Gilead Announces Multiple Scientific Presentations Demonstrating High Cure Rates in Difficult-to-Cure HCV Patients and Improved Long-Term Bone and Renal Safety of Vemlidy® in HBV Patients Switched from Viread®

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– Results Presented at The Liver Meeting® 2017–

WASHINGTON--(BUSINESS WIRE)--Oct. 20, 2017-- Gilead Sciences, Inc. (NASDAQ: GILD) today announced results from Phase 2 and Phase 3 studies of its approved medicines for chronic hepatitis C virus (HCV) and hepatitis B virus (HBV) infection, adding to the body of evidence supporting Gilead's viral hepatitis therapies in diverse patient populations. These and other data from more than 25 abstracts will be presented this week at The Liver Meeting® 2017, which begins today in Washington, D.C.

Positive results from studies of Harvoni® (ledipasvir 90mg/sofosbuvir 400mg) in HCV-infected patients with severe renal impairment, Epclusa® (sofosbuvir 400mg/velpatasvir 100mg) in HCV-infected liver transplant recipients and Vosevi® (sofosbuvir 400mg/velpatasvir 100mg/voxilaprevir 100mg) in NS5A-inhibitor experienced HCV-infected patients will be presented during poster sessions on October 21 and October 22. In addition, updated results from two Phase 3 studies demonstrating improved long-term bone and renal safety in HBV-infected patients one year after switching from Viread® (tenofovir disoproxil fumarate 300mg) to Vemlidy® (tenofovir alafenamide 25mg) will be presented on October 21.

"Gilead continues to study the effectiveness of our once-daily sofosbuvir-based single tablet regimens in diverse chronic HCV-infected patient populations to provide the opportunity for cure for all patient populations, including those most difficult to cure," said Norbert Bischofberger, PhD, Executive Vice President of Research and Development and Chief Scientific Officer at Gilead. "We are also committed to advancing the long-term care of patients with chronic HBV infection, and are pleased to share multiple new data presentations demonstrating the ongoing improvements in bone and renal safety observed when patients switch from Viread to Vemlidy."

Harvoni, Epclusa and Vosevi have Boxed Warnings in their product labels regarding the risk of hepatitis B virus reactivation in HCV/HBV coinfected patients, and Vemlidy has a Boxed Warning regarding the risk of post-treatment severe acute exacerbation of hepatitis B. See below for important safety information for all products.

Harvoni in Renally Impaired Patients (Poster #1587)

In an open-label Phase 2 study evaluating once-daily Harvoni for 12 weeks among HCV genotype 1 patients with severe renal impairment (creatinine clearance ≤ 30 mL/min), 100 percent (18/18) of patients achieved SVR12, including patients with compensated cirrhosis (n=2) and those who had failed prior treatment (n=4).

Safety events were consistent with those expected for the patient population. The most common adverse events (AEs) (>15 percent) were fatigue (22 percent), headache (22 percent) and hyperkalemia (17 percent). Four patients (22 percent) reported serious AEs, none of which was related to study drug. There were no deaths and no patients discontinued treatment in the study.

Harvoni is approved for adults with chronic HCV genotype 1, 4, 5 or 6 infection without cirrhosis or with compensated cirrhosis, adults with genotype 1 infection with decompensated cirrhosis in combination with ribavirin (RBV), and adults with genotype 1 or 4 infection who are liver transplant recipients without cirrhosis or with compensated cirrhosis, in combination with RBV. The safety and efficacy of Harvoni have not been established in patients with severe renal impairment.

Epclusa in Liver Transplant Patients (Poster #1069)

In an open-label Phase 2 study evaluating once-daily Epclusa for 12 weeks among 79 liver transplant patients with

genotype 1-4 chronic HCV infection, treatment with Epclusa resulted in an overall SVR12 rate of 96 percent, including patients with cirrhosis and prior treatment failure, and was well tolerated.

Patient Population	SVR12	Patient Population	SVR12
Genotype 1	95% (35/37)	Genotype 1-4 without cirrhosis	97% (70/72)
Genotype 2	100% (3/3)	Genotype 1-4 with cirrhosis	86% (6/7)
Genotype 3	97% (34/35)	Genotype 1-4, treatment-naïve	94% (30/32)
Genotype 4	100% (4/4)	Genotype 1-4, treatment-experienced	99% (46/47)

Baseline resistance mutations did not impact SVR rates. Two patients relapsed in this study – one treatment-naïve non-cirrhotic patient with HCV genotype 1a and one treatment-experienced non-cirrhotic patient with HCV genotype 3.

Common adverse effects (AEs) (>10 percent) were headache (24 percent), fatigue (20 percent) and cough (10 percent). Three patients (4 percent) experienced serious AEs; none was related to study drug. One patient discontinued treatment after one week due to hyperglycemia. There were no deaths, graft loss or episodes of acute liver transplant rejection.

Epclusa is approved for patients with genotype 1-6 without cirrhosis or with compensated cirrhosis, and in combination with RBV for patients with decompensated cirrhosis. The safety and efficacy of Epclusa in liver transplant recipients has not been established.

