Phase 2 Results for Madrigal's MGL-3196 in Non-Alcoholic Steatohepatitis (NASH) Presented during Presidential Plenary Clinical Session of The Liver Meeting® 2018

-- Statistically significantly more NASH resolution in MGL-3196 as compared with placebo in a Phase 2 clinical trial support MGL-3196 as a first- and potentially best-in class thyroid hormone receptor (THR) β-selective agonist for treating patients with NASH

--The fact that MGL-3196 lowers LDL cholesterol and other atherogenic lipids while resolving NASH offers the potential to provide protection from cardiovascular morbidity and mortality in fatty liver and NASH patients who die more often from cardiovascular disease than cirrhosis

-- Live webcast to discuss these Phase 2 results scheduled for 7:00 p.m PT / 10:00 p.m. ET today --

SAN FRANCISCO, CA and CONSHOHOCKEN, PA., November 12, 2018 -- Madrigal Pharmaceuticals, Inc. (NASDAQ:MDGL) today announced the oral presentation of statistically significant results from a double-blind, placebo-controlled 36-week Phase 2 clinical trial in patients with biopsy-proven non-alcoholic steatohepatitis (NASH). These results were presented during a Presidential Plenary Session at The Liver Meeting® 2018 during the American Association for the Study of Liver Diseases 2018 Annual Meeting being held in San Francisco.

"Statistically significantly greater resolution of NASH in MGL-3196 treated compared with placebo patients provides evidence for efficacy in an accepted registrational endpoint for Phase 3 development in NASH," stated Dr. Stephen Harrison, M.D., Principal Investigator of the study, as well as Medical Director for Pinnacle Clinical Research, San Antonio, Texas, and Visiting Professor of Hepatology, Oxford University.

Dr. Harrison, who presented the results, added, "The correlation of NASH resolution with reduction in liver fat on MRI-PDFF adds to the growing database indicating the importance of hepatic fat reduction in the effective treatment of NASH."

In this 36-week serial liver biopsy Phase 2 study in patients with NASH, fibrosis stage 1-3, there was:

- sustained highly statistically significant reduction in liver fat based on MRI-PDFF in MGL-3196 treated as compared with placebo patients;
- sustained statistically significant lowering of multiple atherogenic lipids including LDL-C, ApoB, triglycerides, ApoCIII and lipoprotein(a);
- lowering and normalization of liver enzymes;
- statistically significant resolution of NASH that is correlated with reduction in liver fat on MRI-PDFF and provides evidence for efficacy at an approvable endpoint for Phase 3 development in NASH.

To view the MGL-3196 AASLD Plenary Presentation by Dr. Harrison go to: https://www.madrigalpharma.com/wp-content/uploads/2018/11/MGL-3196-Plenary-presentation-Nov-10-NASDAQ.pdf

“These highly significant and sustained potential benefits demonstrated in our Phase 2 clinical trial in patients with NASH, combined with the significant results MGL-3196 achieved in our Phase 2 clinical trial in patients with heterozygous familial hypercholesterolemia, further support our confidence in the broad therapeutic benefits of MGL-3196,” stated Paul Friedman, M.D., Chief Executive Officer of Madrigal.

“The key findings in this Phase 2 clinical trial are that once daily oral doses of MGL-3196 were effective in reducing and resolving NASH, and were well tolerated, which gives us confidence that these results will be confirmed in our planned registration study.” Becky Taub, M.D., CMO and Executive VP, Research & Development of Madrigal stated, “Additionally, we are encouraged by the lipid lowering results in NASH patients and believe that MGL-3196 could provide a safe additional LDL-cholesterol and atherogenic lipid lowering therapy for patients at increased CV risk, particularly those with metabolic risk factors, such as increased blood pressure, high blood sugar, excess body fat and abnormal cholesterol and/or triglyceride levels who require better lipid control. This patient group includes patients with type 2 diabetes, nonalcoholic fatty liver disease and early stages of NASH fibrosis.”

