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): December 19, 2022

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 7.01 Regulation FD Disclosure.

On December 19, 2022, Madrigal Pharmaceuticals, Inc. ("Madrigal" or the "Company") issued a press release announcing Phase 3 MAESTRO-NASH clinical trial topline results, which are summarized under Item 8.01 below. This press release was posted to the Company's website coincident with its public release.

Item 8.01 Other Events.

Madrigal is conducting a pivotal Phase 3 MAESTRO-NASH clinical trial of resmetirom for the treatment of nonalcoholic steatohepatitis (NASH). On December 19**,** 2022, Madrigal announced topline results, which are summarized below.

Efficacy Data

Dual Primary Endpoints (52 Weeks) and Key Secondary Endpoint (24 weeks) Were Met

Primary Endpoint	Resmetirom 80 mg (n=316)	p-value	Resmetirom 100 mg (n=321)	p-value	Placebo (n=318)
NASH resolution (ballooning 0, inflammation 0,1) with ≥2-point reduction in NAS and no worsening of fibrosis	26%	<0.0001	30%	<0.0001	10%
≥1-stage improvement in fibrosis with no worsening of NAS	24%	0.0002	26%	<0.0001	14%
Key Secondary Endpoint					
LDL-C lowering (24 weeks)	-12%	<0.0001	-16%	<0.0001	1%

All biopsies were read independently by two central pathologists. Each pathologist's scores showed a similar statistically significant magnitude of response at both doses for both liver biopsy endpoints. Biopsy endpoints were achieved independent of baseline fibrosis stage or diabetes status, including similar statistical significance and magnitude of effect at both doses in subgroups of F2, F3, and F2/F3 patients. Other secondary liver biopsy endpoints that were achieved at both doses include ≥2 point reduction in NAS with no worsening of fibrosis, ≥2 point reduction in NAS with ≥1-stage improvement in fibrosis, NASH resolution (with ≥2 point reduction in NAS) with ≥1-stage improvement in fibrosis, and a 2-stage reduction in fibrosis without worsening of NAS.

Safety Data

Resmetirom was safe and well-tolerated at both the 80 mg and 100 mg doses. The frequency of serious adverse events (SAEs) was similar across treatment arms: 11.8%, 12.7% and 12.1% for the 80 mg, 100 mg, and placebo, respectively. The rate of study discontinuation for adverse events was low: 2.8%, 7.7% and 3.7% for the 80 mg, 100 mg and placebo groups, respectively. SAEs occurred at expected rates based on the patient population. The Company believes that, consistent with previous Phase 2 and Phase 3 data, the most common adverse events reported with greater frequency in the resmetirom groups vs placebo were an excess of generally mild and transient diarrhea at the beginning of therapy, in 28%, 34%, 16% in the 80 mg, 100 mg and placebo groups, respectively, and generally mild nausea that occurred at rates of 22%, 19% and 13% in the 80 mg, 100 mg and placebo arms, respectively.

New Drug Application Planning

In the first half of 2023, Madrigal Pharmaceuticals intends to file a new drug application seeking Subpart H accelerated approval of resmetirom.

Other MAESTRO-NASH Study Details

MAESTRO-NASH is a multicenter, randomized, double-blind, placebo-controlled Phase 3 study of resmetirom in patients with liver biopsy-confirmed NASH and was initiated in March 2019. The subpart H portion of the study enrolled more than 1,000 patients with biopsy-proven NASH (at least half with F3 (advanced) fibrosis, the remainder F2 or F1B (moderate fibrosis) with a few earlier F1 patients.

In the MAESTRO-NASH study, patients were randomized 1:1:1 to receive resmetirom 80 mg, resmetirom 100 mg or placebo taken orally once daily. A second biopsy was conducted after 52 weeks of treatment for assessment of the dual primary endpoints. The

primary efficacy analysis assessed histological response at 52 weeks in 955 patients with biopsy-confirmed NASH with fibrosis (modified intent-to-treat (mITT) population) that excluded eleven ITT patients who had their Week 52 biopsy after Week 60 due to COVID-related reasons per regulatory guidelines. Patients without a second biopsy due to early study discontinuation or missing liver biopsy (~17% across treatment arms) were included and considered as non-responders in the primary efficacy analyses (mITT).

MAESTRO-NASH is an ongoing blinded study and all patients continue on therapy after the Week 52 liver biopsy for up to a total of 54 months to accrue hepatic clinical outcome events including histologic conversion to cirrhosis and hepatic decompensation events.

Forward Looking Statements

This Current Report 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; include all statements that are not historical facts; include statements referenced by forward-looking statement identifiers, including the examples in the paragraph below; and include but are not limited to 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 plan (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 and timing 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; 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," "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, generally and in relation to COVID-19 related measures and individual precautionary measures that may be implemented or continued for an uncertain period of time; 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, 2021, filed with the SEC on February 24, 2022, as updated by the risk factors discussed in Part II, Item 1A of the Quarterly Report on Form 10-Q filed with the SEC on May 9, 2022, as well as in Madrigal's other filings with the SEC.

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: December 19, 2022

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