Madrigal Receives Positive CHMP Opinion for Resmetirom (Rezdiffra™) for the Treatment of MASH with Moderate to Advanced Liver Fibrosis

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- *Positive recommendation based on resmetirom's favorable profile including positive results from the pivotal Phase 3 MAESTRO-NASH trial*
- *European Commission decision expected in August 2025; if approved, resmetirom will be the first medication for people living with MASH in the E.U.*

CONSHOHOCKEN, Pa., June 20, 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 Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending approval of resmetirom (Rezdiffra) for the treatment of adults with noncirrhotic MASH with moderate to advanced liver fibrosis. The European Commission decision is anticipated in August.

Bill Sibold, Chief Executive Officer of Madrigal, stated, "Madrigal is singularly focused on leading the fight against MASH globally. Resmetirom was the first medication to achieve fibrosis improvement and MASH resolution in a Phase 3 trial, the first medication to receive FDA-approval for MASH, and today's positive CHMP opinion represents another historic first for the global MASH community. MASH is the fastest-growing indication for liver transplantation in Europe, and we believe resmetirom has the potential to address the urgent unmet need for a foundational, liver-directed therapy to treat patients with this serious disease."

MASH 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 MASH. The CHMP opinion was based on resmetirom's favorable profile including the positive results from the pivotal Phase 3 MAESTRO-NASH trial, which achieved both fibrosis reduction and MASH resolution primary endpoints.

Jörn M. Schattenberg, M.D., Professor of Medicine and Director of the Department of Medicine at the University Medical Center Homburg and University of the Saarland in Germany, stated, "I'm encouraged by the CHMP's positive opinion recommending approval of resmetirom. After years of clinical research and growing appreciation of the burden of MASH on patients and health systems across Europe, we are finally on the cusp of having an approved therapy that targets the underlying disease. Importantly, resmetirom is already included in European clinical practice guidelines, which provide a framework for identifying and monitoring patients with noninvasive tests. If approved, I believe the medication has the potential to transform care for my patients with MASH."

The U.S. Food and Drug Administration (FDA) granted accelerated approval in March 2024 for Rezdiffra 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). Continued approval for this indication may be contingent upon verification and description of clinical benefit in ongoing confirmatory trials.

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 U.S. In the pivotal Phase 3 MAESTRO-NASH biopsy trial, Rezdiffra achieved both fibrosis improvement and MASH resolution primary endpoints, and 91% of patients treated with Rezdiffra 100 mg experienced improvement or stabilization of liver stiffness. In the U.S., Rezdiffra 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). Continued approval for this indication may be contingent upon verification and description of clinical benefit in ongoing

confirmatory trials.

Rezdiffra is not approved in Europe for the treatment of patients with MASH with moderate to advanced liver fibrosis and 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.

What is Rezdiffra?
Rezdiffra is a prescribed medicine used along with diet and exercise to treat adults with nonalcoholic steatohepatitis (NASH) with moderate to advanced liver scarring (fibrosis), but not with cirrhosis of the liver.

It is not known if Rezdiffra is safe and effective in children (under 18 years old).
This indication is approved based on improvement of NASH and liver scarring (fibrosis). There are ongoing studies to confirm the clinical benefit of Rezdiffra.

Before you take Rezdiffra, tell your healthcare provider about all of your medical conditions, including if you:

- have any liver problems other than NASH.
- have gallbladder problems or have been told you have gallbladder problems, including gallstones.
- are pregnant or plan to become pregnant. It is not known if Rezdiffra will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if Rezdiffra passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you take Rezdiffra.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

- Rezdiffra and other medicines may affect each other, causing side effects. Rezdiffra may affect the way other medicines work, and other medicines may affect how Rezdiffra works.
- Especially tell your healthcare provider if you take medicines that contain gemfibrozil to help lower your triglycerides, or cyclosporine to suppress your immune system, because Rezdiffra is not recommended in patients taking these medicines.
- Tell your healthcare provider if you are taking medicines such as clopidogrel to thin your blood or statin medicines to help lower your cholesterol.
- Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

What are the possible side effects of Rezdiffra?
Rezdiffra may cause serious side effects, including:

- liver injury (hepatotoxicity). Stop taking Rezdiffra and call your healthcare provider right away if you develop the following signs or symptoms of hepatotoxicity: tiredness, nausea, vomiting, fever, rash, your skin or the white part of your eyes turns yellow (jaundice), pain or tenderness in the upper middle or upper right area of your stomach (abdomen).
- gallbladder problems. Gallbladder problems such as gallstones, inflammation of the gallbladder, or inflammation of the pancreas from gallstones can occur with NASH and may occur if you take Rezdiffra. Call your healthcare provider right away if you develop any signs or symptoms of these conditions including nausea, vomiting, fever, or pain in your stomach area (abdomen) that is severe and will not go away. The pain may be felt going from your abdomen to your back and the pain may happen with or without vomiting.

The most common side effects of Rezdiffra include: diarrhea, nausea, itching, stomach (abdominal) pain, vomiting, dizziness, constipation. These are not all the possible side effects of Rezdiffra. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Madrigal at 1-800-905-0324.

Please see the full Prescribing Information, including Patient Information, for Rezdiffra.

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 the FDA for the treatment of MASH with moderate to advanced fibrosis (consistent with stages F2 to F3). An ongoing Phase 3 outcomes trial is evaluating Rezdiffra for the treatment of compensated MASH cirrhosis (consistent with stage 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 a decision for marketing authorization by the European Commission and resmetirom's role as a potential foundational therapy for the treatment of MASH in Europe. 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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