Madrigal Pharmaceuticals Announces U.S. Availability of Rezdiffra™ (resmetirom) for the Treatment of Patients with Noncirrhotic NASH with Moderate to Advanced Liver Fibrosis

April 9, 2024

- *Rezdiffra is the first and only medication approved by the FDA for the treatment of NASH (also known as "MASH")*
- *First patients have received Rezdiffra via Madrigal's specialty pharmacy network*

CONSHOHOCKEN, Pa., April 09, 2024 (GLOBE NEWSWIRE) -- Madrigal Pharmaceuticals, Inc. (NASDAQ:MDGL), a biopharmaceutical company focused on delivering novel therapeutics for nonalcoholic steatohepatitis (NASH), today announced that Rezdiffra (resmetirom) is now available in the U.S. Rezdiffra is indicated in conjunction with diet and exercise for the treatment of adults with noncirrhotic NASH 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.

Bill Sibold, Chief Executive Officer of Madrigal, stated, "The introduction of Rezdiffra as the first and only FDA-approved therapy in NASH marks a turning point for Madrigal and the NASH community. Since approval, we have been partnering with healthcare providers, payers, and patient advocates to build new care pathways that will help patients access Rezdiffra and achieve their treatment goals. Our field teams are fully deployed, our specialty pharmacy network is processing prescriptions, our supply chain is fully operational, and most importantly, the first patients are now receiving Rezdiffra."

Donna R. Cryer, JD, founder and Chief Executive Officer of the Global Liver Institute, stated, "Years of advocacy from the NASH community helped pave the way for Rezdiffra as the first approved medication for this long-neglected disease. We were thrilled to see that the Rezdiffra prescribing information is patient-centric: there is no biopsy requirement for diagnosis. Moving the field away from biopsy has been a long-time goal for the Global Liver Institute and I believe the availability of Rezdiffra will help grow patient awareness of noninvasive testing options for NASH."

Naim Alkhouri, MD, FAASLD, Chief Medical Officer, Chief of Transplant Hepatology, Director of the Fatty Liver Program, Arizona Liver Health, stated, "The introduction of Rezdiffra is completely changing the conversation about NASH in our practice. I can finally tell my appropriate patients with moderate to advanced fibrosis that we have an approved treatment to help improve fibrosis and resolve NASH. Our team at Arizona Liver Health has never felt more energized, and we recently celebrated when our first patient received Rezdiffra."

Rezdiffra is a once-daily, oral THR-β agonist designed to target key underlying causes of NASH. The accelerated approval of Rezdiffra was based on results from the Phase 3 MAESTRO-NASH trial, which was published in the *New England Journal of Medicine* in February 2024. MAESTRO-NASH remains ongoing as an outcomes study designed to generate confirmatory data that, if positive, will help verify clinical benefit and may support full approval. A second ongoing outcomes trial is evaluating progression to liver decompensation events in patients with well-compensated NASH cirrhosis treated with Rezdiffra versus placebo.

The recommended dosage of Rezdiffra is based on actual body weight. For patients weighing <100 kg (220 lbs.), the recommended dosage is 80 mg orally once daily. For patients weighing ≥100 kg (220 lbs.), the recommended dosage is 100 mg orally once daily.

Rezdiffra should not be used in patients with decompensated cirrhosis. The most common adverse reactions reported in patients treated with Rezdiffra included diarrhea, nausea, pruritis, vomiting, constipation, abdominal pain, and dizziness. Diarrhea and nausea typically began early in treatment initiation and were mild to moderate in severity. See full prescribing information for dosage modifications with concomitant use of moderate CYP2C8 inhibitors.

Rezdiffra is distributed through a limited specialty pharmacy network. Madrigal is committed to helping appropriate patients who may benefit from Rezdiffra access the medication through the Madrigal Patient Support program. This program is designed to help patients navigate insurance and affordability challenges and provide co-pay support for eligible patients. Madrigal has also established a patient assistance program (PAP) to help patients with no insurance access Rezdiffra.

About NASH

Nonalcoholic steatohepatitis (NASH) is a more advanced form of nonalcoholic fatty liver disease (NAFLD). NASH is a leading cause of liver-related mortality and an increasing burden on healthcare systems globally. Additionally, patients with NASH, especially those with more advanced metabolic risk factors (hypertension, concomitant type 2 diabetes), are at increased risk for adverse cardiovascular events and increased morbidity and mortality.

Once patients progress to NASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis), the risk of adverse liver outcomes increases dramatically. NASH is rapidly becoming the leading cause of liver transplantation in the U.S.

Madrigal estimates that approximately 1.5 million patients have been diagnosed with NASH in the U.S., of which approximately 525,000 have NASH with moderate to advanced liver fibrosis. Madrigal plans to focus on approximately 315,000 diagnosed patients with NASH with moderate to advanced liver fibrosis under the care of the liver specialist physicians during the launch of Rezdiffra.

