Madrigal Pharmaceuticals Provides an Overview of Upcoming Resmetirom Data Presentations and Reports 2022 Third Quarter Financial Results

November 3, 2022

- *Two resmetirom oral abstracts to be presented at the AASLD Liver Meeting®:*
  - *Phase 3 MAESTRO-NAFLD-1 data demonstrate the potential of resmetirom for the treatment of patients with compensated NASH cirrhosis*
  - *Screening data from the Phase 3 MAESTRO-NASH biopsy study provide new insights on noninvasive strategies for patient identification*
- *Madrigal remains on track to announce topline data from the Phase 3 MAESTRO-NASH biopsy study in the fourth quarter*

CONSHOHOCKEN, Pa., Nov. 03, 2022 (GLOBE NEWSWIRE) -- Madrigal Pharmaceuticals, Inc. (NASDAQ:MDGL), a clinical-stage biopharmaceutical company pursuing novel therapeutics for nonalcoholic steatohepatitis (NASH), today provides an overview of upcoming resmetirom Phase 3 data presentations and reports third quarter 2022 financial results.

Paul Friedman, M.D., Chief Executive Officer of Madrigal, stated, “The Madrigal team is focused on delivering topline data from the pivotal MAESTRO-NASH biopsy study in Q4 2022. Positive results from the study would allow us to finalize our new drug application for resmetirom, with the goal of filing for Subpart H accelerated approval in the first half of 2023. The efficacy and safety data we are generating across four Phase 3 MAESTRO studies put Madrigal in a strong position to navigate this accelerated approval pathway and potentially address the unmet needs of patients who currently have no approved therapy to treat NASH with significant fibrosis.”

Becky Taub, M.D., Chief Medical Officer and President of Research & Development of Madrigal, stated, "The MAESTRO program continues to generate data that reinforce our conviction in the potential of resmetirom to become a foundational therapy for patients with NASH. At the upcoming American Association for the Study of Liver Diseases (AASLD) Liver Meeting, we’ll be presenting results from the compensated NASH cirrhosis cohort studied in MAESTRO-NAFLD-1. The safety and efficacy data in this more advanced patient population helped support our decision to initiate the Phase 3 MAESTRO-NASH Outcomes study, a noninvasive clinical endpoint study that assesses the rate of progression from early well-compensated NASH cirrhosis to decompensated NASH cirrhosis.”

Dr. Taub continued, “A second oral presentation at AASLD will examine the ability of several noninvasive strategies to identify NASH patients with significant liver fibrosis using screening data from the MAESTRO-NASH biopsy study. Given the comprehensive diagnostic strategies included in MAESTRO studies, Madrigal has a unique opportunity to define noninvasive measures to diagnose and manage patients with NASH in real world clinical practice.”

Presentations at the AASLD Liver Meeting

The following abstracts have been accepted for presentation at the AASLD Liver Meeting, taking place November 4-8 in Washington, DC:

Oral Presentation (abstract 100): Sunday, November 6th
A 52-week Phase 3 clinical trial of resmetirom in 180 patients with well-compensated NASH cirrhosis. Presenter: Stephen Harrison

In patients with well-compensated cirrhosis included in an open-label active resmetirom treatment arm of the Phase 3 MAESTRO-NAFLD-1 safety study, resmetirom lowered markers of cardiovascular risk and NASH fibrosis. Following 52 weeks of treatment with resmetirom, patients achieved reductions in magnetic resonance imaging proton density fat fraction (MRI-PDFF), FibroScan controlled attenuation parameter (CAP), FibroScan vibration-controlled transient elastography (VCTE), magnetic resonance elastography (MRE), liver and spleen volume, ALT, AST, GGT, LDL-C, triglycerides, ApoB, and lipoprotein (a). Resmetirom appeared safe and was well-tolerated during 52 weeks of treatment.

