



Metacrine Initiates Phase 2a Combination Trial of MET409 with Empagliflozin in Patients with Type 2 Diabetes and NASH

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Trial Designed to Evaluate Potential of FXR-Based Combination Therapy in a Growing Segment of NASH Patient Population with Significant Unmet Needs

SAN DIEGO, Jan. 05, 2021 (GLOBE NEWSWIRE) -- Metacrine, Inc. (Nasdaq: MTCR), a clinical-stage biopharmaceutical company focused on discovering and developing differentiated therapies for patients with liver and gastrointestinal diseases, today announced that the first patient has been treated in the company's Phase 2a trial evaluating MET409 (50 mg) in combination with empagliflozin (Jardiance®), a sodium-glucose cotransport-2 (SGLT2) inhibitor, in patients with both type 2 diabetes mellitus (T2DM) and nonalcoholic steatohepatitis (NASH). T2DM and NASH co-exist in many patients, with abnormal liver fat content seen in up to approximately 70% of patients with T2DM and biopsy-proven NASH in up to approximately 25% of patients.

"NASH is a multifactorial liver disease associated with a number of co-morbidities, including type 2 diabetes," said Eric J. Lawitz, M.D., vice president of scientific and research development at The Texas Liver Institute, clinical professor of medicine at the University of Texas Health San Antonio and primary investigator for the Phase 2a trial. "Even though patients with T2DM are perceived to have a more aggressive form of NASH and fibrosis, there has been a lack of innovative treatments for these patients. I am encouraged by MET409's monotherapy clinical data in patients with NASH, as well as its potential to combine with a SGLT2 inhibitor. I look forward to evaluating MET409 in this combination, potentially enabling its clinical use in the future."

Metacrine has developed a proprietary farnesoid X receptor (FXR) platform utilizing a unique chemical scaffold, which has demonstrated a differentiated and improved therapeutic profile in the clinic. MET409, Metacrine's lead product candidate, is a once-daily, orally administered FXR agonist that is being evaluated as both a monotherapy and a combination therapy for the treatment of NASH. In a 12-week trial in patients with NASH, MET409 (50 mg) achieved approximately 38% mean relative liver fat reduction and was associated with a 16% overall pruritus rate, with no discontinuations due to pruritus, and a 7% LDL-cholesterol increase, findings that are favorable and perceived as class-leading for FXR agonists.

SGLT2 inhibitors, such as empagliflozin, are once-daily, oral anti-diabetic medications that are increasingly viewed as a paradigm-shifting therapeutic class for T2DM. In addition to beneficial effects on metabolic control and cardio-renal protection, SGLT2 inhibitors have demonstrated positive effects on liver fat reduction. In a proof-of-concept trial in patients with NASH and T2DM, empagliflozin (10 mg) achieved approximately 30% relative liver fat reduction after 20 weeks of treatment. SGLT2 inhibitors therefore have the potential to complement the liver-targeting therapeutic effects of FXR agonism on hepatic steatosis, inflammation and fibrosis.

"We are pleased to begin this trial, given the meaningful impact this combination could demonstrate in patients affected by these challenging and often overlapping conditions," said Hubert C. Chen, M.D., chief medical officer of Metacrine. "MET409 has already shown significant liver fat reductions and a differentiated tolerability profile as a monotherapy in patients with NASH. Importantly, as a once-daily, oral therapy, MET409 has the potential to be an ideal backbone for use in combination treatment. We look forward to advancing the trial in a key segment of the NASH patient population."

The Phase 2a clinical trial is a 12-week, randomized, placebo-controlled, multi-center trial evaluating the safety, tolerability and pharmacological activity (as measured by reductions in liver fat content with magnetic resonance imaging-derived proton density fat fraction) of MET409 in combination with empagliflozin in patients with T2DM and NASH. Eligible patients will be randomized into one of four cohorts: MET409 (50 mg), MET409 (50 mg) plus empagliflozin (10 mg), placebo alone or placebo plus empagliflozin (10 mg). Each trial drug will be given once-daily by oral administration. The trial will enroll up to 120 patients in the United States. Metacrine expects to report topline data in the first half of 2022.

About Metacrine

Metacrine, Inc. (Nasdaq: MTCR) is a clinical-stage biopharmaceutical company building a differentiated pipeline of therapies to treat liver and gastrointestinal (GI) diseases. Metacrine has developed a proprietary farnesoid X receptor (FXR) platform utilizing a unique chemical scaffold, which has demonstrated a differentiated and improved therapeutic profile in clinical trials. The company's two product candidates, MET409 and MET642, are currently being investigated in clinical trials as potential new treatments for non-alcoholic steatohepatitis (NASH). MET409 has completed a 12-week monotherapy trial in patients with NASH and is being evaluated in a 12-week combination trial with empagliflozin in patients with both NASH and type 2 diabetes. MET642 has completed a 14-day Phase 1 trial in healthy volunteers and is being advanced into a 16-week monotherapy trial in patients with NASH.

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. Forward-looking statements contained in this press release include statements regarding the therapeutic potential of MET409; statements regarding Metacrine's timelines; the differentiated nature of Metacrine's FXR program; plans underlying Metacrine's clinical trials; plans for advancing the clinical development of Metacrine's FXR program; the potential for its FXR product candidates to be long-term therapies 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 therapies for patients with both NASH and T2DM. Many factors may cause differences between current expectations and actual results, including unexpected safety or efficacy data observed during preclinical or clinical studies and uncertainties related to the regulatory approval path for the NASH indication. Words such as "may," "could," "will," "encourage," "expect," "plan," "aim," "anticipate," "estimate," "intend," "potential," "prepare" 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: 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 November 12, 2020, 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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