Madrigal Pharmaceuticals Announces EMA Validation of its Marketing Authorization Application for Resmetirom for the Treatment of NASH/MASH with Liver Fibrosis

March 5, 2024

- *MAA submission is supported by positive results from MAESTRO-NASH, the only Phase 3 trial in NASH to achieve fibrosis reduction and NASH resolution primary endpoints*
- *Resmetirom new drug application is currently under review with the FDA with a PDUFA date of March 14, 2024*

CONSHOHOCKEN, Pa., March 05, 2024 (GLOBE NEWSWIRE) -- Madrigal Pharmaceuticals, Inc. (NASDAQ:MDGL), a clinical-stage biopharmaceutical company pursuing novel therapeutics for nonalcoholic steatohepatitis (NASH), today announced that the Company's Marketing Authorization Application (MAA) for resmetirom for the treatment of NASH/metabolic dysfunction-associated steatohepatitis (MASH) with liver fibrosis has been validated and is now under evaluation with the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP).

NASH is a leading cause of liver-related mortality and an increasing burden on healthcare systems globally. Resmetirom is a once-daily, oral, liver-directed THR-β agonist designed to target key underlying causes of NASH. The clinical development program for resmetirom is comprised of 18 clinical studies supporting the MAA: twelve Phase 1 studies, two Phase 2 studies, and four Phase 3 studies. The pivotal MAESTRO-NASH trial of resmetirom is the only Phase 3 trial in NASH to achieve both fibrosis reduction and NASH resolution primary endpoints, an efficacy standard for NASH therapies described in the EMA's Reflection Paper on Regulatory Requirements for the Development of Medicinal Products for Chronic Non-infectious Liver Diseases.

"NASH with fibrosis represents a serious burden for both patients and health systems. Without treatment, the disease can lead to cirrhosis, liver failure, liver cancer and premature death," said Becky Taub, M.D., Chief Medical Officer and President of Research & Development of Madrigal. "Based on the positive results from our Phase 3 MAESTRO trials, we believe resmetirom has the potential to become the first therapy for patients with NASH with liver fibrosis to receive approval in Europe."

In the United States, resmetirom received Breakthrough Therapy designation from the FDA and was granted Priority Review with a Prescription Drug User Fee Act (PDUFA) date of March 14, 2024, the target date by which FDA intends to complete its review.

"As we near an FDA decision on accelerated approval of resmetirom in the U.S. and advance our application in Europe, Madrigal is generating new momentum for the NASH field," said Bill Sibold, Chief Executive Officer of Madrigal. "The results from our pivotal Phase 3 trial recently published in the *New England Journal of Medicine* provide a robust dataset to support regulatory evaluation globally, and our two ongoing outcomes trials carry the potential to reinforce Madrigal's long-term leadership position in NASH. Our regulatory, R&D and commercial activities continue to accelerate, and each day brings us one step closer to delivering the first foundational therapy to patients with this serious disease."

About NASH

Nonalcoholic steatohepatitis (NASH) is a more advanced form of nonalcoholic fatty liver disease (NAFLD). NASH is a leading cause of liver-related mortality and an increasing burden on healthcare systems globally. Additionally, patients with NASH, especially those with more advanced metabolic risk factors (hypertension, concomitant type 2 diabetes), are at increased risk for adverse cardiovascular events and increased morbidity and mortality.

Once patients progress to NASH with significant fibrosis (consistent with fibrosis stages 2 and 3), the risk of adverse liver outcomes increases dramatically. NASH is rapidly becoming the leading cause of liver transplantation in the U.S.

Madrigal estimates that approximately 1.5 million patients have been diagnosed with NASH in the U.S., of which approximately 525,000 have NASH with significant fibrosis. Madrigal plans to focus on approximately 315,000 diagnosed patients with NASH with significant fibrosis under the care of the liver specialist physicians during the launch of resmetirom.

There are currently no FDA-approved therapies available for the treatment of NASH.

NASH is also known as "metabolic dysfunction-associated steatohepatitis (MASH)" following a change in disease nomenclature introduced by hepatology medical societies in 2023.

About Madrigal Pharmaceuticals

Madrigal Pharmaceuticals, Inc. (Nasdaq: MDGL) is a clinical-stage biopharmaceutical company pursuing novel therapeutics for nonalcoholic steatohepatitis (NASH), a liver disease with high unmet medical need. Madrigal's lead candidate, resmetirom, is a once-daily, oral, liver-directed THR-β agonist designed to target key underlying causes of NASH. For more information, visit www.madrigalpharma.com.