Live Webcast Information

Madrigal will host an investor meeting to discuss these Phase 2 results in NASH, which will be webcast live today at 7:00 p.m. PT / 10:00 p.m. ET. To access the webcast please go to: http://www.madrigalpharma.com/newsroom/presentations/ in the “Events and Presentations” section of the Madrigal website.
Webcast link: https://edge.media-server.com/m6/p/ugohg5f8

A dial-in number is also available should you be unable to access the live webcast:
Toll-free 833-660-2754
Toll 409-350-3497
Conference ID: 2277179

If you are unable to listen to the webcast live, a replay will be available on the website under http://www.madrigalpharma.com/newsroom/presentations/.

Clinical Program Summaries for MGL-3196

NASH

Non-alcoholic Steatohepatitis (NASH) is a common liver disease in the United States and worldwide, unrelated to alcohol use, that is characterized by a build-up of fat in the liver, inflammation, damage (ballooning) of hepatocytes 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 in a high percentage of patients.

In October 2016, the first patient was treated in the ongoing Phase 2 trial of MGL-3196 for the treatment of NASH. The randomized, double-blind, placebo-controlled, multi-center Phase 2 study enrolled 125 patients 18 years of age and older with liver biopsy-confirmed NASH and included approximately 25 clinical sites in the United States. Patients were randomized to receive either MGL-3196 or placebo in a 2:1 ratio.

The primary endpoint of the study was the reduction of liver fat at 12 weeks compared with baseline (relative change), assessed by MRI-PDFF. Key secondary endpoints at 36 weeks included: reduction in liver fat compared with baseline (relative change), also assessed by MRI-PDFF; a two-point reduction in NAS (NALFD activity score) on biopsy; resolution of NASH on biopsy; and, safety and tolerability based on adverse events and changes in laboratory values.

The primary endpoint of the study at 12 weeks was achieved. Liver fat was reduced by 36.3% in all MGL-3196 treated patients and 42.0% in a pre-specified group of high exposure MGL-3196 treated patients, as compared with 9.6% median reduction in liver fat in placebo treated patients. These results were statistically significant ($p<0.0001$) for both MGL-3196 treatment groups. Further, 75% of the high-exposure MGL-3196 treated patients showed liver fat reductions of ≥30%.

At 36 weeks, MGL-3196 achieved multiple key secondary endpoints including a sustained highly significant ($p<0.001$) reduction in liver fat compared to placebo as measured by MRI-PDFF; mean relative fat reduction for MGL-3196 was 37% versus 8.9% for placebo. MGL-3196 was associated with a greater percentage of subjects with a 2-point improvement in NAS (56% vs 32% in MGL-3196 compared with placebo subjects, $p=0.02$). NASH resolution (NR) was seen in 27% of MGL-3196 compared with 6% of placebo subjects, $p=0.02$. MGL-3196 patients with ≥ 30% fat reduction on Week 12 MRI-PDFF demonstrated a higher percentage of 2-point improvement in NAS (70%,

p=0.001) and NR (39%, p=0.001) compared with placebo, demonstrating a strong relationship between early reduction in liver fat as demonstrated by week 12 MRI-PDFF and NASH improvement on liver biopsy at Week 36.

At Week 36, MGL-3196 treated patients showed sustained reduction of fibrosis biomarkers. In MGL-3196 patients with NASH resolution, fibrosis also resolved in 50% of patients and was decreased statistically significantly relative to all placebo patients. There were statistically significant reductions in liver enzymes in MGL-3196 treated patients compared to placebo treated patients; reductions of greater magnitude were achieved with longer duration of MGL-3196 treatment. Statistically significantly more MGL-3196 treated patients than placebo treated patients had normalization of ALT (alanine transaminase).

Similar to week 12, at week 36 there were sustained, statistically significant reductions in low-density lipoprotein cholesterol (LDL-C), triglycerides, ApoB and lipoprotein(a). MGL-3196 was well tolerated in this trial with mostly mild and a few moderate AEs which were balanced between drug treated and placebo patients. There was an increase in incidence of mild loose stools in MGL-3196-treated, often a single episode, at the start of treatment and incidence of loose stools was not increased later in the study.

Based on liver enzyme inclusion criteria, some patients are receiving extended treatment beyond 36 weeks for up to 36 additional weeks. All patients in this extension study have received MGL-3196 and only non-invasive assessments are made, including serial MRI-PDFF, safety labs, and circulating biomarkers. Additional information about the study [NCT02912260] can be obtained at www.ClinicalTrials.gov.

