Merck Announces Presentation of New Findings for ZEPATIER™ (Elbasvir and Grazoprevir) in Patients with Chronic Hepatitis C at The Liver Meeting®

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KENILWORTH, N.J.--(BUSINESS WIRE)--Merck (NYSE:MRK), known as MSD outside of the United States and Canada, today announced results from multiple analyses at The Liver Meeting® 2016, which provide additional evidence supporting the use of ZEPATIER™ (elbasvir and grazoprevir) 50mg/100mg tablets in chronic hepatitis C virus (HCV) genotype (GT) 1- or GT4-infected patient populations, including those who receive opioid agonist therapy (OAT), are infected with chronic HCV GT1b, use proton pump inhibitors (PPIs) or have moderate kidney disease.

“Work remains to be done in the community’s efforts to reduce the global burden of chronic hepatitis C, and Merck is committed to pursuing this goal,” said Dr. Eliav Barr, senior vice president, global clinical development, infectious diseases and vaccines, Merck Research Laboratories. “Our clinical development program continues to yield meaningful evidence for ZEPATIER in specific patient populations.”

C-EDGE CO-STAR: Interim Results from the Three Year Follow-Up (3YFU) Trial (Abstract #871)
The CO-STAR Three Year Follow-Up (3YFU) Trial is an observational cohort study to evaluate chronic HCV reinfection and injecting risk behaviors in patients who were treated with ZEPATIER during the C-EDGE CO-STAR study. C-EDGE CO-STAR is a Phase 3 clinical trial including patients with chronic HCV GT1, GT4 and/or GT6 infection who are on OAT (methadone and buprenorphine). The study does not exclude patients who are actively using drugs with high abuse potential. Primary efficacy and safety results from C-EDGE CO-STAR were previously presented at The Liver Meeting® in November 2015. Interim results presented today are from the ongoing 3YFU study.

The median time from the end-of-treatment (EOT) in the C-EDGE CO-STAR study to the first visit as part of the 3YFU study was 330 days (range: 206-485). Of the 199 patients in the 3YFU study, 108 (54%) reported any drug use (non-injecting or injecting) in the past six months, 40 of whom (37%) reported injection drug use in the past month. At the first visit in the 3YFU study, two individuals (1%) tested positive for evidence of HCV, suggesting that chronic HCV reinfection was uncommon among patients on OAT in the first year following treatment with ZEPATIER, despite ongoing drug use.

GT1b Integrated Analysis (Abstract #874)
A retrospective integrated analysis of data from 11 Phase 2 and Phase 3 trials in the clinical development program for ZEPATIER was conducted to evaluate its efficacy in patients infected with GT1b, the most common chronic HCV genotype globally and the second-most common in the United States. The analysis included 1,070 patients with chronic HCV GT1b infection who received ZEPATIER for 12 weeks, including: patients who were treatment naïve or had prior experience with peginterferon alfa/interferon and ribavirin (RBV), with or without an NS3/4A protease inhibitor; those who were compensated cirrhotic or non-cirrhotic; and those with or without HIV-1 co-infection.

The analysis showed 97 percent of patients (1040/1070) achieved sustained virologic response 12 weeks after the completion of therapy (SVR12, considered virologic cure). Of the patients who did not achieve SVR12, 15 were virologic failures (1%) and 15 patients were lost to follow-up (1%). Rates of SVR12 were consistently high regardless of patient characteristics, including prior treatment experience (97%, 212/219), presence of compensated cirrhosis (99%, 188/189) and HIV-1 co-infection (94%, 51/54).

Serious adverse events occurred in 3 percent of patients (35/1070) who received active treatment, and 2.9 percent (3/105) of those who received placebo in studies that included a placebo arm.

Pooled Analysis in Patients with Self-Reported PPI Use (Abstract #869)
This post-hoc analysis of patients with chronic HCV GT1 and GT4 infection in six studies in the Phase 3 clinical program for ZEPATIER assessed SVR12 among patients who self-reported concomitant use of proton pump inhibitors (PPIs). Pharmacokinetic interactions leading to reduced drug concentrations have previously been reported for some HCV NS5A inhibitors when given concomitantly with PPIs.

Overall, 12 percent (162/1322) of patients in the post-hoc analysis who received ZEPATIER reported baseline use of PPIs. Of
those patients, 96 percent (155/162) achieved SVR12, compared to 97 percent (1129/1160) of patients without PPI use, suggesting that PPI use was not a predictive factor in achieving SVR12.

This abstract received Presidential Poster of Distinction recognition at The Liver Meeting® 2016.

**Pooled Dataset Analysis in Patients with Moderate Kidney Disease (Abstract #889)**

This integrated analysis of data from the Phase 2 and Phase 3 clinical development program for ZEPATIER was conducted to evaluate its impact on renal function, including in patients with chronic kidney disease (CKD) stage 3 (estimated glomerular filtration rate [eGFR] less than 60 and greater than or equal to 30 mL/min/1.73 m²). The safety and efficacy profile of ZEPATIER in patients with more severe renal disease was described in the C-SURFER study, presented at the International Liver Congress™ in April 2015 and subsequently published in The Lancet by Roth et al.

