

## Gilead Announces Phase 2 Results for GS-0976 in Nonalcoholic Steatohepatitis (NASH)

October 24, 2017 8:37 AM ET

**- Oral ACC Inhibitor Led to Significant Reductions in Measures of Liver Fat and Fibrosis -**

**- Results from the GS-0976 Phase 2 Study and 18 Other Abstracts from Across Gilead's Liver Fibrosis Pipeline Presented at The Liver Meeting® 2017 -**

WASHINGTON--(BUSINESS WIRE)--Oct. 24, 2017-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced results from a Phase 2, randomized, placebo-controlled trial evaluating two doses of GS-0976, an oral, investigational inhibitor of Acetyl-CoA carboxylase (ACC), in patients with nonalcoholic steatohepatitis (NASH). The data demonstrate that the higher dose of GS-0976 (20 mg taken orally once daily) when administered for 12 weeks was associated with statistically significant reductions in hepatic steatosis (buildup of fat in the liver) and a noninvasive marker of fibrosis (TIMP-1) compared to placebo. These results are being presented during a late-breaking abstract session at The Liver Meeting® 2017 in Washington, D.C. (Abstract #LB-9). Eighteen other abstracts on Gilead's NASH and liver fibrosis pipeline were also presented at the meeting.

“In patients with advanced fibrosis, NASH may lead to severe complications including end-stage liver disease, hepatocellular carcinoma and the requirement for liver transplantation,” said Rohit Loomba, MD, MHS, lead study author, Director of the NAFLD Research Center, Director of Hepatology, Professor of Medicine, and Vice Chief of the Division of Gastroenterology at University of California San Diego School of Medicine. “Unfortunately, there are no treatments available for these patients. In this first randomized, placebo-controlled, Phase 2 study of an ACC inhibitor in NASH, the data suggest that GS-0976 has the potential to play an important role in treating patients with this disease.”

ACC plays a role in one of several biologically relevant pathways associated with disease progression in NASH. ACC catalyzes the first step in hepatic *de novo* lipogenesis, the synthesis of fatty acids that contribute to hepatic steatosis and, subsequently, inflammation and liver fibrosis.

The study included 126 patients who were randomized to receive GS-0976 20 mg (n=49), GS-0976 5 mg (n=51), or placebo (n=26) once daily for 12 weeks. All patients in the study were diagnosed with NASH and liver fibrosis stages F1 through F3 based on biopsy, or by magnetic resonance elastography (MRE) and MRI proton density fat fraction (MRI-PDFF).

Patients receiving GS-0976 20 mg demonstrated significant decreases in liver fat content (measured by MRI-PDFF) compared to placebo after 12 weeks of treatment. Patients treated with GS-0976 20 mg also experienced a significant decrease in TIMP-1, a serum marker associated with liver fibrosis. Differences between GS-0976 5 mg and placebo were not statistically significant. Data for these efficacy endpoints are summarized in the table below.

### Relative (%) Changes in Imaging, ALT and Serum Fibrosis Markers at Week 12\*

Endpoint (Week 12)	GS-0976	GS-0976	P-values		
	20 mg	5 mg		20 mg vs. Placebo	5 mg vs. Placebo
	(n=49)	(n=51)	Placebo (n=26)		
MRI-PDFF	-28.9	-13.0	-8.4	<b>0.002</b>	0.142
≥30% reduction in MRI-PDFF, % (n/N)	48% (22/46)	23% (11/47)	15% (4/26)	<b>0.004</b>	0.433
MRE-stiffness	-5.5	-9.6	-12.5	0.100	0.743
Liver stiffness by FibroScan	-11.1	-8.4	-3.1	0.212	0.364

ALT	-20.5	-9.8	-6.7	0.176	0.765
TIMP-1	-7.9	-2.9	-1.5	<b>0.022</b>	0.301
PIII-NP	-13.9	-7.0	-0.5	0.107	0.605

\*Unless indicated, all data are median relative (%) changes from baseline.

In other measures, including liver stiffness by FibroScan, liver stiffness by MRE, serum ALT and PIII-NP, a serum marker of fibrogenesis, no statistically significant differences were observed between the treatment and placebo arms of the study.

