

Madrigal Pharmaceuticals Announces the Initiation of a Phase 2 Study of MGL-3196 in Patients with Heterozygous Familial Hypercholesterolemia (HeFH)

-- 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 build up requiring aggressive lipid lowering treatment --

-- Primary endpoint is the reduction of LDL cholesterol, with secondary endpoints including reduction of Lp(a), a highly atherogenic lipid particle --

Conshohocken, PA – February 23, 2017 – 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 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 in a Phase 2 clinical trial for the treatment of non-alcoholic steatohepatitis (NASH).

“Because individuals with HeFH have a life-long burden of cholesterol buildup in their bodies, current standard of care employs aggressive therapy, often combinations of drugs, to attempt to lower this burden. Despite such aggressive therapy, more than one third of HeFH patients do not reach their cholesterol reduction goals,” said 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. “Confirming the potential for MGL-3196 to safely lower LDL cholesterol and Lp(a) with this study will bring us closer to adding a much-needed new treatment option for this population.”

“MGL-3196 has demonstrated impressive LDL cholesterol lowering in Phase I; MGL-3196 acts by mechanisms distinct from and complementary with statins, as our studies to date have suggested, and should readily combine with high dose statins and ezetimibe, thus having the potential to provide significant additional LDL cholesterol lowering. The data we have generated with MGL-3196 as well as what is known about THR- β agonism, gives us a high degree of confidence that MGL-3196 will perform well in these patients,” said Paul A. Friedman, M.D., Chairman and CEO of Madrigal. “We expect to have topline data from this study near year end.”

“Madrigal is conducting the Phase 2 study in Europe, with the first patient dosed in Denmark. The European patient registries for HeFH should help support rapid trial recruitment by our clinical trial sites,” said Becky Taub, M.D., CMO and Executive VP, Research & Development of Madrigal. “In addition to the efficacy and safety endpoints, the results of this study will provide additional confirmation that we have selected the appropriate dose of MGL-3196 for these patients.”

About the Study

The 12-week, randomized, double-blind, placebo-controlled, multi-center Phase 2 study will enroll 105 patients with HeFH in several European countries. Patients will be randomized in a 2:1 ratio to receive either MGL-3196 or placebo, in addition to their current drug regimen (including high dose statins and/or ezetimibe). The primary endpoint of the study is 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 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) 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. 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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