China National Medical Products Administration (NMPA) Approves Gilead's Vemlidy® (Tenofovir Alafenamide) for Chronic Hepatitis B Virus (HBV) Infection

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- First New Oral Treatment Approved for HBV in Ten Years Offers Improved Renal and Bone Laboratory Safety Parameters Compared to Tenofovir Disoproxil Fumarate (TDF) –

FOSTER CITY, Calif.--(BUSINESS WIRE)--Nov. 18, 2018-- Gilead Sciences, Inc. (NASDAQ: GILD) announced today that the China National Medical Products Administration (NMPA) has approved Vemlidy® (tenofovir alafenamide, TAF) 25 mg, a once-daily treatment for chronic hepatitis B in adults and adolescents (aged 12 years and older with body weight at least 35 kg).

Vemlidy is a novel, targeted prodrug of tenofovir that has demonstrated antiviral efficacy similar to Gilead's Viread® (tenofovir disoproxil fumarate, TDF) 300 mg but at one-tenth of the dose. Data show that because Vemlidy has greater plasma stability and more efficiently delivers tenofovir to hepatocytes compared to Viread, it can be given at a lower dose, resulting in less tenofovir in the bloodstream. In clinical trials, Vemlidy demonstrated improved renal and bone laboratory safety parameters compared to Viread.

"With the approval of Vemlidy, physicians can now offer their patients a treatment that retains the efficacy of TDF while improving renal and bone safety parameters in clinical trials," said Prof. Jinlin Hou, Nanfang Hospital of Southern Medical University.

HBV is highly prevalent in China with an estimated 20 million people meeting current guidelines for therapy – accounting for almost one-third of all patients currently requiring therapy worldwide. Each year, approximately 300,000 people in China die from cirrhosis of the liver related to HBV.

"Chronic hepatitis B remains an urgent public health issue in China, and many people still need well tolerated and effective treatment options with a high barrier to resistance, especially as therapy can be life-long," said Gregg Alton, Gilead Chief Patient Officer. "Gilead is committed to working with health officials and affected communities to help address the ongoing hepatitis B challenge in China."

Vemlidy's approval is supported by data from two international Phase 3 studies (Studies 108 and 110) among 1,632 treatment-naive and treatment-experienced adult patients with HBeAg-negative and HBeAg-positive HBV disease (including 334 treated in China). In an integrated analysis of both studies, patients receiving Vemlidy demonstrated improvements in certain bone and renal laboratory parameters compared to those treated with Viread. In addition, no patient developed resistance to tenofovir during the studies through 96 weeks of therapy.

The most commonly reported adverse events through 96 weeks in both studies included headache, abdominal pain, fatigue, cough, nausea and back pain and occurred at similar rates in patients receiving either Vemlidy or Viread.

The U.S. Prescribing Information for Vemlidy has a Boxed Warning for the risk of post-treatment severe acute exacerbation of hepatitis B. See below for U.S. Important Safety Information and Indication. In the U.S., Vemlidy is only indicated for adult patients with compensated liver disease.

Vemlidy received marketing approval from the U.S. Food and Drug Administration (FDA) and the Japanese Ministry of Health, Labour and Welfare in 2016, and from the European Commission in 2017.

U.S. IMPORTANT SAFETY INFORMATION

BOXED WARNING: POST TREATMENT SEVERE ACUTE EXACERBATION OF HEPATITIS B

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. Monitor renal function in all patients – See Dosage and Administration.
- **Lactic Acidosis and Severe Hepatomegaly with Steatosis:** Fatal cases have been reported with the use of nucleoside analogs, including TDF. Discontinue VEMLIDY 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 $\geqslant$5%; all grades) were headache, abdominal pain, cough, back pain, fatigue, nausea, arthralgia, diarrhea, and dyspepsia.

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, Screening, and Monitoring:** VEMLIDY is not recommended in patients with CrCl <15 mL/min. In all patients, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein prior to initiating and during treatment, on a clinically appropriate schedule. In patients with chronic kidney disease, also assess serum phosphorus.
- **Hepatic Impairment:** Not recommended in patients with decompensated (Child-Pugh B or C) hepatic impairment.
- **Testing prior to initiation:** HIV infection.

U.S. 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, 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.

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. 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, 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 Vemlidy and Viread including **BOXED WARNINGS** is available at www.gilead.com*

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For more information on Gilead Sciences, please visit the company's China website at www.gileadchina.com, or follow Gilead on WeChat.by scanning the QR code below: