



Madrigal's MGL-3196 Achieves Primary Endpoint in Patients with Heterozygous Familial Hypercholesterolemia (HeFH)

-- Statistically significant improvement achieved in the reduction of LDL cholesterol (LDL-C) with MGL-3196 compared to placebo, the primary endpoint of this 12-week Phase 2 clinical trial in HeFH patients on maximal statin therapy --

-- Statistically significant results also achieved for MGL-3196 compared to placebo for multiple secondary endpoints including reduction of triglycerides, apolipoprotein B (ApoB), and lipoprotein(a) (Lp(a)), a highly atherogenic lipid particle commonly elevated in HeFH patients and not adequately controlled by existing therapies --

-- MGL-3196 was well tolerated in this trial as compared to placebo; mostly mild and some moderate AEs balanced between drug -treated and placebo, only 2 unrelated SAEs, 1 in placebo, 1 in drug-treated --

-- HeFH is the most common dominantly inherited disease, present in up to 1 in 200 people, in which there is a life-long burden of high LDL cholesterol levels leading to increased risk of premature coronary artery disease and cardiovascular-related death --

- Conference call scheduled for 9:00 AM Eastern Time today -

CONSHOHOCKEN, Pa. - February 8, 2018 - Madrigal Pharmaceuticals, Inc. (NASDAQ:MDGL) today announced positive results from a double-blind, placebo-controlled, multi-center, 12-week Phase 2 clinical trial in patients with heterozygous familial hypercholesterolemia (HeFH), a severe genetic dyslipidemia that causes early onset cardiovascular disease. MGL-3196 is a first-in-class, oral, once-daily, liver-directed, thyroid hormone receptor (THR) β -selective agonist medication. MGL-3196 is also being developed as a treatment for patients with non-alcoholic steatohepatitis (NASH).

In this Phase 2 HeFH trial, 116 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 ($p < 0.0001$) and numerically similar results were observed with ApoB. Highly significant ($p < 0.0001$) triglyceride (TG) (25-31%),

apolipoprotein CIII (Apo CIII) and Lp(a) lowering (25-40%) were observed in all MGL-3196 treated patients and prespecified subgroups, irrespective of statin treatment. Full results from the Phase 2 trial will be submitted to a future medical conference and for publication.

MGL-3196 was well-tolerated with primarily mild and some moderate AEs, the numbers of which were balanced between placebo and drug-treatment groups. Fewer than 7% of patients did not complete the study, and patients who discontinued for AEs, all mild to moderate, were balanced between drug-treated and placebo patients. There were 2 serious adverse events in the study, both unrelated to treatment, one in a placebo and one in a drug-treated patient.

Dr. John J. P. Kastelein, Professor of Medicine in the Department of Vascular Medicine at the Academic Medical Center (AMC) of the University of Amsterdam and the principal investigator of the study, stated, "These Phase 2 results confirm the potential of MGL-3196 to safely lower LDL cholesterol in high-risk HeFH patients whose disease is not well-controlled, despite the use of maximally tolerated lipid-lowering therapies. There is clearly an unmet need for additional therapeutic options for these patients; based on the results of this study, MGL-3196 has the potential to offer one such option. Moreover, the effect of MGL-3196 on other lipid parameters that are associated with unfavorable cardiovascular (CV) outcomes including TGs, ApoCIII, Lp(a) and ApoB provides multiple potential opportunities to lower cardiovascular risk in HeFH and other high CV risk patients."

"With many HeFH and other high risk CV patients unable to reach LDL cholesterol goals despite being on maximal lipid-lowering therapy, it is gratifying to see MGL-3196 treated patients achieve such significant improvements in the primary and secondary endpoints of the trial as compared to placebo-treated patients. These results, together with the positive top-line results we recently reported from our Phase 2 NASH trial, provide further evidence that MGL-3196, a first- and we believe potentially best-in-class, oral, once-daily, liver-directed, thyroid hormone receptor (THR) β -selective agonist, has the potential to become an important and much needed new medicine," said Becky Taub, M.D., CMO and Executive VP, Research & Development of Madrigal.

Paul A. Friedman, M.D., Chairman and CEO of Madrigal, added, "Because MGL-3196 acts by mechanisms distinct from and complementary with statins, we were confident that the compound could safely and effectively combine with high dose statins and ezetimibe, and potentially provide significant LDL cholesterol lowering, allowing additional patients to reach their LDL cholesterol targets and provide benefits on multiple lipids associated with increased CV risk. Importantly, we are in a strong position to expeditiously advance MGL-3196 forward."

Conference Call and Webcast Information

Madrigal will hold a conference call and webcast this morning at 9:00 a.m. ET. To access the conference call, please dial (833) 660-2754 for domestic callers or (409) 350-3497 for international callers. When prompted, provide the conference identification number, 5097096.

The conference call will also be webcast and can be accessed at:

<http://www.madrigalpharma.com/newsroom/presentations/> in the “Events and Presentations” section of the Madrigal website.

If you are unable to participate, a replay of the conference call will be available on the website under <http://www.madrigalpharma.com/newsroom/presentations/>.

About the Study

The 12-week, randomized, double-blind, placebo-controlled, multi-center Phase 2 study enrolled 116 patients with HeFH in several European countries. Patients were randomized in a 2:1 ratio to receive either 100 mg MGL-3196 or placebo, in addition to their current drug regimen including high dose statins (80 mg Lipitor; 40 mg Crestor) with ezetimibe. Based on a prespecified drug exposure level measured at Week 2, some patients with higher than target MGL-3196 levels were treated with 60 mg MGL-3196 from Week 4-12. The primary endpoint of the study was reduction of LDL cholesterol, with secondary endpoints including reductions in triglycerides, Lp(a), and ApoB, as well as safety. Lp(a) is a severely atherogenic lipid particle, commonly elevated in familial hypercholesterolemia patients, the levels of which are not adequately reduced by existing lipid lowering therapies. THR- β agonism is one of the few therapeutic approaches that can substantially lower Lp(a).

About 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% 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.

About 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 MGL-3196 is the first orally administered, small-molecule, liver-directed, truly β -selective THR agonist. MGL-3196 has demonstrated the potential for a broad array of therapeutically beneficial effects, improving components of both metabolic syndrome,

such as insulin resistance and dyslipidemia, and fatty liver disease, including lipotoxicity and inflammation. These pleiotropic actions, coupled with an excellent safety profile, suggest that MGL-3196 could be the preferred treatment option for NASH.

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, MGL-3196, is a first-in-class, orally administered, small-molecule, liver-directed, thyroid hormone receptor (THR) β -selective agonist that is currently in Phase 2 development for NASH and HeFH. 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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