Oral Presentation (abstract 102): Sunday, November 6th
Utility of FIB-4, MRE, MRI and FibroScan to identify patients with at-risk F2-F3 NASH based on screening data from a 2000 patient biopsy confirmed cohort of the resmetirom Phase 3 clinical trial, MAESTRO-NASH. Presenter: Rohit Loomba

FIB-4 of ≥1.3 is frequently used to identify potential at-risk patients with NASH, but an analysis of screening data from the MAESTRO-NASH biopsy study found this threshold lacked the sensitivity to accurately identify patients with NASH with significant fibrosis (F2-F3). The authors concluded the influence of age on FIB-4 may require an age adjustment to ensure younger patients are not removed from consideration for therapy. MRE, MAST (MRI-AST) and FAST (FibroScan-AST) showed reasonable accuracy for identifying patients with NASH with significant fibrosis.

Financial Results for the Nine Months Ended September 30, 2022

As of September 30, 2022, Madrigal had cash, cash equivalents and marketable securities of $153.2 million, compared to $270.3 million at December 31, 2021. This decrease in cash and marketable securities resulted primarily from cash used in operations for the nine months ended September 30, 2022 of $166.3 million, partially offset by the net proceeds ($49 million) from the Loan Facility (“Loan Facility”) with Hercules Capital, Inc. (“Hercules”).

Operating expenses were $80.4 million and $208.3 million for the three month and nine month periods ended September 30, 2022, compared to $63.2 million and $177.9 million in the comparable prior year periods.

Research and development expenses for the three and nine month periods ended September 30, 2022 were $68.3 million and $174.7 million, compared to $54.9 million and $152.3 million in the comparable prior year periods. The increase is attributable primarily to additional activities related to the Phase 3 clinical trials, and an increase in head count.

General and administrative expenses for the three and nine month periods ended September 30, 2022 were $12.1 million and $33.6 million, compared to $8.3 million and $25.6 million in the comparable prior year periods. The increase is due primarily to increases in commercial preparation activities, including an increase in headcount and an increase in non-cash stock compensation.

Interest income for the three and nine month periods ended September 30, 2022 was $0.7 million and $1.1 million, compared to $0.1 million and $0.3 million in the comparable prior year periods. These increases in interest income were due primarily to higher average interest rates in 2022.

Interest expense for the three and nine month periods ended September 30, 2022 was $1.5 million and $2.3 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 with Hercules, which we closed in May of 2022.

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 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 biopsy is performed. The dual primary surrogate endpoints on biopsy are 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 NASH. Achievement of either primary endpoint is considered a successful trial outcome. A key secondary endpoint is lowering of LDL-C. The planned target enrollment was announced as completed on June 30, 2021.

All 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.

