Madrigal Announces New Real-World Data at AASLD 2026 Demonstrating Improvements in Liver Stiffness and Cardiometabolic Health Markers with Rezdiffra

November 5, 2026

- *In real-world studies, up to 93% of patients experienced improvement or stabilization in liver stiffness with ultrasound elastography, with many patients moving into lower liver stiffness categories one year after treatment initiation*
- *Treatment persistence studies showed up to 72% of patients remained on Rezdiffra® (resmetirom) at one year, with high adherence*
- *Improvements in liver stiffness and other measures of liver health were observed regardless of concomitant GLP-1 use, with up to 53% of patients receiving GLP-1 therapies alongside Rezdiffra*
- *Safety findings were consistent with the established safety profile of Rezdiffra observed in clinical trials*

CONSHOHOCKEN, Pa., Nov. 05, 2026 (GLOBE NEWSWIRE) -- Madrigal Pharmaceuticals, Inc. (NASDAQ: MDGL), a biopharmaceutical company focused on delivering novel therapeutics for metabolic dysfunction-associated steatohepatitis (MASH), today announced results from multiple real-world studies of Rezdiffra presented at the American Association for the Study of Liver Diseases (AASLD) The Liver Meeting®, taking place Nov. 5–9 in Denver.

The studies provide new insights into clinical outcomes and treatment patterns among patients with MASH receiving Rezdiffra in routine U.S. clinical practice, including those with cardiometabolic comorbidities. Across multiple independent real-world data sources, patients achieved meaningful improvements (based on a 25% threshold) or stabilization in liver stiffness measurements, a noninvasive marker associated with liver fibrosis, approximately one year after treatment initiation. Additional analyses demonstrated improvements in transaminase levels, liver fat and cardiometabolic markers, alongside encouraging trends in treatment persistence and adherence.

"These new data represent an important expansion of the real-world evidence supporting Rezdiffra as a foundational therapy for patients with MASH," said David Soergel, M.D., Chief Medical Officer of Madrigal. "Across multiple studies and diverse patient populations, we are seeing robust improvements in noninvasive measures of liver health consistent with the positive results observed in the pivotal Phase 3 trial of Rezdiffra. The findings also provide encouraging evidence that most patients are staying on therapy over time. Together, these results reinforce the strong real-world effectiveness, safety and tolerability profile of Rezdiffra, and provide valuable insight into how the medication is being used in everyday clinical practice."

Real-world studies demonstrate consistent improvements in liver stiffness at one year

Several studies presented at AASLD evaluated changes in liver stiffness measurements (LSM) using ultrasound elastography, which is increasingly used in clinical practice to assess liver fibrosis and monitor patients with MASH. Across studies, approximately 37% to 55% of patients with paired measurements achieved a ≥25% improvement in liver stiffness after approximately one year; most improved or remained stable.[1-3, 9]

Key findings included:

- Truveta Data: Among 150 patients with paired LSMs, 55% achieved a ≥25% improvement in liver stiffness and 48.0% achieved a ≥30% improvement at 12 months. Overall, 93% improved or remained stable, and 67% transitioned to a lower pre-defined liver stiffness range.[1]
- Trio Health Data: Among 195 patients with paired LSMs, 45% achieved a ≥25% improvement and 38% achieved a ≥30% improvement at 12 months; 88% improved or remained stable. Separately, 44% of 347 patients with documented fibrosis stages improved by at least one stage.[2]
- Gastro Health/Latica: Among 112 patients with paired LSMs, 47% achieved a ≥25% improvement and approximately 38% achieved a ≥30% improvement at follow-up; approximately 89% improved or remained stable using the 25% threshold. Moreover, 32 of 46 patients starting between 10 and <20 kPa moved below 10 kPa at follow-up.[3]
- Methodist Dallas Medical Center: Among 35 patients with paired LSMs, 37% achieved a ≥25% improvement and 26% achieved a ≥30% improvement at 12 months; 83% improved or remained stable.[9]

“Not every medicine delivers the same results in real-world clinical practice that we see in carefully controlled clinical trials, particularly when treating a complex, chronic disease like MASH,” said Parvez Mantry, M.D., at The Liver Institute at Methodist Dallas Medical Center. “What makes these findings so encouraging is the remarkable consistency of improvement we're seeing across multiple real-world studies of Rezdiffra, involving different patient populations and clinical settings. For physicians treating MASH, this growing body of evidence provides important reassurance that the benefits observed in these trials are translating into everyday patient care.”

