NEWS RELEASE

Merck's ZEPATIER™ (Elbasvir and Grazoprevir) Showed Superiority on Efficacy and Safety Endpoints Compared to Sofosbuvir Plus Peginterferon and Ribavirin Treatment Regimen in Phase 3 Trial

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Results From C-EDGE Head-to-Head Study in Patients with Chronic Hepatitis C Genotypes 1 or 4 Infection Presented at The International Liver Congress™ 2016

KENILWORTH, N.J.--(**BUSINESS WIRE**)--Merck (NYSE: MRK), known as MSD outside of the United States and Canada, today announced the presentation of results from **C-EDGE Head-to-Head**, the company's comparative, Phase 3, open-label clinical trial evaluating the efficacy and safety of ZEPATIER™ (elbasvir and grazoprevir) 50mg/100mg tablets versus a regimen of sofosbuvir 400mg tablets plus peginterferon and ribavirin (pegIFN/RBV) in treatment-naïve and pegIFN/RBV treatment-experienced patients with chronic hepatitis C (HCV) genotype (GT) 1 or GT4 infection (abstract #PS002). In this study, ZEPATIER demonstrated superiority on efficacy and safety endpoints compared to sofosbuvir plus pegIFN/RBV, based on pre-specified analyses. In the full analysis set (FAS) (n=255), the efficacy endpoint of sustained virologic response (SVR) 12 weeks after the completion of therapy (SVR12, considered virologic cure) was achieved in 99 percent (128/129) of patients receiving ZEPATIER for 12 weeks versus 90 percent (114/126) of patients receiving sofosbuvir plus pegIFN/RBV for 12 weeks. The study's safety endpoint was the frequency of pre-specified (Tier 1) safety events focusing on tolerability, hematologic side effects, and liver-related laboratory abnormalities.1 ZEPATIER – Merck's once-daily, fixed-dose combination tablet indicated with or without RBV for the treatment of chronic HCV GT1 or GT4 infection in adults – was approved by the U.S. Food and Drug Administration (FDA) on Jan. 28, 2016, based in part on prior studies from the Phase 3 program. The results of C-EDGE Head-to-Head will be featured today in the official press program at **The International Liver Congress™**

2016.

“Overall in this study, the elbasvir and grazoprevir regimen showed superior SVR rates and improvement on pre-specified safety endpoints compared to the sofosbuvir plus peginterferon and ribavirin regimen in these genotype 1- or 4-infected patients,” said Dr. Jan Sperl, Department of Hepatogastroenterology, Institute for Clinical and Experimental Health, Prague, Czech Republic and lead study investigator. “Sofosbuvir in combination with peginterferon and ribavirin continues to be a prescribed treatment regimen in many regions, and this comparative study versus combination treatment with elbasvir and grazoprevir provides interesting and important insights.”

C-EDGE Head-to-Head is a comparative Phase 3, randomized, open-label, parallel-group trial conducted at multiple sites in the European Union, Norway and Turkey, and was designed to evaluate the efficacy and safety of 12 weeks of ZEPATIER (elbasvir and grazoprevir) versus a 12 week treatment regimen of sofosbuvir plus pegIFN/RBV. The trial enrolled treatment-naïve and pegIFN/RBV treatment-experienced patients, with or without cirrhosis, with chronic HCV GT1 or GT4 infection. Investigators were to enroll only patients whom, in their opinion, were appropriate candidates for 12 weeks of pegIFN/RBV-based therapy; this assessment included consideration of factors associated with lower response rates to interferon-based therapies (e.g., advanced fibrosis/cirrhosis, high baseline viral concentrations, black race, IL28B non-CC genotype, or prior null-response to pegIFN/RBV therapy). The study randomized 255 GT1- or GT4-infected patients to 12 weeks of treatment with either ZEPATIER (elbasvir and grazoprevir) 50mg/100mg tablets (n=129) or sofosbuvir 400mg tablets plus pegIFN/RBV (n=126). Overall, at baseline, 17 percent of patients had compensated cirrhosis; 67 percent had HCV RNA greater than 800,000 IU/mL; 99 percent were white; 78 percent had IL28B non-CC genotype; and approximately 25 percent had failed prior treatment with pegIFN/RBV (10% prior null-responders, 5% prior partial-responders, 10% prior relapsers).

