Gilead Presents New Data on Viral Hepatitis at the International Liver Congress™ 2019

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– Data Demonstrate Role of Gilead HCV Medicines in Difficult–to-Treat Patient Populations and in Real-World Settings –

– Latest HBV Data Reinforce Role of Treatment with Vemlidy and Demonstrate Progress in Cure Research –

FOSTER CITY, Calif.--(BUSINESS WIRE)--Apr. 11, 2019-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced new data on the use of its chronic hepatitis B (HBV) and hepatitis C (HCV) medicines including safety and efficacy data on Vemlidy® (tenofovir alafenamide 25mg, TAF) in HBV patients previously treated with tenofovir disoproxil fumarate (TDF) and data on Epclusa® (sofosbuvir 400mg/velpatasvir 100mg) and Harvoni® (ledipasvir 90mg/sofosbuvir 400mg) in difficult-to-cure HCV patient populations. These results, along with data from Gilead's HBV cure research program, will be presented at The International Liver Congress™ (ILC) 2019 in Vienna, Austria.

"As part of our ongoing commitment to patients living with viral hepatitis, we continue to research the roles of our HBV and HCV medicines across the broadest range of patient populations. These latest data demonstrate that the efficacy of our HCV medicines is consistent in clinical trials and in real-world settings, even in difficult-to-cure patients," said John McHutchison, AO, MD, Chief Scientific Officer, Head of Research and Development, Gilead Sciences. "In HBV, our latest research reinforces the role of Vemlidy in chronic HBV management and the importance of ongoing research in pursuit of an HBV cure."

HBV Treatment: Switching from TDF to Vemlidy

In a Phase 3 study, 488 virologically suppressed adult patients with chronic HBV infection receiving once-daily TDF (300 mg) were randomized to remain on TDF or switch to Vemlidy (TAF 25 mg) for 48 weeks. Vemlidy demonstrated non-inferior viral suppression (HBV DNA ≥20 IU/mL) compared to TDF at Week 48. Switching from TDF to Vemlidy also resulted in improvements in glomerular filtration rate ($eGFR_{CG}$), a measure of kidney function, and increases in hip and spine bone mineral density (BMD), a measure of bone health, as compared with patients who continued taking TDF. Rates of adverse events and serious adverse events were similar between the two groups. Similar findings were also presented from secondary analyses of two Phase 3 studies of 1,298 patients initially randomized to receive Vemlidy or TDF. Among patients switched from TDF to Vemlidy at Week 96 or Week 144, virologic suppression (HBV DNA <29 IU/mL) was maintained in both groups at Week 192. Increases in both hip and spine BMD and $eGFR_{CG}$ were observed in each group switching to Vemlidy treatment.

In clinical trials, the most common adverse reaction (incidence greater than or equal to 10 percent, all grades) in patients taking Vemlidy was headache. These latest data will support supplementary regulatory filings in the European Union and the United States.

HBV Cure Research

Gilead is actively pursuing multiple research approaches with the goal of identifying a functional cure for patients with chronic HBV infection. Results of an *in vitro* study of GS-9688, an investigational oral selective toll-like receptor 8 (TLR8) agonist, presented at the meeting, provide evidence of its antiviral immune response. Blood samples from HBV patients were treated with GS-9688 for two to seven days and analyzed for cytokine response, a marker of immunity. In this study, GS-9688 induced cytokines and also reduced the frequency of conventional regulatory T cells (T_{regs}), which suppress immune response. In addition, GS-9688 triggered dose-dependent activation of natural killer (NK) cells associated with immune response. GS-9688 is now being studied in a Phase 2 trial of patients with chronic HBV infection.

The safety and efficacy of GS-9688 has 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. In the U.S., 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.