Improvements observed across diverse patient populations and measures of liver health

Additional analyses demonstrated consistent improvements in liver-related and cardiometabolic biomarkers among patients initiating Rezdiffra, including those with comorbidities such as type 2 diabetes, obesity and cardiovascular disease and those receiving concomitant GLP-1 receptor agonists or statins.

A subgroup analysis from the Truveta Data of 2,488 patients found statistically significant improvements in mean liver stiffness and liver fat measurements across subgroups defined by diabetes, obesity, GLP-1 receptor agonist use and statin use. Across these subgroups, approximately 89% to 98% of patients with paired measurements experienced improvement (based on 25% threshold) or stabilization in liver stiffness.[4]

The broader Truveta Data analysis also demonstrated statistically significant reductions compared to baseline in markers of liver injury and cardiometabolic health at 12 months, including:

- Mean ALT decreased by 16.2 U/L.
- Mean liver stiffness decreased by 2.5 kPa.
- Mean LDL cholesterol decreased by 15.5 mg/dL.
- Mean triglycerides decreased by 41.0 mg/dL.

Similar trends were observed in the Trio Health study, where 54% of patients achieved a clinically meaningful reduction in liver fat, measured by controlled attenuation parameter (CAP, based on >40 dB/m), and 48% achieved a reduction in ALT of at least 20% from baseline.[2]

A separate real-world analysis using Optum Market Clarity data also found statistically significant reductions in liver enzymes and select cardiometabolic measures at 12 months, providing additional evidence of consistent trends across different healthcare datasets.[5]

Real-world studies demonstrate encouraging treatment persistence and adherence

Three additional studies evaluated Rezdiffra treatment adherence and persistence using pharmacy and administrative claims data;[6-8] one retrospective cohort analysis included 11,469 patients from a large U.S. specialty and retail pharmacies database (CVS Healthspire database).

Across these analyses, up to 72% of patients remained persistent with Rezdiffra at 12 months using a 60-day treatment-gap definition. Persistence at six months was up to 89%.

The studies provide early benchmarks for understanding long-term treatment patterns in routine clinical practice. Most patients remained on treatment at one year, and adherence among patients continuing therapy was high.

Safety findings were generally consistent with the established safety profile of Rezdiffra observed in clinical trials. In a real-world analysis evaluating treatment-related adverse events, reported events were infrequent, with 11% of patients experiencing ≥1 adverse event. The most frequently reported events were diarrhea (7%), nausea (4%), pruritus (2%), vomiting (2%) and fatigue (≤1%).[3]

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 F2 to F4c MASH is growing.

About Rezdiffra
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. Forward-looking statements are based on Madrigal's beliefs and assumptions on information currently available to it and are subject to a number of risks and uncertainties including, but not limited to: the assumptions underlying the forward-looking statements; Madrigal's ability to successfully commercialize Rezdiffra in the U.S. and Europe; conditions imposed by regulators relating to the scope and design of Madrigal's clinical trials; risks related to obtaining and maintaining regulatory approvals, including, but not limited to, potential regulatory delays or rejections; Madrigal's history of operating losses and the possibility that it may never achieve or maintain consistent 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 or of any other product candidate; market demand for and acceptance of Rezdiffra; Madrigal's ability to service indebtedness and otherwise comply with debt covenants; outcomes or trends from competitors; future topline data timing or results; Madrigal's ability to prevent and/or mitigate cyber-attacks; Madrigal's ability to protect its 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 Madrigal's business and its 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, 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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