Gilead Presents Data on Multiple Investigational Regimens for the Treatment of Patients With Nonalcoholic Steatohepatitis (NASH) and Advanced Fibrosis at The International Liver Congress™ 2018

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-- Combination Therapy Data Presented from First 12-Week Study --

-- Enrollment Complete for Phase 3 STELLAR Trials of ASK1 Inhibitor Selonsertib --

FOSTER CITY, Calif.--(BUSINESS WIRE)--Apr. 13, 2018-- Gilead Sciences, Inc. (Nasdaq: GILD) today presented data from a proof-of-concept study of investigational combination therapies for patients with advanced fibrosis due to nonalcoholic steatohepatitis (NASH), combining the apoptosis signal-regulating kinase 1 (ASK1) inhibitor selonsertib with either the Acetyl-CoA carboxylase (ACC) inhibitor GS-0976 or the selective, non-steroidal Farnesoid X receptor (FXR) agonist GS-9674. The data were presented at The International Liver Congress™ 2018 in Paris.

More than 25 additional Gilead abstracts on NASH and other fibrotic liver diseases are also being presented, including data from predictive modeling studies using noninvasive tests for the diagnosis and monitoring of NASH that aim to reduce the need for liver biopsy.

"Gilead is focused on addressing the greatest unmet need in NASH, which is in patients with advanced fibrosis. Reflective of this unmet need, the STELLAR-3 and STELLAR-4 studies of selonsertib in patients with F3 and F4 fibrosis have completed enrollment ahead of schedule. We expect data from these Phase 3 studies in the first half of 2019," said Norbert Bischofberger, PhD, Executive Vice President of Research and Development and Chief Scientific Officer at Gilead. "We are now exploring combination therapy approaches with compounds with distinct and potentially complementary mechanisms of action. The initial data presented today are important advances toward our goal of improving outcomes for patients with advanced fibrosis due to NASH."

Investigational Combination Therapies in Patients with NASH

The proof-of-concept study (Oral #105) included 70 patients treated with either selonsertib 18 mg plus GS-0976 20 mg (n=20), selonsertib 18 mg plus GS-9674 30 mg (n=20), or each monotherapy (n=10 per group) once daily for 12 weeks. All patients in the study were diagnosed with NASH and liver fibrosis stages F2 to F3 based on biopsy, or by magnetic resonance elastography (MRE) and MRI proton density fat fraction (MRI-PDFF). The greatest changes observed after 12 weeks of treatment in the study were decreases in liver fat content (measured by MRI-PDFF), which occurred in regimens containing GS-0976. Improvements in liver biochemistry and/or markers of fibrosis were also observed across both combination arms of the study compared to baseline. In patients treated with selonsertib plus GS-0976, kinetic labeling revealed the largest reduction in the fractional synthesis rate of lumican, a marker of fibrogenesis. Similar rates of adverse events were observed between patients treated with single-agent and combination therapies. No patient discontinued treatment prematurely.

"These encouraging results suggest that combination therapy with selonsertib and either GS-0976 or GS-9674 warrants further exploration in longer-term studies in patients with NASH and F3 and F4 fibrosis," said Stephen Harrison, MD, presenting author and Visiting Professor of Hepatology at the Radcliffe Department of Medicine, University of Oxford, UK. "Patients with advanced fibrosis due to NASH urgently need effective therapeutic options because they may face more serious health risks, including development of complications of end-stage liver disease, liver cancer and the need for liver transplantation. Combination therapy may be a way forward to achieving greater benefit for this patient population."

Gilead also presented data from a pre-clinical study of another combination treatment approach for NASH, evaluating GS-9674 and GS-0976 together and as single-agents in rodent models of NASH and liver fibrosis (Poster #077). The data indicate that combining agents had greater anti-fibrotic and anti-steatotic effects and led to greater improvements in liver biochemistry and fibrosis markers, compared with either agent alone.

Based on these promising pre-clinical results and data from the proof-of-concept clinical study, Gilead has initiated a larger Phase 2b study of combination treatment with selonsertib, and/or GS-0976, and/or GS-9674 in patients with advanced fibrosis due to NASH.

Data from Noninvasive Tests Help Predict Histological Severity and Clinical Outcomes in Patients with NASH

Currently, the diagnosis and monitoring of NASH requires liver biopsy, an invasive and costly procedure with the potential for serious complications. At the meeting, Gilead presented results from two studies utilizing machine learning techniques which suggest that noninvasive tests perform as effectively as liver biopsy for predicting clinical outcomes in patients with advanced fibrosis due to NASH. Both studies utilized data from two previous Phase 2b trials of simtuzumab that involved 477 NASH patients with F3-F4 fibrosis. While simtuzumab was ineffective, data from these trials have revealed important insights into the natural history of disease progression and the potential utility of noninvasive fibrosis markers.

One study (Poster #466) showed that models using noninvasive testing data can predict the risk of clinical disease progression in patients with advanced fibrosis due to NASH. Another study (Oral #178) identified models that can predict which patients are most likely to experience spontaneous fibrosis improvement. Both studies incorporated noninvasive tests such as Enhanced Liver Fibrosis (ELF) score, FIB-4 and NAFLD fibrosis score.

Additional presentations at The International Liver Congress™ describe the accuracy of other noninvasive markers, including proteomics (Poster #432), serum bile acids (Poster #422), micro-RNAs (Poster #463), and the stool microbiome (Poster #004) to predict liver histology and/or its change over time. These novel approaches will be evaluated in future Gilead studies.

About Gilead's Clinical Programs in NASH

NASH is a chronic and progressive liver disease characterized by the accumulation of fat in the liver, as well as inflammation, which can lead to liver damage and fibrosis. Gilead is advancing multiple novel investigational compounds for the treatment of advanced fibrosis due to NASH.

Gilead is currently planning or conducting Phase 2 and 3 clinical trials evaluating single-agent and combination therapy approaches against multiple

biologically relevant pathways associated with NASH – metabolic dysregulation, inflammation and fibrosis. Compounds in development include:

- **Selonsertib (formerly GS-4997)** – A small-molecule inhibitor of apoptosis signal-regulating kinase 1 (ASK1), which promotes inflammation, apoptosis and fibrosis in settings of increased oxidative stress, which is characteristic of NASH and associated with its pathogenesis.
- **GS-9674** – A selective, non-steroidal agonist of the Farnesoid X receptor (FXR), a nuclear hormone receptor that is highly expressed in the gastrointestinal tract and liver. FXR is the primary regulator of bile acid synthesis and plays important roles in glucose and lipid metabolism.
- **GS-0976** – A small-molecule inhibitor of Acetyl-CoA carboxylase (ACC), an enzyme that is involved in de novo lipogenesis, which is the synthesis of lipids, including mediators of inflammation and fibrosis. ACC also upregulates the burning of fat in the liver through beta oxidation.

Selonsertib, GS-9674 and GS-0976, alone and in combination, are investigational therapies and their efficacy and safety have not been determined.

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 35 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 single-agent and combination therapy approaches, including selonsertib, and/or GS-9674 and/or 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, and/or GS-9674 and/or GS-0976 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 Annual Report on Form 10-K for the year ended December 31, 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, follow Gilead on Twitter (@GileadSciences) or call Gilead Public Affairs at 1-800-GILEAD-5 or 1-650-574-3000

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