Gilead Presents New Data on Biktarvy® (Bictegravir, Emtricitabine and Tenofovir Alafenamide) and TAF-Based Regimens for the Treatment of HIV-1 in Children, Older Adults and Women

March 6, 2019

FOSTER CITY, Calif.--(BUSINESS WIRE)--Mar. 6, 2019-- Gilead Sciences, Inc. (NASDAQ: GILD) today announced 48-week results from a Phase 2/3 study (Study GS-US-380-1474) evaluating the efficacy and safety of Biktarvy®(bictegravir 50 mg/emtricitabine 200 mg/tenofovir alafenamide 25 mg tablets, BIC/FTC/TAF), a once-daily single tablet regimen, in virologically suppressed adolescents and children at least 6 years of age who are living with HIV. Through Week 48, Biktarvy maintained high rates of virologic suppression with a low incidence of study drug-related adverse events and no treatment-emergent resistance. The data were presented at the 2019 Conference on Retroviruses and Opportunistic Infections (CROI) in Seattle.

“These findings indicate that Biktarvy, an oral single-tablet regimen that can be taken with or without food, has the potential to be an effective and well-tolerated treatment option for some children and adolescents living with HIV,” said Aditya H. Gaur, MD, Clinical Director, Department of Infectious Diseases at St. Jude Children’s Research Hospital and lead study investigator. “Importantly, Biktarvy was not associated with any cases of treatment-emergent resistance through 48 weeks of treatment, a result observed consistently to date across the Biktarvy clinical research programs and a significant consideration for children and adolescents who are facing the prospect of long-term treatment.”

Biktarvy is indicated in the U.S. as a complete regimen for the treatment of HIV-1 infection in adults who have no antiretroviral treatment history. Biktarvy is also indicated to replace the current antiretroviral regimen in those adults who are virologically suppressed on a stable antiretroviral regimen for at least three months. Virologically suppressed adults must have no history of treatment failure and no known substitutions associated with resistance to the individual components of Biktarvy. Biktarvy carries a Boxed Warning in its U.S. product label regarding the risk of post-treatment acute exacerbation of hepatitis B. See below for Important Safety Information.

Studies of Biktarvy and other TAF-based regimens in specific populations presented at the conference included:

Oral 2571: Biktarvy Single-Tablet Regimen in Adolescents & Children: Week 48 results

The 48-week, single-arm, open-label trial enrolled 50 virologically suppressed adolescents aged 12 to <18 years old and weighing ≥35 kg and 50 virologically suppressed children aged 6 to <12 years old and weighing ≥25 kg. All study participants had an undetectable viral load (HIV-1 RNA <50 c/mL) for at least six months before screening and CD4 cell counts of ≥200 cells/μL. Patients received a full adult strength Biktarvy tablet once daily.

At Week 48, 98 percent (n=74/75) of patients maintained an undetectable viral load, as defined by the US FDA snapshot algorithm. The remaining one patient had a reported HIV-1 RNA level of 85 c/ml at Week 48, but re-suppressed and achieved an undetectable viral load within two weeks. No participant in the study developed treatment-emergent resistance. Abdominal discomfort (grade 1) was the only study drug-related adverse event (AE) reported in more than one patient (2 percent; n=2).

In addition to efficacy and safety, the study evaluated the impact of the Biktarvy tablet on adherence in this patient population. All participants reported that the size and shape of the Biktarvy tablet was acceptable and the taste was palatable. The median percent adherence to Biktarvy, measured by pill count, was 99 percent.

The efficacy and safety profile of Biktarvy in adolescents and children has not been established; its use in these populations is investigational.

Poster 2586: 96 Week Efficacy and Safety of Biktarvy in Treatment-Naïve Adults and Adults ≥50 Years

A post-hoc analysis of data from two randomized, double-blind, Phase 3 studies (Studies 1489 and 1490) evaluated Biktarvy in treatment-naïve adults aged 50 and older (n=96/634), at Week 96. Treatment with Biktarvy resulted in high rates of virologic suppression regardless of age. Biktarvy was well tolerated in both the overall and the 50 year and older patient subgroups. There was no clinically significant impact on bone mineral density and renal laboratory parameters in patients aged 50 and older, a population at higher risk for comorbidities.