Forward Looking Statements

This communication includes "forward-looking statements" made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, that are based on Madrigal's beliefs and assumptions and on information currently available to it, but are subject to factors beyond its control. Forward-looking statements reflect management's current knowledge, assumptions, judgment and expectations regarding future performance or events. Forward-looking statements include: all statements that are not historical facts; statements referenced by forward-looking statement identifiers, including the examples in the paragraph below; prospects for, and uncertainties associated with, obtaining EMA/European Commission approval of our MAA submission for resmetirom; estimates of patients diagnosed with and/or under care for NASH; the relationship between NASH progression and adverse patient outcomes; the estimated clinical burden of uncontrolled NASH; analyses for patients with NASH with significant fibrosis concerning potential progression to cirrhosis, decompensated cirrhosis, liver transplant or death, and cardiovascular risks, comorbidities and outcomes; health economics assessments or projections; resmetirom's potential to be the first specialty therapy for NASH patients with significant liver fibrosis, in the U.S. and/or Europe; projections or objectives for obtaining accelerated or full approval for resmetirom, including all statements concerning potential clinical benefit to support potential accelerated approval and/or approval; and statements or references concerning - the potential efficacy and safety of resmetirom for noncirrhotic NASH patients and cirrhotic NASH patients, possible or assumed future results of operations and expenses, business strategies and plans (including ex-US. Launch/partnering plans), research and development activities, and the timing and results associated with the future development of resmetirom, the timing and completion of projected future clinical milestone events, including enrollment, additional studies, top-line data and open label projections, plans, Madrigal's primary and key secondary study endpoints for resmetirom and the potential for achieving such endpoints and projections, the potential to support an additional indication for resmetirom in patients with well-compensated NASH cirrhosis, optimal dosing levels for resmetirom, projections regarding potential NASH or NAFLD and potential patient benefits with resmetirom, including future NASH resolution, safety, fibrosis treatment, cardiovascular effects, lipid treatment, and/or biomarker effects with resmetirom, and strategies, objectives and commercial opportunities, including potential prospects or results.

Forward-looking statements can be identified by terms such as "accelerate," "achieve," "allow," "anticipates," "appear," "be," "believes," "can," "confidence," "continue," "could," "demonstrates," "design," "estimates," "expectation," "expects," "forecasts," "future," "goal," "help," "hopeful," "inform," "intended," "intends," "may," "might," "on track," "planned," "planning," "plans," "positions," "potential," "powers," "predicts," "predictive," "projects," "seeks," "should," "will," "will achieve," "will be," "would" or similar expressions and the negatives of those terms.

Forward-looking statements are subject to a number of risks and uncertainties including, but not limited to: the assumptions underlying the forward-looking statements; general risks of obtaining and maintaining regulatory approvals, including, but not limited to, potential regulatory delays or rejections; specific risks of, and uncertainties concerning, obtaining EMA regulatory approval; our belief that resmetirom could meet the efficacy standard for NASH therapies described in the EMA's Reflection Paper on Regulatory Requirements; risks associated with meeting the objectives of Madrigal's clinical studies, including, but not limited to Madrigal's ability to achieve enrollment objectives concerning patient numbers (including an adequate safety database), outcomes objectives and/or timing objectives for Madrigal's studies; any delays or failures in enrollment, and the occurrence of adverse safety events; risks related to the effects of resmetirom's mechanism of action; the achievement of enrollment objectives concerning patient number, safety database and/or timing for Madrigal's studies; enrollment and trial conclusion uncertainties; market demand for and acceptance of our products; the potential inability to raise sufficient capital to fund ongoing operations as currently planned or to obtain financings on terms similar to those arranged in the past; the ability to service indebtedness and otherwise comply with debt covenants; outcomes or trends from competitive studies; future topline data timing or results; our ability to prevent and/or mitigate cyber-attacks, unauthorized exfiltration of data or other security incidents; the risks of achieving potential benefits in studies that includes substantially more patients, and patients with different disease states, than prior studies; the timing and outcomes of clinical studies of resmetirom; the uncertainties inherent in clinical testing; and uncertainties concerning analyses or assessments outside of a controlled clinical trial. 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 submissions filed with the U.S. Securities and Exchange Commission, or SEC, 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. Madrigal specifically discusses these risks and uncertainties in greater detail under the captions "Cautionary Note Regarding Forward-Looking Statements" and "Risk Factors Summary" and within Part I, Item 1A of its Annual Report on Form 10-K for the year ended December 31, 2023, filed with the SEC on February 28, 2024, and as updated from time to time by Madrigal's other filings with the SEC.

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