HCV Treatment: Epclusa and Harvoni in Clinical Practice

Gilead continues to research treatment options for difficult to treat HCV patient populations. In a 32-patient open-label, single-arm clinical study, treatment with Epclusa plus ribavirin (RBV) demonstrated efficacy (78 percent of patients achieved SVR12, defined as maintaining undetectable viral load 12 weeks after completion of therapy) and tolerability in HCV patients with Child-Pugh-Turcotte (CPT) Class B and C decompensated cirrhosis (Class B signifies CPT scores of 7-9, or moderate cirrhosis; Class C signifies CPT scores of 10-15, or severe cirrhosis). No grade 3-4 serious adverse events or deaths in the study were considered to be related to study drug. Also presented is an open-label clinical study of Harvoni that demonstrated its effectiveness (94 percent of patients achieved SVR 12) in patients with chronic HCV infection with and without cirrhosis undergoing dialysis. The most frequent adverse events (incidence greater than or equal to 10 percent, all grades) in patients taking Harvoni were muscle spasms and nasopharyngitis, and non-serious adverse events were assessed to relate to Harvoni.

Gilead also continues to assess the real-world impact of its approved medicines including Epclusa, a pan-genotypic, pan-fibrotic single-tablet regimen. An analysis of real-world data assessed the efficacy of Epclusa patients with HCV genotype 1-6 who were treated at 12 clinical cohorts across North America and the European Union. Among the 5,541 patients included in the initial assessment, 98.5 percent achieved SVR12. Subgroup analyses of patients with compensated cirrhosis and treatment-experienced patients were also presented.

"To achieve the World Health Organization's goal of eliminating HCV globally by 2030, we will require treatments that are highly effective and have simple dosing regimens with broad clinical utility," said Alessandra Mangia, MD, Chief of Liver Unit, IRCCS-Ospedale Casa Sollievo Della Sofferenza, San Giovanni Rotondo, Italy, who presented the data at the ILC 2019. "This real-world analysis demonstrates that Epclusa can cure HCV patients irrespective of genotype or cirrhosis status, which is essential for implementing test and treat strategies in populations with HCV around the world."

Epclusa and Harvoni are each indicated in the U.S. for the treatment of chronic HCV infection in patients with no cirrhosis or compensated cirrhosis: Epclusa for adults with genotypes 1-6; and Harvoni for patients 12 years and older with genotypes 1, 4, 5 and 6. The U.S. product labels for Epclusa

and Harvoni each contain 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 Indications for Harvoni and 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 HARVONI or 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 HARVONI or 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 HARVONI or 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 CYP: Rifampin, St. John's wort and carbamazepine are not recommended for use with HARVONI or with EPCLUSA. P-gp inducers may significantly decrease ledipasvir, sofosbuvir and/or velpatasvir plasma concentrations. Moderate to potent inducers of CYP2B6, CYP2C8 or CYP3A4 may significantly decrease sofosbuvir and/or velpatasvir plasma concentrations.

Adverse Reactions

The most common adverse reactions (≥10%, all grades) with HARVONI were fatigue, headache, and asthenia.

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

HARVONI: Coadministration is not recommended withoxcarbazepine, phenobarbital, phenytoin, rifabutin, rifapentine, and tipranavir/ritonavir due to decreased concentrations of ledipasvir and sofosbuvir; or with co-formulated elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate due to increased concentrations of tenofovir; or with simeprevir due to increased concentrations of ledipasvir and simeprevir; or with rosuvastatin due to increased concentrations of rosuvastatin.

EPCLUSA: 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 HARVONI and EPCLUSA for more information on potentially significant drug interactions, including clinical comments.

INDICATION for HARVONI

HARVONI is indicated for the treatment of adults with chronic hepatitis C virus genotype (GT) 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis. HARVONI is used with ribavirin in GT 1 adults with decompensated cirrhosis and in GT 1 or 4 adult liver transplant recipients without cirrhosis or with compensated cirrhosis.

INDICATION for EPCLUSA

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.

U.S. Important Safety Information and Indications 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

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.

INDICATION

VEMLIDY is indicated for the treatment of chronic hepatitis B virus 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 possibility of unfavorable results from ongoing and additional clinical trials involving GS-9688. Further, it is possible that the parties may make a strategic decision to discontinue development of GS-9688, and as a result, the 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 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 Epclusa, Harvoni and Vemlidy including **BOXED WARNINGS**, are available at www.gilead.com.*

Epclusa, Harvoni 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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