Sagimet Biosciences Presents Positive Phase 2b FASCINATE-2 Clinical Trial Interim Data for Denifanstat for the Treatment of NASH at EASL Congress 2023

06/23/2023 at 2:30 AM EDT

Denifanstat was well-tolerated and met primary endpoint in planned interim readout with 67% of treated patients achieving ≥30% reductions in liver fat at week 26 compared to 18% placebo (p<0.001) as assessed by MRI-PDFF

Denifanstat statistically significantly decreased LDL cholesterol in treated patients and improvements in the circulating blood lipid profile were observed

Topline week 52 liver biopsy results expected in the first quarter of 2024

SAN MATEO, Calif., June 23, 2023 (GLOBE NEWSWIRE) -- Sagimet Biosciences Inc., a clinical-stage biopharmaceutical company developing novel therapeutics targeting dysfunctional metabolic pathways, today announced an oral presentation of data from the planned interim analysis of a prespecified subset of patients at week 26 of the Phase 2b FASCINATE-2 clinical trial of denifanstat, an investigational fatty acid synthase (FASN) inhibitor, in nonalcoholic steatohepatitis (NASH) patients with moderate to advanced fibrosis, stages F2 or F3, as confirmed by liver biopsy. These results were presented at the European Association for the Study of the Liver (EASL) Congress being held in Vienna from June 21-24, 2023, and were previously presented at The Liver Meeting of the American Association for the Study of Liver Diseases (AASLD) in November 2022.

Rohit Loomba, M.D., M.H.Sc., Director, NAFLD Research Center, University of California San Diego, who presented the data, commented, “The level of response observed in denifanstat-treated patients at week 26 is consistent with prior clinical results and encouraging, especially given the favorable tolerability profile. We are excited by the observed improvement across biomarkers, including a statistically significant 12.4 mg/dL reduction in LDL cholesterol and an increase in endogenous FGF21 by 73.1%. FGF21 is a hormone that regulates important metabolic pathways, in particular insulin sensitivity, and has been known to decrease hepatocyte injury while suppressing inflammation and fibrosis. At week 26, denifanstat-treated patients had an observable change in circulating blood lipid composition with a decrease in the di-/triglycerides that are unregulated in NASH and an increase in cardioprotective polyunsaturated di-/triglycerides. These denifanstat-driven improvements are consistent with the Phase 2a FASCINATE-1 findings.”

Improvement Across Biomarkers at Week 26 of Denifanstat Treatment

	Denifanstat 50 mg (n=30)	**Placebo (n=22)**	**P-value vs placebo**
Relative reduction in liver fat	- 34.1%	- 1.5%	p<0.001
≥30% reduction of liver fat (responder rate)*	67.0%	18.0%	p<0.01
ALT (U/L)	- 16.5	- 4.0	p<0.05
Dual liver fat & ALT responder >30% + >17U/L decrease	37.0%	9.0%	p<0.05
PRO-C3**	- 8.2%	-1.5%	p<0.05
Enhanced liver fibrosis (ELF) score	- 0.34	- 0.02	p<0.05
LDL cholesterol (mg/dL)	- 12.4	0.0	p<0.05
FGF21	+ 73.1%	+ 0.9%	p<0.01

** approximately half of denifanstat responders decreased liver fat by ≥50%*
***Roche Diagnostics cobas® assay*

As of the cut-off date for this interim analysis population, no treatment-related serious adverse events were reported, and the majority of adverse events reported were mild to moderate in nature (Grades 1 and 2). The incidence of treatment-related treatment emergent adverse events (TEAEs) was 46.7% (denifanstat) and 27.3% (placebo), and all were Grade 1 or Grade 2. The incidence of TEAEs leading to treatment discontinuation were 6.7% (denifanstat) and 4.6% (placebo) Additionally, there was no evidence of drug-induced liver injury (DILI) and no deaths.

Advanced Lipid Analysis
Denifanstat improved measures of metabolic health by demonstrating a statistically significant decrease in LDL cholesterol and statistically significant increase in FGF21, an endogenous hormone primarily expressed in the liver that is associated with improvements in metabolic regulation. Using advanced lipid analyses, denifanstat improved circulating blood lipid composition by reducing the saturated diglycerides and triglycerides that are elevated in NASH while increasing polyunsaturated diglycerides and triglycerides, and reducing lipotoxic ceramides. Changes in these measures are consistent with improved cardiometabolic health.

“As we continue to advance denifanstat for the treatment of NASH, we are pleased with the significant improvement across multiple biomarkers of disease, which are consistent with FASCINATE-1 results,” said David Happel, Chief Executive Officer of Sagimet. “We believe the interim Phase 2b data continues to highlight denifanstat’s differentiated mechanism of action and reinforces our confidence in its favorable tolerability profile and broad application potential in NASH. We look forward to presenting the topline biopsy data in the first quarter of 2024 and are working towards a subsequent initiation of a pivotal Phase 3 trial.”

About Phase 2b FASCINATE-2 Clinical Trial

The Phase 2b FASCINATE-2 study is a 52-week randomized, double-blind, placebo-controlled trial evaluating the safety and histological impact of a

50mg daily oral dose of denifanstat compared to placebo in 168 biopsy-confirmed NASH patients with moderate-to-severe fibrosis (stage F2 or F3). The primary efficacy endpoint is histological (liver biopsy) improvement at week 52 in nonalcoholic fatty liver disease (NAFLD) activity score (NAS) without worsening of fibrosis or resolution of steatohepatitis without worsening of fibrosis. Secondary endpoints include biomarkers of inflammation, fibrosis and liver injury.

About Sagimet Biosciences

Sagimet is a clinical-stage biopharmaceutical company developing novel therapeutics targeting dysfunctional metabolic pathways in diseases, such as NASH, certain cancers and acne. Sagimet compounds are designed to inhibit FASN, an enzyme involved in the production of fatty acids normally used for energy storage. In NASH, the activity of FASN enzyme is upregulated, resulting in excess accumulation of liver fat, inflammation and fibrosis. Sagimet's lead product candidate, denifanstat, an oral, once-daily pill, is currently being tested in FASCINATE-2, a Phase 2b clinical trial in NASH with liver biopsy as the primary endpoint. In June 2020, Sagimet announced positive results from FASCINATE-1, its Phase 2 clinical trial for denifanstat. The results of the Phase 2 clinical trial were published in ***Gastroenterology,*** the official journal of the American Gastroenterological Association. For additional information about Sagimet Biosciences, please visit www.sagimet.com.

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