Madrigal Presents Data Demonstrating Rezdiffra Reduced Markers of Cardiovascular and Liver-Related Risk in Patients with MASH

May 27, 2026

- *Growing body of clinical and real-world evidence supports the role of Rezdiffra® (resmetirom) as the foundational therapy for patients with MASH*
- *Rezdiffra improved atherogenic lipid profiles associated with cardiovascular risk, including LDL-C, ApoB and Lp(a), in a secondary analysis from the Phase 3 MAESTRO program*
- *In patients with well-compensated MASH cirrhosis (F4c), Rezdiffra improved a risk score – ANTICIPATE-NASH – that predicts the probability of experiencing severe liver-related events*
- *Multiple real-world analyses evaluating the use of Rezdiffra in routine clinical practice demonstrated early and sustained improvements in cardiometabolic parameters, liver-related biomarkers, and liver stiffness measurements; 49% of patients achieved ≥25% reduction in liver stiffness over a nine-month follow-up period*

CONSHOHOCKEN, Pa., May 27, 2026 (GLOBE NEWSWIRE) -- Madrigal Pharmaceuticals, Inc. (NASDAQ: MDGL), a biopharmaceutical company focused on delivering novel therapeutics for metabolic dysfunction-associated steatohepatitis (MASH), today announced new analyses of Phase 3 data and real-world evidence demonstrating Rezdiffra reduced markers of cardiovascular and liver-related risk in patients with MASH. The data are featured across eight poster presentations at the European Association for the Study of the Liver (EASL) Congress 2026, taking place May 27-30 in Barcelona, Spain.

“New analyses from the Phase 3 MAESTRO program and a growing body of real-world evidence reinforce Rezdiffra’s position as the foundational therapy for MASH,” said David Soergel, M.D., Chief Medical Officer of Madrigal. “The data we are presenting at the EASL Congress give us new insight into Rezdiffra’s potential to reduce clinically significant portal hypertension risk in patients with well-compensated MASH cirrhosis, a population with no approved therapies. Additionally, we continue to generate evidence supporting the medication’s broad and consistent effects on key biomarkers used to monitor treatment response in everyday clinical practice, as well as markers of cardiovascular risk.”

“Cardiovascular disease is the leading cause of death in people with MASH, so the secondary analysis from the Phase 3 MAESTRO program demonstrating that Rezdiffra improved LDL-C, ApoB and Lp(a) is highly relevant for clinicians and patients,” said Meena B. Bansal, M.D., F.A.A.S.L.D., System Chief, Division of Liver Diseases Director, MASH/NASH Center of Excellence, Icahn School of Medicine at Mount Sinai. “Patients achieved key MASH endpoints and significant improvements in multiple atherogenic lipids and lipoproteins regardless of baseline statin use. This is particularly important because statins are not known to meaningfully lower certain lipoproteins such as Lp(a). These results suggest Rezdiffra may provide additional cardiometabolic benefit for patients with MASH, whether or not they are receiving statin therapy. Further research is warranted to evaluate Rezdiffra’s potential to improve cardiovascular outcomes in patients with MASH.”

Key Madrigal Data Presentations at the EASL Congress 2026

Poster Presentation: *Reducing CV risk in patients with MASH independent of baseline statin use: Lp(a) and LDL lowering by resmetirom* [Abstract # ID-FRI-149, Presenter: Meena B. Bansal]

Data from a secondary analysis of the Phase 3 MAESTRO-NASH and MAESTRO-NAFLD-1 trials demonstrated that Rezdiffra improved key histologic MASH endpoints and significantly reduced multiple atherogenic lipids and lipoproteins associated with cardiovascular risk, including LDL-C and Lp(a), regardless of baseline statin use.

Among statin-treated patients (n=473) receiving Rezdiffra 100mg:

- 44.4% of patients with baseline LDL-C ≥70mg/dL shifted to <70mg/dL at week 52.
- 50.0% of patients with baseline LDL-C ≥100mg/dL shifted to <100mg/dL at week 52.
- Among patients with elevated baseline Lp(a), 36.3% of patients with baseline Lp(a) ≥30mg/dL and 37.5% of patients with baseline Lp(a) ≥50mg/dL shifted below those thresholds.
- No significant statin-related safety signals were observed.

Among patients receiving Rezdiffra 100mg and no statins (n=493):

- 13.8% of patients with baseline LDL-C ≥70mg/dL shifted to <70mg/dL at week 52.
- 51.5% of patients with baseline LDL-C ≥100mg/dL shifted to <100mg/dL at week 52.
- Among patients with elevated baseline Lp(a), 45.4% of patients with baseline Lp(a) ≥30mg/dL and 62.5% of patients with baseline Lp(a) ≥50mg/dL shifted below those thresholds.

These findings support the concomitant use of Rezdiffra with statin therapy and suggest the potential for Rezdiffra to address both liver disease and cardiometabolic risk in patients with MASH.

EASL Top Poster: *Baseline ANTICIPATE score and response predicts liver outcome events in a 180 patient MASH cirrhosis cohort treated with resmetirom* [Abstract # ID-TOP-177, Presenter: Naim Alkhouri]

In patients with compensated MASH cirrhosis, clinically significant portal hypertension (CSPH) is a key driver of disease progression and severe liver-related complications. While Baveno criteria are used to identify patients likely to have CSPH, ANTICIPATE-NASH is a noninvasive risk stratification model developed for MASH that integrates liver stiffness measurements, platelet count and body mass index (BMI) to estimate future CSPH risk and predict the likelihood of liver-related events over the subsequent three years.

