



Metacrine Reports Topline Results for MET409 Phase 2a Combination Trial In Patients with Type 2 Diabetes and NASH

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- Validates therapeutic benefit of combination approaches for a large segment of NASH patients
- Demonstrates additive efficacy results and favorable tolerability profile

SAN DIEGO, Nov. 02, 2021 (GLOBE NEWSWIRE) -- Metacrine, Inc. (NASDAQ:MTCR), a clinical-stage biopharmaceutical company pioneering differentiated therapies for patients with gastrointestinal and liver diseases, today reported topline results from its Phase 2a trial evaluating MET409, a farnesoid X receptor (FXR) agonist, in combination with empagliflozin (Jardiance®), a sodium-glucose cotransport-2 (SGLT2) inhibitor, in patients with type 2 diabetes and non-alcoholic steatohepatitis (NASH).

The Phase 2a study ([NCT04702490](#)) is a 12-week, randomized, placebo-controlled, multi-center trial that evaluated the safety, tolerability and pharmacological activity, as measured by reductions in liver fat content with magnetic resonance imaging-derived proton density fat fraction (MRI-PDFF), of MET409 (50 mg) and empagliflozin (10 mg) versus individual treatments and placebo. A total of 132 patients were randomized (33 per treatment group).

All regimens had favorable safety profiles and were generally well-tolerated, with no treatment-related serious adverse events (AEs). Mild-moderate pruritus was reported in 0%-6% of patients across all groups. No pruritus-related treatment discontinuations occurred in any of the cohorts. LDL-cholesterol increases with MET409 were consistent with previous studies and were comparable alone or in combination with empagliflozin. Secondary assessment of liver fat content at 12 weeks indicated reduction in liver fat, as measured by MRI-PDFF, in both monotherapy arms and demonstrated additive effects in the combination regimen.

"NASH is closely linked to several co-morbidities, with an estimated 65% of type 2 diabetes patients also having NASH," said Hubert C. Chen, M.D., chief medical officer, Metacrine. "These results showcase the multiple mechanisms that drive NASH and the promise of novel combination approaches in bringing new therapies to patients. We are pleased by the MET409 combination trial results, as this product candidate achieved improvements in liver fat both as a monotherapy and additively when combined with empagliflozin. Treating this large and important patient segment effectively will likely require combination therapies."

MET409 Phase 2a Combination Trial Selected Data

Endpoint	Placebo	MET409 50 mg	Empagliflozin 10 mg	MET409 50 mg + Empagliflozin 10 mg
Mean relative liver fat change (±SD)	3% ± 24%	-16% ± 45%	-16% ± 22%	-28% ± 33%
% of patients with >30% relative liver fat reduction	3%	50%	23%	47%
Mean change in LDL-C	0%	12%	-2%	9%
Overall pruritus rate	0%	6%	0%	3%
Pruritus-related treatment discontinuation	0%	0%	0%	0%

MET409 Phase 2a Combination Trial Monotherapy Arm and MET642 Phase 2a Interim Results Comparison

Endpoint (12 weeks for MET409, 16 weeks for MET642)	MET409 50 mg	MET642 3 mg
Relative liver fat reduction (Placebo-corrected)	19%	19%
% of patients with >30% relative liver fat reduction	50%	47%
Mean change in LDL-C (Placebo-corrected)	12%	15%
Overall pruritus rate	6%	5%
Pruritus-related treatment discontinuation	0%	0%

Chen continued, "With the additional data from this study's MET409 individual cohort, it has also become clear that MET409 and MET642 have comparable therapeutic profiles. Both compounds were developed from the same unique chemical scaffold, and these data along with the MET642 interim results we recently shared provide a comprehensive view of our FXR program and highlight the similarity of these two assets."

As the Company previously stated, it has halted future development of its FXR program in NASH and is prioritizing its clinical development effort and resources to advance MET642 into a Phase 2 trial in inflammatory bowel disease (IBD).

About Metacrine

Metacrine, Inc. is a clinical-stage biopharmaceutical company building a pipeline of differentiated therapies to treat gastrointestinal and liver diseases. Metacrine has developed a proprietary farnesoid X receptor (FXR) platform utilizing a unique chemical scaffold. To learn more, visit www.metacrine.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Statements in this press release that are not purely historical are forward-looking statements. Such forward-looking statements include, among other things, the potential for MET409 to be used in combination therapies; the potential for MET409 to be used in therapies for patients with both NASH and type 2 diabetes, the uncertainties inherent in clinical testing; future plans or expectations for MET409 or MET642, as well as the dosing, safety and tolerability of MET409 or MET642, plans for initiating future clinical trials and studies; statements regarding the therapeutic potential of MET409 or MET642. Words such as "could," "may," "will," "expect," "plan," "aim," "projected," "likely," "anticipate," "estimate," "intend," "potential," "prepare," "perceived," "believes" and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. These forward-looking statements are based on Metacrine's expectations and assumptions that may never materialize or prove to be incorrect. Each of these forward-looking statements involves risks and uncertainties. Actual results may differ materially from those projected in any forward-looking statements due to numerous risks and uncertainties, including but not limited to: positive results from a clinical study may not necessarily be predictive of the results of future or ongoing clinical studies, risks and uncertainties regarding regulatory approvals for MET409 or MET642; potential delays in initiating, enrolling or completing any clinical trials; potential adverse side effects or other safety risks associated with Metacrine's product candidates; competition from third parties that are developing products for similar uses; and Metacrine's ability to obtain, maintain and protect its intellectual property. Information regarding the foregoing and additional risks may be found in the section entitled "Risk Factors" in Metacrine's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (the "SEC") on August 12, 2021, and in Metacrine's other filings with the SEC. All forward-looking statements contained in this press release speak only as of the date on which they were made. Except as required by law, Metacrine assumes no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

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