Madrigal Pharmaceuticals Provides Corporate Updates and Reports 2022 Fourth Quarter and Full Year Financial Results

February 23, 2023

- *Positive Phase 3 MAESTRO-NASH study results reported in December 2022 position Madrigal for a resmetirom new drug application filing in the first half of 2023*
- *Madrigal reports year end cash, cash equivalents and marketable securities of $358.8M*

CONSHOHOCKEN, Pa., Feb. 23, 2023 (GLOBE NEWSWIRE) -- Madrigal Pharmaceuticals, Inc. (NASDAQ:MDGL), a clinical-stage biopharmaceutical company pursuing novel therapeutics for nonalcoholic steatohepatitis (NASH), today provides a summary of corporate updates and reports fourth quarter and full year 2022 financial results.

Paul Friedman, M.D., Chief Executive Officer of Madrigal, stated, “The positive Phase 3 MAESTRO-NASH results reported in Q4 2022 have allowed us to advance our regulatory filing preparations, accelerate our prelaunch market development programs, and strengthen our financial position with funding to support the company’s operations through the potential accelerated approval of resmetirom in the U.S. The results have also reinforced our conviction in the value of resmetirom. The Institute for Clinical and Economic Review (ICER), a non-profit organization that conducts pharmacoeconomic assessments of new therapies, recently published a draft Evidence Report indicating that resmetirom has the potential to be a cost-effective treatment for NASH patients with significant fibrosis.”

Becky Taub, M.D., Chief Medical Officer and President of Research & Development of Madrigal, stated, "We remain on track to file our NDA for resmetirom in the first half of 2023. The filing will be supported by positive Phase 3 biopsy results, a standalone Phase 3 safety study, and two ongoing outcomes studies designed to verify clinical benefit following accelerated approval. Based on current screening and enrollment trends, we anticipate that the 54-month outcomes portion of MAESTRO-NASH will be fully enrolled prior to NDA filing in the first half of 2023. We believe that data from the 52-week liver biopsy primary endpoints of MAESTRO-NASH, in which both the NASH resolution and fibrosis reduction primary endpoints were achieved, support NDA and market authorization filings for accelerated approval in the U.S. and Europe. In addition, the noninvasive data from MAESTRO-NASH will provide a framework for identification and monitoring of patients treated with resmetirom in real world clinical practice following a potential approval.”

Remy Sukhija, Chief Commercial Officer of Madrigal, added, “The positive results from MAESTRO-NASH reinforce and increase our confidence in the resmetirom commercial opportunity. Our market research indicates specialist healthcare providers, patients and payers in the U.S. and Europe view NASH with significant fibrosis as an urgent unmet need and understand the potential value that resmetirom can deliver. I’m pleased with the momentum we have established with our market development initiatives and we look forward to launching our new disease education campaign for patients in the coming days.”

Summary of Madrigal 2022 Accomplishments

In 2022, Madrigal achieved multiple business and clinical milestones, including two positive Phase 3 data readouts from the MAESTRO program.

- In January, Madrigal announced topline data from the Phase 3 MAESTRO-NAFLD-1 safety study of resmetirom. Primary and key secondary endpoints from the study were achieved: resmetirom was safe, well-tolerated and provided statistically significant improvements in key measures of liver and cardiovascular health.
- In May, Madrigal secured a $250 million term loan facility with Hercules Capital, Inc. to support the resmetirom clinical program and ramp-up for a potential launch in the U.S.
- In June, Madrigal presented results from the MAESTRO-NAFLD-1 study in a late-breaking oral abstract at the European Association for the Study of the Liver’s (EASL) International Liver Congress.
- Also in June, Madrigal launched the NASHExplored website for healthcare professionals and expanded its partnerships with leading patient advocacy groups.
- In August, Madrigal initiated the Phase 3 MAESTRO-NASH OUTCOMES trial. This noninvasive trial will evaluate the effects of resmetirom on progression to liver decompensation events in patients with compensated NASH cirrhosis. Positive results from this trial have the potential to expand the indication for resmetirom to include patients with compensated NASH cirrhosis and provide a faster route to full approval in noncirrhotic NASH.
- In November, Madrigal presented additional data from the Phase 3 MAESTRO trials in oral presentations at the American Association for the Study of Liver Disease (AASLD) Liver Meeting.
- In December, Madrigal announced positive topline results from the Phase 3 MAESTRO-NASH trial. Resmetirom achieved both primary endpoints with both daily oral doses, 80 mg and 100 mg, relative to placebo. The results established resmetirom as the first and only investigational medication to demonstrate both NASH resolution and fibrosis improvement in Phase 3.
- Also in December, Madrigal announced $300+ million in financing events to support planned commercial and clinical activities through potential accelerated approval of resmetirom in the U.S.

Financial Results for the Three and Twelve Months Ended December 31, 2022

As of December 31, 2022, Madrigal had cash, cash equivalents and marketable securities of $358.8 million, compared to $270.3 million at December 31, 2021. The increase in cash and marketable securities was primarily from equity offerings and our Loan Facility, partially offset by cash used in operations of $224.9 million.

