Gilead Announces SVR12 Rates From Three Phase 3 Studies Evaluating a Once-Daily Fixed-Dose Combination of Sofosbuvir and Ledipasvir for Genotype 1 Hepatitis C Patients

December 18, 2013 8:31 AM ET

-- High Cure Rates Observed with Single Tablet Regimen May Eliminate Interferon and Ribavirin from HCV Therapy for Genotype 1 Patients --

-- U.S. NDA Submission Planned for Q1 2014--

FOSTER CITY, Calif.--(BUSINESS WIRE)--Dec. 18, 2013-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced topline results from three Phase 3 clinical trials (ION-1, ION-2 and ION-3) evaluating the investigational once-daily fixed-dose combination of the nucleotide analog polymerase inhibitor sofosbuvir (SOF) 400 mg and the NS5A inhibitor ledipasvir (LDV) 90 mg, with and without ribavirin (RBV), for the treatment of genotype 1 chronic hepatitis C virus (HCV) infection.

Across the three studies, 1,952 patients with genotype 1 HCV infection were randomized to receive SOF/LDV with or without RBV for eight, 12 or 24 weeks of therapy. Of these, 1,512 patients were treatment-naïve, 440 were treatment experienced and 224 had compensated cirrhosis.

The intent-to-treat SVR12 rates observed to date in the ION studies are summarized in the table below. Results of the 24-week arms from ION-1 will be available in the first quarter of 2014 and will be presented at a future scientific meeting.

Study	Population	Treatment	Duration	SVR12 Rates
ION-1	GT 1 treatment-naïve (including 15.7 percent (136/865) with cirrhosis)	SOF/LDV	12 weeks	97.7% (209/214)
		SOF/LDV + RBV	12 weeks	97.2% (211/217)
		SOF/LDV	24 weeks	NA (n=217)
		SOF/LDV + RBV	24 weeks	NA (n=217)
ION-2	GT 1 treatment-experienced (including 20.0 percent (88/440) with cirrhosis)	SOF/LDV	12 weeks	93.6% (102/109)
		SOF/LDV+RBV	12 weeks	96.4% (107/111)
		SOF/LDV	24 weeks	99.1% (108/109)
		SOF/LDV+RBV	24 weeks	99.1% (110/111)
ION-3	GT 1 treatment-naïve	SOF/LDV	8 weeks	94.0% (202/215)
		SOF/LDV + RBV	8 weeks	93.1% (201/216)
		SOF/LDV	12 weeks	95.4% (206/216)

Of the 1,518 patients randomized to the 12-week arms of ION-1 and to all arms of ION-2 and ION-3, 1,456 patients (95.9 percent) achieved the primary efficacy endpoint of SVR12. Of the 62 patients (4.1 percent) who failed to achieve SVR12, 36 patients (2.4 percent) experienced virologic failure: 35 due to relapse and only one patient due to on-treatment breakthrough (with documented non-compliance). Twenty-six patients (1.7 percent) were lost to follow-up or withdrew consent.

Fewer adverse events were observed in the RBV-free, fixed-dose combination arms compared to the RBV-containing arms in all ION studies. Adverse events observed in those taking the SOF/LDV tablet were generally mild and included fatigue and headache. In the RBV-containing arms of the ION studies, the most common adverse events were fatigue, headache, nausea and insomnia. Anemia, which is a common side effect associated with RBV, was reported in 0.5 percent of patients in the SOF/LDV arms versus 9.2 percent of patients in the RBV-containing arms. Less than 1 percent of patients in the studies discontinued treatment due to treatment-emergent adverse events.

“The results of the ION studies demonstrate that a simple, safe and short course of therapy with a single tablet regimen of sofosbuvir/ledipasvir can provide high cure rates among patients with genotype 1 HCV infection, while eliminating the need for both interferon and ribavirin,” said Norbert Bischofberger, PhD, Executive Vice President of Research and Development and Chief Scientific Officer. “With the availability of these results, Gilead is finalizing its regulatory filing for sofosbuvir/ledipasvir, with the goal of submitting a New Drug Application in the first quarter of 2014.”

The FDA has assigned the SOF/LDV fixed-dose combination a Breakthrough Therapy designation, which is granted to investigational medicines that may offer major advances in treatment over existing options. Sofosbuvir was approved as Sovaldi™ in the United States on December 6 and in Canada on December 13. Applications are pending in the European Union, Australia and New Zealand, Switzerland and Turkey.

About the ION Studies

The Phase 3 ION studies are randomized, open-label Phase 3 clinical trials evaluating the efficacy and safety of a once-daily fixed-dose combination of SOF/LDV for 8, 12 or 24 weeks, with and without RBV, among 1,952 genotype 1 HCV patients. The studies included patients who were treatment-naïve or who had failed previous treatment, including protease inhibitor-based regimens. The primary endpoint for each study was SVR12. Complete results from all three studies will be presented at a future scientific conference.

In ION-1, 865 treatment-naïve genotype 1 HCV patients, including those with cirrhosis, received SOF/LDV with or without RBV for 12 or 24 weeks. In March 2013, a planned review by the study's Data and Safety Monitoring Board (DSMB) of interim safety and efficacy data from an initial enrollment of patients concluded that the trial should continue without modification. Enrollment of the remaining patients was completed in May 2013. Prior to the DSMB meeting, the statistical analysis plan was amended to allow for the analysis of the primary efficacy endpoint for the two 12-week arms, independent of the 24-week arms. Per the amendment, if SVR12 rates in the 12-week arms were >90 percent (including among those with cirrhosis), early regulatory filings could be pursued, given that longer treatment durations would not be able to show statistically significantly higher SVR12 rates.

The ION-2 study evaluated 440 treatment-experienced genotype 1 HCV patients who had failed past therapy with regimens containing Peg-IFN (including Peg-IFN plus a protease inhibitor). Patients received SOF/LDV with or without RBV for 12 or 24 weeks.

In ION-3, 647 non-cirrhotic treatment-naïve genotype 1 HCV patients received SOF/LDV with or without RBV for 8 weeks or without RBV for 12 weeks.

The SOF/LDV fixed-dose combination is an investigational product and its safety and efficacy has not yet been established.

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 worldwide. Headquartered in Foster City, California, Gilead has operations in North and South America, Europe and Asia Pacific.

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 be unable to file for U.S. regulatory approval of the SOF/LDV fixed-dose combination in the currently anticipated timelines. In addition, the FDA and other regulatory agencies may not approve the SOF/LDV fixed-dose combination, and any marketing approvals, if granted, may have significant limitations on its use. Additional clinical studies of sofosbuvir and the SOF/LDV fixed-dose combination, including results from the 24-week arms of ION-1, may not produce favorable results. As a result, Gilead may not be able to successfully commercialize the SOF/LDV fixed-dose combination, and may make a strategic decision to discontinue its development if, for example, the market for the product fails to materialize as expected. 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, 2013, 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 Sovaldi is available at www.Sovaldi.com.

Sovaldi is a 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, follow Gilead on Twitter (@GileadSciences) or call Gilead Public Affairs at 1-800-GILEAD-5 or 1-650-574-3000.

Source: Gilead Sciences, Inc.

Gilead Sciences, Inc.
Patrick O'Brien, 650-522-1936 (Investors)
Cara Miller, 650-522-1616 (Media)