Sagimet Biosciences Announces Positive Topline Results from Phase 2b FASCINATE-2 Clinical Trial of Denifanstat in Biopsy-Confirmed F2/F3 NASH

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Denifanstat achieved statistically significant results on primary and multiple secondary endpoints in a 52-week clinical trial of 168 NASH patients with stage 2 or 3 fibrosis

- *Primary efficacy endpoints:*
  - *NASH resolution without worsening of fibrosis with ≥2-point reduction in NAS (NAFLD Activity Score) in 36% of denifanstat-treated patients vs 13% with placebo* ***(p=0.002)***
  - *≥2-point reduction in NAS without worsening of fibrosis in 52% of denifanstat-treated patients vs 20% with placebo* ***(p=0.0001)***

- *Multiple secondary endpoints:*

  - *Fibrosis improvement by ≥ 1 stage with no worsening of NASH in 41% of denifanstat-treated patients vs 18% with placebo* ***(p=0.005)***
  - *NASH resolution with no worsening of fibrosis in 38% of denifanstat-treated patients vs 16% with placebo* ***(p=0.002)***
  - *MRI-PDFF decline from baseline ≥30% (responders) in 65% of denifanstat-treated patients vs 21% with placebo* ***(p<0.0001)***

Statistically significant improvements in additional markers of liver health, including artificial intelligence (AI) digital pathology-based fibrosis assessment, FAST Score, and ALT, and numerical improvements in LDL

Denifanstat was generally well-tolerated

Management to host live webcast at 8:00 a.m. ET on Monday, January 22, 2024

SAN MATEO, Calif., Jan. 22, 2024 (GLOBE NEWSWIRE) -- Sagimet Biosciences Inc. (Sagimet, Nasdaq: SGMT), a clinical-stage biopharmaceutical company developing novel fatty acid synthase (FASN) inhibitors designed to target dysfunctional metabolic and fibrotic pathways, today announced positive topline results from its FASCINATE-2 Phase 2b clinical trial of denifanstat versus placebo in biopsy-confirmed non-alcoholic steatohepatitis (NASH) patients with stage 2 or stage 3 fibrosis (F2/F3) at week 52. In this trial, denifanstat, an oral, selective FASN inhibitor, showed statistically significant improvements relative to placebo on both of the primary endpoints of NASH resolution without worsening of fibrosis with ≥2-point reduction in NAS, and ≥2-point reduction in NAS without worsening of fibrosis. Denifanstat-treated patients also showed statistically significant fibrosis improvement by ≥ 1 stage with no worsening of NASH, and a greater proportion of MRI-derived proton density fat fraction (MRI-PDFF) ≥30% responders relative to placebo.

“Denifanstat is designed to reduce the three main drivers of NASH, including fat accumulation, inflammation, and fibrosis, both independently and in parallel. The week 52 biopsy results showed that denifanstat achieved statistical superiority over placebo in reduction of fibrosis, via two independent processes of traditional histopathology and AI digital pathology,” said Dave Happel, Chief Executive Officer of Sagimet. “Sagimet is committed to creating novel approaches to target dysfunctional metabolic pathways, and we believe these positive results represent a major advancement in that endeavor. Our next step will be holding an End-of-Phase 2 meeting with the FDA and starting our Phase 3 program for development of denifanstat in NASH with related fibrosis, which we anticipate to begin in the second half of 2024.”

“The over-activity of fatty acid synthase and increased de-novo lipogenesis or DNL plays a critical role in the development of NASH and its progression to cirrhosis,” commented 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, who serves as a scientific advisor for Sagimet on its ongoing development of denifanstat. “Denifanstat is the only FASN inhibitor currently in clinical development for the treatment of NASH with related fibrosis. These data show that blocking fatty acid synthesis in the liver and DNL is a critical approach for NASH resolution and improvements in fibrosis. These results support denifanstat’s mechanism of action and the impact of addressing these multiple pathways simultaneously. Moreover, the safety profile supports the further development of denifanstat in NASH patients.”

