Metacrine Presents Positive MET409 Phase 1b Clinical Data in NASH Patients at the Digital International Liver Congress™ 2020

August 27, 2020

MET409 demonstrated notable improvements in decreased liver fat content and differentiated impacts on pruritus and LDL cholesterol after 12 weeks of treatment in NASH patients

SAN DIEGO, Aug. 27, 2020 (GLOBE NEWSWIRE) -- Metacrine, Inc., a clinical-stage biotechnology company focused on discovering and developing differentiated therapies to treat liver and gastrointestinal (GI) diseases, announced positive, final results from its 12-week, randomized, placebo-controlled Phase 1b study of MET409, the company's lead farnesoid X receptor (FXR) agonist, in patients with non-alcoholic steatohepatitis (NASH). These data are being presented in a late-breaking poster presentation[1] as part of the Digital International Liver Congress™ being held August 27-29, 2020.

In the Phase 1b proof-of-concept trial, 58 patients with NASH were randomized 1:1:1 to receive oral, once-daily MET409 at 80 mg or 50 mg, or to placebo. Study findings show that MET409 lowered liver fat content, with mean relative reductions of 55% in the 80 mg cohort and 38% in the 50 mg cohort, compared with 6% in the placebo cohort (P<0.001). Notably, MET409 achieved a 30% or greater relative liver fat reduction in 93% of patients (13/14) in the 80 mg cohort and 75% (12/16) in the 50 mg cohort, compared with 11% (2/18) in the placebo cohort (P<0.001). MET409 also normalized liver fat content to 5% or lower in 29% of patients (4/14) in the 80 mg cohort and 31% of patients (5/16) in the 50 mg cohort, compared with 0% in the placebo cohort (P<0.05).

"NASH is a highly prevalent, potentially life-threatening liver disease for which there are no approved treatments today," said Eric J. Lawitz, M.D., vice president of scientific research and development at the Texas Liver Institute, clinical professor of medicine at the University of Texas Health San Antonio and a principal investigator of the study. "The magnitude of liver fat reduction observed after 12 weeks of MET409 treatment is highly encouraging and I look forward to further investigating MET409 as a potential new therapeutic approach to treating patients with NASH."

In addition to liver fat reduction, there was a trend towards 30% or greater relative alanine aminotransferase (ALT) reduction with MET409 treatment: 50% (7/14) of patients in the 80 mg cohort and 31% (5/15) in the 50 mg cohort, versus 17% (3/18) with placebo (P>0.05). MET409 also showed a 30% or greater relative gamma-glutamyl transferase (GGT) reduction in 64% (9/14) of patients in the 80 mg cohort and 81% (13/16) in the 50 mg cohort, compared to 0% with placebo (P<0.0001). A transient, asymptomatic ALT and AST elevation was observed in a subset of patients at Week 8, without increased GGT or total bilirubin.

MET409 was generally well-tolerated in patients treated, with no treatment-related serious adverse events reported. Generalized pruritus (mild-moderate grade) was reported in 40% (8/20) of patients in the MET409 80 mg cohort and 16% (3/19) in the 50 mg cohort, which was determined to be related to treatment with MET409. Only two (10%) pruritus-related early discontinuations occurred, both at 80 mg. MET409 resulted in on-target increases in low-density lipoprotein cholesterol (LDL-C) of 23.7% with the 80 mg dose and 6.8% with the 50 mg dose, versus a reduction of 1.5% with placebo (P<0.05 for 80 mg only), from baseline to day 84.

"MET409 significantly decreased liver fat and improved liver enzymes in NASH patients, with encouraging safety and tolerability results, particularly showing a differentiated and favorable pruritus and LDL-C cholesterol profile at the 50 mg dose," said Hubert C. Chen, M.D., chief medical officer of Metacrine. "These results provide the first clinical evidence that the therapeutic index of FXR agonists can be enhanced through structural optimization. The profile observed to date with MET409 relative to other treatments in development demonstrates the potential of our sustained, non-bile acid FXR agonist program for patients with NASH, and we look forward to advancing MET409 into our planned combination study next year."

About Non-alcoholic Steatohepatitis (NASH)
Non-alcoholic steatohepatitis, or NASH, is a liver disease characterized by excess liver fat, inflammation and fibrosis. In 2015, there were an estimated 17 million people in the United States with NASH, which is expected to increase to an estimated 27 million people by 2030. Left untreated, patients' disease may progress to liver failure, which is life-threatening without a successful liver transplant. NASH is expected to become the leading cause for liver transplants in the United States. Additionally, patients with NASH often present with metabolic disease and other co-morbidities, which is likely to require combination therapy. Currently, there are no approved therapies for NASH.

About Metacrine
Metacrine is a clinical-stage biopharmaceutical company building a differentiated pipeline of drugs to treat liver and gastrointestinal (GI) diseases. The company's most advanced programs, MET409 and MET642, target the farnesoid X receptor (FXR), which is central to modulating liver and GI diseases. Both MET409 and MET642 are currently being investigated in clinical trials as a potential new treatment for non-alcoholic steatohepatitis (NASH). For additional information, please visit www.metacrine.com.

Contact:
Caton Morris
THRUST Strategic Communications
336.403.0669
investors@metacrine.com

1. Lawitz, E. J., et al. "MET409, an optimized farnesoid X receptor agonist, decreased liver fat and improved liver enzymes in patients with non-alcoholic steatohepatitis: a 12-week, randomized, placebo-controlled study." The Digital International Liver Congress™, August 27-29, 2020.