The ANTICIPATE-NASH risk model was applied to the open-label extension (OLE) cohort from the MAESTRO-NAFLD-1 trial, which included patients with well-compensated MASH cirrhosis (F4c) treated with Rezdiffra for up to two years. Results demonstrated progressive improvements in ANTICIPATE-NASH risk scores over time:

- The proportion of patients classified as high risk for CSPH decreased from 75% at baseline to 60.3% at Year 1 and 54.5% at Year 2.
- Mean ANTICIPATE-NASH scores declined by up to 37.6% over two years of treatment.
- Liver-related events were infrequent and occurred exclusively in patients with baseline ANTICIPATE-NASH scores associated with elevated CSPH risk.

These findings support the potential use of ANTICIPATE-NASH as a risk stratification tool to identify patients with a high-risk of disease progression, informing prognosis and clinical decision-making.

Additional Poster Presentations (Real-World Data):

- ***Early real-world effectiveness of resmetirom in adults with metabolic dysfunction associated steatohepatitis and moderate-to-advanced- fibrosis [Abstract #ID-FRI-141, Presenter: Naim Alkhouri]***
- ***Twelve-month changes in liver function enzymes and lipids in patients receiving resmetirom [Abstract # ID-FRI-186, Presenter: Anthony Martinez]***
- ***Non-invasive test-driven modeling of patient eligibility for resmetirom therapy in MASLD: Data from the German SLD-Registry [Abstract #ID-WED-155, Presenter: Maurice Michel]***

Multiple real-world studies evaluating patients treated with Rezdiffra for up to 12 months in routine clinical practice are also being presented at EASL. Collectively, these studies demonstrated that patients achieved clinically meaningful improvements in biomarkers of liver disease and cardiometabolic risk. Improvements were observed as early as approximately six months following treatment initiation and sustained through approximately 12 months. Rezdiffra was generally well tolerated, with low rates of treatment-related adverse events and discontinuations reported in routine clinical practice.

- Abstract #ID-FRI-141: In an analysis of data from a large gastroenterology practice, Rezdiffra use was associated with clinically meaningful improvements in laboratory and non-invasive clinical measures. Over a mean follow-up period of approximately nine months, 48.6% of patients achieved ≥25% reduction in liver stiffness, a key measure of treatment response. Rezdiffra was well tolerated in this analysis, and discontinuation due to treatment-related adverse events was <1%.

- Abstract # ID-FRI-186: In another electronic health record analysis of 728 patients treated with Rezdiffra over 12 months, statistically significant reductions in ALT and AST were observed; these reductions in liver enzymes were consistent across all subgroups, irrespective of baseline type 2 diabetes status, obesity, GLP-1 and statin use. LDL-C levels also decreased significantly in the overall cohort and showed directional reductions across all subgroups.

- Abstract #ID-WED-155: A prospective registry study (Germany Steatotic Liver Disease [SLD]) aimed to characterize patients eligible for Rezdiffra treatment based on noninvasive tests (NITs) in a real-world cohort in Germany. Of the 1,308 patients analyzed, approximately one in five met the criteria for treatment. The treatment-eligible cohort showed a higher distribution of three or more metabolic comorbidities simultaneously. Identification of such patients using NITs such as liver stiffness may support risk stratification and inform treatment strategies in routine clinical practice.

About Rezdiffra
Rezdiffra (resmetirom) is a once-daily, oral, liver-directed thyroid hormone receptor (THR)-β agonist designed to address key underlying causes of MASH. It was the first medication approved 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.

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 any geography for the treatment of patients with cirrhosis.

About MASH
Metabolic dysfunction-associated steatohepatitis (MASH) is a serious liver disease that can progress to cirrhosis, liver failure, liver cancer, the 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 to 17 times higher risk of liver-related mortality as compared to patients without fibrosis.

Patients with MASH 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 disease awareness improves and disease prevalence increases, the number of diagnosed patients with F2 to F4c MASH is growing.

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

This indication is approved based on improvement of MASH 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 MASH.
- 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.
    - A pregnancy safety study for women who take Rezdiffra during pregnancy collects information about the health of you and your baby. You or your healthcare provider can report your pregnancy by visiting https://pregnancyregistry.madrigalpharma.com/ or calling 1-800-905-0324.
- 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, 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) or stomach pain/tenderness.
- gallbladder problems. Gallbladder problems such as gallstones, or inflammation of the gallbladder, or inflammation of the pancreas from gallstones can occur with MASH 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 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 was the first 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 and follow us on LinkedIn.

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 Rezdiffra's ability to potentially improve cardiovascular outcomes in patients with MASH and the potential benefit of Rezdiffra in patients with compensated MASH cirrhosis. Forward-looking statements are subject to a number of risks and uncertainties including, but not limited to: the assumptions underlying the forward-looking statements; our ability to successfully commercialize Rezdiffra in the U.S. and Europe; risks related to obtaining and maintaining regulatory approvals, including, but not limited to, potential regulatory delays or rejections; our history of operating losses and the possibility that we may never achieve or maintain profitability; risks associated with meeting the objectives of our clinical trials, including, but not limited to our ability to achieve enrollment objectives concerning patient numbers (including an adequate safety database), outcomes objectives and/or timing objectives for our 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 or of any other product candidate; market demand for and acceptance of Rezdiffra; our ability to service indebtedness and otherwise comply with debt covenants; outcomes or trends from competitors; future topline data timing or results; our ability to prevent and/or mitigate cyber-attacks; our ability to protect our intellectual property rights; 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 1A of its Annual Report on Form 10-K for the year ended December 31, 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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Source: Madrigal Pharmaceuticals, Inc.