Poster 0519: Tenofovir Alafenamide vs Tenofovir DF in Women: Pooled Analysis of 7 Clinical Trials

A pooled analysis of data from 779 women in seven randomized, double-blind clinical trials (two in treatment-naïve adults and five in virologically suppressed adults) evaluated the efficacy and safety of TAF-based versus TDF-based regimens for antiretroviral treatment initiation or switch through Week 96. All participants who initiated or switched to TAF-based regimens, including Biktarvy, were compared with those who initiated or continued TDF-based regimens. Women who initiated or switched to TAF-based regimens had significantly improved bone and renal safety parameters compared to those who initiated or continued TDF-based regimens, with similar rates of virologic suppression. Discontinuations due to AEs were low in both groups.

“Gilead’s ongoing investment in HIV treatment research and development is focused on bringing the latest innovations and the potential for successful, long-term treatment to as many people living with HIV as possible,” said John McHutchison, AO, MD, Chief Scientific Officer and Head of Research and Development, Gilead Sciences. “Results from these studies in specific populations presented at CROI demonstrate that Biktarvy has the potential to be appropriate for use in a broad range of patients who are new to therapy or switching therapies, including young people and aging adults, as well as women who have been traditionally underrepresented in HIV clinical trials.”

Biktarvy does not cure HIV infection or AIDS.

IMPORTANT U.S. SAFETY INFORMATION AND INDICATION FOR BIKTARVY

BOXED WARNING: POST TREATMENT ACUTE EXACERBATION OF HEPATITIS B

- **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 (FTC) and/or tenofovir disoproxil fumarate (TDF), and may occur with discontinuation of Biktarvy. Closely monitor hepatic function with both clinical and laboratory follow-up for at least several months in patients who are coinfected with HIV-1 and HBV and discontinue Biktarvy. If appropriate, anti-hepatitis B therapy may be warranted.

Contraindications

- **Coadministration:** Do not use Biktarvy with dofetilide or rifampin.

Warnings and precautions

- **Drug interactions:** See Contraindications and Drug Interactions sections. Consider the potential for drug interactions prior to and during Biktarvy therapy and monitor for adverse reactions.
- **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 Biktarvy, there have been no cases of Fanconi syndrome or proximal renal tubulopathy (PRT). Do not initiate Biktarvy 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 Biktarvy in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome.
  Renal monitoring: Prior to or when initiating Biktarvy and during therapy, assess serum creatinine, CrCl, urine glucose, and urine protein in all patients as clinically appropriate. In patients with chronic kidney disease, also assess serum phosphorus.

- **Lactic acidosis and severe hepatomegaly with steatosis:** Fatal cases have been reported with the use of nucleoside analogs, including FTC and TDF. Discontinue Biktarvy 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** (incidence ≥5%; all grades) in clinical studies through week 96 were diarrhea (6%), nausea (6%), and headache (5%).

Drug interactions

- **Prescribing information:** Consult the full prescribing information for Biktarvy for more information on Contraindications, Warnings, and potentially significant drug interactions, including clinical comments.
- **Enzymes/transporters:** Drugs that induce P-gp or induce both CYP3A and UGT1A1 can substantially decrease the concentration of components of Biktarvy. Drugs that inhibit P-gp, BCRP, or inhibit both CYP3A and UGT1A1 may significantly increase the concentrations of components of Biktarvy. Biktarvy can increase the concentration of drugs that are substrates of OCT2 or MATE1.
- **Drugs affecting renal function:** Coadministration of Biktarvy 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.

Pregnancy and lactation

- **Pregnancy:** There is insufficient human data on the use of Biktarvy during pregnancy. An Antiretroviral Pregnancy Registry (APR) has been established. Available data from the APR for FTC shows no difference in the rates of birth defects compared with a US reference population.
- **Lactation:** Women infected with HIV-1 should be instructed not to breastfeed, due to the potential for HIV-1 transmission.

Dosage and administration

- **Dosage:** 1 tablet taken once daily with or without food.
- **Renal impairment:** Not recommended in patients with CrCl <30 mL/min.
- **Hepatic impairment:** Not recommended in patients with severe hepatic impairment.
- **Prior to or when initiating:** Test patients for HBV infection.
- **Prior to or when initiating, and during treatment:** As clinically appropriate, assess serum creatinine, CrCl, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, assess serum phosphorus.

INDICATION

Biktarvy is indicated as a complete regimen for the treatment of HIV-1 infection in adults who have no antiretroviral (ARV) treatment history or to

replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA <50 copies per mL) on a stable ARV regimen for ≥3 months with no history of treatment failure and no known resistance to any component of Biktarvy.

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 nearly 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 11.5 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 Biktarvy may not be approved for the treatment of HIV-1 infection in adolescents and children and the possibility of unfavorable results from additional clinical trials involving Biktarvy. 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, 2018, 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 Biktarvy, including **BOXED WARNING**, is available at www.gilead.com.*

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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