Gilead Presents 96-week DISCOVER Trial Data Demonstrating Favorable Renal and Bone Safety Profile of Descovy® for HIV PrEP in At-Risk Populations

March 10, 2020

BOSTON--(BUSINESS WIRE)-- Gilead Sciences, Inc. (Nasdaq: GILD) today presented longer-term results from the DISCOVER trial of Descovy (emtricitabine 200 mg and tenofovir alafenamide 25 mg tablets, F/TAF) for pre-exposure prophylaxis (PrEP), demonstrating continued non-inferior efficacy and continued favorable changes in key markers of renal and bone safety at Week 96 compared with Truvada® (emtricitabine 200 mg and tenofovir disoproxil fumarate 300 mg, F/TDF) for PrEP. These results were achieved in the overall study population of men and transgender women at risk for HIV infection, as well as in study sub-populations of participants age 50 and older, those younger than 25 years, and those with moderate renal impairment. A separate analysis of the DISCOVER trial demonstrated that Descovy and Truvada were effective and well-tolerated in Black and Hispanic/Latinx participants. These data were presented at the 2020 Conference on Retroviruses and Opportunistic Infections (CROI) in Boston.

“At Gilead, we believe continued scientific innovation is essential to altering the future of the HIV epidemic,” said Diana Brainard, MD, Senior Vice President, HIV and Emerging Viral Infections, Gilead Sciences. “The longer-term efficacy and safety outcomes from the DISCOVER trial continue to demonstrate that Descovy is effective for HIV prevention with non-inferior efficacy to Truvada, and that Descovy has an improved bone and renal safety profile compared with Truvada.”

In addition to new data from the DISCOVER trial, the company also presented the results of a preclinical study with an investigational combination of bictegravir, emtricitabine and tenofovir alafenamide (BIC+F/TAF; 100+200/25 mg) for event-driven post-exposure prophylaxis (PEP).

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.

96-Week Safety Data from the DISCOVER Trial

This 96-week analysis of the DISCOVER trial (Oral 2940) demonstrated significant differences in key markers of bone and renal safety in study participants across different age groups. These differences were also observed in the overall population, in addition to differences in lipid parameters and change in baseline weight. The long-term clinical significance of these differences in renal, bone and lipid parameters are not known; however, these measures are important to consider as people at risk increasingly use PrEP for longer periods of time.

At Week 96, statistically significant differences in measurements of renal safety favoring Descovy were observed in the overall trial population, as well as in older participants and in those with moderate renal impairment (baseline eGFR=60-≤90 mL/min). In participants older than 50 years of age, those receiving Descovy showed a smaller decrease in median estimated glomerular filtration rate (eGFR) compared with those receiving Truvada (-1 mL/min vs. -6 mL/min) at Week 96. Key differences favoring Descovy were also observed in markers of proximal tubular function (β2-microglobulin:creatinine ratio and retinol binding protein:creatinine ratio). Among participants with moderate renal impairment, those randomized to Descovy also had smaller changes in eGFR and markers of proximal tubular function. In this sub-group, eGFR increased by 3 mL/min among those taking Descovy and decreased by 1 mL/min in those taking Truvada.

The analysis also found changes in bone mineral density (BMD) favoring Descovy in the overall trial population and among participants younger than 25 years of age. At Week 96 in participants younger than 25 years, spine BMD increased by 1.39 percent in the Descovy group and decreased by 1.2 percent in the Truvada group. Hip BMD increased 1.21 percent from baseline in the Descovy group and decreased by 1.7 percent in the Truvada group.

Study participants receiving Descovy had stable lipid levels through 96 weeks, whereas those receiving Truvada had decreases in lipid levels after 48 and 96 weeks. Fasting glucose levels were similar between the 2 groups. Participants in the Truvada group showed smaller mean weight increases than those in the Descovy group (+0.5 kg vs. +1.7 kg at Week 96). These findings are consistent with the lower lipid levels and decreased weight previously observed with TDF.

“These data continue to support the role of Descovy for PrEP as an option for a range of appropriate individuals at risk for HIV infection,” said Onyema Ogbuagu, MD, FACP, Director of HIV Clinical Trials program at Yale School of Medicine. “We are especially pleased to see that Descovy, unlike Truvada, did not result in a decrease in bone mineral density among younger participants and that more favorable measures of renal function were observed among study participants including older individuals and those with moderate renal impairment.”

Additional Data and Results from the DISCOVER Trial

On Monday, March 9, data were presented from 96-week follow-up of Black (n=474; 9%) and Hispanic/Latinx (n=1,318; 24%) participants in the DISCOVER trial (Poster 4033), which showed that both Descovy and Truvada were effective and well-tolerated in Black and Hispanic/Latinx participants.

Additional results presented from the DISCOVER trial included an analysis of transgender female trial participants who were taking high-dose gender-affirming hormone therapy (n=27) during the study (Poster 4018). This analysis of concomitant hormone therapy on the pharmacokinetics, efficacy and safety profile of Descovy or Truvada builds on the data from the dedicated Phase 1 studies that demonstrated lack of an effect of oral contraceptive hormones on the plasma exposure of TAF, TFV and FTC, and the lack of effect of plasma TAF, TFV, and FTC on ethinyl estradiol exposures, FSH, LH, or progesterone levels.

An analysis of drug levels and adherence in the DISCOVER trial (Poster 3815) will be presented tomorrow, March 11.

Descovy, Truvada, and BIC/FTC/TAF do not prevent other sexually transmitted infections or cure HIV or AIDS.

About the DISCOVER Trial

The DISCOVER trial is a multi-year global Phase 3 registrational clinical trial evaluating the safety and efficacy of once-daily Descovy for PrEP compared with Truvada for PrEP® in men and transgender women who have sex with men and are at risk for sexually acquired HIV infection. The primary analysis of the study was at Week 48; the Week 96 analysis was a prespecified secondary analysis. At both Weeks 48 and 96, Descovy for PrEP demonstrated non-inferior efficacy to Truvada for PrEP.

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.

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, Truvada for PrEP and the combination of BIC/FTC/TAF for post-exposure prophylaxis, and the possibility that we are unable to complete one or more of such trials on the currently anticipated timelines or at all. In addition, it is possible that Gilead may make a strategic decision to discontinue development of BIC/FTC/TAF for post-exposure prophylaxis, and as a result, it may never be successfully commercialized. 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 Annual Report on Form 10-K for the year ended December 31, 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 and Gilead 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.

View source version on businesswire.com: https://www.businesswire.com/news/home/20200310005729/en/

Douglas Maffei, PhD, Investors
(650) 522-2739

Brian Plummer, Media
(650) 524-7708

Source: Gilead Sciences, Inc.