Sagimet Biosciences Presents Clinical Denifanstat and Preclinical FASN Inhibitor Data at AASLD - The Liver Meeting® 2024

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Subset analysis of FASCINATE-2 Phase 2 trial demonstrated denifanstat improved fibrosis in difficult-to-treat MASH patients

Both artificial intelligence (AI) and conventional pathology demonstrated denifanstat's strong anti-fibrotic activity

FASN inhibitor treatment reduced atherosclerosis development in mouse model of dyslipidemia and MASH

SAN MATEO, Calif., Nov. 18, 2024 (GLOBE NEWSWIRE) -- Sagimet Biosciences Inc. (Sagimet, Nasdaq: SGMT), a clinical-stage biopharmaceutical company developing novel therapeutics targeting dysfunctional metabolic and fibrotic pathways, today announced the presentation of Phase 2b data demonstrating the anti-fibrotic activity of its fatty acid synthase (FASN) inhibitor denifanstat, and preclinical data demonstrating potential benefit of FASN inhibition in atherosclerosis, at the American Association for the Study of Liver Disease (AASLD) - The Liver Meeting 2024®, November 15-19, 2024 in San Diego, California.

"Our presentations of data from the Phase 2b FASCINATE-2 study highlight denifanstat's impact on liver fibrosis, particularly in difficult-to-treat subsets of MASH patients who are at the highest risk of disease progression," said Dave Happel, Chief Executive Officer of Sagimet. "Using an AI-based digital pathology approach, we observed pronounced fibrosis reduction in the peri-portal and portal zones of the liver, which as part of composite scores have recently been shown to correlate with liver outcomes and mortality, that may not be captured using conventional histological scoring. Finally, our preclinical data in a mouse model of MASH and dyslipidemia treated with a FASN inhibitor that is a surrogate for denifanstat showed that a FASN inhibitor may reduce circulating cholesterol and atherosclerosis development. Together, these results demonstrate the anti-fibrotic effects and potential cardiometabolic benefits of FASN inhibition and support the advancement of denifanstat into Phase 3 development."

A poster titled "*Denifanstat significantly improves liver fibrosis in difficult-to-treat MASH patients – Results from conventional and AI-based pathology from the phase 2b FASCINATE-2, a 52-week randomized, double-blind, placebo-controlled trial*," was presented by Rohit Loomba, M.D., M.H.Sc., Professor of Medicine, Chief, Division of Gastroenterology and Hepatology, and Director, MASLD Research Center, University of California San Diego, the primary investigator of the FASCINATE-2 trial. Denifanstat treatment improved fibrosis by ≥ 1 stage without worsening of MASH in the higher-risk patient subgroups described below. Observed improvements by conventional pathology reading included:

- F3 population: 49% denifanstat (n=47) vs 13% placebo (n=23) (p=0.0032)
- GLP1 receptor agonist population: 42% denifanstat (n=12) vs 0% placebo (n=4) (p=0.034)
- Type 2 diabetes population: 40% denifanstat (n=55) vs 19% placebo (n=27) (p=0.0382)
- PNPLA3 I148 carrier population: 30% denifanstat (n=33) vs 6% placebo (n=17) (p=0.022)

Strong consistency in fibrosis improvement was observed between conventional and AI-based pathology in the F3 population. Denifanstat treatment improved fibrosis by ≥ 1 stage in more than 50% of F3 patients as follows:

- AI-based: 62% denifanstat (n=47) and 26% placebo (n=23) (p=0.005)
- Conventional: 55% denifanstat (n=47) and 26% placebo (n=23) (p=0.021)

An oral presentation titled "*AI-based digital pathology shows that denifanstat improves multiple parameters of fibrosis and reduces progression to cirrhosis in MASH patients with F2/F3 fibrosis – results of the FASCINATE-2 study*," was presented by Mary Rinella, M.D. (University of Chicago). In this analysis, second harmonic generation (SHG) microscopy AI-based digital pathology was used to evaluate pre- and post-treatment liver biopsies. Denifanstat showed statistically significant liver fibrosis improvement, particularly in the portal and peri-portal regions. Improvement was observed with AI-based digital pathology not only in patients with >1-stage fibrosis improvement but also in patients with "no change" in fibrosis stage by conventional reading, representing important mechanistic insights provided by the AI-based platform. Select fibrosis parameters in the periportal and portal regions are part of AI-based composite score that have been recently linked to liver outcomes and mortality. Overall, both AI and conventional pathology readings demonstrated denifanstat's strong anti-fibrotic activity in MASH patients, including those with high risk of progression. These data reflect the unique mechanism of action of denifanstat and support the initiation of phase 3 trials.

