UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 12, 2023

MADRIGAL PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-33277**	**04-3508648**
(State or other jurisdiction of incorporation)	**(Commission File No.)**	**(I.R.S. Employer Identification No.)**

Four Tower Bridge **200 Barr Harbor Drive, Suite 200** **West Conshohocken, Pennsylvania**	**19428**
(Address of principal executive office)	**(Zip Code)**

Registrant's telephone number, including area code: (267) 824-2827

(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.0001 Par Value Per Share	MDGL	The NASDAQ Stock Market LLC

Item 8.01 Other Events.

On September 13, 2023, Madrigal Pharmaceuticals, Inc. (the "Company") issued a press release announcing that the U.S. Food and Drug Administration has accepted for review the Company's New Drug Application for resmetirom for the treatment of adult patients with NASH with liver fibrosis and granted a Priority Review designation. A copy of the press release is filed as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press release of Madrigal Pharmaceuticals, Inc. issued on September 13, 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL file)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Madrigal Pharmaceuticals, Inc.

Date: September 13, 2023

By: /s/ Brian J. Lynch
Name: Brian J. Lynch
Title: Senior Vice President and General Counsel

Madrigal Pharmaceuticals Announces NDA Acceptance and Priority Review of the New Drug Application for Resmetirom for the Treatment of NASH with Liver Fibrosis

CONSHOHOCKEN, PA, September 13, 2023 – Madrigal Pharmaceuticals, Inc. (NASDAQ:MDGL), a clinical-stage biopharmaceutical company pursuing novel therapeutics for nonalcoholic steatohepatitis (NASH), today announced that the U.S. Food and Drug Administration (FDA) has accepted for review its New Drug Application (NDA) for resmetirom for the treatment of adult patients with NASH with liver fibrosis. The FDA has granted Priority Review and assigned a Prescription Drug User Fee Act date for resmetirom of March 14, 2024, the target date by which the FDA intends to complete its review and take action on the NDA. The Agency noted that it is not currently planning to hold an advisory committee meeting to discuss the application.

Resmetirom is a once daily, oral, thyroid hormone receptor (THR)-ß selective agonist designed to target key underlying causes of NASH in the liver. The clinical development program for resmetirom is comprised of 18 clinical studies supporting the NDA: twelve Phase 1 studies, two Phase 2 studies, and four Phase 3 studies. Madrigal is seeking approval of resmetirom for the treatment of patients with NASH and liver fibrosis under the FDA's accelerated approval pathway.

Bill Sibold, Chief Executive Officer of Madrigal, stated, "NASH with liver fibrosis represents a significant unmet need in healthcare today: the disease has a serious impact on patients and, without treatment, it can lead to increased risk of cirrhosis, liver failure, liver cancer, and premature mortality. Resmetirom is a liver-directed therapy that has demonstrated the potential to treat the liver fibrosis that is associated with these negative outcomes, while resolving the underlying steatohepatitis that drives the disease. The FDA's acceptance of our NDA with priority review is an important step forward as we pursue our goal of delivering the first approved treatment to patients with NASH with liver fibrosis."

The FDA grants Priority Review to applications for medicines that, if approved, would be significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions. A Priority Review designation means FDA's goal is to take action on an application within 6 months (compared to 10 months under standard review).

Becky Taub, M.D., Chief Medical Officer and President of Research & Development of Madrigal, stated, "We believe that we have delivered a compelling data package to support the FDA's benefit-risk evaluation of resmetirom for the treatment of NASH with liver fibrosis. The NDA is supported by the positive efficacy results observed in our pivotal Phase 3 trial, the large safety database we have established through the MAESTRO program, and two ongoing outcomes studies that are designed to verify clinical benefit following a potential accelerated approval. We look forward to beginning this critical next phase of the review process."

About the Resmetirom Phase 3 Registration Program for the Treatment of NASH

Resmetirom is a once daily, oral, thyroid hormone receptor (THR)-ß selective agonist designed to target key underlying causes of NASH in the liver.