NASH is also known as metabolic dysfunction associated steatohepatitis (MASH). In 2023, global liver disease medical societies and patient groups came together to rename the disease, with the goal of establishing an affirmative, non-stigmatizing name and diagnosis. Nonalcoholic fatty liver disease (NAFLD) was renamed metabolic dysfunction-associated steatotic liver disease (MASLD), NASH was renamed MASH, and an overarching term, steatotic liver disease (SLD), was established to capture multiple types of liver diseases associated with fat buildup in the liver. In addition to liver disease, patients with MASH have at least one related comorbid condition (e.g., obesity, hypertension, dyslipidemia, or type 2 diabetes).

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, 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 Pharmaceuticals

Madrigal Pharmaceuticals, Inc. (Nasdaq: MDGL) is a biopharmaceutical company pursuing novel therapeutics for nonalcoholic steatohepatitis (NASH), 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 NASH. 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, that are based on Madrigal's beliefs and assumptions and on information currently available to it, but are subject to factors beyond its control. Forward-looking statements reflect management's current knowledge, assumptions, judgment and expectations regarding future performance or events. Forward-looking statements include all statements that are not historical facts; statements referenced by forward-looking statement identifiers; and statements regarding: Rezdiffra (resmetirom) and its expected use for treating NASH with moderate to advanced fibrosis; the initiation of the commercial launch of Rezdiffra, including statements regarding commercial insurance and the anticipated time to fill prescriptions; estimates of patients diagnosed with NASH and market opportunities; the relationship between NASH progression and adverse patient outcomes; the estimated clinical burden of uncontrolled NASH; analyses for patients with NASH with moderate to advanced fibrosis concerning potential progression to cirrhosis, decompensated cirrhosis, liver transplant or death; cardiovascular risks, comorbidities and outcomes; health economics assessments or projections; that Rezdiffra has been shown to improve the fibrosis that is associated with progression to cirrhosis and its complications and resolve the underlying inflammation that drives the disease; projections or objectives for obtaining full approval for Rezdiffra, including those concerning potential clinical benefit to support potential full approval; post-approval requirements and commitments; reduced risk of progression to cirrhosis, liver failure, need for liver transplant and premature mortality; treatment paradigm, including new care pathways to help patients access Rezdiffra and achieve their treatment goals; improved liver enzymes, fibrosis biomarkers and imaging tests; the potential efficacy and safety of Rezdiffra for noncirrhotic NASH patients and cirrhotic NASH patients; possible or assumed future results of operations and expenses, business strategies and plans (including ex-US. Launch/partnering plans); research and development activities, the timing and results associated with the future development of Rezdiffra, the timing and completion of projected future clinical milestone events, including enrollment, additional studies, the potential to support an additional indication for Rezdiffra in patients with well-compensated NASH cirrhosis; optimal dosing levels for Rezdiffra ; potential NASH or NAFLD and potential patient benefits with Rezdiffra, including future NASH resolution, safety, fibrosis treatment, cardiovascular effects, lipid treatment, and/or biomarker effects with Rezdiffra; and strategies, objectives and commercial opportunities, including potential prospects or results.

Forward-looking statements can be identified by terms such as "accelerate," "achieve," "allow," "anticipates," "appear," "be," "believes," "can," "confidence," "continue," "could," "demonstrates," "design," "estimates," "expectation," "expects," "forecasts," "future," "goal," "help," "hopeful," "inform," inform," "intended," "intends," "may," "might," "on track," "planned," "planning," "plans," "positions," "potential," "powers," "predicts," "predictive," "projects," "seeks," "should," "will," "will achieve," "will be," "would" or similar expressions and the negatives of those terms.

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 does not have commercial experience; risks associated with meeting the objectives of Madrigal's clinical studies, 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 studies; 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; enrollment and trial conclusion uncertainties; market demand for and acceptance of our product; the potential inability to raise sufficient capital to fund ongoing operations as currently planned or to obtain financings on terms similar to those arranged in the past; the ability to service indebtedness and otherwise comply with debt covenants; outcomes or trends from competitive studies; future topline data timing or results; our ability to prevent and/or mitigate cyber-attacks; the timing and outcomes of clinical studies of Rezdiffra (resmetirom); the uncertainties inherent in clinical testing; and uncertainties concerning analyses or assessments outside of a controlled clinical trial. 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, or 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, 2023, filed with the SEC on February 28, 2024, and as updated from time to time by Madrigal's other filings with the SEC.

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A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/699742ee-b5cf-4bac-8fe0-131c989b4210

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Rezdiffra



Rezdiffra product image