In the FAS (n=255), the efficacy analyses demonstrated superiority of ZEPATIER compared to sofosbuvir plus pegIFN/RBV, as measured by SVR12. 2 Higher SVR rates were observed among those receiving ZEPATIER (elbasvir and grazoprevir) in subgroups of patients who had previously experienced a non-response to pegIFN/RBV therapy and in those with cirrhosis, higher baseline viral load, or IL28B non-CC genotype. Efficacy results for the overall population as well as those for selected subgroups are shown in Table 1. In the ZEPATIER group, one patient (1%) discontinued from the trial after completing treatment. There were no virologic failures in the ZEPATIER group. In the sofosbuvir plus pegIFN/RBV group, virologic failure occurred in 11 patients (9%) and one patient (1%) discontinued from the trial after the first week of treatment.

Table 1: Summary of Efficacy (SVR12) Findings in FAS, Overall and Selected Subgroups

Population	ZEPATIER (n=129)	Sofosbuvir + PegIFN/RBV (n=126)
All Patients	99% (128/129)	90% (114/126)
Genotype		
GT1a	100% (18/18)	100% (17/17)
GT1b	99% (104/105)	90% (94/104)
GT4	100% (6/6)	60% (3/5)
Cirrhotic/Non-cirrhotic		
Non-cirrhotic	99% (106/107)	93% (98/105)
Cirrhotic	100% (22/22)	76% (16/21)
Prior Treatment Experience		
Treatment-naïve	99% (99/100)	96% (87/91)
PegIFN/RBV Null-response	100% (11/11)	50% (7/14)
PegIFN/RBV Partial-response	100% (6/6)	88% (7/8)
PegIFN/RBV Relapse	100% (12/12)	100% (13/13)

The primary safety analysis compared the incidence of adverse events (AEs) of special relevance (Tier 1 AEs) between the ZEPATIER and sofosbuvir plus pegIFN/RBV treatment groups. Additional AEs (Tier 2 AEs) also were recorded. Safety results are shown in Table 2. Overall, the incidence of Tier 1 AEs, including those commonly associated with pegIFN and/or RBV such as hematological side effects of decreased hemoglobin and decreased neutrophil count, were lower in the ZEPATIER treatment group versus the sofosbuvir plus pegIFN/RBV treatment group. In the ZEPATIER (elbasvir and grazoprevir) treatment group, headache was the only AE reported at a frequency of greater than 10 percent. In the sofosbuvir plus pegIFN/RBV treatment group, AEs reported in greater than 10 percent of patients were pyrexia, headache, fatigue, asthenia, influenza-like illness, chills, myalgia, decreased appetite, anemia, nausea and cough. No grade three or four abnormalities of alanine aminotransferase (ALT), aspartate aminotransferase (AST) or hemoglobin were observed in the ZEPATIER group. In the sofosbuvir plus pegIFN/RBV group, one patient had a grade three ALT abnormality and five patients had grade three or four hemoglobin reduction.

Table 2: Summary of Safety Findings

	ZEPATIER (n=129)	Sofosbuvir + PegIFN/RBV (n=126)
Tier 1 Adverse Events	1% (1/129)	28% (35/126)
Serious Drug Related Adverse Events (DRAEs)	0% (0/129)	2% (3/126)
Discontinuations due to DRAE	0% (0/129)	1% (1/126)
Neutrophil Count <0.75 x 109/L	0% (0/129)	13% (16/126)
Hemoglobin <10 g/dL	1% (1/129)	14% (18/126)
Tier 2 Adverse Events	52% (67/129)	93% (117/126)
One or more adverse events	52% (67/129)	93% (117/126)
One or more drug related adverse events	25% (32/129)	90% (114/126)
Serious adverse events	1% (1/129)	4% (5/126)
Other Safety Events		
ALT Grade 3 or 4: >5.1 x ULN (IU/L)	0% (0/129)	1% (1/126)
AST Grade 3 or 4: >5.1 xULN (IU/L)	0% (0/129)	0% (0/126)
Hemoglobin Grade 3 or 4: <9.0 (mg/dL)	0% (0/129)	4% (5/126)

“Treatment regimens containing peginterferon and ribavirin are associated with certain serious side effects,” said Dr. Jan Gerstoft, Clinic for Infectious Diseases and Rheumatology, Copenhagen, Denmark. “This study provides evidence for the clinical potential of elbasvir and grazoprevir in chronic HCV genotype 1- or 4-infection as compared with a regimen containing peginterferon and ribavirin along with sofosbuvir.”

