Madrigal Pharmaceuticals to Present Multiple Rezdiffra™ (resmetirom) and Health Economics Outcomes Research Abstracts in NASH/MASH at the EASL Congress

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CONSHOHOCKEN, Pa., May 29, 2024 (GLOBE NEWSWIRE) -- Madrigal Pharmaceuticals, Inc. (NASDAQ:MDGL), a biopharmaceutical company focused on delivering novel therapeutics for nonalcoholic steatohepatitis (NASH), today announced ten data presentations at the upcoming European Association for the Study of the Liver (EASL) Congress, taking place from June 5-8, 2024 in Milan, Italy.

“The data we will be presenting at EASL further support Rezdiffra as the foundational therapy in NASH and Madrigal as the leading company in the field," said Bill Sibold, Chief Executive Officer of Madrigal. "We look forward to sharing multiple new data analyses from the MAESTRO Phase 3 program, including the first quality of life data, further analysis of noninvasive test results, and the first look at Rezdiffra in patients with metabolic dysfunction- and alcohol associated liver disease (MetALD)."

Mr. Sibold continued, “Additionally, we will be presenting important new real-world data examining the burden of uncontrolled NASH on patients and the health system. The serious human and economic costs of this disease are coming into focus, and we’re learning that patients can progress to cirrhosis and decompensated cirrhosis at a faster rate than previously understood.”

Rezdiffra is a once-daily, oral, liver-directed thyroid hormone receptor (THR)-β agonist designed to target key underlying causes of NASH. It is the first approved medication for the treatment of NASH. In the pivotal Phase 3 MAESTRO-NASH biopsy trial, Rezdiffra achieved both fibrosis improvement and NASH resolution primary endpoints, and 80% of patients treated with Rezdiffra 100 mg experienced improvement or stabilization of fibrosis. 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.

Madrigal data presentations at the EASL Congress 2024

- Late-breaking oral presentation: “Identification and validation of pre-identified morphological baseline features for prediction of fibrosis progression in MAESTRO-NASH” [Friday, June 7 at 17:45 CEST. Presenter: Jörn Schattenberg]
- Oral presentation: “Assessment of resmetirom efficacy (80 mg vs. 100 mg) stratified by baseline body mass index and weight in patients from the MAESTRO-NASH trial” [Saturday, June 8 at 11:15 CEST. Presenter: Mazen Noureddin]
- Poster: “Health-related quality of life assessments in a 52-week, double-blind, randomized, placebo-controlled Phase 3 study of resmetirom in patients with NASH and fibrosis (MAESTRO-NASH)” [Presenter: Zobair Younossi]
- Poster: “Noninvasive predictive markers of resmetirom biopsy response” [Presenter: Jörn Schattenberg]
- Poster: “Resmetirom treatment of a subgroup of patients with possible MetALD enrolled in MAESTRO-NASH, a Phase 3 NASH/MASH serial liver biopsy study” [Presenter: Vlad Ratziu]
- Poster: “Analyses of fibrosis biomarkers PRO-C3 and ELF in resmetirom treated patients from MAESTRO-NASH, a 52 Week NASH/MASH serial liver biopsy study” [Presenter: Quentin Anstee]
- Poster: “Using machine learning models to predict baseline fibrosis stage in patients from phase 3 resmetirom trials (MAESTRO-NAFLD and MAESTRO-NASH)” [Presenter: Jörn Schattenberg]
- Poster: “Risk of nonalcoholic steatohepatitis disease progression to more severe liver disease in Medicare patients” [Presenter: Robert Gish]
- Poster: “Costs associated with nonalcoholic steatohepatitis disease progression in Medicare patients” [Presenter: Robert Gish]
- Poster: “Healthcare cost and resource utilization among patients with nonalcoholic steatohepatitis, stratified by glucagon-like peptide 1 receptor agonist use in real world data” [Presenter: Yestle Kim]

About the Phase 3 MAESTRO-NASH Trial of Rezdiffra

MAESTRO-NASH is an ongoing Phase 3 trial that enrolled 1759 patients with biopsy-confirmed NASH. Patients were randomly assigned in a 1:1:1 ratio to receive once-daily Rezdiffra at a dose of 80 mg or 100 mg or placebo. The two primary endpoints at week 52 were NASH resolution with no worsening of fibrosis and an improvement in fibrosis by at least one stage with no worsening of the NAFLD activity score. The key secondary endpoint was the percent change from baseline in LDL cholesterol at week 24.

Rezdiffra achieved both primary endpoints and the key secondary endpoint of the MAESTRO-NASH trial. Additionally, Rezdiffra improved liver enzymes, fibrosis biomarkers and imaging tests as compared with placebo. The primary results of the trial were published in the *New England Journal of Medicine* in February 2024.

Patients enrolled in the MAESTRO-NASH trial continue on therapy after the initial 52-week treatment period for up to 54 months to

accrue and measure hepatic clinical outcome events including progression to cirrhosis on biopsy and hepatic decompensation events, as well as all-cause mortality. The 54-month outcomes portion of the trial is designed to generate confirmatory data that, if positive, will help verify Rezdiffra's clinical benefit and may support full approval.

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; indicating 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 (resmetirom), including those concerning potential clinical benefit to support potential full approval; regarding post-approval requirements and commitments; reduced risk of progression to cirrhosis, liver failure, need for liver transplant and premature mortality; treatment paradigm; improved liver enzymes, fibrosis biomarkers and imaging tests; the potential efficacy and safety of Rezdiffra (resmetirom) 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 (resmetirom), the timing and completion of projected future clinical milestone events, including enrollment, additional studies, the potential to support an additional indication for Rezdiffra (resmetirom) in patients with well-compensated NASH cirrhosis; optimal dosing levels for Rezdiffra (resmetirom); potential NASH or NAFLD and potential patient benefits with Rezdiffra (resmetirom), including future NASH resolution, safety, fibrosis treatment, cardiovascular effects, lipid treatment, and/or biomarker effects with Rezdiffra (resmetirom); 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 Part II, Item 1A of its Quarterly Report on Form 10-Q for the quarter ended March 31, 2024, filed with the SEC on May 7, 2024, and as updated from time to time by Madrigal's other filings with the SEC.

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