Madrigal Pharmaceuticals Announces the Initiation of a Phase 2 Study of MGL-3196 in Patients with Non-alcoholic Steatohepatitis (NASH)

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-- Study expected to provide proof-of-concept data in NASH for the first liver-directed, thyroid hormone receptor (THR) ß-selective agonist –

-- Primary endpoint is the reduction of liver fat, assessed by MRI-PDFF, at 12 weeks, with confirmation of NASH resolution by biopsy at 36 weeks --

CONSHOHOCKEN, Pa., Oct. 20, 2016 (GLOBE NEWSWIRE) -- Madrigal Pharmaceuticals, Inc. (Nasdaq:MDGL) today announced that the first patient has been dosed in its Phase 2 study of MGL-3196 for the treatment of non-alcoholic steatohepatitis (NASH). MGL-3196 is a first-in-class, oral, once-daily, liver-directed, thyroid hormone receptor (THR) ß-selective agonist medication.

"Thyroid hormone, through activation of its ß receptor, plays a central role in controlling lipid metabolism, impacting many health parameters from levels of serum cholesterol and triglycerides to the pathological buildup of fat in the liver," said Paul A. Friedman, M.D., Chairman and CEO of Madrigal. "The lack of selectivity of older compounds limited their clinical utility, so we designed this study to provide clinical proof-of-concept for the role of highly-specific THR ß activation in regulating lipid metabolism in the liver to treat the cause of NASH. It will also allow us to confirm the value of assessing the early reduction of liver fat with imaging as a meaningful and predictive treatment endpoint."

"NASH is the leading liver disease in the United States with a growing prevalence for which no FDA approved treatment is yet available," said Dr. Stephen Harrison, Principal Investigator of the study as well as Medical Director for Pinnacle Clinical Research, San Antonio, Texas, and Visiting Professor of Hepatology, Oxford University. "We are hopeful that this novel approach, by targeting an underlying pathophysiologic mechanism of NASH, will eventually address a significant unmet need in this patient population."

Becky Taub, M.D., CMO and Executive VP, Research & Development of Madrigal added, "Madrigal's 36-week NASH study has a unique design based on the mechanism of action of MGL-3196 that allows us to determine the primary endpoint after 12 weeks of treatment, the percent change in hepatic fat fraction from baseline as measured by MRI-PDFF (magnetic resonance imaging-estimated proton density fat fraction), an imaging-based biomarker."

The randomized, double-blind, placebo-controlled, multi-center Phase 2 study will enroll 117 patients 18 years of age and older with biopsy-confirmed NASH. Patients are randomized to receive either placebo or MGL-3196, twice as many receiving MGL-3196 as placebo. Efficacy will be confirmed at the end of the trial (36 weeks) by repeat MRI-PDFF and conventional liver biopsy to examine histological evidence for the resolution of NASH. Recent published data show a high correlation of reduction of liver fat measured by MRI-PDFF to NASH scoring on liver biopsy. Other secondary endpoints include changes in clinically relevant biomarkers at 12 and 36 weeks, improvement in fibrosis by at least one stage with no worsening of steatohepatitis, and safety and tolerability. Additional information about the study [NCT02912260] can be obtained at www.ClinicalTrials.gov.

About NASH
NASH (non-alcoholic steatohepatitis) is a common liver disease in the United States and world-wide, unrelated to alcohol use, characterized by a build-up of fat in the liver, inflammation, and increasing fibrosis. Although people with NASH may feel well and often do not know they have the disease, NASH can lead to permanent damage, including cirrhosis, and impaired liver function. According to the National Institutes of Health (NIH), NASH affects approximately 2-5% of American adults,[1] or more than 15 million people. It is the fastest growing reason for liver transplants and is also associated with an increasing incidence of liver cancer. There are currently no treatments approved by the U.S. Food and Drug Administration (FDA) for NASH.

About Madrigal Pharmaceuticals
Madrigal Pharmaceuticals, Inc. (Nasdaq:MGDL) is a clinical-stage biopharmaceutical company pursuing novel therapeutics that target a specific thyroid hormone receptor pathway in the liver, which is a key regulatory mechanism common to a spectrum of cardio-metabolic and fatty liver diseases with high unmet medical need. The Company's lead candidate, MGL-3196, is a first-in-class, orally administered, small-molecule, liver-directed, thyroid hormone receptor (THR) ß-selective agonist. Based on evidence of broad activity and a favorable safety profile from pre-clinical and Phase 1 studies, MGL-3196 is entering Phase 2 clinical trials for the treatment of non-alcoholic steatohepatitis (NASH) and familial dyslipidemias/hypercholesterolemias. For more information, visit: www.madrigalpharma.com.

Forward-Looking Statements
This communication contains "forward-looking statements" made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements reflect management's current knowledge, assumptions, judgment and expectations regarding future performance or events. Although management believes that the expectations reflected in such

statements are reasonable, they give no assurance that such expectations will prove to be correct and you should be aware that actual results could differ materially from those contained in the forward-looking statements. Forward-looking statements are subject to a number of risks and uncertainties including, but not limited to, the company's clinical development of MGL-3196, the timing and outcomes of clinical studies of MGL-3196, and the uncertainties inherent in clinical testing. Undue reliance should not be placed on forward-looking statements, which speak only as of the date they are made. Madrigal undertakes no obligation to update any forward looking statements to reflect new information, events or circumstances after the date they are made, or to reflect the occurrence of unanticipated events. Please refer to Madrigal's filings with the U.S. Securities and Exchange Commission for more detailed information regarding these risks and uncertainties and other factors that may cause actual results to differ materially from those expressed or implied.

[1] https://www.niddk.nih.gov/health-information/health-topics/liver-disease/nonalcoholic-steatohepatitis/Pages/facts.aspx

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