Gilead Presents New Data From the Company's HIV Clinical Development Program and Latest Findings on the Impact of HIV Pre-exposure Prophylaxis (PrEP) at IDWeek 2019

October 4, 2019

- Results from DISCOVER Trial Provide Bone and Renal Safety Profile Data from Participants who Switched from Truvada for PrEP® to Descovy for PrEP ™ -

- Analysis Illustrates the Significant and Independent Impact of High PrEP Use on HIV Diagnoses Rate in Major U.S. Cities -

FOSTER CITY, Calif.--(BUSINESS WIRE)--Oct. 4, 2019-- Gilead Sciences, Inc. (NASDAQ: GILD) today announced important findings from the DISCOVER trial evaluating Descovy® (emtricitabine 200 mg and tenofovir alafenamide 25 mg tablets; F/TAF) for HIV pre-exposure prophylaxis (PrEP), showing significant improvements in key measures of bone and renal safety parameters in a subset of study participants who switched from Truvada® (emtricitabine 200 mg and tenofovir disoproxil fumarate 300 mg tablets; F/TDF) for PrEP to Descovy for PrEP ™. The company also released the latest data demonstrating that major metropolitan areas in the United States with the highest use of HIV PrEP experienced the greatest decreases in new diagnoses. The data will be presented at the IDWeek 2019 conference being held in Washington, D.C. from October 2-6.

"The results presented at IDWeek reflect Gilead's ongoing commitment to expanding awareness of HIV prevention efforts and the impact of PrEP use in the United States, and continuing to research and develop new prevention options for people at risk for HIV," said Diana Brainard, MD, Senior Vice President, HIV and Emerging Viruses, Gilead Sciences. "The data being shared at this year's meeting underscore the opportunity to reverse the HIV epidemic by supporting and accelerating the use of a broad range of prevention efforts."

Descovy is approved for HIV-1 pre-exposure prophylaxis in at-risk adults and adolescents weighing at least 35 kg who are HIV-negative, excluding individuals at risk from receptive vaginal sex. The indication does not include use of Descovy in individuals at risk of HIV-1 from receptive vaginal sex because effectiveness in this population has not been evaluated.

Descovy and Truvada have Boxed Warnings in their U.S. product labels regarding the risk of drug resistance with use of Descovy for PrEP and Truvada for PrEP® in undiagnosed early HIV infection and the risk of post-treatment acute exacerbation of hepatitis B. See below for Indications and Important Safety Information. Descovy and Truvada do not prevent other sexually transmitted infections or cure HIV or AIDS.

DISCOVER Trial: Renal and Bone Safety Profile Data Among Participants Switching from Truvada to Descovy for HIV Pre-exposure Prophylaxis

Two sub-analyses of data from the DISCOVER trial, a multi-year global Phase 3 clinical study of HIV prevention in 5,387 men and transgender women who have sex with men (MSM, TGW) will be presented. These findings provide new bone and renal safety profile data from a subgroup of 905 study participants (17 percent) who were using Truvada for PrEP at baseline and were randomized 1:1 to either continue Truvada or to switch to Descovy for PrEP.

The first study (oral abstract 1962) reports 48-week renal safety parameters among 465 participants who switched from Truvada for PrEP to Descovy for PrEP after enrolling in the DISCOVER trial, finding statistically significant improvements in key prespecified laboratory measures of kidney function, including urine protein:creatinine (CR) ratio (UPCR), estimated glomerular filtration rate ($eGFR_{CG}$) and markers of proximal tubular function (β2-microglobulin:Cr ratio [β2M:Cr] and retinol binding protein:Cr ratio [RBP Cr]). Improvements were statistically significant as early as Week 4 of the trial. At Week 48, $eGFR_{CG}$ increased by 3.9 mL/min from baseline for those randomized to F/TAF and decreased by 0.6 mL/min in those who continued to receive F/TDF ($p<0.001$). Greater declines in RBP:CR and β2M:Cr were observed among participants randomized to F/TAF compared with those who received F/TDF. Additional renal outcomes data from the 5,387 DISCOVER trial participants through 48 weeks will also be presented, including that study participants randomized to F/TAF for PrEP had fewer study drug-related renal adverse effects (AEs) and fewer discontinuations due to renal AEs compared with study participants randomized to F/TDF. Common adverse reactions (≥2 percent; all grades) in the DISCOVER trial included diarrhea, nausea, headache, fatigue, and abdominal pain.

"These latest findings from the DISCOVER trial continue to support the clinical and public health potential of Descovy for PrEP," said Tony Mills, MD, Assistant Professor of Clinical Medicine, UCLA and Chief Medical Officer, SoCal Men's Medical Group and lead author of the DISCOVER study. "The improvements observed in these important markers of kidney health in the overall study population and in those who switched from Truvada to Descovy point to the potential for Descovy to be a preventive option for appropriate people at risk for HIV who may require longer-term PrEP use, including those who have previously taken Truvada for PrEP."

