Madrigal Presents New Data Demonstrating Rezdiffra® (resmetirom) Significantly Improved Multiple Noninvasive Imaging Tests and Biomarkers in Patients with Compensated MASH Cirrhosis

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- *Rezdiffra® treatment significantly improved liver stiffness, fibrosis biomarkers, and markers of clinically significant portal hypertension risk in patients with compensated MASH cirrhosis*
- *Rezdiffra also improved disease-specific quality of life measures in patients with and without cirrhosis, with sustained effect through two years of treatment*
- *New analysis examining effects of Rezdiffra treatment interruption underscores the need for sustained therapy to prevent disease progression*

CONSHOHOCKEN, Pa., Nov. 10, 2025 (GLOBE NEWSWIRE) -- Madrigal Pharmaceuticals, Inc. (NASDAQ: MDGL), a biopharmaceutical company focused on delivering novel therapeutics for metabolic dysfunction-associated steatohepatitis (MASH), today announced positive two-year data from the open-label compensated MASH cirrhosis (F4c) arm of the Phase 3 MAESTRO-NAFLD-1 trial, evaluating the use of Rezdiffra in an advanced, difficult-to-treat patient population with no approved therapies. The F4c data, and multiple additional Rezdiffra abstracts from the Phase 3 MAESTRO program, were presented at the American Association for the Study of Liver Diseases (AASLD) The Liver Meeting®, taking place from November 7-11, 2025, in Washington, D.C.

In a new analysis examining a population of patients with more advanced compensated MASH cirrhosis (those with a platelet count of <100,000/µL at baseline), Rezdiffra demonstrated improvements from baseline across multiple imaging tests and biomarkers including liver stiffness, liver enzymes and lipids, as well as Baveno risk scores for clinically significant portal hypertension (CSPH).

“Patients with platelet count <100,000/µL have been excluded from other trials in F4c MASH, so these new data from MAESTRO-NAFLD-1 offer unique insights about a population that is on the cusp of progressing to liver decompensation events,” said Naim Alkhouri, M.D., Chief Academic Officer at Summit Clinical Research and the Director of the Steatotic Liver Disease Program at the Clinical Research Institute of Ohio. “Rezdiffra reduced multiple imaging and biomarker parameters in these vulnerable patients despite their advanced state of compensated cirrhosis and a period of treatment interruption between the first and second year of treatment. These data give me greater confidence in the ongoing Phase 3 MAESTRO-NASH OUTCOMES trial of Rezdiffra, which also includes patients with platelet count <100,000/µL.”

“MASH cirrhosis carries a 42 times higher risk of liver-related mortality, so there is an urgent need for an approved therapy that can protect patients from progressing to adverse outcomes,” said David Soergel, M.D., Chief Medical Officer of Madrigal. “Madrigal is determined to pioneer treatment in compensated MASH cirrhosis, and we are currently executing a fully enrolled Phase 3 outcomes study in this population. Overall, the breadth of data we are presenting at AASLD reinforces our conviction that Rezdiffra has the potential to benefit patients across the full spectrum of F2 to F4c MASH.”

Rezdiffra is not approved in any geography for the treatment of patients with cirrhosis; safety and efficacy have not been confirmed in this patient population.

Key Madrigal Data Presentations at AASLD’s The Liver Meeting

Oral Presentation: *“Two-Year Time Course of Biomarker and Imaging Responses in Well-Compensated MASH Cirrhosis Patients Treated with Resmetirom”* [Abstract #0167, Presenter: Naim Alkhouri]

In this open-label analysis, Rezdiffra treatment for two years showed statistically significant improvements from baseline in multiple imaging and biomarker parameters in patients with compensated MASH cirrhosis (n=122; 113 completed two years of treatment). Improvements were also observed in a group of more advanced patients with platelet counts <100,000/µL at baseline (n=30). More than 90% of patients with platelets <100,000/µL at baseline had clinically significant portal hypertension (CSPH) or probable CSPH. Interruption of treatment between year one and two (mean=77 days) led to temporary attenuation of beneficial effects, which generally reversed when treatment resumed.

