



Data Showing Potential for Machine Learning to Advance Understanding of Nonalcoholic Steatohepatitis (NASH) Presented at the Liver Meeting® 2019

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-- AI-Based Tools for Liver Histology Assessment Contribute to Gilead's Broader Efforts to Improve Understanding of NASH --

-- Data Support Utility of Noninvasive Tests (NITs) for Risk Stratification and Monitoring of NASH Patients --

-- New Results Show Fenofibrate Mitigates Increases in Serum Triglycerides in NASH Patients Treated With Investigational Firsocostat --

BOSTON--(BUSINESS WIRE)--Nov. 8, 2019-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced new data from the company's nonalcoholic steatohepatitis (NASH) research and development program, including studies evaluating machine learning approaches to the interpretation of liver histology, noninvasive tests (NITs) for the characterization and monitoring of disease severity, and novel therapies for the treatment of this disease. The data are being presented at The Liver Meeting® 2019 in Boston this week.

"By combining data from across our NASH clinical development program with artificial intelligence (AI)-based tools, we have the opportunity to better characterize this complex disease and understand how potential therapies can impact disease progression," said Mani Subramanian, MD, Senior Vice President, Liver Diseases, Gilead Sciences. "Applying PathAI's deep learning research platform for liver histology assessment will enable a more rigorous review of treatment response and has potential for the exploration of novel biology in patients with advanced fibrosis due to NASH."

Machine Learning in NASH

In a collaboration with PathAI, a leader in AI-powered research in pathology, Gilead is evaluating machine learning approaches to liver histology assessment for use in the diagnosis and staging of NASH and monitoring of treatment response in clinical trials. A study of images from liver biopsies from patients screened for the Phase 3 STELLAR program compared the staging and characterization of liver disease as assessed by experienced pathologists and by the PathAI research platform. The pathologists scored biopsies using the NASH Clinical Research Network (CRN) and Ishak fibrosis classifications, and the PathAI research platform, a convolutional neural network, evaluated these biopsies following training on more than 68,000 annotations from 75 board-certified pathologists.

The results showed that the machine learning models and the consensus of readings from the independent pathologists demonstrated high consistency for the key histologic features of NASH. Importantly, for the staging of fibrosis, the predictions of the machine learning model were highly correlated with those of the central pathologist for both the NASH CRN ($r=0.83$) and Ishak ($r=0.86$) staging systems.

"The evaluation of new therapies for NASH can be advanced with quantitative and reproducible assessment of liver pathology," said Andy Beck, MD, PhD, PathAI co-founder and Chief Executive Officer. "We are thrilled to apply the PathAI research platform to support development of new treatment approaches."

In a separate analysis, machine learning models were developed to recognize patterns associated with each fibrosis stage, using slide-level pathologist Ishak fibrosis stages. Images of liver biopsies from 674 patients with compensated cirrhosis (F4) enrolled in the Phase 3 STELLAR-4 clinical trial demonstrated that machine learning models are predictive of disease progression, illustrate the heterogeneity of fibrosis in NASH cirrhosis, and correlate with noninvasive markers of fibrosis. These data highlight the potential of machine learning models to characterize patients with cirrhosis beyond conventional histological staging.

NITs for Risk Stratification and Monitoring of NASH Patients

Analyses of the Phase 3 STELLAR clinical trials indicate that NITs can play an important role in the risk stratification and monitoring of NASH patients. Results from a poster presentation demonstrated that greater fibrosis burden at baseline, as assessed by NITs (e.g., Enhanced Liver Fibrosis (ELF) test and NAFLD Fibrosis Score (NFS)), and greater increases in these markers over time, are both associated with an increased risk of disease progression. An additional analysis showed that in patients with advanced fibrosis due to NASH, treatment response defined by improvements in ELF or liver stiffness by transient elastography (TE) are associated with consistent improvements in other clinical parameters, including liver biochemistry, liver stiffness, and glycemic indices, whereas only histologic parameters improved in responders defined by liver histology. These data support the potential utility of NITs for the monitoring of NASH patients and as endpoints in clinical trials.

Combination Therapy with Fenofibrate Mitigates Triglyceride Elevations in NASH Patients Treated With Investigational Firsocostat

Gilead is investigating the potential role of acetyl-CoA carboxylase (ACC) inhibitors in the treatment of NASH. In a late-breaker session, Gilead will present results from a study evaluating the safety and efficacy of fenofibrate in mitigating increases in serum triglycerides (TGs) in patients with hypertriglyceridemia and advanced fibrosis due to NASH who were treated with the ACC inhibitor firsocostat. Patients were randomized to receive treatment with fenofibrate 48 mg or 145 mg orally once daily for two weeks, followed by the combination of fenofibrate and firsocostat 20 mg daily for 24 weeks. Results indicate that after 24 weeks of combination treatment, TGs were not significantly different from baseline in the 48 mg group ($p=0.09$) and 145 mg group ($p=0.99$). These results indicate that in patients with advanced fibrosis due to NASH, fenofibrate mitigates firsocostat-induced increases in serum triglycerides. The combination of firsocostat and fenofibrate also led to significant improvements in hepatic fat, liver biochemistry and markers of fibrosis. Fenofibrate alone and in combination with firsocostat was well-tolerated; no grade 3 or 4 adverse events, treatment-related discontinuations or hepatotoxicity were observed.

Firsocostat is an investigational compound and is not approved by the U.S. Food & Drug Administration (FDA) or any other regulatory authority. Safety and efficacy have not been established.

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, which are being studied in the Phase 2 ATLAS trial in advanced fibrosis due to NASH.

These investigational compounds 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 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 the risk that Gilead and PathAI may not realize the potential benefits of this collaboration. There is also the possibility of unfavorable results from ongoing and additional Gilead clinical programs in NASH, including clinical trials involving firsocostat, and the possibility that Gilead may be unable to complete these clinical studies in the currently anticipated timelines or at all. Further, it is possible that Gilead may make a strategic decision to discontinue development of firsocostat and other investigational compounds for the treatment of NASH 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 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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