The analysis included 32 patients with stage 3 CKD and 1,657 patients with eGFR greater than or equal to 60 mL/min/1.73 m² who were treated with ZEPATIER with or without RBV for 8 (n=91, 5%), 12 (n=1238, 73%), 16 (n=211, 12%), or 18 (n=149, 9%) weeks. Among the 32 patients with stage 3 CKD, kidney function improved or remained stable in 38 percent (12/32) and 63 percent (20/32), respectively, at the end of treatment.

**About ZEPATIER™ (elbasvir and grazoprevir) 50mg/100mg Tablets**

ZEPATIER is a fixed-dose combination product containing elbasvir, an HCV NS5A inhibitor, and grazoprevir, an HCV NS3/4A protease inhibitor. In the United States, ZEPATIER is indicated with or without ribavirin (RBV) for treatment of chronic HCV GT1 or 4 infection in adults. ZEPATIER is not indicated to treat chronic HCV GT6 infection. ZEPATIER was approved in the United States on January 28, 2016, and is also approved in the European Union, Canada, Japan, Australia, Saudi Arabia, Israel and Switzerland, with additional regulatory approvals anticipated.

**Selected Safety Information about ZEPATIER™**

ZEPATIER is not for use in patients with moderate or severe hepatic impairment (Child Pugh B or C). ZEPATIER is also not for use with organic anion transporting polypeptides 1B1/3 (OATP1B1/3) inhibitors (e.g., atazanavir, darunavir, lopinavir, saquinavir, tipranavir, cyclosporine), strong cytochrome P450 3A (CYP3A) inducers (e.g., carbamazepine, phenytoin, rifampin, St. John's Wort), and efavirenz. If ZEPATIER is administered with RBV, healthcare professionals should refer to the prescribing information for RBV as the contraindications, warnings and precautions, adverse reactions and dosing for RBV also apply to this combination regimen.

Elevations of alanine transaminase (ALT) to greater than 5 times the upper limit of normal (ULN) occurred in 1% of subjects, generally at or after treatment week 8. These late ALT elevations were typically asymptomatic and most resolved with ongoing or completion of therapy. Healthcare professionals should perform hepatic lab testing on patients prior to therapy, at treatment week 8, and as clinically indicated. For patients receiving 16 weeks of therapy, additional hepatic lab testing should be performed at treatment week 12.

Patients should be instructed to consult their healthcare professional without delay if they have onset of fatigue, weakness, lack of appetite, nausea and vomiting, jaundice or discolored feces. Healthcare providers should consider discontinuing ZEPATIER if ALT levels remain persistently greater than 10 times ULN. ZEPATIER should be discontinued if ALT elevation is accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or international normalized ratio.

The concomitant use of ZEPATIER with certain drugs may lead to adverse reactions or reduced therapeutic effect due to drug interactions. Certain strong CYP3A inhibitors may increase the plasma concentration of ZEPATIER, leading to possibly clinically significant adverse reactions. Moderate CYP3A inducers may decrease the plasma concentration of ZEPATIER, leading to reduced therapeutic effect and possible development of resistance. Co-administration of ZEPATIER with these drugs is not recommended. Physicians should consult the Prescribing Information for potential drug interactions.

In subjects receiving ZEPATIER for 12 weeks, the most commonly reported adverse reactions of all intensity (greater than or equal to 5%) in placebo-controlled trials were fatigue, headache and nausea. In subjects receiving ZEPATIER with RBV for 16 weeks, the most commonly reported adverse reactions of moderate or severe intensity (greater than or equal to 5%) were anemia and headache.

**Selected Dosage and Administration Information for ZEPATIER (elbasvir and grazoprevir)**

ZEPATIER is a single tablet taken once daily. The recommended dosing is 12 or 16 weeks with or without RBV, depending on HCV genotype, prior treatment history and, for patients with genotype 1a infection, presence of certain baseline NS5A resistance-associated polymorphisms. See Prescribing Information for ZEPATIER for specific dosage regimens and durations. Refer to RBV prescribing information for RBV dosing and dosage modifications when ZEPATIER is given with RBV. To determine dosage regimen and duration of ZEPATIER for genotype 1a patients, testing for the presence of virus with one or more baseline NS5A resistance-associated polymorphisms at positions 28, 30, 31, or 93 is recommended prior to initiating treatment.

**Merck’s Commitment to HCV**

For more than 30 years, Merck has been at the forefront of the response to the HCV epidemic. Merck’s chronic HCV clinical development programs have included more than 135 clinical trials in approximately 40 countries and have enrolled nearly 10,000 participants. As part of our longstanding leadership in infectious diseases, Merck collaborates with the scientific and patient communities to develop and deliver innovative solutions to support people living with chronic HCV worldwide.

**About Merck**

For 125 years, Merck has been a global health care leader working to help the world be well. Merck is known as MSD outside the United States and Canada. Through our prescription medicines, vaccines, biologic therapies, and animal health products,
we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. For more information, visit www.merck.com and connect with us on Twitter, Facebook, YouTube and LinkedIn.

Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the “company”) includes “forward-looking statements” within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company’s management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company’s ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company’s patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company’s 2015 Annual Report on Form 10-K and the company’s other filings with the Securities and Exchange Commission (SEC) available at the SEC’s Internet site (www.sec.gov).


1 Estimated glomerular filtration rate (eGFR) is a measure of kidney function.