Japan's Ministry of Health, Labour and Welfare Approves Gilead's Vemlidy® for Patients With Chronic Hepatitis B Virus Infection

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-- A Once-Daily Treatment that Demonstrated Comparable Efficacy with Improved Renal and Bone Laboratory Safety Parameters Compared to Tenofovir Disoproxil Fumarate (TDF) --

FOSTER CITY, Calif.--(BUSINESS WIRE)--Dec. 19, 2016-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced that the Japanese Ministry of Health, Labour and Welfare (MHLW) has approved Vemlidy® (tenofovir alafenamide) 25mg, a once-daily treatment for suppression of viral replication in chronic hepatitis B patients with evidence of hepatitis B virus replication and abnormal liver function.

Vemlidy is a novel targeted prodrug of tenofovir that has demonstrated antiviral efficacy similar to and at a dose less than one-tenth that of tenofovir disoproxil fumarate (TDF) 300mg. Data show that Vemlidy has greater plasma stability and delivers tenofovir to hepatocytes more efficiently compared to TDF. As a result, Vemlidy can be given at a lower dose, reducing the concentration of tenofovir in the bloodstream. Vemlidy has also shown improvements in renal and bone laboratory safety parameters compared to TDF.

"It is very exciting that a new treatment with improvements in renal and bone safety parameters is now approved for patients with chronic hepatitis B. This is an important advancement, as these patients often require lifelong therapy," said Namiki Izumi, MD, the President of Musashino RedCross Hospital.

Vemlidy's approval is supported by 48-week data from two international Phase 3 studies (Studies 108 and 110) among 1,298 treatment-naïve and treatment-experienced adult patients with HBeAg-negative and HBeAg-positive chronic HBV infection. Study 108 randomized and treated 425 HBeAg-negative patients with either Vemlidy or TDF, and Study 110 randomized and treated 873 HBeAg-positive patients with either Vemlidy or TDF. Study 108 enrolled 27 patients from 11 sites in Japan and Study 110 enrolled 46 patients from 16 sites in Japan. Both studies met their primary endpoint of non-inferiority to TDF based on the percentage of patients with chronic hepatitis B with plasma HBV DNA levels below 29 IU/mL at 48 weeks of therapy.

In an integrated analysis of both studies, patients receiving Vemlidy demonstrated improvements in bone and renal laboratory parameters compared to those treated with TDF. Patients in the Vemlidy arm also experienced numerically higher rates of normalization of serum alanine aminotransferase (ALT) levels.

Vemlidy and TDF were generally well-tolerated by patients in both studies and discontinuations due to adverse events were 1% and 1.2%, respectively. In both studies, the most commonly reported adverse events included headache, abdominal pain, fatigue, cough, nausea and back pain and occurred at similar rates in patients receiving either Vemlidy or TDF.

"There are currently more than one million people in Japan chronically infected with hepatitis B, and we believe Vemlidy is an important option for patients living with this disease," said Norbert Bischofberger, PhD, Gilead's Executive Vice President, Research and Development, and Chief Scientific Officer. "We have been pleased to partner with the medical community here in Japan to demonstrate the efficacy and safety profile of Vemlidy, and we look forward to making the medication available in Japan soon."

Gilead is now preparing to launch Vemlidy as quickly as possible.

In Japan, TDF is sold by GlaxoSmithKline K.K.

Important Safety Information and Indication for Vemlidy in the U.S.

BOXED WARNING: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT SEVERE ACUTE EXACERBATION OF HEPATITIS B

- **Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs.**
- **Discontinuation of anti-hepatitis B therapy, including VEMLIDY, may result in severe acute exacerbations of hepatitis B. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue anti-hepatitis B therapy, including VEMLIDY. If appropriate, resumption of anti-hepatitis B therapy may be warranted**.

Warnings and Precautions

- **Risk of Development of HIV-1 Resistance in HBV/HIV-1 Coinfected Patients:** Due to this risk, VEMLIDY alone is not recommended for the treatment of HIV-1 infection. Safety and efficacy of VEMLIDY have not been established in HBV/HIV-1 coinfected patients. HIV antibody testing should be offered to all HBV-infected patients before initiating therapy with VEMLIDY, and, if positive, an appropriate antiretroviral combination regimen that is recommended for HBV/HIV-1 coinfected patients should be used.
- **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 VEMLIDY, there have been no cases of Fanconi syndrome or proximal renal tubulopathy (PRT). Patients with impaired renal function and/or taking nephrotoxic agents (including NSAIDs) are at increased risk of renal-related adverse reactions. Discontinue VEMLIDY in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome.
  Renal monitoring: Assess serum creatinine, serum phosphorus, CrCl, urine glucose, and urine protein prior to initiating and during therapy in all patients as clinically appropriate.

Adverse Reactions

Most common adverse reactions (incidence ≥5%; all grades) were headache, abdominal pain, fatigue, cough, nausea and back pain.

Drug Interactions

- Coadministration of VEMLIDY with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of tenofovir and the risk of adverse reactions.
- Coadministration of VEMLIDY is not recommended with the following: oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine, or St. John's wort. Such coadministration is expected to decrease the concentration of tenofovir alafenamide, reducing the therapeutic effect of VEMLIDY. Drugs that strongly affect P-gp and BCRP activity may lead to changes in VEMLIDY absorption.

Consult the full prescribing information for VEMLIDY for more information on potentially significant drug interactions, including clinical comments.

Dosage and Administration

- **Dosage:** Adults; 1 tablet taken once daily with food.
- **Renal Impairment:** Not recommended in patients with CrCl <15 mL/min.
- **Hepatic Impairment:** Not recommended in patients with decompensated (Child-Pugh B or C) hepatic impairment.
- **Testing prior to initiation:** HIV infection.

Indication

VEMLIDY is indicated for the treatment of chronic hepatitis B virus (HBV) infection in adults with compensated liver disease.

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 30 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 Vemlidy for the treatment of chronic HBV. 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 September 30, 2016, 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 Vemlidy, including **BOXED WARNING**, is available at www.gilead.com.*

Vemlidy is a registered trademark 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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