Selected Safety Information about ZEPATIER (elbasvir and grazoprevir)

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 possible clinically significant adverse reactions from greater exposure to ZEPATIER or concomitant drugs. Coadministration of ZEPATIER is not recommended with certain strong CYP3A inhibitors (e.g., ketoconazole or the cobicistat-containing regimens of elvitegravir/cobicistat/emtricitabine/tenofovir [disoproxil fumarate or alafenamide]). Healthcare professionals should not exceed atorvastatin 20mg/daily or rosuvastatin 10mg/daily when given with ZEPATIER. If ZEPATIER is given with fluvastatin, lovastatin or simvastatin, healthcare professionals should give the lowest statin dose necessary and closely monitor for statin-associated adverse events. If ZEPATIER (elbasvir and grazoprevir) and tacrolimus are coadministered, frequent monitoring of tacrolimus whole blood concentrations, changes in renal

function and tacrolimus-associated adverse events is recommended.

The concomitant use of ZEPATIER and certain drugs may cause significant decrease of elbasvir and grazoprevir plasma concentrations, which may lead to reduced therapeutic effect of ZEPATIER and possible development of resistance. Coadministration of ZEPATIER is not recommended with moderate CYP3A inducers (e.g., nafcillin, bosentan, etravirine, modafinil).

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.

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

ZEPATIER is a fixed-dose combination product containing elbasvir, a hepatitis C virus (HCV) NS5A inhibitor, and grazoprevir, an HCV NS3/4A protease inhibitor, and is indicated with or without ribavirin (RBV) for treatment of chronic HCV genotype (GT) 1 or GT4 infection in adults. The dosing regimens and durations for treatment with once-daily ZEPATIER for chronic HCV GT1 or GT4 infection in patients with or without cirrhosis, HIV-1 co-infection or renal impairment are as follows:

- Twelve weeks of treatment with ZEPATIER is recommended for: GT1a-infected patients who are treatment-naïve or who failed prior treatment with peginterferon alfa plus RBV (PegIFN/RBV-experienced) without baseline NS5A resistance-associated polymorphisms (amino acid positions 28, 30, 31 or 93); GT1b-infected patients who are treatment-naïve or PegIFN/RBV-experienced; and GT4-infected patients who are treatment-naïve.
- Twelve weeks of treatment with ZEPATIER in combination with RBV is recommended for GT1a- or GT1b-infected patients who failed prior treatment with PegIFN/RBV + a HCV NS3/4A protease inhibitor (PI) (boceprevir, simeprevir or telaprevir). For GT1a-infected PegIFN/RBV/PI-experienced patients with one or more baseline NS5A resistance-associated polymorphisms, the optimal ZEPATIER-based treatment regimen and duration of therapy has not been established.
- Sixteen weeks of treatment with ZEPATIER (elbasvir and grazoprevir) in combination with RBV is recommended for: GT1a-infected patients who are treatment-naïve or PegIFN/RBV-experienced with baseline NS5A resistance-associated polymorphisms; and GT4-infected patients who are PegIFN/RBV-experienced.

For patients with chronic HCV GT1a infection, testing for the presence of NS5A resistance-associated polymorphisms is recommended prior to starting treatment with ZEPATIER to determine the optimal dosage regimen and duration.

Merck's Commitment to HCV

For nearly 30 years, Merck has been at the forefront of the response to the HCV epidemic. Merck employees are dedicated to applying their scientific expertise, resources and global reach to develop and deliver innovative healthcare 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**).

Please see Prescribing Information for ZEPATIER (elbasvir and grazoprevir) at **http://www.merck.com/product/usa/pi_circulars/z/zepatier/zepatier_pi.pdf** and the Patient Information for ZEPATIER at **http://www.merck.com/product/usa/pi_circulars/z/zepatier/zepatier_ppi.pdf**

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1 See Table 2

2 Per the trial protocol, in the FAS all randomized patients received at least one (1) dose of study medication. Superiority was concluded if the lower bound of the two-sided 95% CI for the difference between SVR12 rates in the treatment groups was greater than zero.

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