Phase 2 Data for Selonsertib in Nonalcoholic Steatohepatitis (NASH) Presented at The Liver Meeting® 2016

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-- Results Demonstrate Improvement in Fibrosis Stage among NASH Patients with Moderate to Severe Fibrosis --

BOSTON--(BUSINESS WIRE)--Nov. 14, 2016-- Gilead Sciences (Nasdaq:GILD) today announced detailed results from an open-label Phase 2 trial evaluating the investigational apoptosis signal-regulating kinase 1 (ASK1) inhibitor selonsertib (formerly GS-4997) alone or in combination with the monoclonal antibody simtuzumab (SIM) in patients with nonalcoholic steatohepatitis (NASH) and moderate to severe liver fibrosis (fibrosis stages F2 or F3). The data demonstrate regression in fibrosis that was, in parallel, associated with reductions in other measures of liver injury in patients treated with selonsertib for 24 weeks. These data were presented in a late-breaking abstract session at The Liver Meeting® 2016 in Boston (#LB-3).

Patients receiving selonsertib demonstrated improvements in several measures of liver disease severity, including fibrosis stage, progression to cirrhosis, liver stiffness (measured by magnetic resonance elastography, MRE) and liver fat content (measured by magnetic resonance imaging (MRI)-proton density fat fraction, PDFF). Data for these efficacy endpoints are summarized in the table below. As no differences were observed between combination and monotherapy, results are presented for selonsertib (18 mg and 6 mg) with/without SIM and for SIM alone. Additionally, patients with fibrosis improvement demonstrated reductions in hepatic collagen content, liver biochemistry (e.g., serum ALT) and the apoptosis marker, cytokeratin-18, supporting the biological activity of selonsertib.

Endpoint (Week 24)	**Selonsertib 18 mg ± SIM**	**Selonsertib 6 mg ± SIM**	**SIM**
Fibrosis Improvement ≥1 Stage from Baseline*	43% (n=13/30)	30% (n=8/27)	20% (n=2/10)
Progression to Cirrhosis	3% (n=1/30)	7% (n=2/27)	20% (n=2/10)
≥15% Reduction in Liver Stiffness by MRE	20% (n=5/25)	32% (n=7/22)	0% (n=0/7)
≥30% Reduction in Liver Fat by MRI-PDFF	26% (n=8/31)	13% (n=3/24)	10% (n=1/10)

**Fibrosis staged according to the NASH Clinical Research Network (CRN) classification by a central pathologist blinded to treatment group.*

Selonsertib demonstrated no dose-related increases in treatment-emergent adverse events or serious adverse events. Headache, nausea and sinusitis were the most common adverse events in patients receiving selonsertib.

“Currently, no approved treatments exists for NASH, and patients with advanced fibrosis would potentially benefit from new options to halt and/or reverse the progression of their disease,” said Rohit Loomba, MD, MHSc, lead study author and Director, NAFLD Research Center, Director of Hepatology, Professor of Medicine, Vice Chief, Division of Gastroenterology, University of California San Diego School of Medicine. “After only 24 weeks of therapy, selonsertib exhibited promising anti-fibrotic activity in this study, which was the first known multi-center NASH clinical trial to use centrally-assessed MRE, MRI-PDFF, in addition to liver biopsy as endpoints. Based on these data, selonsertib represents an important investigational drug candidate for further clinical trials in patients with NASH and significant fibrosis.”

Other Gilead NASH data being presented at The Liver Meeting include results from Phase 1 studies evaluating the investigational selective, non-steroidal Farnesoid X receptor (FXR) agonist GS-9674. Data from a Phase 1 study demonstrated the biological activity and safety profile of GS-9674 in healthy volunteers and support the evaluation of this compound in patients with NASH and cholestatic liver disorders (#1077 and #1140). Phase 2 studies with GS-9674 are ongoing in patients with NASH, primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC).

Additionally, preclinical data for the combination of selonsertib and GS-9674 in a rodent model of advanced fibrosis suggested that the combination of selonsertib and GS-9674 resulted in greater anti-fibrotic activity than either agent alone (#1588). These preclinical data support clinical evaluation of combination approaches with selonsertib and GS-9674 in patients with NASH and advanced fibrosis.

Selonsertib, GS-9674 and simtuzumab have not been determined to be safe or efficacious.

About Selonsertib and the Study

Selonsertib is an investigational small molecule inhibitor of ASK1, a protein that promotes inflammation, apoptosis (cell death) and fibrosis in settings of oxidative stress. Oxidative stress can be increased in many pathological conditions including liver diseases such as NASH.

This Phase 2, randomized, open-label trial evaluated the safety, tolerability and efficacy of selonsertib alone or in combination with SIM in 72 patients with NASH and fibrosis stages F2 (n=25) or F3 (n=47). Eligible patients were randomized (2:2:1:1:1) to receive selonsertib 6 mg (n=20), selonsertib 18 mg (n=22), selonsertib 6 mg plus SIM 125 mg (n=10), selonsertib 18 mg plus SIM 125 mg (n=10) or SIM 125 mg alone (n=10) for 24 weeks. Selonsertib was administered orally once daily and SIM was administered via weekly subcutaneous injection.

About Gilead's Clinical Programs in NASH

Gilead is advancing a pipeline of novel investigational therapies for the treatment of NASH with advanced fibrosis. Gilead is currently planning or conducting Phase 2 and Phase 3 clinical trials evaluating single-agent and combination therapy approaches against multiple core pathways associated with NASH – metabolic dysfunction, inflammation and fibrosis. Compounds in development include the ASK1 inhibitor, selonsertib; the FXR agonist, GS-9674; and an inhibitor of acetyl-coA carboxylase (ACC), GS-0976, currently being evaluated in a Phase 2 study in patients with NASH.

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 Gilead's ability to initiate or complete its Phase 2 and Phase 3 clinical trial programs evaluating selonsertib, GS-9674 and GS-0976 in patients with NASH in the currently anticipated timelines or at all. In addition, there is the possibility of unfavorable results from further clinical trials involving these compounds. Further, it is possible that Gilead may make a strategic decision to discontinue development of selonsertib, GS-9674 and GS-0976 if, for example, Gilead believes commercialization will be difficult relative to other opportunities in its pipeline. As a result, selonsertib, GS-9674 and GS-0976 may never be successfully commercialized. 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, 2016, 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.

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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