Gilead Announces New Data from Viral Hepatitis Research Programs at The Liver Meeting® 2019

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-- Data Demonstrate Reductions in Hepatocellular Carcinoma in Hepatitis B (HBV) Patients Treated with Vemlidy --

-- Improved Markers of Bone and Renal Safety Also Seen with Vemlidy in Separate Analysis of HBV Patients with Hepatic or Renal Impairment --

-- Data on Investigational TLR8 Agonist GS-9688 Support Continued Advancement of the Company's HBV Cure Research Program --

BOSTON--(BUSINESS WIRE)--Nov. 8, 2019-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced new data on Vemlidy® (tenofovir alafenamide 25 mg, TAF) that continue to support an improved safety profile compared with tenofovir disoproxil fumarate (TDF) in patients with chronic hepatitis B (HBV) infection. These results, along with new data from Gilead's HBV cure and hepatitis C (HCV) research programs, are being presented at The Liver Meeting® 2019 in Boston this week.

Chronic HBV infection is a leading risk factor for the development of hepatocellular carcinoma (HCC) globally. The impact of HBV treatment on HCC incidence was evaluated in a long-term analysis of two Phase 3 studies of Vemlidy (Oral 0194), in which 1,632 HBV patients were randomized to receive either Vemlidy or TDF once daily in two cohorts. Through three or five years of follow-up, dependent on cohort, HCC was observed in 21 patients (1.0 percent in the TAF group; 1.9 percent in the TDF group), with a median time to onset of 104 weeks. The HCC incidence observed in this study was significantly lower than the predicted incidence using the REACH-B model, particularly for patients without cirrhosis. Additional follow-up is needed to further characterize the impact of longer-term treatment on HCC risk reduction.

In the United States, Vemlidy is indicated for the treatment of chronic HBV infection in adults with compensated liver disease. The U.S. product label for Vemlidy contains a BOXED WARNING for the risk of severe post-treatment acute exacerbation of HBV. See below for U.S. Important Safety Information.

"Chronic infection with hepatitis B virus can lead to an increased risk of developing serious and life-threatening liver damage," said Young-Suk Lim, M.D., Ph.D., lead study author and professor, Department of Gastroenterology, Liver Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea. "This analysis suggests that sustained viral suppression from treatment with Vemlidy may reduce the risk of hepatocellular carcinoma in chronic hepatitis B patients, which is the most common type of liver cancer in adults."

Markers of Bone and Renal Safety with Vemlidy

Data from multiple studies presented at AASLD demonstrate continued viral suppression (HBV DNA <20 IU/mL) and improvements in bone and renal markers with Vemlidy in patients with chronic HBV and also in high-risk HBV patients with hepatic or renal impairment.

In an analysis from a Phase 3 study evaluating virally suppressed chronic HBV patients (Poster 0455), 243 patients who had previously been treated with TDF for a median of four years were switched to Vemlidy for 48 weeks. Switching from TDF to Vemlidy resulted in improvement in certain bone and renal markers regardless of the duration (<4 years vs ≥ 4 years) of prior TDF use.

In an open-label Phase 2 study (Poster 0483), 93 HBV patients with moderate to severe renal impairment and those with end-stage renal disease (ESRD) on chronic hemodialysis (HD) who were virally suppressed taking TDF and/or other antivirals for at least 48 weeks, were switched to Vemlidy for 96 weeks. At week 24, all patients with ESRD and 97 percent of patients with moderate or severe renal impairment met the primary endpoint of maintaining viral load suppression. In renally-impaired HBV patients, switching to Vemlidy from TDF resulted in increases in hip and spine bone mineral density and decreases in most bone turnover markers including in ESRD patients on HD, as well as decreases in renal tubular markers and increases in glomerular filtration rate ($eGFR_{CG}$). Similar results were achieved in a Phase 2 open-label study of 31 virally suppressed HBV patients with moderate or severe hepatic impairment (Child-Turcotte-Pugh Class B or C) who were switched to Vemlidy and treated for 24 weeks (Poster 0501).

The use of Vemlidy in chronic HBV patients with moderate or severe hepatic impairment is investigational; its safety and efficacy have not been established.

HBV Functional Cure Research

GS-9688 is an investigational oral selective small molecule agonist of toll-like receptor 8 (TLR8). In a Phase 2 multicenter, randomized, double-blind study of 48 virally suppressed chronic HBV patients (Poster 0697), GS-9688, taken in combination with oral antivirals, was well-tolerated over an extended dosing period and demonstrated dose-dependent pharmacodynamic activity. Clinical activity was also evaluated; five percent of patients receiving GS-9688 achieved a ≥ 1 $\log_{10}$ IU/mL decline in hepatitis B surface antigen (HBsAg) levels or hepatitis B e-antigen (HBeAg) loss at 24 weeks. These data support ongoing studies of GS-9688 as well as novel combinations aimed at achieving a functional cure of HBV.

The safety and efficacy of GS-9688 have not been established. GS-9688 is an investigational compound and is not approved by the U.S. Food & Drug Administration (FDA) or any other regulatory authority.