A second presentation (abstract 1288) reports 48-week data on bone mineral density (BMD) outcomes among a subgroup of DISCOVER trial participants who received additional bone strength evaluations. Of these individuals (n=383), 53 participants were on baseline F/TDF PrEP at enrollment, 26 of whom were randomized to F/TAF. Participants who were randomized to switch to F/TAF experienced statistically significant improvements in BMD of the hip and spine compared with those randomized to continue F/TDF. In addition, participants taking F/TAF for PrEP were significantly less likely to develop osteopenia of the spine. The prevalence of osteopenia among the 2,694 study participants who took F/TAF for PrEP was 0.4 percent. The prevalence of osteopenia among the 2,693 study participants who took F/TDF for PrEP was 0.6 percent. Rates of fracture incidence were similar across the F/TAF and F/TDF groups. Among the subset of participants who were taking F/TDF for PrEP prior to randomization to F/TAF, significant improvements in hip BMD compared with baseline were observed, while spine BMD was unchanged.

"Maintaining bone mineral density is important when considering the potential impact of longer-term PrEP for people at risk for HIV infection," David Alain Wohl, MD, Professor of Medicine, Division of Infectious Diseases, the University of North Carolina at Chapel Hill and lead author of the DISCOVER study. "These results provide valuable insight into the potential impact of Descovy for PrEP on important measures of bone strength in a diverse population over the course of nearly a year."

Increased PrEP Use Associated with Significant Reductions in New HIV Diagnoses in Major U.S. Metropolitan Areas

A new analysis (abstract 1963) demonstrates the significant impact of PrEP for reducing new HIV diagnoses since the approval of the biomedical intervention, finding that between 2012 and 2017 metropolitan statistical areas (MSAs) in the United States with the highest rates of PrEP use experienced the greatest decreases in HIV diagnoses. Importantly, this effect was independent of the impact of treatment as prevention (TasP).

The analysis evaluates U.S. Centers for Disease Control and Prevention (CDC) HIV surveillance data collected between 2012 and 2017 from 105 MSAs, national pharmacy and medical claims databases and proxy data for TasP from HIV-suppressed individuals in 38 states and Washington, D.C. Between 2012 and 2017, the rate of PrEP use among at-risk individuals increased by greater than nine-fold, at an average rate of 2.95 percent per year, and HIV viral suppression increased by 1.34 percent per year during the same period. Overall, from 2012 to 2017, there was a 15.2 percent decline in the total rate of new HIV diagnoses. In MSAs with the highest rates of PrEP use, HIV diagnoses decreased by as much as 4.24 percent per year, whereas in MSAs with the lowest rates of PrEP use, HIV diagnoses decreased by 0.23 percent per year; these declines were statistically significant and independent of TasP. Comparatively, TasP independent of PrEP contributed to a 2.87 percent decline in HIV diagnoses for each percent increase in the proportion of HIV-infected people achieving viral suppression.

Projecting out five years, the analysis suggests that if PrEP utilization among individuals at high risk of HIV could reach 50 percent by 2022 in the MSAs analyzed, a 40.7 percent decline in the rate of new HIV diagnoses is possible.

These data support a multi-prong approach to reducing the number of new HIV diagnoses, combining TasP and 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.

Important U.S. Safety Information and Indication for Truvada for PrEP

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

- **Truvada for PrEP must only be prescribed to individuals 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 Truvada for 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 HBV-infected patients who discontinued Truvada. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients with HBV after discontinuing Truvada. If appropriate, initiation of anti-hepatitis B therapy may be warranted**

Contraindications

- Do not use Truvada for PrEP in individuals with unknown or positive HIV status

Warnings and precautions: Comprehensive risk reduction strategies

- **Reduce HIV-1 risk:** Truvada for PrEP is not always effective in preventing HIV-1. Use only as part of a comprehensive prevention strategy that includes safer sex practices, regular testing for HIV-1 and other STIs, and counseling on reducing sexual risk behaviors

- **Reduce potential for drug resistance:** Truvada for PrEP should only be used in individuals confirmed to be HIV-negative immediately prior to initiation, at least every 3 months while taking Truvada, and upon an STI diagnosis. HIV-1 resistance substitutions may emerge in individuals with undetected HIV-1 infection who are taking only Truvada. Truvada alone is not a complete regimen for treating HIV-1

    - HIV antibody tests may not detect acute HIV infection. If recent exposures are suspected or symptoms of acute HIV infection are present (e.g., fever, fatigue, myalgia, skin rash), delay initiating (≥1 month) or discontinue use and confirm HIV-negative status with a test approved by U.S. Food and Drug Administration (FDA) for the diagnosis of acute HIV infection

    - If a screening test indicates possible HIV-1 infection, convert the HIV-1 PrEP regimen to an HIV treatment regimen until HIV-negative status is confirmed.

