# Madrigal Pharmaceuticals Completes Enrollment of the 52 Week Liver Biopsy Patient Population in the Phase 3 MAESTRO-NASH Study of Resmetirom

June 30, 2021

CONSHOHOCKEN, Pa., June 30, 2021 (GLOBE NEWSWIRE) -- Madrigal Pharmaceuticals, Inc. (NASDAQ:MDGL) announced today achievement of the planned target enrollment in the Phase 3 clinical trial, MAESTRO-NASH. Serial liver biopsy and safety data from patients enrolled in MAESTRO-NASH coupled with safety data from MAESTRO-NAFLD-1, an additional large Phase 3 study, are expected to support the planned Subpart H (Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses) submission to the US Food and Drug Administration (FDA). Madrigal will continue to enroll additional patients beyond those required for accelerated approval to provide for the clinical outcomes portion of the MAESTRO-NASH Phase 3 clinical trial of resmetirom.

Becky Taub, M.D., Chief Medical Officer and President of Research & Development of Madrigal, commented, “Based on conservative powering assumptions for patient number and completion rates, we believe the enrollment readily powers both NASH resolution and fibrosis endpoints.” Dr Taub continued, “We are grateful for the tremendous support we are receiving from our clinical trial sites and enthusiasm and willingness of patients to participate in the MAESTRO-NASH study”.

“We expect that the timing of the MAESTRO- NASH study will enable us to report topline 52-week data by the third quarter of 2022. The 52-week data from MAESTRO-NASH and the MAESTRO-NAFLD-1 safety study, together comprising well over 2,000 patients, are expected to support filing of the NDA Subpart H (accelerated approval) to the FDA,” stated Paul Friedman, M.D., Chief Executive Officer of Madrigal.

Stephen Harrison, M.D., Medical Director for Pinnacle Clinical Research, San Antonio, Texas, Visiting Professor of Hepatology, Oxford University, and Principal Investigator of the MAESTRO studies commented, “Patients with NASH fibrosis have a very large unmet need, with no current approved therapy. The MAESTRO Phase 3 studies are designed to provide liver biopsy support for the effective treatment of NASH by resmetirom, coupled with state-of-the-art imaging and biomarker data that support liver biopsy outcomes and have the potential utility to diagnose and follow NASH patients non-invasively.”

**About the Phase 3 Registration Program for the Treatment of NASH (Non-alcoholic steatohepatitis)**

Madrigal is currently conducting two Phase 3 Clinical trials, MAESTRO-NASH and MAESTRO-NAFLD-1, to demonstrate the safety and efficacy of resmetirom for the treatment of NASH.

**MAESTRO-NASH** is a Phase 3 multi-center, double-blind, randomized, placebo-controlled study of resmetirom in patients with liver biopsy confirmed NASH and was initiated in March 2019. The study targets enrollment of 900 patients with biopsy-proven NASH (fibrosis stage 2 or 3, at least 450 fibrosis stage 3), randomized 1:1:1 to receive resmetirom 80 mg once a day, 100 mg once a day, or placebo. After 52 weeks of treatment a second biopsy is performed. The primary surrogate endpoint on biopsy will be NASH resolution, with at least a 2-point reduction in NAS (NASH Activity Score), and with no worsening of fibrosis. Two key secondary endpoints are liver fibrosis reduction of at least one stage, with no worsening of NASH on liver biopsy, and lowering of LDL-cholesterol [ClinicalTrials.gov/NCT03900429].

The first 900 patients in the MAESTRO-NASH study will continue on therapy after the initial 52-week treatment period; and up to another 1,100 patients are to be added using the same randomization plan and the study is expected to continue for up to 54 months to accrue and measure hepatic clinical outcome events including progression to cirrhosis on biopsy (52 weeks and 54 months) and hepatic decompensation events.

**MAESTRO-NAFLD-1** is a 52-week Phase 3 multi-center, double-blind, randomized, placebo-controlled study of resmetirom, and was initiated in December 2019 in patients with non-alcoholic fatty liver disease (NAFLD), presumed NASH. The primary endpoint for this study is to evaluate the safety and tolerability of resmetirom. Completion of enrollment of over 1,200 patients into the study was announced in November 2020. Top-line data from the study is targeted by end of year 2021.