Operating expenses were $85.3 million and $293.6 million for the three and twelve month periods ended December 31, 2022, compared to $64.6 million and $242.5 million in the comparable prior year periods.

Research and development expenses for the three and twelve month periods ended December 31, 2022 were $70.7 million and $245.4 million, compared to $52.9 million and $205.2 million in the comparable prior year periods. The increases are attributable primarily to additional activities related to the Phase 3 clinical trials, an increase in head count, and an increase in non-cash stock compensation expense.

General and administrative expenses for the three and twelve month periods ended December 31, 2022 were $14.6 million and $48.1 million, compared to $11.7 million and $37.3 million in the comparable prior year periods. The increases are attributable primarily to increases in commercial preparation activities, including an increase in headcount and an increase in non-cash stock compensation expense.

Interest income for the three and twelve month periods ended December 31, 2022 was $1.1 million and $2.2 million, compared to $0.1 million and $0.4 million in the comparable prior year periods. The increases in interest income for the latest three and twelve month periods were due primarily to a higher average interest rates in 2022.

Interest expense for the three and twelve month periods ended December 31, 2022 was $1.7 million and $4.0 million, compared to $0 million and $0 million in the comparable prior year periods. The increase in interest expense was as a result of the Loan Facility we entered with Hercules and increases in interest rates throughout the year.

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

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 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, randomized 1:1:1 to receive once-daily resmetirom 80 mg, resmetirom 100 mg, or placebo. After 52 weeks of treatment, a second liver biopsy is performed. 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. Achievement of either primary endpoint was considered a successful trial outcome. A key secondary endpoint was lowering of LDL-C.

Patients enrolled in the MAESTRO-NASH study (up to 2,000 in total) 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.

MAESTRO-NAFLD-1 was initiated in December 2019 and the 52-week multicenter, randomized, placebo-controlled Phase 3 study of resmetirom in over 1,200 patients with NAFLD, presumed NASH, has completed the double-blind arms and an open-label 100 mg arm. An additional open-label active treatment arm in patients with early (well-compensated) NASH cirrhosis is ongoing. The primary endpoint was to evaluate the safety and tolerability of resmetirom. A separate 52 week Phase 3 clinical trial, an open-label extension study of MAESTRO-NAFLD-1 (MAESTRO-NAFLD-OLE), is ongoing.

Patients in the 52-week Phase 3 MAESTRO-NAFLD-1 study were randomized 1:1:1:1 to receive once-daily resmetirom 80 mg, resmetirom 100 mg, placebo in double-blind arms or resmetirom 100 mg in an open-label arm. MAESTRO-NAFLD-1 (unlike MAESTRO-NASH), did not include a liver biopsy and represents a “real-life” NASH study. Patients with 3 metabolic risk factors were documented with NASH or NAFLD by historical liver biopsy or noninvasive techniques. 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 and several key secondary endpoints were met, including LDL-C, apolipoprotein B, and triglyceride lowering and reduction of liver fat as determined by MRI-PDFF. Additional secondary and exploratory endpoints were assessed including reduction in liver enzymes, FibroScan, and MRE scores, and other NASH biomarkers.

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, will form the basis for a planned subpart H submission to FDA for accelerated approval of resmetirom for treatment of NASH.

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.

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)-β 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 referenced by forward-looking statement identifiers, including the examples in the paragraph below; resmetirom's potential to be a cost-effective specialty therapy for NASH patients with significant liver fibrosis; 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, 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," "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, 2022, filed with the SEC on February 23, 2023, as updated from time to time by Madrigal's other filings with the SEC.

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Madrigal Pharmaceuticals, Inc.
Condensed Consolidated Statements of Operations
(in thousands, except share and per share amounts)
(unaudited)

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2022	**2021**	**2022**	**2021**
Revenues:				
Total revenues	$ -	$ -	$ -	$ -
Operating expenses:				
Research and development	70,742	52,889	245,441	205,164
General and administrative	14,557	11,712	48,130	37,318
Total operating expenses	85,299	64,601	293,571	242,482

Loss from operations	(85,299)	(64,601)	(293,571)	(242,482)
Interest income, net	1,076	52	2,185	363
Interest expense	(1,682)	-	(3,964)	-
Other income	-	-	-	273
Net loss	$ (85,905)	$ (64,549)	$ (295,350)	$ (241,846)
Basic and diluted net loss per common share	$ (4.98)	$ (3.78)	$ (17.23)	$ (14.63)
Basic and diluted weighted average number of common shares outstanding	17,237,517	17,074,543	17,137,201	16,535,188

Madrigal Pharmaceuticals, Inc.
Condensed Consolidated Balance Sheets
(in thousands)
(unaudited)

	December 31, 2022	December 31, 2021
Assets		
Cash, cash equivalents and marketable securities	$ 358,774	$ 270,346
Other current assets	2,595	1,338
Other non-current assets	1,203	1,648
Total assets	$ 362,572	$ 273,332
Liabilities and Equity		
Current liabilities	$ 115,894	$ 76,838
Long-term liabilities	49,289	387
Stockholders' equity	197,389	196,107
Total liabilities and stockholders' equity	$ 362,572	$ 273,332

Source: Madrigal Pharmaceuticals, Inc.