U.S. FDA Approves Two Supplemental Indications for Harvoni® in Chronic Hepatitis C Patients With Advanced Liver Disease

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– Liver Transplant Patients and Those with Decompensated Cirrhosis Can Now be Treated With 12 Weeks of All-Oral Therapy –

FOSTER CITY, Calif.--(BUSINESS WIRE)--Feb. 16, 2016-- Gilead Sciences, Inc. (NASDAQ: GILD) today announced that the U.S. Food and Drug Administration (FDA) has approved additional indications for Harvoni® (ledipasvir/sofosbuvir) for use in chronic hepatitis C patients with advanced liver disease. Harvoni in combination with ribavirin (RBV) for 12 weeks was approved for use in chronic hepatitis C virus (HCV) genotype 1- or 4-infected liver transplant recipients without cirrhosis or with compensated cirrhosis (Child-Pugh A), and for HCV genotype 1-infected patients with decompensated cirrhosis (Child-Pugh B or C), including those who have undergone liver transplantation. Harvoni is now approved for use in a broader range of patient populations, including HCV genotypes 1, 4, 5 and 6, HCV/HIV-1 coinfection, HCV genotype 1 and 4 liver transplant recipients, and genotype 1-infected patients with decompensated cirrhosis.

“Hepatitis C-infected patients who have decompensated cirrhosis and those who have previously received a liver transplant have an urgent need for treatment, but historically their options have been limited,” said Norbert Bischofberger, Ph.D., Executive Vice President of Research and Development and Chief Scientific Officer at Gilead. “We are pleased that health care providers now have the information needed to offer these patients an all-oral, 12-week duration therapy with high cure rates and a tolerable side effect profile.”

Decompensated Cirrhosis and Post-Liver Transplantation

The supplemental new drug application (sNDA) approval for genotype 1 or 4 HCV liver transplant recipients without cirrhosis or with compensated cirrhosis, and for genotype 1 HCV patients with decompensated cirrhosis, was supported by data from the Phase 2 SOLAR-1 and SOLAR-2 trials. These open-label studies evaluated 12 and 24 weeks of treatment with Harvoni in combination with RBV in HCV treatment-naïve and treatment-experienced patients with genotype 1 and 4 infection who had undergone liver transplantation and/or who had decompensated liver disease.

Pooled data from SOLAR-1 and SOLAR-2 among genotype 1 HCV patients are summarized in the table below:

**HARVONI + RBV 12 weeks**

<table>
<thead>
<tr>
<th>Pre-transplant</th>
<th>SVR12 (N=300)</th>
<th>Relapse (N=288)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child-Pugh-Turcotte (CPT) B</td>
<td>87% (45/52)</td>
<td>12% (6/51)</td>
</tr>
<tr>
<td>CPT C</td>
<td>88% (35/40)</td>
<td>5% (2/37)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Post-transplant</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Metavir score F0-F3</td>
<td>95% (94/99)</td>
<td>3% (3/97)</td>
</tr>
<tr>
<td>CPT A</td>
<td>98% (55/56)</td>
<td>0% (0/55)</td>
</tr>
<tr>
<td>CPT B</td>
<td>89% (41/46)</td>
<td>2% (1/42)</td>
</tr>
<tr>
<td>CPT C</td>
<td>57% (4/7)</td>
<td>33% (2/6)</td>
</tr>
</tbody>
</table>

Five subjects transplanted prior to post-treatment Week 12 with HCV RNA<LLOQ at last measurement prior to transplant were excluded.

Two subjects were excluded due to failure to meet the inclusion criteria for any of the treatment groups (i.e., did not have decompensated cirrhosis and had also not received a liver transplant).
Twelve subjects were excluded from relapse analysis because they died (N=11) or withdrew consent (N=1) prior to reaching the 12 week post-treatment follow-up visit.

SVR12 rates among genotype 4 HCV post-transplant patients without cirrhosis or with compensated cirrhosis (n=12) were similar to the reported genotype 1 SVR12 rates; no subjects relapsed. Available data in subjects with genotype 4 HCV who had decompensated cirrhosis (pre- and post-liver transplantation) were insufficient for dosing recommendations.

A total of seven patients in the 12-week treatment arms of SOLAR-1 and SOLAR-2 had fibrosing cholestatic hepatitis (FCH), and all achieved SVR12. FCH is a rare and severe form of recurrent hepatitis that occurs following liver transplantation and is associated with high morbidity and mortality. Previously, there were no approved treatment options for FCH.

Adverse events observed in the two SOLAR studies were consistent with the expected clinical sequelae of liver transplantation and/or decompensated liver disease, or the known safety profile of Harvoni and/or RBV. Among liver transplant and decompensated liver disease patients, 1 percent and 2 percent of patients discontinued Harvoni with RBV due to an adverse event, respectively. The most common adverse reactions (≥10 percent, all grades) observed with treatment with Harvoni in combination with RBV for 12 weeks were asthenia, headache and cough.

Important Safety Information for Harvoni

Contraindications

If Harvoni 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

Risk of Serious Symptomatic Bradycardia When Coadministered with Amiodarone: Amiodarone is not recommended for use with 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. 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 of Harvoni Due to P-gp Inducers: Rifampin and St. John’s wort are not recommended for use with Harvoni as they may significantly decrease ledipasvir and sofosbuvir plasma concentrations.

Related Products Not Recommended: Harvoni is not recommended for use with other products containing sofosbuvir.

Adverse Reactions

Most common (≥10%, all grades) adverse reactions were fatigue, headache and asthenia.

Drug Interactions

In addition to rifampin and St. John’s wort, coadministration of Harvoni is also not recommended with carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifapentine, and tipranavir/ritonavir. Such coadministration is expected to decrease the concentration of ledipasvir and sofosbuvir, reducing the therapeutic effect of Harvoni.

Coadministration of Harvoni is not recommended with simprevir due to increased concentrations of ledipasvir and simeprevir. Coadministration is also not recommended with rosvastatin or co-formulated elvitegravir/cobicistat/emeriticitabine/tenofovir disoproxil fumarate due to increased concentrations of rosvastatin and tenofovir, respectively.
Consult the full Prescribing Information for Harvoni for more information on potentially significant drug interactions, including clinical comments.

**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 risks that physicians may not see the benefits of Harvoni for the additional indications. 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, 2015, 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 is available at [www.gilead.com](http://www.gilead.com).*

*Harvoni is a registered trademark of Gilead Sciences, Inc. or its related companies.*

*For more information on Gilead Sciences, please visit the company’s website at [www.gilead.com](http://www.gilead.com), follow Gilead on Twitter (@GileadSciences) or call Gilead Public Affairs at 1-800-GILEAD-5 or 1-650-574-3000.*


Source: Gilead Sciences, Inc.

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