Gilead Presents Latest Data from Viral Hepatitis Research Programs at The Liver Meeting® 2018

November 9, 2018

– Data Demonstrate Sofosbuvir-Based Regimens Achieve High Cure Rates in Hepatitis C Patient Populations with Unmet Need –

– Early Data from Gilead's Functional Hepatitis B Cure Program Suggest Activation of Immune Cells Crucial to Viral Clearance –

SAN FRANCISCO--(BUSINESS WIRE)--Nov. 9, 2018-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced results from studies investigating Epclusa® (sofosbuvir 400mg/velpatasvir 100mg) in chronic hepatitis C virus (HCV) infected patients with severe renal impairment undergoing dialysis and Harvoni® (ledipasvir/sofosbuvir) in pediatric HCV patients aged three to five years, adding to the efficacy and safety profile of sofosbuvir-based regimens across diverse patient populations. These results, along with data from Gilead's hepatitis B virus (HBV) cure development program, are being presented at The Liver Meeting® 2018 in San Francisco this week.

"Our scientific leadership has helped transform the treatment of patients with chronic hepatitis C infection and we remain committed to ensuring effective and well-tolerated treatment options for a broad range of patient populations." said John McHutchison, AO, MD, Chief Scientific Officer, Head of Research and Development, Gilead Sciences. "For patients with chronic hepatitis B infection, we are intensifying our efforts to advance research and development toward a functional cure."

Further Progress in the Treatment of Hepatitis C

Results from an open-label Phase 2 study demonstrated that treatment with the once-daily single-tablet regimen of Epclusa for 12 weeks in patients with genotype 1, 2, 3, 4 or 6 HCV and severe renal impairment undergoing dialysis resulted in cure rates (SVR12, or undetectable viral load 12 weeks after completion of therapy) of 95 percent (n=56/59) with only two patients experiencing virologic failure. The most common adverse events (AEs) (>10 percent) were headache, fatigue, nausea, vomiting and insomnia. No patients discontinued therapy due to an adverse event.

In another open-label Phase 2 study, children aged three to five years old with genotype 1 or 4 HCV infection received weight-based oral dosing of ledipasvir/sofosbuvir granules 33.75 mg/150 mg if < 17 kg or 45 mg/ 200 mg if ≥ 17 kg) once-daily for 12 weeks. Overall, 97 percent (n=33/34) of the patients were cured, and none experienced virologic failure. The most common AEs (>10 percent) were vomiting, cough, pyrexia, rhinorrhea and streptococcal pharyngitis. One patient discontinued treatment due to an adverse event of abnormal drug taste.

The use of Epclusa and Harvoni, including granules formulation, in the aforementioned patient populations is investigational; their safety and efficacy have not been established. The granule formulation is not approved. Epclusa and Harvoni are both indicated in the US 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 (or ≥35 kg) with genotypes 1, 4, 5 and 6. The US 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 US Important Safety Information.

Hepatitis B Cure Research

Gilead is presenting data on GS-9688, an investigational, oral selective toll-like receptor 8 (TLR8) agonist, one of several compounds under investigation as part of Gilead's HBV cure program. The data support continued development of GS-9688 as a potential therapeutic approach for achieving a functional cure for patients with chronic HBV infection.

In the first-in-human, healthy volunteer safety study, GS-9688 was well-tolerated at single ascending doses up to 5mg and resulted in pharmacodynamic activity as demonstrated by the production of the systemic cytokines IL-1RA and IL-12p40 and by the activation of key relevant immune cells including natural killer (NK) cells and mucosal-associated invariant T (MAIT) cells. The most commonly reported AEs among people receiving doses up to and including 5 mg were nausea and vomiting. There were no reports of Grade 3 or higher AEs, laboratory AEs or serious adverse events (SAEs) and no discontinuations or deaths.

In a Phase 1b safety and tolerability study of GS-9688 in HBV chronically infected patients, dose-dependent activation of the cytokines IL-12p40 and IL-1RA was demonstrated with once weekly dosing for up to 4 weeks in viremic and virally-suppressed patients. There were no reports of SAEs; the most common AEs were headache and nausea. Based on these data, GS-9688 is currently being evaluated in Phase 2 studies in patients with chronic hepatitis B.

GS-9688 is an investigational agent and not approved; its safety and efficacy have not been established.

Latest Research in Hepatitis B Treatment

Presentations on Vemlidy® (tenofovir alafenamide 25mg, TAF) add further evidence to its established safety and efficacy profile in adults with chronic HBV and compensated liver disease, including longer term data on the safety of Vemlidy in virologically suppressed HBV patients. Through three years of treatment, patients originally randomized to receive TAF continued to show an improved bone and renal safety profile compared to treatment with tenofovir disoproxil fumarate 300mg (TDF) with maintained viral suppression. In a separate study in post-liver transplant patients virally suppressed on TDF-based regimens, switching to TAF maintained viral suppression in all TAF-treated patients with improvements in renal function and bone mineral density, after 48 weeks of treatment.

The use of Vemlidy in post-liver transplant patients is investigational; its safety and efficacy have not been established. Vemlidy is indicated in the US for the treatment of chronic HBV infection in adults with compensated liver disease. The US Prescribing Information for VEMLIDY contains a Boxed Warning regarding the risk of post treatment severe acute exacerbation of hepatitis B; see below for Important Safety Information.

US Important Safety Information About Epclusa and Harvoni

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 or HARVONI. 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.

Warnings and Precautions

Serious Symptomatic Bradycardia When Coadministered with Amiodarone: Amiodarone is not recommended for use with EPCLUSA or HARVONI 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 EPCLUSA or with HARVONI. 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 EPCLUSA were headache and fatigue.

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

Drug Interactions

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.

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.

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

US Important Safety Information About 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 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, 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.

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. For more information on Gilead Sciences, please visit the company's website at www.gilead.com

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, Harvoni, 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, 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**, is 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.

View source version on businesswire.com: https://www.businesswire.com/news/home/20181109005281/en/

Source: Gilead Sciences, Inc.

Gilead Sciences, Inc.
Investors
Sung Lee, 650-524-7792
or
Media
Arran Attridge, 650-425-8975