Madrigal Receives European Commission Approval for Rezdiffra™ (resmetirom) for the Treatment of MASH with Moderate to Advanced Liver Fibrosis

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- *Rezdiffra is the first and only medication approved for people living with MASH in the European Union*
- *Conditional marketing authorization is based on positive results from the pivotal Phase 3 MAESTRO-NASH trial demonstrating Rezdiffra reduced fibrosis, resolved MASH and improved key noninvasive tests*
- *Rezdiffra is already included in European MASH treatment guidelines as a first-line treatment*
- *Madrigal is planning for its first European launch in Germany in the fourth quarter of 2025*

CONSHOHOCKEN, Pa., Aug. 19, 2025 (GLOBE NEWSWIRE) -- Madrigal Pharmaceuticals, Inc. (NASDAQ: MDGL), a biopharmaceutical company focused on delivering novel therapeutics for metabolic dysfunction-associated steatohepatitis (MASH), today announced that the European Commission (EC) has granted conditional marketing authorization for Rezdiffra (resmetirom) for the treatment of adults with noncirrhotic MASH with moderate to advanced liver fibrosis. Rezdiffra is now the first and only approved therapy in the European Union (EU) for the treatment of MASH.

Bill Sibold, Chief Executive Officer of Madrigal, stated, “This approval of Rezdiffra marks a historic breakthrough for patients in Europe living with MASH, a serious and progressive liver disease. MASH is the fastest-growing indication for liver transplantation in Europe, but until now, had no approved treatment. The European labelling for Rezdiffra will set an important precedent for the entire field, with no biopsy required to qualify for treatment with Rezdiffra and a clear focus on a distinct MASH patient population with high unmet need: those with moderate to advanced fibrosis (F2-F3). These patients require liver-directed treatment because they have a 10 to 17 times higher risk of liver-related mortality and are just one or two steps away from progressing to cirrhosis.”

MASH is a leading cause of liver-related mortality and an increasing burden on healthcare systems globally. Madrigal estimates that approximately 370,000 patients with MASH with moderate to advanced fibrosis are currently diagnosed and under the care of a liver specialist across Europe.

Rezdiffra is a once-daily, oral, liver-directed THR-β agonist designed to target key underlying causes of MASH. The EC Decision was based on Rezdiffra’s favorable benefit-risk profile – including the positive results from the pivotal Phase 3 MAESTRO-NASH trial, which achieved both fibrosis reduction and MASH resolution primary endpoints. Rezdiffra also reduced liver stiffness, liver fat, liver enzymes, and atherogenic lipids in the MAESTRO-NASH trial, and improved health-related quality of life. At one year, 91% of patients treated with Rezdiffra 100 mg achieved improvement or stabilization of liver stiffness as measured by vibrational-controlled transient elastography (VCTE), a test that is frequently used to monitor treatment response in clinical practice.

Frank Tacke, MD, PhD, MBHA, Chairman of Hepatology & Gastroenterology at the Charité – Universitätsmedizin Berlin, Germany, stated, “The approval of Rezdiffra is a transformational moment for the European MASH community and I’m looking forward to offering this important new treatment option to my patients with moderate to advanced fibrosis. Rezdiffra is included in the European MASH treatment guidelines and hundreds of patients participated in the Phase 3 studies, so there is already sound clinical experience with Rezdiffra in Europe.”

This approval follows a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) adopted in June 2025. The EC Decision is valid in all 27 Member States of the EU, as well as in Iceland, Liechtenstein and Norway. The timing for access to Rezdiffra in individual countries will depend on multiple factors, including the completion of reimbursement procedures. Madrigal expects to launch Rezdiffra in Europe on a country-by-country basis commencing with Germany in the fourth quarter of 2025.

About MASH
Metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH), is a serious liver disease that can progress to cirrhosis, liver failure, liver cancer, need for liver transplantation, and premature mortality. MASH is the leading cause of liver transplantation in women and the second leading cause of all liver transplantation in the U.S., and the fastest-growing indication for liver transplantation in Europe.

