Metacrine Reports Interim Results for MET642 Phase 2a Trial in Patients with NASH and Announces a Strategic Re-Prioritization of Its Clinical Development Programs

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SAN DIEGO, Oct. 21, 2021 (GLOBE NEWSWIRE) -- Metacrine, Inc. (NASDAQ:MTCR), a clinical-stage biopharmaceutical company pioneering differentiated therapies for patients with liver and gastrointestinal diseases, today reported interim results from a Phase 2a clinical trial evaluating the efficacy and safety of MET642, a farnesoid X receptor (FXR) agonist, in approximately 60 non-alcoholic steatohepatitis (NASH) patients after 16 weeks of treatment. The Company also announced it is prioritizing its clinical development effort and resources to advance MET642 into a Phase 2 trial in inflammatory bowel disease (IBD) in the first half of 2022.

The Phase 2a trial (NCT04773964) is a 16-week, randomized, placebo-controlled, multi-center trial evaluating the safety, tolerability and pharmacological activity of MET642, as measured by reductions in liver fat content with magnetic resonance imaging-derived proton density fat fraction (MRI-PDFF), changes in liver enzymes, low-density lipoprotein cholesterol (LDL-C) levels and incidence of pruritus, at 3 mg and 6 mg dose levels.

MET642 lowered liver fat content, with mean relative reductions of 26.9±27.8 percent in the 3 mg cohort and 9.3±55.8 percent in the 6 mg cohort, compared with 7.5±21.0 percent in the placebo arm. Post-hoc comparative assessment of relative liver fat reduction in the interim cohort found the decrease with 3 mg to be statistically significant compared to placebo (p=0.006). MET642 achieved greater than 30 percent liver fat reduction in 47 percent of patients (8/17) in the 3 mg cohort and 35 percent (6/17) in the 6 mg cohort, compared with 12 percent (2/17) in the placebo arm.

MET642 was generally well-tolerated, with no treatment-related serious adverse events (AEs). All treatment-related AEs were mild-moderate with no apparent dose relationship. Mild-moderate pruritus was reported in one patient in the 3 mg cohort and one patient in the 6 mg cohort. No pruritus-related treatment discontinuations occurred. MET642 treatment resulted in on-target mean increases in LDL-C of 5 percent with the 3 mg dose and 19 percent with the 6 mg dose, versus a decline of 10 percent with placebo, from baseline to week 16.

Mean Change (Baseline to Week 16)	Placebo (N=20)	3 mg (N=21)	6 mg (N=20)
Liver Fat Reduction (MRI-PDFF) % ±SD	-7.5% ± 21.0%	-26.9% ± 27.8%	-9.3% ± 55.8%
Median Liver Fat Reduction (MRI-PDFF) %	-1.5%	-28.6%	-26.9%
% of patients with >30% Liver Fat Reduction (MRI-PDFF)	11.8%	47.1%	35.3%
LDL-C %	-10.5%	4.5%	19.4%
Overall Pruritus Rate %	10.0%	5.0%	5.0%
Pruritus-Related Treatment Discontinuation %	0.0%	0.0%	0.0%

In addition, the Company is conducting an independent review of preliminary findings from a recently completed nine-month animal toxicology study for MET642, which may result in the need for an additional long-term animal toxicology study to support Phase 3 clinical trials in IBD. Metacrine expects the independent review to be completed before the end of 2021.

“We are encouraged by the MET642 interim clinical trial results, as this product candidate demonstrated meaningful liver fat reduction at 3 mg and a potentially class-leading tolerability profile for the treatment of NASH at both 3 mg and 6 mg,” said Preston Klassen, M.D., MHS, CEO, Metacrine. “In this small interim analysis, the 6 mg cohort displayed a non-normal distribution in liver fat changes, as evidenced by differences between the mean and median results. Further clarification of the impact on liver fat at the 6 mg dose will require examination of the complete trial data set, which is anticipated in the first half of 2022. NASH is a complex and chronic disease that we believe will likely require combination regimes to most effectively treat patients. MET642 can potentially serve as an important part of these novel combination approaches.”

Klassen continued, “After a rigorous assessment of our NASH and IBD programs, including the significant capital and resources required to progress these large clinical development programs, we have made the decision to focus Metacrine’s clinical development effort and financial resources on moving MET642 into a Phase 2 trial in IBD in the first half of 2022 and to halt future development of the FXR program in NASH. This decision was influenced in part by a potential delay in confirming appropriate safety margins in our long-term toxicology work that would impact the timing of future NASH studies, but is unlikely to impact timelines for the IBD clinical program.”

Klassen concluded, “The rationale for FXR-based therapies in IBD holds great promise and is anchored on the potential to address multiple aspects of IBD pathogenesis without the immunosuppression inherent to other advanced-line therapies. FXR is highly expressed by intestinal epithelial cells and plays a key role in healthy intestinal function by maintaining the epithelial barrier, reducing bacterial translocation into the intestinal wall and regulating the innate immune response. Metacrine’s preclinical studies supporting a role for FXR agonism in IBD are corroborated by significant evidence from the scientific literature. FXR therapy could potentially change the IBD treatment paradigm by bringing an oral, once-daily, well-tolerated and non-immunosuppressive medicine to patients. New approaches are clearly needed that expand therapeutic options for people living with IBD and we are excited to advance MET642 into clinical investigation in this important disease.”

About Metacrine

Metacrine, Inc. is a clinical-stage biopharmaceutical company building a pipeline of differentiated therapies to treat liver and gastrointestinal diseases. Metacrine has developed a proprietary farnesoid X receptor (FXR) platform utilizing a unique chemical scaffold, which has demonstrated an improved therapeutic profile in clinical trials. 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, Metacrine's clinical development of MET642, the uncertainties inherent in clinical testing; future plans or expectations for MET642, as well as the dosing, safety and tolerability of MET642, plans for initiating future clinical trials and studies; statements regarding the therapeutic potential of MET642; the timing, outcome and potential impact of the independent review of the animal toxicology study of MET642; plans for advancing the clinical development of Metacrine's FXR and IBD programs; the potential leading nature of MET642 and Metacrine's FXR program; the potential for combination therapies to be used for NASH, the potential for its FXR product candidates to be used in combination therapies; and the potential for its FXR product candidates to be long-term therapies for NASH and IBD. 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 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.

Investor & Media Contact

Steve Kunszabo
Metacrine, Inc.
+1 (858) 369-7892
skunszabo@metacrine.com