Madrigal Pharmaceuticals to Present Additional Analyses of Data from The Phase 2 NASH Study with MGL-3196 (resmetirom) at The International Liver Congress™ 2019

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-- MRI-PDFF response (≥30% reduction in hepatic fat) at 12 weeks correlated with reduction in the ballooning and inflammation components of NAS and was predictive of NASH resolution on liver biopsy at 36 weeks --

-- The data suggest that reduction of hepatic fat is a critical component of NASH improvement and resolution --

CONSHOHOCKEN, Penn., April 08, 2019 (GLOBE NEWSWIRE) -- Madrigal Pharmaceuticals, Inc. (NASDAQ:MDGL) announced today that on Thursday, April 11, 2019 at the International Liver Congress ™2019, European Association for the Study of the Liver (EASL) in Vienna, further in depth analyses of the Phase 2 NASH study with MGL-3196 (resmetirom) will be presented. Resmetirom is currently in Phase 3 development for the treatment of NASH patients with stage 2-3 fibrosis (ClinicalTrials.gov NCT03900429).

Stephen Harrison, M.D., Principal Investigator of the resmetirom Phase 2 study, and Medical Director for Pinnacle Clinical Research, San Antonio, Texas, and Visiting Professor of Hepatology, Oxford University, will present the poster during an Oral ePoster Session: Fatty Liver Disease-Clinical on Thursday April 11, 12-1 PM CET, at Poster pod 4 on the ground floor, Hall B. The poster will also be on display in Saturday's poster session (SAT-347).

MGL-3196-05 (NCT02912260) was a 36-week multicenter, randomized, double-blind, placebo-controlled serial MRI-PDFF, paired liver biopsy study in adults with biopsy-confirmed NASH (NAS ≥4, FI-F3) and hepatic fat fraction ≥10%. In 12 week interim and 36 week final analyses, MGL-3196 (resmetirom) treated patients had significantly more reduction of liver fat compared with placebo on MRI-PDFF and up to 77% of resmetirom-treated patients showed at least a 30% reduction of liver fat (defined as a positive PDFF response) ($p<0.0001$ relative to placebo). NASH resolution was attained on biopsy in 39% of resmetirom patients who had a positive PDFF response. At 36 weeks 107 paired biopsies (73 resmetirom-treated; 34 placebo-treated) were assessed to examine the predictive power of PDFF response on histologic response of NAS, NASH resolution and reduction of ALT. In resmetirom-treated patients, a 12 week PDFF response versus non-response was predictive of NASH resolution at week 36 ($p=0.001$) and correlated with improvements in steatosis, hepatocyte ballooning and inflammation as well as reduction in ALT. Placebo patients with weight loss ≥5% were likely PDFF responders (71%; $p=0.007$), and a PDFF response in placebo patients also predicted reductions in inflammation and hepatocyte ballooning.

Dr. Harrison stated, "These analyses show that positive MRI-PDFF responses correlate with reductions in hepatocyte ballooning, inflammation and NASH resolution on liver biopsy and are

associated with decreases in ALT. The data suggest that reduction of hepatic fat is a critical component of NASH improvement and resolution."

Rebecca Taub, M.D., Madrigal Chief Medical Officer, added, "The steatosis score on liver biopsy, a non-continuous measure, does not always accurately reflect the reduction in liver fat following resmetirom treatment. Correlations between MRI-PDFF and a new measure of steatosis on biopsy slides, second harmonic generation (SHG), will also be presented on the poster as late-breaking data. These technologies provide more precise measurements of liver fat and offer the potential to more accurately predict a response to treatment."

About resmetirom (MGL-3196)
Among its many functions in the human body, thyroid hormone, through activation of its beta receptor, plays a central role in controlling lipid metabolism, impacting a range of health parameters from levels of serum cholesterol and triglycerides to the pathological buildup of fat in the liver. Attempts to exploit this pathway for therapeutic purposes in cardio-metabolic and liver diseases have been hampered by the lack of selectivity of older compounds for the thyroid hormone receptor (THR)-β, chemically-related toxicities and undesirable distribution in the body.

Madrigal recognized that greater selectivity for thyroid hormone receptor (THR)-β and liver targeting might overcome these challenges and deliver the full therapeutic potential of THR-β agonism. Madrigal believes that resmetirom is the first orally administered, small-molecule, liver- directed, truly β-selective THR agonist.

Based on the positive Phase 2 clinical study results in patients with NASH (Phase 2 36-Week Results Press Release), Madrigal recently announced the initiation of a Phase 3 multinational, double-blind, randomized, placebo-controlled study of resmetirom in patients with non-alcoholic steatohepatitis (NASH) and fibrosis to resolve NASH and reduce progression to cirrhosis and/or hepatic decompensation (Phase 3 Initiation Press Release and ClinicalTrials.gov NCT03900429). Additionally, in both the NASH Phase 2 study, and a second positive Phase 2 clinical study in patients with heterozygous familial hypercholesterolemia (Phase 2 HeFH Results Press Release), significant reductions in multiple atherogenic lipids were observed. As a result, Madrigal is designing a Phase 3 study intended to treat the prevalent dyslipidemias in NAFLD and NASH patients and improve the fatty liver phenotype in this population.

About Madrigal Pharmaceuticals
Madrigal Pharmaceuticals, Inc. (Nasdaq: MDGL) 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. Madrigal's lead candidate, resmetirom, is a first-in- class, orally administered, small-molecule, liver-directed, thyroid hormone receptor (THR) β- selective agonist. 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. Such statements contain words such as "expect," "could," "may," "might," "will," "be, "predict," "project," "intend," "believe," "estimate," "continue," "future," or the negative thereof or comparable terminology and the use of future dates. Forward-looking statements reflect management's current knowledge, assumptions, judgment and expectations regarding future performance or events. Such forward-looking

statements include but are not limited to statements or references concerning: our primary and secondary study endpoints and their achievement potential; optimal dosing levels for resmetirom; projections regarding potential future NASH resolution, fibrosis treatment, cardiovascular effects and lipid treatment; the achievement of enrollment objectives concerning patient number and/or timing; and potential NASH or NAFLD patient risk profile benefits. 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 resmetirom, enrollment uncertainties, outcomes or trends from competitive studies, the risks of achieving potential benefits in a study that includes substantially more patients than our prior study, the timing and outcomes of clinical studies of resmetirom, 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.

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