Gilead Presents Data on Biktarvy® (Bictegravir, Emtricitabine and Tenofovir Alafenamide) in Virologically Suppressed Adults, Including Those With Pre-Existing NRTI Resistance

March 6, 2019

FOSTER CITY, Calif.--(BUSINESS WIRE)--Mar. 6, 2019-- Gilead Sciences, Inc. (NASDAQ: GILD) today announced data from two studies evaluating the resistance profile of Biktarvy® (bictegravir 50 mg/emtricitabine 200 mg/tenofovir alafenamide 25 mg tablets, BIC/FTC/TAF) in virologically suppressed adults switching from dolutegravir/abacavir/lamivudine (DTG/ABC/3TC) or a boosted protease inhibitor (PI)-based regimen for the treatment of HIV-1. The studies found high rates of virologic suppression with Biktarvy in treatment-experienced adults, regardless of pre-existing resistance to nucleoside reverse transcriptase inhibitors (NRTIs). The data were presented at the 2019 Conference on Retroviruses and Opportunistic Infections (CROI) in Seattle.

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.

“Maintaining virologic suppression, even in the setting of resistance to certain classes of HIV medicines, when switching to Biktarvy, speaks to the versatility of Biktarvy,” said John McHutchison, AO, MD, Chief Scientific Officer and Head of Research and Development, Gilead Sciences. “These data add to the growing body of evidence supporting Biktarvy as a single tablet regimen that can be used in a wide range of clinical settings.”

Key abstracts for data presented at the conference included:

Poster 2141: Long-Term Biktarvy Switch Efficacy in Patients with Archived Pre-Existing Resistance

Participants in two Phase 3 Biktarvy switch studies (Studies 1844 and 1878) were followed through two years of therapy in the open-label continuation of these studies past the Week 48 primary endpoints. Documented resistance to study drugs was exclusionary; for the purposes of this retrospective analysis, archived preexisting HIV-1 drug resistance was assessed by historical genotypes and retrospective baseline proviral DNA genotyping. Among adults who switched to Biktarvy from DTG/ABC/3TC or a boosted protease inhibitor (PI)-based regimen, high rates of virologic suppression were observed in the overall population (n=561/570; 98 percent) as well as the population with preexisting drug resistance (n=155/159; 97 percent), including those with archived M184V/I (n=42/44; 95 percent). No patients developed treatment-emergent resistance during the course of the study.

Poster 3362: High Level of Pre-Existing NRTI Resistance Prior to Switching to Biktarvy

This ongoing, randomized, double-blind Phase 3 study (Study 4030) evaluated 565 virologically suppressed adults who switched 1:1 from a regimen of DTG+F/TAF or DTG+F/TDF to DTG+F/TAF or Biktarvy for 48 weeks. Participants with any documented nucleoside reverse transcriptase inhibitor (NRTI), non-nucleoside reverse-transcriptase inhibitor (NNRTI), and protease inhibitor (PI) resistance were allowed to enroll; patients with documented INSTI resistance were excluded. Archived preexisting HIV-1 drug resistance was assessed by historical genotype and retrospective baseline proviral DNA genotyping. In the study, 14 percent (n=78/565) of participants had NRTI resistance known or suspected at screening. This increased to 24 percent (n=138/565) using historical data combined with additional baseline proviral HIV-1 DNA genotyping. In this pooled, blinded *interim* analysis, 99 percent (n=557/562) of all participants with any post-baseline visit and 99 percent (n=220/222) of participants with resistance to any class of ARV, including those with archived M184V/I (n=79/81; 98 percent), had undetectable viral load (HIV-1 RNA <50 copies/mL) with no emergent drug resistance.

The efficacy and safety profile of Biktarvy in patients with preexisting resistance to its components has not been established; its use in these populations is investigational. 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 were diarrhea (6%), nausea (5%), 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 physicians may not see the benefits of prescribing Biktarvy for the treatment of HIV-1 infection 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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