Gilead Presents Data at the International Liver Congress™ 2017 Supporting the Efficacy and Safety of Vemlidy in Patients with Chronic Hepatitis B After 96 Weeks, and Also After Switching From Viread

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-- Additional Presentations Highlight Early Research of Investigational Agents For HBV Cure --

FOSTER CITY, Calif.--(BUSINESS WIRE)--Apr. 20, 2017-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced 96-week results from two ongoing Phase 3 studies evaluating the safety and efficacy of daily Vemlidy® (tenofovir alafenamide, TAF 25mg) in immune active patients and in patients switching from Gilead's Viread® (tenofovir disoproxil fumarate, TDF 300mg). Vemlidy is a once-daily treatment approved for adults with chronic hepatitis B virus (HBV) infection with compensated liver disease. In addition, Gilead presented data from preclinical studies of investigational compounds being studied for their potential role in HBV cure strategies. Data are being presented this week at The International Liver Congress™ 2017 in Amsterdam.

Vemlidy is a novel, targeted prodrug of tenofovir that has demonstrated antiviral efficacy that is noninferior to that of Viread at Week 48 in patients with chronic HBV. Vemlidy treatment at the same time point also demonstrated a beneficial impact on renal and bone laboratory safety parameters compared to Viread. Analyses now conducted at Week 96 of treatment demonstrate continued benefits of Vemlidy including high rates of viral suppression, with no evidence of resistance, and less impact on renal and bone safety parameters as compared to Viread (#PS-042, #FRI-153). Additionally, patients switching from Viread to Vemlidy after Week 96 demonstrated maintenance of viral suppression, improvement in serum alanine aminotransferase (ALT) normalization rates, and improvement in bone and renal parameters 24 weeks after switching to Vemlidy (#PS-041: "Hepatitis B and D: emerging treatment options").

"The results observed in these studies reinforce Vemlidy as an important treatment option for patients living with chronic HBV infection," said Norbert Bischofberger, PhD, Executive Vice President of Research and Development and Chief Scientific Officer at Gilead. "Additionally, the preclinical data presented at this EASL meeting illustrate our scientific approach to evaluating compounds with distinct mechanisms of action aimed at curing HBV infection."

Vemlidy has a boxed warning in its U.S. product label regarding the risk of post-treatment severe acute exacerbation of hepatitis B. See below for important safety information.

Vemlidy

The two randomized, double-blinded Phase 3 studies (Studies 108 and 110) from which the data are presented evaluated the use of Vemlidy given once-daily versus Gilead's Viread given once-daily in treatment-naïve and treatment-experienced adults with HBeAg-negative and HBeAg-positive chronic HBV infection.

Results demonstrate continued advantages of treatment with Vemlidy over Viread between Week 48 and Week 96. Virologic response rates at Week 96 were 90 percent (n=257/285) and 91 percent (n=127/140) in HBeAg-negative patients (Study 108) receiving Vemlidy and Viread, respectively. In HBeAg-positive patients (Study 110), virologic response rates at Week 96 were 73 percent (n=423/581) and 75 percent (n=218/292) in the Vemlidy and Viread groups, respectively. In both studies, a greater percentage of patients taking Vemlidy achieved normalization of ALT levels relative to patients taking Viread as measured by both central laboratory criteria, and by the American Association for the Study of Liver Diseases (AASLD) criteria. Patients receiving Vemlidy also demonstrated ongoing benefits at Week 96 in bone and renal safety parameters, including smaller declines from baseline in hip and spine bone mineral density (BMD) and smaller declines from baseline in estimated creatinine clearance compared with patients taking Viread in both studies. Similar rates of adverse events and low and similar rates of adverse events leading to discontinuation were observed in both treatment arms. Viral resistance analyses showed no resistance to Vemlidy or Viread at Week 96.

A post-hoc analysis evaluated a subset of 541 patients from Studies 108 and 110 who completed 96 weeks of treatment

with double-blind Vemlidy or Viread and were then switched to open-label treatment with Vemlidy. Among patients switched from Viread to Vemlidy at Week 96 (n=180), virologic suppression was maintained and the rates of ALT normalization by central laboratory criteria and AASLD criteria significantly increased during the subsequent 24 weeks of Vemlidy therapy. These patients also demonstrated further improvements in hip and spine BMD and had significant improvements in estimated creatinine clearance. Longer-term data are required to confirm the benefits of switching from Viread to Vemlidy for the treatment of chronic HBV.

Hepatitis B Pipeline

In addition, Gilead has several ongoing research programs with the goal of achieving functional cure for HBV-infected patients. Preclinical data with some of Gilead's novel investigational compounds are being presented at the Congress.

GS-5801 is an oral liver-targeted prodrug of a small molecule inhibitor of KDM5, a histone lysine demethylase. Results from *in vitro* preclinical studies (#SAT-160) demonstrated activity of GS-5801 in HBV-infected primary human hepatocytes with significant declines in viral proteins and HBV RNA. In addition, *in vivo* data (#THU-171) demonstrated the pharmacodynamic response of GS-5801 within the liver, in animal models. GS-5801 is currently being evaluated in Phase 1 trials in healthy subjects and in patients with chronic HBV infection.

GS-9688, an oral selective toll-like receptor 8 (TLR8) agonist, demonstrated *in vitro* and *in vivo* pharmacodynamic effects consistent with selective TLR8 activation, including the production of antiviral cytokines (#SAT-168). Further, in an efficacy animal model of chronic HBV infection, GS-9688 treatment demonstrated a sustained antiviral response in chronically infected woodchucks (#SAT-165). GS-9688 is currently being evaluated in Phase 1 trials in healthy subjects and in patients with chronic HBV infection.

Further information about the clinical studies described above can be found at http://anzctr.org.au/.

GS-5801 and GS-9688 are investigational products and have not been determined to be safe or efficacious.

U.S. Important Safety Information for Vemlidy

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.
  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.
- **Lactic Acidosis and Severe Hepatomegaly with Steatosis:** Fatal cases have been reported with the use of

nucleoside analogs, including tenofovir DF. 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 ≥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.

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 HBV. In addition, Gilead may be unable to achieve a functional cure for HBV with any of its product candidates, including GS-5801 and GS-9688. 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 quarter ended December 31, 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 including **BOXED WARNING** for Vemlidy is available at www.gilead.com.*

Vemlidy and Viread are registered 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.

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