risk of sexually transmitted infections (STIs)
  - **HIV-1 risk factors:** Behavioral, biological, or epidemiologic HIV-1 risk factors may include, but are not limited to: condomless sex, past or current STIs, self-identified HIV risk, having sexual partners of unknown HIV-1 viremic status, or sexual activity in a high-prevalence area or network
  - **Reduce STI risk:** Counsel on the use of STI prevention measures (e.g., consistent and correct condom use, knowledge of partner's HIV-1 viremic status, regular testing for STIs
  - **Reduce potential for drug resistance:** Only prescribe DESCOVY FOR PrEP to patients confirmed to be HIV negative immediately prior to initiation, at least every 3 months while taking DESCOVY, and upon an STI diagnosis. HIV-1 resistance substitutions may emerge in patients with undetected HIV-1 infection who are taking only DESCOVY because DESCOVY alone is not a complete regimen for treating HIV-1
  - Some HIV tests may not detect acute HIV infection. Prior to initiating DESCOVY FOR PrEP, ask patients about potential recent exposure events. If recent (<1 month) exposures are reported or suspected, or symptoms of acute

HIV infection (e.g., fever, fatigue, myalgia, skin rash) are present, confirm HIV-negative status with a test approved by the FDA for use in the diagnosis of acute HIV infection

- If HIV-1 infection is suspected or if symptoms of acute infection are present while taking DESCOVY FOR PrEP, convert the DESCOVY FOR PrEP regimen to a complete HIV treatment regimen until HIV-negative status is confirmed by a test approved by the FDA for use in the diagnosis of acute HIV infection
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Counsel on adherence: Counsel patients to strictly adhere to daily dosing, as efficacy is strongly correlated with adherence. Some patients, such as adolescents, may benefit from more frequent visits and counseling

- **New onset or worsening renal impairment:** Cases of acute renal failure and Fanconi syndrome have been reported with the use of tenofovir prodrugs. Do not initiate DESCOVY 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 DESCOVY in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome. Monitor renal function in all patients (see Dosage and Administration section)

- **Lactic acidosis and severe hepatomegaly with steatosis:** Fatal cases have been reported with the use of nucleoside analogs, including FTC and TDF. Discontinue use if clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity develop, including hepatomegaly and steatosis in the absence of marked transaminase elevations

Adverse reactions

- **Most common adverse reactions** (≥2%) in the DESCOVY FOR PrEP clinical trial were diarrhea, nausea, headache, fatigue, and abdominal pain

Drug interactions

- **Prescribing information:** Consult the full Prescribing Information for DESCOVY for more information, warnings, and potentially significant drug interactions, including clinical comments

- **Metabolism:** Drugs that inhibit P-gp can increase the concentrations of tenofovir alafenamide (TAF), a component of DESCOVY. Drugs that induce P-gp can decrease the concentrations of TAF, which may lead to loss of efficacy

- **Drugs affecting renal function:** Coadministration of DESCOVY with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of FTC and tenofovir and the risk of adverse reactions

Dosage and administration

- **Dosage:** One tablet taken once daily with or without food
- **HIV screening:**Test for HIV-1 infection immediately prior to initiating, at least every 3 months during use, and upon diagnosis of an STI (see Warnings and Precautions section)
- **HBV screening:**Test for HBV infection prior to or when initiating DESCOVY
- **Renal impairment and monitoring:** Not recommended in patients with creatinine clearance (CrCl) <30 mL/min. Prior to or when initiating DESCOVY, and during use on a clinically appropriate schedule, assess serum creatinine, CrCl, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, assess serum phosphorus

About Gilead Sciences

Gilead Sciences, Inc. is a research-based biopharmaceutical company that discovers, develops and commercializes innovative medicines in areas of unmet medical need. The company strives to transform and simplify care for people with life-threatening illnesses around the world. Gilead has operations in more than 35 countries worldwide, with headquarters in Foster City, California.

For more than 30 years, Gilead has been a leading innovator in the field of HIV, driving advances in treatment, prevention, testing and linkage to care, and cure research. Today, it's estimated that more than 12 million people living with HIV globally receive antiretroviral therapy provided by Gilead or one of the company's manufacturing partners.

For more information on Gilead Sciences, please visit the company's website at www.gilead.com.

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 possibility of unfavorable results from ongoing and additional clinical trials involving Descovy for PrEP. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. 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 June 30, 2019, 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 Descovy and Truvada, including BOXED WARNINGS, is available at www.gilead.com.

Descovy, Descovy for PrEP, Truvada, Truvada for PrEP, Advancing Access, Gilead and the Gilead logo are trademarks of Gilead Sciences, Inc. or its related companies.

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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Source: Gilead Sciences, Inc.

Sung Lee, Investors
(650) 524-7792

Ryan McKeel, Media
(650) 377-3548