Statistical Significance Achieved in Primary Endpoints and Improvements Across Other Endpoints at Week 52 of Denifanstat Treatment

	Denifanstat 50 mg (n=81)	Placebo (n=45)	P-value vs placebo
Primary Endpoints			
NASH resolution without worsening of fibrosis with ≥2-point reduction in NAS	36%	13%	0.002
≥ 2-point decrease in NAS without worsening of fibrosis	52%	20%	0.0001
Other Endpoints			
Improvement of fibrosis by ≥ 1 stage with no worsening of NASH	41%	18%	0.005

NASH resolution with no worsening of fibrosis	38%	16%	0.002
AI digital pathology (qFibrosis)*	-0.3	0.1	0.002
ALT % change from baseline	-30.5%	-17.2%	0.03
MRI-PDFF responder rate**	65%	21%	<0.0001
FibroScan AST (FAST) score	-0.3	-0.1	<0.0001
LDL cholesterol (mg/dL)***	-19.1	-9.1	--

Modified intent-to-treat population (mITT) includes all patients with paired biopsies; includes Secondary Endpoints for which analysis has been completed as of the date of this press release.
**Artificial Intelligence (AI) digital pathology assessed by second harmonic generation (SHG, HistoIndex)*
*** MRI-PDFF responders are patients with ≥30% relative reduction of liver fat at the end of treatment*
**** Baseline LDL-C greater than 100 mg/dL; exploratory analysis shown for n=32 and n=27 denifanstat and placebo patients, respectively*

Safety and Tolerability

As in prior studies, no treatment-related serious adverse events (SAEs) were observed, and the majority of adverse events (AEs) were mild to moderate in nature (Grades 1 and 2). There were no Grade ≥3 treatment-related AEs. The most common treatment-related AEs by system organ class (observed in ≥5% of patients in the study) were eye disorders (denifanstat 15.2%, placebo 16.1%), gastrointestinal disorders (denifanstat 11.6%, placebo 8.9%), and skin and subcutaneous tissue disorders (denifanstat 22.3%, placebo 7.1%). The incidence of treatment emergent adverse events (TEAEs) leading to treatment discontinuation was 19.6% in the denifanstat group compared to 5.4% in placebo.

Webcast Information

Management will host a live webcast at 8:00 a.m. ET on Monday, January 22, 2024 to discuss the data; participants will have the opportunity to participate in a chat-based Q&A session. The webcast will be available here and in the Events & Presentation section of Sagimet's website at www.sagimet.com, with an archived replay available for approximately 90 days following the event.

About Phase 2b FASCINATE-2 Clinical Trial

The Phase 2b FASCINATE-2 clinical trial was a 52-week randomized, double-blind, placebo-controlled trial that evaluated the safety and histological impact of denifanstat compared to placebo in 168 biopsy-confirmed NASH patients with moderate-to-severe fibrosis (stage F2 or F3) with NAS ≥4.

Patients were randomized 2:1 to receive 50 mg denifanstat or placebo, taken orally once daily. An end-of-trial biopsy was assessed by a central pathologist for histological endpoints. Liver biopsies were also analyzed using AI-based digital pathology.

About Sagimet Biosciences

Sagimet is a clinical-stage biopharmaceutical company developing novel fatty acid synthase (FASN) inhibitors that are designed to target dysfunctional metabolic 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 NASH, for which there are no treatments currently approved in the United States or Europe. FASCINATE-2, a Phase 2b clinical trial of denifanstat in NASH with liver biopsy-based primary endpoints, was successfully completed with positive results. For additional information about Sagimet, please visit www.sagimet.com.

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 presentation of data from 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 risks that top-line clinical trial results may not be predictive of, and may differ from, final clinical data and later-stage clinical trials; that unfavorable new clinical trial data may emerge in other clinical trials of denifanstat, including Phase 3 clinical trials; that clinical trial data are subject to differing interpretations and assessments, including by regulatory authorities; 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; 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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