At week 12, a median relative change in triglycerides (TG) from baseline of +11 percent, +13 percent and -4 percent was observed in patients receiving GS-0976 20 mg, GS-0976 5 mg and placebo, respectively. Asymptomatic Grade 3 or 4 TG elevations (>500 mg/dL) were observed in 16 patients receiving GS-0976 20 mg (n=7) or 5 mg (n=9); the primary factor associated with such elevations was a baseline TG level >250 mg/dL (p<0.001). The majority of patients with such elevations either responded to fibrate or fish oil therapy (n=4) or resolved without additional treatment or cessation of GS-0976 (n=7). GS-0976 was well-tolerated. Nausea, abdominal pain and diarrhea were the most common adverse events.

Other Gilead studies being presented at The Liver Meeting include preclinical data examining the combination of inhibitors of ACC and apoptosis signal-regulating kinase 1 (ASK1) in rodent models of NASH. These data suggest that the combination of agents resulted in greater anti-fibrotic and anti-steatotic efficacy than either agent alone (Abstract #425; named a Presidential Poster of Distinction). Gilead is currently conducting clinical studies evaluating combinations of the ASK1 inhibitor selonsertib, ACC inhibitor GS-0976 and the selective, non-steroidal Farnesoid X receptor (FXR) agonist GS-9674 in patients with NASH. Additional abstracts describe the accuracy of noninvasive markers to predict improvements in liver histology in response to treatment in a Phase 2 study of selonsertib, including reductions in fibrosis with MRE (Abstract #2104) and liver fat with MRI-PDFF (Abstract #2169). Phase 3 studies are ongoing with selonsertib in patients with advanced fibrosis due to NASH.

Gilead is also presenting multiple abstracts regarding primary sclerosing cholangitis (PSC), a progressive cholestatic liver disease with no approved therapies. These include presentations on the role of magnetic resonance cholangiopancreatography (MRCP) in PSC including a Presidential Plenary Oral Presentation (Abstract #140) describing a novel MRCP-based risk score for predicting PSC-related complications; an innovative technique for quantifying biliary tree volume in PSC (Abstract #292); prospective data describing the natural history of radiologic progression in PSC (Abstract #279; a Presidential Poster of Distinction); and the development and validation of a PSC-specific patient reported outcome (PRO) measure (Abstract #1351; a Presidential Poster of Distinction). These studies will enhance our understanding of PSC and aid in the development of novel therapies. Gilead is currently conducting a Phase 2 study of the FXR agonist GS-9674 in patients with PSC.

### **About Gilead's Clinical Programs in NASH**

NASH is a chronic liver disease associated with steatosis, or accumulation of fat within the liver, which can lead to inflammation, progressive fibrosis and cirrhosis. Gilead is advancing multiple novel investigational compounds for the treatment of NASH with advanced fibrosis. Gilead is currently planning or conducting Phase 2 and 3 clinical trials evaluating single-agent and combination therapy approaches against multiple core pathways associated with NASH – metabolic dysregulation, inflammation and fibrosis. Compounds in development include the ASK1 inhibitor selonsertib; the selective, non-steroidal FXR agonist GS-9674; and the ACC inhibitor GS-0976. The STELLAR Phase 3 trial program evaluating selonsertib among NASH patients with bridging fibrosis (F3) or cirrhosis (F4) is ongoing. GS-9674 and GS-0976 are currently in Phase 2 studies in NASH.

Selonsertib, GS-9674 and GS-0976, alone and in combination, are investigational therapies and have not been determined to be safe or efficacious.

## **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 complete its Phase 2 and Phase 3 clinical trial programs evaluating GS-0976, selonsertib and GS-9674 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 GS-0976, selonsertib and/or GS-9674 if, for example, Gilead believes commercialization will be difficult relative to other opportunities in its pipeline. As a result, the compounds 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 June 30, 2017, 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](http://www.gilead.com), follow Gilead on Twitter (@GileadSciences) or call Gilead Public Affairs at 1-800-GILEAD-5 or 1-650-574-3000.*

View source version on businesswire.com: <http://www.businesswire.com/news/home/20171024005952/en/>

Source: Gilead Sciences, Inc.

Gilead Sciences, Inc.

Sung Lee, 650-524-7792 (Investors)

Nathan Kaiser, 650-522-1853 (Media)