Patients in both platelet groups experienced improvements in liver stiffness as measured by vibration-controlled transient elastography (VCTE): mean -7.9 kPa in patients with platelets <100,000/µL; mean -6.4 kPA in patients with platelets >100,000/µL.

At baseline, 50% of patients with platelets <100,000/µL met Baveno criteria for CSPH, 43% for probable CSPH, and 7% for no/low CSPH. Following two years of treatment, 35% had CSPH, 26% had probable CSPH, and 39% had no/low CSPH. Two thirds of patients overall shifted to lower Baveno CSPH risk scores by year two, regardless of platelet count.

Additionally, patients achieved improvements in liver enzymes (ALT, GGT); fibrosis and liver injury biomarkers (CK-18, PRO-C3, Adiponectin); and atherogenic lipids and lipoproteins, in both platelet groups.

Safety data were consistent with previous studies and Rezdiffra was well-tolerated in this high-risk population, with a low rate of discontinuation due to adverse events.

No changes in bone mineral density or fracture risk were observed over two years.

Oral Presentation: *"Improvement in Health-Related Quality of Life After Treatment with Resmetirom in Cirrhotic and Non-Cirrhotic Patients with Metabolic Dysfunction-Associated Steatotic Liver Disease: Data from MAESTRO-NAFLD"* [Abstract #0181, Presenter: Zobair Younossi]

In a pooled analysis across the MAESTRO clinical program (n=1,323), patients treated with Rezdiffra reported significant and sustained improvements from baseline across multiple domains of the Liver Disease Quality of Life (LDQOL) and Chronic Liver Disease Questionnaire-Nonalcoholic Steatohepatitis (CLDQ-NASH) – disease-specific tools assessing fatigue, worry, emotional function, and abdominal and systemic symptoms. Improvements were observed in both patients without cirrhosis and with compensated cirrhosis.

In noncirrhotic MASH (n=1,143), Rezdiffra significantly improved abdominal symptoms, worry, and health distress scores, and attenuated declines in physical and emotional role functioning compared with placebo. In compensated MASH cirrhosis (n=180), by week 24 of treatment with Rezdiffra, worry and health distress improved, and were sustained by week 52 and throughout Year 2.

Poster of Distinction: *"Durability of Resmetirom Response in MASLD Patients After Two Years of Treatment in MAESTRO-NAFLD-OLE"* [Abstract #4003, Presenter: Naim Alkhouri]

In the open-label extension of the Phase 3 MAESTRO-NAFLD-1 trial, patients with MASH with moderate to advanced fibrosis (n=515) who paused therapy (mean of 111 days between years one and two) experienced a reversal of earlier gains and evidence of renewed disease progression. When treatment resumed, improvements in MRI-PDFF, VCTE, and liver biochemistry were restored. In addition, patients who continued treatment for two years maintained consistent biomarker improvements, and those initially on placebo before entering the open-label extension achieved comparable benefits after switching to Rezdiffra. The therapy remained well tolerated, and transient gastrointestinal events did not generally recur after reinitiation.

"These data from the Phase 3 MAESTRO-NAFLD-1 trial help answer an important question that many clinicians and patients ask about pausing treatment after a positive early treatment response to Rezdiffra," said Soergel. "We now have compelling evidence that continuous treatment with Rezdiffra maintained benefit and prevented progression; stopping therapy at one year resulted in an immediate return of disease activity in this analysis. In most cases, patients with MASH will require continuous treatment, similar to other chronic diseases like diabetes."

Rezdiffra (resmetirom) is a once-daily, oral, liver-directed thyroid hormone receptor (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. and Europe. In the pivotal Phase 3 MAESTRO-NASH biopsy trial, Rezdiffra achieved both fibrosis improvement 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 100mg 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.

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). This indication is approved under accelerated approval based on improvement of NASH and 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
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, and 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 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 potential benefit of Rezdiffra in patients with compensated MASH cirrhosis and the potential impact of positive results from the MAESTRO-NASH OUTCOMES trial. 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; 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; 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.

Madrigal may use its website to comply with its disclosure obligations under Regulation FD. Therefore, investors should monitor Madrigal's website in addition to following its press releases, filings with the SEC, public conference calls, and webcasts.

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