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 and other data, including safety parameters, will form the basis for a potential 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 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 our beliefs and assumptions and on information currently available to us, but are subject to factors beyond our control. Forward-looking statements include but are not limited to statements or references concerning: anticipated or estimated future results, including the risks and uncertainties associated with our future operating performance and financial position; our possible or assumed future results of operations and expenses, business strategies and plan (including ex-US. Launch/partnering plans), including incurrence of indebtedness and compliance with debt covenants under the Loan and Security Agreement with Hercules Capital, Inc., as agent and lender, market trends, market sizing, competitive position, industry environment and potential growth opportunities, among other things; our ability to delay certain research activities and related clinical expenses as necessary; our clinical trials, including the anticipated timing of disclosure, presentations of data from, or outcomes from our trials; research and development activities, and the timing and results associated with the future development of our lead product candidate, resmetirom (formerly known as MGL-3196), including projected market size, sector leadership, and patient treatment estimates for NASH and NAFLD patients; 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 for noncirrhotic NASH patients with compensated cirrhosis; our primary and key secondary study endpoints for resmetirom and the potential for achieving such endpoints and projections, including NASH resolution, safety, fibrosis treatment, cardiovascular effects, and lipid treatment with resmetirom; our ability to address the unmet needs of patients suffering from NASH with significant fibrosis; 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; the potential efficacy and safety of resmetirom for noncirrhotic NASH patients and cirrhotic NASH patients; the potential for resmetirom to become the best-in-class and/or first-to-market treatment option for patients with NASH and liver fibrosis; anticipated or estimated future results of operations and expenses as we expand our resmetirom clinical development program and our commercial development program; ex-U.S. launch/partnering plans; the ability to develop clinical evidence demonstrating the utility of noninvasive tools and techniques to screen and diagnose NASH and/or NAFLD patients; the predictive power of liver fat reduction with resmetirom, as measured by noninvasive tests, on NASH resolution and/or fibrosis reduction or improvement, and potential NASH or NAFLD patient risk profile benefits with resmetirom; the predictive power of liver fat, liver volume changes or MAST scores for NASH and/or NAFLD patients; the predictive power of NASH resolution and/or liver fibrosis reduction or improvement with resmetirom using noninvasive tests, including the use of ELF, FibroScan, MRE and/or MRI-PDFF; the predictive power of noninvasive tests generally, including for purposes of diagnosing NASH, monitoring patient response to resmetirom, or recruiting and conducting a NASH clinical trial; market demand for and acceptance of our products; research, development and commercialization of new products; obtaining and maintaining regulatory approvals, including, but not limited to, potential regulatory delays or rejections; risks associated with meeting the objectives of our clinical studies, including, but not limited to our ability to achieve enrollment objectives concerning patient numbers (including an adequate safety database), outcomes objectives and/or timing objectives for our studies, any delays or failures in enrollment, the occurrence of adverse safety events, and the risks of successfully conducting trials that are substantially larger, and have patients with different disease states, than our past trials; risks related to the effects of resmetirom' s mechanism of action and our ability to accomplish our business and business development objectives and realize the anticipated benefit of any such transactions; the achievement of enrollment objectives concerning patient number, safety database and/or timing for our studies; and assumptions underlying any of the foregoing.

Forward-looking statements reflect management's current knowledge, assumptions, judgment and expectations regarding forward-looking statements, future performance or events; include all statements that are not historical facts; and 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," informed," "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: our clinical and commercial development of resmetirom; enrollment and trial outlook uncertainties, generally, based on blinded, locked or limited trial data and in relation to COVID-19 related measures and individual precautionary measures that may be implemented or continued for an uncertain period of time; our potential inability to raise sufficient capital to fund our ongoing operations as currently planned or to obtain financings on terms similar to those we have arranged in the past; our ability to service our indebtedness and otherwise comply with our 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 our prior studies; limitations associated with early stage or non-placebo controlled study data; 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 or furnished with the U.S. Securities and Exchange Commission 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. We specifically discuss these risks and uncertainties in greater detail in the section appearing in Part I, Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2021, filed with the SEC on February 25, 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 our other filings with the SEC.

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(Tables follow)

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Revenues:				
Total revenues	$ -	$ -	$ -	$ -
Operating expenses:				
Research and development	68,271	54,873	174,699	152,275

General and administrative	12,141	8,287	33,573	25,606
Total operating expenses	80,412	63,160	208,272	177,881
Loss from operations	(80,412)	(63,160)	(208,272)	(177,881)
Interest income, net	717	60	1,109	311
Interest expense	(1,502)	-	(2,282)	-
Other income	-	-	-	273
Net loss	$ (81,197)	$ (63,100)	$ (209,445)	$ (177,297)
Basic and diluted net loss per common share	$ (4.75)	$ (3.79)	$ (12.25)	$ (10.84)
Basic and diluted weighted average number of common shares outstanding	17,103,395	16,639,776	17,103,395	16,353,428

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

	September 30, 2022	December 31, 2021
Assets		
Cash, cash equivalents and marketable securities	$ 153,192	$ 270,346
Other current assets	3,920	1,338
Other non-current assets	1,532	1,648
Total assets	$ 158,644	$ 273,332
Liabilities and Equity		
Current liabilities	$ 98,920	$ 76,838
Long-term liabilities	49,054	387
Stockholders' equity	10,670	196,107
Total liabilities and stockholders' equity	$ 158,644	$ 273,332

Source: Madrigal Pharmaceuticals, Inc.