Gilead Announces Topline Results From Phase 2 ATLAS Study in Patients With Bridging Fibrosis (F3) and Compensated Cirrhosis (F4) Due to Nonalcoholic Steatohepatitis (NASH)

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-- Study Primary Endpoint Was Not Met; Improvement in Multiple Measures of Fibrosis and Liver Injury Was Observed with Investigational Firsocostat and Cilofexor --

-- Regimens Were Well Tolerated and Safety Measures Were Consistent with Prior Studies –

FOSTER CITY, Calif.--(BUSINESS WIRE)--Dec. 16, 2019-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced topline results from the 48-week, Phase 2 ATLAS study of combination and monotherapy investigational treatments for advanced fibrosis (F3-F4) due to NASH. While no regimen led to a statistically significant increase in the proportion of patients who achieved the primary efficacy endpoint of a ≥1-stage improvement in fibrosis without worsening of NASH, statistically significant improvements in multiple response measures of fibrosis and liver function were observed in patients treated with a combination of the acetyl-CoA carboxylase (ACC) inhibitor firsocostat and the selective, nonsteroidal farnesoid X receptor (FXR) agonist cilofexor, compared with placebo in patients with advanced fibrosis.

The Phase 2 ATLAS study is a randomized, double-blind, placebo-controlled study that evaluated the safety and efficacy of monotherapy and dual combination regimens of cilofexor 30 mg, firsocostat 20 mg and selonsertib 18 mg in patients with advanced fibrosis (F3-F4) due to NASH. The selonsertib monotherapy treatment group was discontinued following termination of the previously reported STELLAR trials of selonsertib.

In the 392 enrolled and dosed patients, of whom 56 percent had compensated cirrhosis, a ≥1-stage improvement in fibrosis without worsening of NASH after 48 weeks of treatment was observed in the following:

Table: Week 48 Primary Endpoint - Histologic Responses*

Endpoint, n (%)	FIR (n=33)	CILO (n=34)	SEL/FIR (n=71)	SEL/CILO (n=68)	FIR/CILO (n=67)	Placebo (n=38)
Fibrosis improvement without NASH worsening	4 (12.1%) p=0.94	4 (11.8%) p=0.96	11 (15.5%) p=0.62	13 (19.1%) p=0.26	14 (20.9%) p=0.17	4 (10.5%)

CILO, cilofexor (FXR agonist); FIR, firsocostat (ACC inhibitor); SEL, selonsertib (ASK1 inhibitor; SEL monotherapy arm [n=39] discontinued mid-trial).

* Observed case analysis assessed by a central pathologist according to the NASH Clinical Research Network (CRN) classification. All p-values (compared with placebo) were adjusted for presence of F4 and diabetes at baseline.

NASH resolution without worsening of fibrosis was uncommon in all treatment groups, including no placebo-treated patients and 4.5 percent of those treated with firsocostat and cilofexor (p=0.35).

Statistically significant improvements in multiple secondary endpoints were observed in patients treated with firsocostat and cilofexor compared with placebo, including a ≥2-point reduction in the NAFLD Activity Score (NAS) and ≥1-point reductions in steatosis, hepatocellular ballooning and lobular inflammation. Statistically significant improvements in noninvasive tests of fibrosis, liver injury and function, including ALT, AST, bilirubin and ELF score, were also observed in patients treated with this regimen compared with placebo.

Firsocostat, cilofexor and selonsertib, as monotherapies and dual combination regimens, were generally well tolerated. The most common adverse events in patients treated with the combination of firsocostat and cilofexor were mild to moderate pruritus (28.2 percent vs 15.4 percent with placebo; no discontinuations), headache, diarrhea and nausea. In patients treated with firsocostat and cilofexor, changes in lipid parameters were similar to those observed previously; 3.9 percent of patients experienced asymptomatic Grade 3 triglyceride elevations (>500 and <1000 mg/dL).

Further results from the ATLAS study will be presented at an upcoming scientific conference.

“NASH is a complex disease driven by multiple mechanisms. The results from the ATLAS study suggest the potential for a combination therapeutic approach for patients with advanced fibrosis by targeting different aspects of this disease,” said Merdad Parsey, MD, PhD, Chief Medical Officer, Gilead Sciences. “We continue to analyze the ATLAS data and will work with regulators to determine appropriate next steps for these therapies.”

“This trial provides novel data showing consistent improvements in liver histology and noninvasive tests, demonstrating the value of a combination approach to deliver meaningful changes in fibrosis, the key determinant of disease severity in NASH,” said Rohit Loomba, MD, MHSc, Director of NAFLD Research Center and Director of Hepatology, University of California, San Diego.

Cilofexor, firsocostat and selonsertib, alone or in combination, are investigational compounds and are not approved by the U.S. Food & Drug Administration (FDA) or any other regulatory authority. Safety and efficacy have not been established for these agents.

About Gilead’s Clinical Programs in NASH

NASH is a chronic and progressive liver disease characterized by fat accumulation and inflammation in the liver, which can lead to scarring, or fibrosis,

that impairs liver function. Individuals with advanced fibrosis, defined as bridging fibrosis (F3) or cirrhosis (F4), are at a significantly higher risk of liver-related and all-cause mortality.

Gilead is advancing multiple novel investigational compounds for the treatment of advanced fibrosis due to NASH, evaluating single-agent and combination therapy approaches against the core pathways associated with NASH – hepatocyte lipotoxicity, inflammation and fibrosis. Investigational compounds in development include the ACC inhibitor firsocostat, the selective, non-steroidal FXR agonist cilofexor, and the ASK1 inhibitor selonsertib. Gilead is also collaborating with Novo Nordisk A/S on a proof-of-concept study combining Gilead's cilofexor and firsocostat and Novo Nordisk's semaglutide (GLP-1 analogue) for the treatment of patients with NASH.

About Gilead Sciences

Gilead Sciences, Inc. is a research-based biopharmaceutical company that discovers, develops and commercializes innovative medicines in areas of unmet medical need. The company strives to transform and simplify care for people with life-threatening illnesses around the world. Gilead has operations in more than 35 countries worldwide, with headquarters in Foster City, California. For more information on Gilead Sciences, please visit the company's website at www.gilead.com.

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 clinical trial programs for the treatment of advanced fibrosis due to NASH, including the evaluation of the investigational monotherapy and dual combination regimens of cilofexor, firsocostat and selonsertib, in the currently anticipated timelines or at all. In addition, there is the possibility of unfavorable results from ongoing and additional clinical trials involving these compounds. Further, it is possible that Gilead may make a strategic decision to discontinue development of these compounds if, for example, Gilead believes commercialization will be difficult relative to other opportunities in its pipeline. As a result, these 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 September 30, 2019, 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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Source: Gilead Sciences, Inc.

Greg Mann, Investors
(424) 322-1795

Arran Attridge, Media
(650) 425-8975