Madrigal is currently conducting four Phase 3 clinical trials to demonstrate the safety and efficacy of resmetirom for the treatment of NASH: MAESTRO-NASH, MAESTRO-NAFLD-1, MAESTRO-NAFLD-OLE, and MAESTRO-NASH-OUTCOMES.

MAESTRO-NASH is a multicenter, randomized, double-blind, placebo-controlled Phase 3 study of resmetirom in patients with liver biopsy-confirmed NASH. The portion of the study designed to support a subpart H approval enrolled more than 1,000 patients with biopsy-proven NASH with fibrosis, randomized 1:1:1 to receive once-daily resmetirom 80 mg, resmetirom 100 mg, or placebo. The dual primary surrogate endpoints on biopsy were NASH resolution with ≥2-point reduction in NAS (NAFLD Activity Score), and with no worsening of fibrosis OR a 1-point decrease in fibrosis with no worsening of NAS after 52 weeks of treatment. Achievement of either primary endpoint was considered a successful trial outcome.

In December 2022, Madrigal announced that both daily oral doses of resmetirom achieved both MAESTRO-NASH primary liver biopsy endpoints. Multiple secondary endpoints were also achieved, including statistically significant reductions by resmetirom as compared with placebo in atherogenic lipids and lipoproteins, liver enzymes, fibrosis biomarkers, and imaging tests.

Resmetirom was generally safe and well-tolerated at both the 80 mg and 100 mg doses. Consistent with previous Phase 2 and Phase 3 data, the most common adverse event reported with greater frequency in the resmetirom groups versus placebo was an excess of generally mild and transient diarrhea and nausea at the beginning of therapy.

Patients enrolled in MAESTRO-NASH (approximately 1,750 total enrollment) 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 (52 weeks and 54 months) and hepatic decompensation events, as well as all-cause mortality. This portion of the study is designed to generate confirmatory data that, if positive, will help verify resmetirom’s clinical benefit and support full approval.

MAESTRO-NAFLD-1 was a 52-week multicenter, randomized, placebo-controlled, double-blind Phase 3 study of resmetirom in ~1,200 patients with NAFLD, presumed NASH. MAESTRO-NAFLD-1 might be considered a “real-world” NASH study in that diagnosis was based on noninvasive measures rather than liver biopsy. The primary endpoint was to evaluate the safety and tolerability of resmetirom.

Patients in the MAESTRO-NAFLD-1 study were randomized 1:1:1:1 to receive once-daily resmetirom 80 mg, resmetirom 100 mg, or placebo in double-blind arms or resmetirom 100 mg in an open-label arm. Using noninvasive measures, MAESTRO-NAFLD-1 was designed to provide incremental safety information to support the NASH indication as well as provide additional data regarding clinically relevant key secondary efficacy endpoints to better characterize the potential clinical benefits of resmetirom on cardiovascular- and liver-related endpoints.

The primary safety endpoint of MAESTRO-NAFLD-1 and key secondary endpoints were achieved: resmetirom was safe, well-tolerated and provided statistically significant improvements in LDL-C, apolipoprotein B, triglycerides, and liver fat as measured by MRI-PDFF.

An additional open-label active treatment arm in 180 patients with early (well-compensated) NASH cirrhosis was conducted. Resmetirom was safe and well tolerated in the MAESTRO-NAFLD-1 open-label cohort of patients with well-compensated NASH cirrhosis. As observed in patients with noncirrhotic NASH, mild GI adverse events were seen at the beginning of therapy. Resmetirom reduced LDL-C, other atherogenic lipids and lipoproteins, and MRI-PDFF in patients with NASH cirrhosis and also reduced liver and spleen volume.

A separate 52 week Phase 3 clinical trial, an open-label active treatment extension study of MAESTRO-NAFLD-1 (MAESTRO-NAFLD-OLE), in about 700 patients is ongoing.