Lastly, a poster titled "*Fatty acid synthase (FASN) inhibitor reduces atherosclerosis development in diet-induced dyslipidaemia LDL receptor knockout mice with MASH*," was presented by Wen-Wei Tsai, Ph.D. (Sagimet Biosciences). In this mouse model, treatment with a FASN inhibitor that is a preclinical surrogate for denifanstat rapidly reduced circulating cholesterol, triglycerides and inflammatory markers associated with atherosclerosis, including CCL4 and CXCL2. The FASN inhibitor also reduced total atherosclerotic lesion area in the aortic root and improved liver steatosis, inflammation and fibrosis. These preclinical results suggest that a FASN inhibitor such as denifanstat could potentially provide benefits in cardiovascular as well as liver health, supporting the clinical evaluation of denifanstat for long term outcomes in MASH patients.

About Sagimet Biosciences

Sagimet is a clinical-stage biopharmaceutical company developing novel fatty acid synthase (FASN) inhibitors that are designed to target

dysfunctional metabolic and fibrotic pathways in diseases resulting from the overproduction of the fatty acid, palmitate. Sagimet's lead drug candidate, denifanstat, is an oral, once-daily pill and selective FASN inhibitor in development for the treatment of metabolic dysfunction associated steatohepatitis (MASH). FASCINATE-2, a Phase 2b clinical trial of denifanstat in MASH with liver biopsy-based primary endpoints, was successfully completed with positive results. Denifanstat has been granted Breakthrough Therapy designation by the FDA for the treatment of non-cirrhotic MASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis), and end-of-Phase 2 interactions with the FDA have been successfully completed, supporting the advancement of denifanstat into Phase 3 development in MASH. For additional information about Sagimet, please visit www.sagimet.com.

About MASH

Metabolic dysfunction associated steatohepatitis (MASH) is a progressive and severe liver disease which is estimated to impact more than 115 million people worldwide, for which there is only one recently approved treatment in the United States and no currently approved treatments in Europe. In 2023, global liver disease medical societies and patient groups formalized the decision to rename non-alcoholic fatty liver disease (NAFLD) to metabolic dysfunction-associated steatotic liver disease (MASLD) and nonalcoholic steatohepatitis (NASH) to MASH. Additionally, an overarching term, steatotic liver disease (SLD), was established to capture multiple types of liver diseases associated with fat buildup in the liver. The goal of the name change was to establish an affirmative, non-stigmatizing name and to improve diagnostic clarity.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of, and made pursuant to the safe harbor provisions of, The Private Securities Litigation Reform Act of 1995. All statements contained in this press release, other than statements of historical facts or statements that relate to present facts or current conditions, including but not limited to, statements regarding: the expected timing of the presentation of data from ongoing clinical trials, Sagimet's clinical development plans and related anticipated development milestones, Sagimet's cash and financial resources and expected cash runway. These statements involve known and unknown risks, uncertainties and other important factors that may cause Sagimet's actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. In some cases, these statements can be identified by terms such as "may," "might," "will," "should," "expect," "plan," "aim," "seek," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "forecast," "potential" or "continue" or the negative of these terms or other similar expressions.

The forward-looking statements in this press release are only predictions. Sagimet has based these forward-looking statements largely on its current expectations and projections about future events and financial trends that Sagimet believes may affect its business, financial condition and results of operations. These forward-looking statements speak only as of the date of this press release and are subject to a number of risks, uncertainties and assumptions, some of which cannot be predicted or quantified and some of which are beyond Sagimet's control, including, among others: the clinical development and therapeutic potential of denifanstat or any other drug candidates Sagimet may develop; Sagimet's ability to advance drug candidates into and successfully complete clinical trials within anticipated timelines, including its Phase 3 denifanstat program; Sagimet's relationship with Ascletis, and the success of its development efforts for denifanstat; the accuracy of Sagimet's estimates regarding its capital requirements; and Sagimet's ability to maintain and successfully enforce adequate intellectual property protection. These and other risks and uncertainties are described more fully in the "Risk Factors" section of Sagimet's most recent filings with the Securities and Exchange Commission and available at www.sec.gov. You should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in these forward-looking statements may not be achieved or occur, and actual results could differ materially from those projected in the forward-looking statements. Moreover, Sagimet operates in a dynamic industry and economy. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that Sagimet may face. Except as required by applicable law, Sagimet does not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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