HCV Treatment in Pediatric Patients

There are limited approved HCV treatment options for children younger than 12 years old, particularly those with HCV genotypes 2 and 3. In an open-label study of patients 6 to <18 years of age with HCV genotypes 1, 2, 3, 4 and 6 (Poster 0748), 12 weeks of treatment with Epclusa® (sofosbuvir/velpatasvir) resulted in a cure rate (SVR12) of 95 percent (97/102) in patients 12 to <18 years old and 92 percent (67/73) in those 6 to <12 years old. Most AEs were mild or moderate in severity; four patients experienced a serious AE, one which was attributed to treatment. The most common AEs (>15 percent of patients) were headache, fatigue and nausea in adolescents, and vomiting, cough and headache in patients 6 to <12

years old. The study is ongoing in children ages 3 to <6 years old.

The use of Epclusa in the aforementioned patient population is investigational; its safety and efficacy have not been established. Epclusa is indicated in the United States for the treatment of adults with chronic HCV genotype 1-6 infection without cirrhosis or with compensated cirrhosis and in combination with ribavirin for those with decompensated cirrhosis. The U.S. product label for Epclusa contains a BOXED WARNING for the risk of hepatitis B reactivation in HCV/HBV co-infected patients. See below for U.S. Important Safety Information.

U.S. Important Safety Information and Indication 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 should not be used 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 tenofovir disoproxil fumarate. 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, 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-glycoprotein (P-gp) and breast cancer resistance protein (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

Testing Prior to Initiation: HIV infection.

Prior to or when initiating, and during treatment: On a clinically appropriate schedule, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, also assess serum phosphorus.

Dosage: Adults; 1 tablet taken once daily with food.

Renal Impairment, Screening, and Monitoring: Not recommended in patients with end stage renal disease (ESRD; eCrCl <15 mL/min) who are not receiving chronic hemodialysis; in patients on chronic hemodialysis, on hemodialysis days, administer VEMLIDY after completion of hemodialysis treatment.

Hepatic Impairment: Not recommended in patients with decompensated (Child-Pugh B or C) hepatic impairment.

INDICATION

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

U.S. Important Safety Information and Indication for Epclusa

BOXED WARNING: RISK OF HEPATITIS B VIRUS REACTIVATION IN HCV/HBV COINFECTED PATIENTS

Test all patients for evidence of current or prior hepatitis B virus (HBV) infection before initiating treatment with EPCLUSA. HBV reactivation has been reported in HCV/HBV coinfected patients who were undergoing or had completed treatment with HCV direct acting antivirals (DAAs) and were not receiving HBV antiviral therapy. Some cases have resulted in fulminant hepatitis, hepatic failure, and death. Cases have been reported in patients who are HBsAg positive, in patients with serologic evidence of resolved HBV, and also in patients receiving certain immunosuppressant or chemotherapeutic agents; the risk of HBV reactivation associated with treatment with HCV DAAs may be increased in patients taking these other agents. Monitor HCV/HBV coinfected patients for hepatitis flare or HBV reactivation during HCV treatment and post-treatment follow-up. Initiate appropriate patient management for HBV infection as clinically indicated.

Contraindications

If EPCLUSA is used in combination with ribavirin (RBV), all contraindications, warnings and precautions, in particular pregnancy avoidance, and adverse reactions to RBV also apply. Refer to RBV prescribing information.

Warnings and Precautions

Serious Symptomatic Bradycardia When Coadministered with Amiodarone: Amiodarone is not recommended for use with EPCLUSA due to the risk of symptomatic bradycardia, particularly in patients also taking beta blockers or with underlying cardiac comorbidities and/or with advanced liver disease. A fatal cardiac arrest was reported in a patient taking amiodarone who was coadministered a sofosbuvir containing regimen.

In patients without alternative, viable treatment options, cardiac monitoring is recommended. Patients should seek immediate medical evaluation if they develop signs or symptoms of bradycardia.

Risk of Reduced Therapeutic Effect Due to Use with P-gp Inducers and/or Moderate to Potent Inducers of CYP2B6, CYP2C8 or CYP3A4: Rifampin, St. John's wort and carbamazepine are not recommended for use with EPCLUSA as they may significantly decrease sofosbuvir and/or velpatasvir plasma concentrations.

Adverse Reactions

The most common adverse reactions (≥10%, all grades) with EPCLUSA were headache and fatigue; and when used with RBV in decompensated cirrhotics were fatigue, anemia, nausea, headache, insomnia, and diarrhea.

Drug Interactions

Coadministration is not recommended with topotecan due to increased concentrations of topotecan; or with proton-pump inhibitors, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifapentine, efavirenz, and tipranavir/ritonavir due to decreased concentrations of sofosbuvir and/or velpatasvir.

Consult the full Prescribing Information for EPCLUSA for more information on potentially significant drug interactions, including clinical comments.

INDICATION

EPCLUSA is indicated for the treatment of adults with chronic hepatitis C virus genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis and in combination with ribavirin for those with decompensated cirrhosis.

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 Gilead's ability to complete its Phase 2 clinical trial program evaluating GS-9688 in the currently anticipated timeline or at all. In addition, there is the possibility of unfavorable results from ongoing and additional clinical trials involving Epclusa, Vemlidy and GS-9688. Further, it is possible that Gilead may make a strategic decision to discontinue development of GS-9688, and as a result, this compound may never be successfully commercialized. 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, 2019, 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 Epclusa and Vemlidy, including **BOXED WARNINGS**, is available at www.gilead.com.*

Epclusa and Vemlidy 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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