Patients in MAESTRO-NAFLD-1 are randomized 1:1:1 to receive resmetirom 80 mg once a day, 100 mg once a day, or placebo. MAESTRO-NAFLD-1 also includes a 100 mg resmetirom open label arm. 52 week data were presented from the open label arm at The International Liver Congress™ 2021 in June and demonstrated that resmetirom is safe and well-tolerated at 100mg per day [view press release here]. MAESTRO-NAFLD-1 (unlike MAESTRO-NASH), does not include a liver biopsy and represents a “real-life” NASH study. NASH or presumed NASH is documented using historical liver biopsy or non-invasive techniques including FibroScan and MRI-PDFF. Using non-invasive measures, MAESTRO-NAFLD-1 is designed to provide incremental safety information to support the NASH indication as well as provide additional data regarding clinically relevant key secondary efficacy endpoints to better characterize the potential clinical benefits of resmetirom on cardiovascular and liver related endpoints. These key secondary endpoints include LDL-cholesterol, apolipoprotein B and triglyceride (TG) lowering; reduction of liver fat as determined by magnetic resonance imaging, proton density fat fraction (MRI-PDFF); and reduction of PRO-C3, a NASH fibrosis

biomarker. [ClinicalTrials.gov/NCT04197479]. Additional secondary and exploratory endpoints will be assessed including reduction in liver enzymes, FibroScan scores and other fibrosis and inflammatory biomarkers.

Data from the 52 week portion of MAESTRO-NASH, together with data from MAESTRO-NAFLD-1 and other data, including safety parameters, will form the basis for a potential subpart H submission to FDA for accelerated approval for the treatment of 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, resmetirom, is a first-in-class, orally administered, small-molecule, liver-directed, thyroid hormone receptor (THR)-β selective agonist that is in currently in two Phase 3 clinical studies, MAESTRO-NASH and MAESTRO- NAFLD-1, designed to demonstrate multiple benefits across a broad spectrum of NASH (non-alcoholic steatohepatitis) and NAFLD (non-alcoholic fatty liver disease) patients. 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, that are based on our beliefs and assumptions and on information currently available to us but are subject to factors beyond our control. Forward-looking statements include but are not limited to statements or references concerning: our clinical trials; research and development activities; the timing and results associated with the future development of our lead product candidate, MGL-3196 (resmetirom); our primary and secondary study endpoints for resmetirom and the potential for achieving such endpoints and projections; plans, objectives and timing for making a Subpart H (Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses) submission to FDA; optimal dosing levels for resmetirom; projections regarding potential future NASH resolution, safety, fibrosis treatment, cardiovascular effects, lipid treatment or biomarker effects with resmetirom; the efficacy and safety of resmetirom for non-cirrhotic NASH patients and cirrhotic NASH patients; the predictive power of liver fat reduction measured by non-invasive tests on NASH resolution with fibrosis reduction or improvement; the achievement of enrollment objectives concerning patient number, safety database and/or timing for our studies; the predictive power of NASH resolution and/or liver fibrosis reduction with resmetirom using non-invasive tests, including the use of ELF, FibroScan, MRE and/or MRI-PDFF; the predictive power of non-invasive tests generally, including for purposes of diagnosing NASH, monitoring patient response to resmetirom, or recruiting a NASH clinical trial; potential NASH or NAFLD patient risk profile benefits with resmetirom; the potential for resmetirom to become the best-in-class and/or first-to-market treatment option for patients with NASH; and our possible or assumed future results of operations and expenses, business strategies and plans, capital needs and financing plans, trends, market sizing, competitive position, industry environment and potential growth opportunities, among other things. Forward-looking statements: reflect management's current knowledge, assumptions, judgment and expectations regarding future performance or events; include all statements that are not historical facts; and can be identified by terms such as "allow," "anticipates," "be," "believes," "continue," "could," "demonstrates," "design," "estimates," "expects," "forecasts," "future," "goal," "hopeful," "inform," "intends," "may," "might," "plans," "positions," "potential," "powers," "predicts," "predictive," "projects," "seeks," "should," "will," "would" or similar expressions and the negatives of those terms. Although management presently believes that the expectations reflected in such forward-looking statements are reasonable, it can 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: our clinical development of resmetirom; enrollment uncertainties, generally and in relation to COVID-19-related measures that may be continued for an uncertain period of time or implemented; outcomes or trends from competitive studies; future topline data timing or results; the risks of achieving potential benefits in studies that include substantially more patients than our prior studies; limitations associated with early stage, non-placebo controlled study data; 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. We specifically discuss these risks and uncertainties in greater detail in the section entitled "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2020, as well as in our other filings with the SEC.*

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