



## Gilead Presents 96-week Discover Trial Data Supporting Non-inferior Efficacy and Key Safety Differences of Descovy For PrEP™ Compared With Truvada For PrEP®

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### **– Results Continue to Demonstrate Statistically Significant Advantages of Descovy® Over Truvada® for Study Measurements of Bone and Renal Safety –**

FOSTER CITY, Calif.--(BUSINESS WIRE)--Nov. 6, 2019-- Gilead Sciences, Inc. (NASDAQ: GILD) today announced 96-week results from the DISCOVER trial, a multi-year global Phase 3 registrational clinical trial evaluating the safety and efficacy of once-daily Descovy (emtricitabine 200 mg and tenofovir alafenamide 25 mg) for HIV pre-exposure prophylaxis (PrEP) compared with Truvada (emtricitabine 200 mg and tenofovir disoproxil fumarate 300 mg) for PrEP, in men and transgender women who have sex with men and are at risk for sexually acquired HIV infection. Descovy demonstrated non-inferior efficacy to Truvada through 96 weeks and statistically significant differences over Truvada for certain key measurements of bone and renal safety assessed in the study, which were pre-specified secondary endpoints. These data are being presented at the 17<sup>th</sup> European AIDS Conference (EACS) in Basel, Switzerland.

“The 96-week data from the DISCOVER trial further support the comparable efficacy of Descovy and Truvada for PrEP and offer new insights into the improved renal and bone safety profile of Descovy as measured by key bone and renal markers,” said Diana Brainard, MD, Senior Vice President, HIV and Emerging Viruses, Gilead Sciences. “As more at-risk people use PrEP for longer periods of time, the data affirm the value of Descovy for PrEP as a new HIV prevention option.”

In the United States, Descovy for PrEP is indicated to reduce the risk of sexually acquired HIV-1 infection in at-risk adults and adolescents weighing at least 35 kg, excluding individuals at risk of HIV-1 from receptive vaginal sex because effectiveness in this population has not been evaluated.

Descovy has a Boxed Warning in its U.S. product label regarding the risk of drug resistance when used for PrEP in undiagnosed early HIV infection, and the risk of post-treatment acute exacerbation of hepatitis B. See below for Indication and Important Safety Information.

In the DISCOVER trial, 5,387 study participants were randomized in a 1:1 ratio to receive either Descovy or Truvada once-daily. The primary endpoint was the incidence rate of HIV infection when 100 percent of participants completed 48 weeks, and at least 50 percent of participants completed 96 weeks. As a secondary endpoint analysis, the incidence rate ratio (IRR) of Descovy to Truvada was evaluated when 100 percent of participants completed 96 weeks. Among the 2,670 participants who received Descovy over 96 weeks, eight acquired HIV (incidence rate: 0.16/100 person-years (PY)). Among the 2,665 participants who received Truvada for the duration of the study, 15 acquired HIV (incidence rate: 0.30/100 PY). These results confirm the continued non-inferiority of Descovy versus Truvada (IRR: 0.54; 95 percent CI 0.23, 1.26). After the primary analysis, there was one new HIV infection in the Descovy arm in a study participant with significantly reduced adherence for several months.

### **Bone and Renal Safety Outcomes**

Bone mineral density (BMD) was measured in a subset of 375 participants at 96 weeks. For measurements of both spine and hip BMD, differences between the Descovy and Truvada arms were statistically significant. At Week 96, lumbar spine BMD increased by 0.95 percent in the Descovy group and decreased by 1.39 percent in the Truvada group ( $p < 0.001$ ). Increases in hip BMD were also observed in participants taking Descovy, with an increase of 0.65 percent from baseline. Among those taking Truvada, hip BMD decreased by 1.01 percent ( $p < 0.001$ ).

For measurements of renal safety, statistically significant differences at Week 96 were observed favoring Descovy in mean serum creatinine level, median creatinine clearance and markers of proximal tubular function ( $\beta_2$ -microglobulin:creatinine ratio and retinol binding protein:creatinine ratio) ( $p < 0.001$  for all markers). Week 96 data also demonstrated fewer cases of treatment-emergent proteinuria among patients taking Descovy than among those taking Truvada ( $p = 0.003$ ) and similar changes in urine protein:creatinine ratio across the two treatment groups ( $p = 0.22$ ).

“These findings give healthcare providers and their patients a deeper understanding of the differences in the renal and bone safety profile of Descovy for PrEP as compared with Truvada,” said Peter Ruane, MD, Ruane Medical and Liver Health Institute. “Descovy for PrEP provides appropriate at-risk people with a new HIV prevention option that can potentially address important safety considerations related to bone mineral density and kidney function.”

Sexually transmitted infections (STIs) were assessed in three anatomic sites (oropharynx, urethra, rectum) at each study visit. Results of these STI screenings demonstrate that participants maintained high-risk sexual risk behavior from study entry through the duration of the study. At 96 weeks, 59 percent of participants had been diagnosed with gonorrhea or chlamydia (from any anatomic site) and 15 percent had been diagnosed with syphilis. All received medical treatment and contact tracing as appropriate.

Study drug-related adverse events were similar in both arms and adverse event-related discontinuations were uncommon, occurring in less than two percent of each arm. Of the nine adverse events that occurred at a frequency of at least 10 percent in either study arm, six of the nine were sexually transmitted infections. The others were diarrhea, nasopharyngitis, and upper respiratory tract infection.

Gilead has committed to conducting a clinical trial that will evaluate the safety and efficacy of Descovy for PrEP in cisgender women and adolescent females weighing at least 35 kg and who are at risk of sexually acquired HIV-1 infection in Africa.

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

### **Important U.S. Safety Information and Indication for Descovy for PrEP**

**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
  - **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

## INDICATION

DESCOVY for 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.

## 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](http://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 September 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](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.*

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Source: Gilead Sciences, Inc.

Greg Mann, Investors  
(424) 322-1795

Ryan McKeel, Media  
(650) 377-3548