Japan's Ministry of Health, Labour and Welfare Approves Gilead's Biktarvy® (Bictegravir, Emtricitabine and Tenofovir Alafenamide) for Treatment of HIV-1 Infection

March 26, 2019

– In Clinical Trials, Biktarvy Demonstrated High Efficacy, Few Interactions with Other Drugs and a High Barrier to Resistance Through 48 Weeks –

FOSTER CITY, Calif.--(BUSINESS WIRE)--Mar. 26, 2019-- Gilead Sciences, Inc. (NASDAQ:GILD) announced today that Japan's Ministry of Health, Labour and Welfare (MHLW) has approved Biktarvy® (bictegravir 50mg/emtricitabine 200mg/tenofovir alafenamide 25mg, BIC/FTC/TAF), a once-daily single tablet regimen (STR) for the treatment of HIV-1 infection. Biktarvy combines the novel, unboosted integrase strand transfer inhibitor (INSTI) bictegravir, with the demonstrated safety and efficacy profile of the Descovy® (emtricitabine 200 mg/tenofovir alafenamide 25 mg; FTC/TAF) dual nucleoside reverse transcriptase inhibitor (NRTI) backbone, and is the smallest INSTI-based triple-therapy STR available. Biktarvy is the first HIV product that Gilead will launch and commercialize in Japan directly through its local subsidiary, Gilead Sciences K.K.

In the United States, Biktarvy has a Boxed Warning in its product label regarding the risk of post-treatment acute exacerbation of hepatitis B. See below for U.S. Important Safety Information as well as the Biktarvy Indication.

The approval of Biktarvy is supported by data from four Phase 3 studies: Studies 1489 and 1490 in treatment-naïve HIV-1 infected adults, and Studies 1844 and 1878 in virologically suppressed adults. The trials are comprised of a diverse population of 2,415 participants on Biktarvy or an active comparator, including a wide range of adult age groups and races/ethnicities. Biktarvy met its primary objective of non-inferiority at 48 weeks across all four studies. Through 48 weeks, no participants in any of the four studies developed treatment-emergent virologic resistance while taking Biktarvy, no patients discontinued Biktarvy due to renal adverse events and there were no cases of proximal renal tubulopathy or Fanconi syndrome. The most common adverse reactions in patients taking Biktarvy were diarrhea, nausea and headache.

"Gilead is pleased that Biktarvy, our latest HIV treatment innovation, will be made available to people living with HIV in Japan," said John McHutchison, AO, MD, Chief Scientific Officer, and Head of Research and Development, Gilead Sciences. "In multiple clinical trials, Biktarvy has demonstrated high efficacy and a high barrier to resistance. With convenient dosing and few pre-screening or ongoing monitoring requirements, it has the potential to simplify treatment initiation, and follow-up over time."

"Gilead's operations in Japan have expanded significantly over the years and we are pleased to now be able to bring our longstanding experience and commitment as a global leader in HIV treatment to the Japanese HIV community," said Luc Hermans, M.D., President and Representative Director, Gilead Sciences, K.K. "Biktarvy adds an important new treatment option to our portfolio of medicines for people living with HIV in Japan."

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.

U.S. 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 is a biopharmaceutical company that discovers, develops and commercializes innovative therapeutics in areas of unmet medical need. The company's mission is to advance the care of patients suffering from life-threatening diseases. Gilead has operations in more than 35 countries worldwide, with headquarters in Foster City, California.

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.*

Biktarvy, Gilead and the Gilead logo 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/20190326005527/en/

Source: Gilead Sciences, Inc.

Sung Lee, Investors
+1 (650) 524-7792

Seiko Noma, Media Japan
+81-3-6837-0790

Ryan McKeel, Media US
+1 (650) 377-3548