HeFH

Heterozygous familial hypercholesterolemia (HeFH), and a much rarer form called homozygous familial hypercholesterolemia (HoFH), are severe genetic dyslipidemias typically caused by inactivating mutations in the LDL receptor. Both forms of FH lead to early onset cardiovascular disease. HeFH, the most common dominantly inherited disease, is present in up to 1 in 200 people; the disease is found in higher frequencies in certain more genetically homogenous populations. Treatments exist for both HeFH and HoFH but many patients (as many as 40 percent of HeFH patients) are not able to reach their cholesterol (LDL-C) reduction goals on these therapies, reflecting the lifetime burden of cholesterol buildup in their bodies. Based on evidence of impressive LDL cholesterol lowering in Phase 1, and data suggesting that MGL-3196 has a mechanism of action that is different from and complementary to statins, Madrigal initiated a Phase 2 proof-of-concept trial in HeFH in February 2017 and enrolled 116 patients.

In this Phase 2 HeFH trial, patients who were not at their LDL-C goal were randomized in a 2:1 ratio to receive either MGL-3196 or placebo, in addition to their current cholesterol lowering regimen, which included approximately 75% taking high intensity statins (20/40 mg rosuvastatin or 80 mg atorvastatin), and about 2/3 of patients also taking ezetimibe. MGL-3196 treated patients (placebo corrected) achieved highly significant ($p< 0.0001$) LDL-C lowering of 18.8%, and 21% LDL-C lowering in those on an optimal dose of MGL-3196. LDL-C lowering was 28.5% in MGL-3196 treated compared to placebo in a prespecified group of patients who did not tolerate high intensity statin doses. Highly significant reductions ($p<0.0001$) relative to placebo were also observed with ApoB, triglycerides (TG) (25-31%), apolipoprotein CIII (Apo CIII) and Lp(a) (25-40%) in all MGL-3196 treated patients and prespecified subgroups, irrespective of statin treatment.

MGL-3196 was well-tolerated with primarily mild and some moderate AEs, the numbers of which were balanced between placebo and drug-treatment groups.

About MGL-3196
MGl-3196 is a first- and potentially best-in class thyroid hormone receptor (THR) β-selective agonist for treating patients with NASH and dyslipimdemias.

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 MGL-3196 is the first orally administered, small-molecule, liver- directed, *truly β-selective* THR agonist.

The discovery of MGL-3196 utilized a novel in vitro functional assay to demonstrate and confirm high β-selectivity (28 fold). In contrast, other thyroid agonists were not β-selective in this assay or in a relevant in vivo heart assay. Additional selectivity of MGL-3196 was conferred by highly specific uptake into the liver and the avoidance of any systemic thyroid receptor effects. Both preclinical and clinical data have confirmed the high liver uptake and safety of MGL-3196 and its ability to avoid activity at the systemic

THR-α receptor as well as no increased heart rate and/or osteoporosis observed. Long-term animal studies have been completed that support Phase 3 development.

MGL-3196 has been tested in over 160 subjects in Phase 1 studies and 150 patients in Phase 2 studies with results suggesting that MGL-3196 provides a broad array of therapeutically beneficial effects including improving components of both metabolic syndrome, such as insulin resistance and dyslipidemia, and fatty liver disease including lipotoxicity and inflammation.

About Madrigal

Madrigal Pharmaceuticals, Inc. (Nasdaq: MDGL) is a clinical-stage biopharmaceutical company pursuing novel therapeutics that target a specific thyroid hormone receptor (THR) 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 product candidate is MGL-3196, a first-in-class, orally administered, small-molecule, liver-directed, THR β-selective agonist. Madrigal has recently completed two successful Phase 2 clinical trials in non-alcoholic steatohepatitis (NASH) and heterozygous familial hypercholesterolemia (HeFH) that confirmed the potential of MGL-3196 to reduce liver fat, lower multiple atherogenic lipids and resolve NASH. Based on this clinical evidence and a favorable safety profile, Madrigal plans to initiate a Phase 3 clinical program in NASH. 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," "will," "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. 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.

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