Vosevi in NS5A Treatment-Experienced Patients (Poster #1178)

A deferred treatment cohort of the POLARIS-1 Phase 3 study confirmed previously reported results demonstrating the effectiveness of 12 weeks of Vosevi as salvage therapy for treatment-experienced patients. The study evaluated once-daily Vosevi in NS5A-inhibitor experienced patients with chronic HCV who were initially randomized to receive placebo in POLARIS-1.

Vosevi treatment was associated with an overall SVR12 rate of 97 percent (143/147), with 97 percent (141/145) of genotype 1 patients achieving SVR12 and 100 percent (2/2) of genotype 6 patients achieving SVR12. Four patients experienced virologic relapse after completing treatment.

The most common adverse effects (>10 percent) were fatigue (21 percent), headache (20 percent), diarrhea (19 percent) and nausea (14 percent). Six patients (4 percent) experienced serious AEs unrelated to study drug, and there were no discontinuations due to AEs.

Vosevi is approved for patients without cirrhosis or with compensated cirrhosis who have HCV genotype 1, 2, 3, 4, 5 or 6 and have been previously treated with an NS5A inhibitor-containing regimen, or with genotype 1a or 3 previously treated with a sofosbuvir-containing regimen without an NS5A inhibitor.

Vemlidy in Patients Switching from Viread (Poster #904) and Two Year Resistance Analysis (Oral #26)

A post-hoc analysis of a subgroup of the 1,298 treatment-naïve and treatment-experienced patients with chronic HBV infection from two Phase 3 studies (Studies 108 and 110, Poster #904) demonstrated that patients who were switched after 96 weeks of treatment with Viread to Vemlidy experienced improvements in renal function, bone mineral density (BMD) and serum alanine aminotransferase (ALT) normalization while maintaining viral suppression, after 48 weeks of treatment with Vemlidy.

In patients initially randomized to Viread, high rates of virologic control (HBV DNA <29 IU/mL) were maintained after

switching from Viread to Vemlidy. When assessed at Week 96 (pre-switch), 88 percent of Viread patients (156/177) had achieved virologic suppression. When these patients were switched to Vemlidy, 89 percent (149/167) had achieved virologic suppression at Week 144.

Median creatinine clearance (CrCL) increased among switch patients by 3.6 (-3.6, +9.0) ml/min ($p<0.001$). Mean hip BMD (n=180) increased by 0.96 percent (2.41) ($p<0.001$) and spine BMD (n=181) increased by 1.83 percent (3.20) ($p<0.001$). In addition, rates of serum ALT normalization (by the AASLD criteria) increased from 47 percent of patients pre-switch at Week 96 to 65 percent after 48 weeks of Vemlidy ($p<0.001$).

A prespecified analysis that will be presented during an oral session (Oral #26) evaluated virologic resistance after 96 weeks of treatment with Vemlidy or Viread. Of the 1,242 patients who entered year two of treatment, similar percentages of patients treated with Vemlidy (10.5 percent; 87/828) or Viread (10.9 percent; 45/414) qualified for evaluation. Using genotypic and phenotypic analyses, no resistance to either Vemlidy or Viread was detected in any patients at 96 weeks.

Vemlidy is approved for the treatment of chronic HBV infection in adults with compensated liver disease. The safety and efficacy of switching virologically suppressed patients onto Vemlidy have not been established.

Important Safety Information About Harvoni, Epclusa and Vosevi

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, Epclusa, or Vosevi. 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

- **Harvoni and Epclusa:** When 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.
- **Vosevi** is contraindicated with rifampin.

Warnings and Precautions

- **Serious Symptomatic Bradycardia When Coadministered with Amiodarone:** Amiodarone is not recommended for use with Harvoni, Epclusa, or Vosevi 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, Epclusa, or Vosevi. P-gp inducers may significantly decrease ledipasvir, sofosbuvir, velpatasvir, and/or voxilaprevir plasma concentrations. Moderate to potent inducers of CYP2B6, CYP2C8 or CYP3A4 may significantly decrease sofosbuvir, velpatasvir, and/or voxilaprevir 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.
- The most common adverse reactions (≥10%, all grades) with Vosevi were headache, fatigue, diarrhea, and nausea.

Drug Interactions

- **Harvoni:** Coadministration is not recommended with oxcarbazepine, 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.
- **Vosevi:** Coadministration is not recommended with phenytoin, phenobarbital, oxcarbazepine, rifabutin, rifapentine, atazanavir, lopinavir, tipranavir/ritonavir, efavirenz, rosuvastatin, pitavastatin, and cyclosporine due to changes (decreased or increased) in concentrations of sofosbuvir, velpatasvir, voxilaprevir, and/or the other agent.

Consult the full Prescribing Information for Harvoni, Epclusa, and Vosevi for more information on potentially significant drug interactions, including clinical comments.

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 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) through Week 48 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 Gilead may observe unfavorable results from additional clinical trials involving Harvoni, Epclusa, Vosevi and Vemlidy in certain difficult-to-treat patient populations. 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 June 30, 2017, 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 Harvoni, Epclusa, Vosevi, Vemlidy and Viread including **BOXED WARNING**, is available at www.gilead.com.*

Harvoni, Epclusa, Vosevi, 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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