- **Counsel on adherence:** Counsel individuals to strictly adhere to their dosing schedule, as efficacy is strongly correlated with adherence. Some individuals, such as adolescents, may benefit from more frequent visits and counseling.

Warnings and precautions

- **New onset or worsening renal impairment:** Cases of acute renal impairment and Fanconi syndrome have been reported with the use of tenofovir disoproxil fumarate (TDF). Truvada is not recommended in individuals with estimated creatinine clearance (CrCl) <60 mL/min. Avoid concurrent or recent use with a nephrotoxic agent. Acute renal failure has been reported after initiation of high dose or multiple NSAIDs in patients at risk for renal dysfunction; consider alternatives to NSAIDs in these patients. Monitor renal function in all patients – See Dosage and Administration

- **Bone effects:** Decreases in bone mineral density (BMD) and mineralization defects, including osteomalacia associated with proximal renal tubulopathy, have been reported with the use of TDF Consider monitoring BMD in patients with a history of pathologic fracture or risk factors for bone loss

- **Lactic acidosis and severe hepatomegaly with steatosis:** Fatal cases have been reported with the use of nucleoside analogs, including Truvada. 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

- **Drug interactions:** See Drug Interactions section. Consider the potential for drug interactions prior to and during use of Truvada and monitor for adverse reactions

Adverse reactions

- **Common adverse reactions** (>2% and more frequently than placebo) of Truvada for PrEP in clinical trials were headache, abdominal pain, and weight loss

Drug interactions

- **Prescribing information:** Consult the full Prescribing Information for Truvada for more information, warnings, and potentially significant drug interactions, including clinical comments
- **Hepatitis C antivirals:** Coadministration with ledipasvir/sofosbuvir, sofosbuvir/velpatasvir, or sofosbuvir/velpatasvir /voxilaprevir increases TDF exposure; monitor for adverse reactions
- **Drugs affecting renal function:** Coadministration of Truvada with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of emtricitabine and/or tenofovir

Pregnancy and lactation

- **Pregnancy:** An Antiretroviral Pregnancy Registry (APR) has been established. Available data from observational studies and the APR show no increase in the rate of major birth defects for Truvada compared with a US reference population. Consider HIV prevention methods, including Truvada for PrEP in at-risk women due to the potential increased risk of HIV-1 infection during pregnancy and mother to child transmission during acute HIV-1 infection
- **Lactation:** Emtricitabine and tenofovir have been detected in human milk. Evaluate the benefits and risks of Truvada for PrEP in breastfeeding women, including the risk of HIV-1 acquisition due to nonadherence, and subsequent mother to child transmission. Health benefits of breastfeeding should be considered along with potential adverse effects of Truvada on the child, which are unknown

Dosage and administration

- **Dosage:** One tablet once daily with or without food
- **HIV screening:** Test for HIV-1 infection prior to initiating and at least every 3 months during treatment
- **HBV screening:** Test for HBV infection prior to or when initiating treatment
- **Renal impairment and monitoring:** Not recommended in individuals with CrCl <60 mL/min. In all patients, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein on a clinically appropriate schedule. In patients with chronic kidney disease, also assess serum phosphorus

INDICATION

Truvada for PrEP (pre-exposure prophylaxis) is indicated to reduce the risk of sexually acquired HIV-1 in adults and adolescents (≥35 kg) who are at risk for HIV, when used in combination with safer sex practices. HIV-negative status must be confirmed immediately prior to initiation

- If clinical symptoms of acute HIV-1 infection are present and recent exposures (<1 month) are suspected, delay initiation for at least 1 month until HIV-negative status is reconfirmed. Alternatively, confirm HIV-negative status with a test cleared by FDA to aid in the diagnosis of acute HIV-1 infection

Individuals at risk for sexually acquired HIV-1 may include those:

- With HIV-1 infected partner(s), or
- Who engage in sexual activity in a high prevalence area or social network and have additional risk factors, such as: inconsistent or no condom use, diagnosis of sexually transmitted infections (STIs), exchange of sex for commodities, use of illicit drugs or alcohol dependence, incarceration, or sexual partners of unknown HIV status with any of these risk factors

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 risk that FDA and other regulatory agencies may not approve Descovy for PrEP in the currently anticipated timelines or at all, and any marketing approvals, if granted, may have significant limitations on its use. As a result, Descovy for PrEP may never be successfully commercialized. There is also the possibility of unfavorable results from additional studies 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 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.

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