Data from the 52-week first 1,000 patient portion of MAESTRO-NASH, together with data from MAESTRO-NAFLD-1, MAESTRO-NAFLD-OLE, Phase 2 and Phase 1 data, including safety parameters, form the basis for Madrigal's subpart H submission to FDA for accelerated approval of resmetirom for treatment of NASH with liver fibrosis.

In August 2022, Madrigal initiated MAESTRO-NASH-OUTCOMES, a randomized double-blind placebo-controlled study in approximately 700 patients with early NASH cirrhosis to allow for noninvasive monitoring of progression to liver decompensation events. A positive outcome is expected to support the full approval of resmetirom for noncirrhotic NASH, potentially accelerating the timeline to full approval. In addition, this study has the potential to support an additional indication for resmetirom in patients with well-compensated NASH cirrhosis.

About NASH

Nonalcoholic steatohepatitis (NASH) is a more advanced form of nonalcoholic fatty liver disease (NAFLD). NAFLD is estimated to afflict more than 20% of adults globally, about 30% in the United States. Of that population, 20% may have NASH.

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.

In NASH, thyroid hormone beta activity in the liver is impaired, leading to a reduction in mitochondrial function and beta-oxidation of fatty acids, which in turn drive inflammation and liver fibrosis.

Once NASH progresses to significant liver fibrosis (stages F2 and F3) the risk of adverse liver outcomes increases dramatically. NASH is rapidly becoming the leading cause of liver transplantation in the U.S. There are currently no FDA-approved therapies available for the treatment of NASH.

About Madrigal Pharmaceuticals

Madrigal Pharmaceuticals, Inc. (Nasdaq: MDGL) is a clinical-stage biopharmaceutical company pursuing novel therapeutics for nonalcoholic steatohepatitis (NASH), a liver disease with high unmet medical need. Madrigal's lead candidate, resmetirom, is a once daily, oral, thyroid hormone receptor (THR)-ß selective agonist designed to target key underlying causes of NASH in the liver. For more information, visit www.madrigalpharma.com.

Forward Looking Statements

This communication 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 concerning the timing and potential impact of FDA acceptance and priority review of our NDA; statements referenced by forward-looking statement identifiers, including the examples in the paragraph below; resmetirom's potential to be the first specialty therapy for NASH patients with significant liver fibrosis; statements concerning potential accelerated approval; and statements or references concerning - the potential efficacy and safety of 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, and the timing and results associated with the future development of resmetirom, the timing and completion of projected future clinical milestone events, including enrollment, additional studies, top-line data and open label projections, plans, objectives, timing and support for making for making a Subpart H (Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses) submission to FDA, projections or objectives for obtaining accelerated or full approval for resmetirom, Madrigal's primary and key secondary study endpoints for resmetirom and the potential for achieving such endpoints and projections, demonstrating clinical benefit to support accelerated approval, the potential to support an additional indication for resmetirom in patients with well-compensated NASH cirrhosis, optimal dosing levels for resmetirom and projections regarding potential NASH or NAFLD and potential patient benefits with resmetirom, including future NASH resolution, safety, fibrosis treatment, cardiovascular effects, lipid treatment, and/or biomarker effects with resmetirom.

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; 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 resmetirom's mechanism of action; the achievement of enrollment objectives concerning patient number, safety database and/or timing for Madrigal's studies; enrollment and trial conclusion uncertainties; market demand for and acceptance of our products; 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; the risks of achieving potential benefits in studies that includes substantially more patients, and patients with different disease states, than prior studies; the timing and outcomes of clinical studies of resmetirom; and the uncertainties inherent in clinical testing. 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 section appearing in Part I, Item 1A of its Annual Report on Form 10-K for the year ended December 31, 2022, filed with the SEC on February 23, 2023, as amended by our Form 10-K/A filed with the SEC on March 3, 2023, and as updated from time to time by Madrigal's other filings with the SEC.

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