Once patients progress to MASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis), the risk of adverse liver outcomes increases dramatically: these patients have a 10-17 times higher risk of liver-related mortality as compared to patients without fibrosis. Those who progress to cirrhosis face a 42 times higher risk of liver-related mortality, underscoring the need to treat MASH before complications of cirrhosis develop. MASH is also an independent driver of cardiovascular disease, the leading cause of mortality for patients.

As MASH disease awareness improves and disease prevalence increases, the number of diagnosed patients with MASH with moderate to advanced fibrosis or compensated MASH cirrhosis (F2-F4c) is expected to grow.

About Rezdiffra
Rezdiffra is a once-daily, oral, liver-directed THR-β agonist designed to target key underlying causes of MASH. It is the first approved medication for the treatment of MASH in the US and EU.

Rezdiffra received accelerated approved from the U.S. Food and Drug Administration (FDA) in March 2024. In the U.S., it is indicated in conjunction with diet and exercise for the treatment of adults with noncirrhotic MASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis). This indication is approved under accelerated approval based on improvement of MASH and fibrosis. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Rezdiffra received conditional marketing authorization from the European Commission (EC) in August 2025. A conditional marketing authorization is granted to a medicinal product that fulfils an unmet medical need when the benefit to public health of immediate availability outweighs the risk inherent in the fact that additional data are still required.

Rezdiffra is not approved in any geography for the treatment of patients with cirrhosis. The ongoing, fully enrolled MAESTRO-NASH OUTCOMES trial is evaluating progression to liver decompensation events in patients with compensated MASH cirrhosis treated with Rezdiffra versus placebo.

About Madrigal
Madrigal Pharmaceuticals, Inc. (Nasdaq: MDGL) is a biopharmaceutical company focused on delivering novel therapeutics for metabolic dysfunction-associated steatohepatitis (MASH), a liver disease with high unmet medical need. Madrigal's medication, Rezdiffra (resmetirom), is a once-daily, oral, liver-directed THR-β agonist designed to target key underlying causes of MASH. Rezdiffra is the first and only medication approved by both the FDA and European Commission for the treatment of MASH with moderate to advanced fibrosis (F2 to F3). An ongoing Phase 3 outcomes trial is evaluating Rezdiffra for the treatment of compensated MASH cirrhosis (F4c). For more information, visit www.madrigalpharma.com.

Forward-Looking Statements
This press release includes "forward-looking statements" made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, as amended, including statements related to the expected timing for commercial launch in Europe on a country-by-country basis. Forward-looking statements are subject to a number of risks and uncertainties including, but not limited to: the assumptions underlying the forward-looking statements; risks of obtaining and maintaining regulatory approvals, including, but not limited to, potential regulatory delays or rejections; the challenges with the commercial launch of a new product, particularly for a company that did not have commercial experience prior to 2024; our history of operating losses and the possibility that we may never achieve or maintain profitability; risks associated with meeting the objectives of Madrigal's clinical trials, 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 trials; any delays or failures in enrollment, and the occurrence of adverse safety events; risks related to the effects of Rezdiffra's (resmetirom's) mechanism of action; market demand for and acceptance of Rezdiffra; the potential inability to raise sufficient capital to fund ongoing operations as currently planned or to obtain financing on acceptable terms; our ability to service indebtedness and otherwise comply with debt covenants; outcomes or trends from competitive trials; future topline data timing or results; our ability to prevent and/or mitigate cyber-attacks; the uncertainties inherent in clinical testing; uncertainties concerning analyses or assessments outside of a controlled clinical trial; and changes in laws and regulations applicable to our business and our ability to comply with such laws and regulations. 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("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 in the sections appearing in Part I, Item 1A of its Annual Report on Form 10-K for the year ended December 31, 2024, filed with the SEC on February 26, 2025, and as updated from time to time by Madrigal's other filings with the SEC.

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