Madrigal Pharmaceuticals Provides Clinical and Business Updates and Reports 2022 First Quarter Financial Results

May 9, 2022

- *MAESTRO-NAFLD-1 late-breaker and three other Madrigal abstracts accepted for oral presentation at the EASL International Liver Congress™*
- *Data from the Phase 3 MAESTRO-NAFLD-1 study continue to reinforce the safety and efficacy profiles of resmetirom*
- *Madrigal remains on track to disclose topline data from MAESTRO-NASH in the fourth quarter and anticipates filing for accelerated approval under Subpart H next year*
- *Planned MAESTRO-NASH Outcomes trial, a non-invasive Phase 3 study designed to accelerate the full approval timeline for non-cirrhotic NASH, will evaluate resmetirom effects on liver decompensation events in patients with early NASH cirrhosis*
- *Madrigal enters into term loan facility with ability to draw up to $250 million to support expansion of clinical development program and preparation for a potential U.S. launch of resmetirom*

Company to host conference call at 8:00 AM ET, May 9th, 2022

CONSHOHOCKEN, Pa., May 09, 2022 (GLOBE NEWSWIRE) -- Madrigal Pharmaceuticals, Inc. (NASDAQ:MDGL), a clinical-stage biopharmaceutical company pursuing novel therapeutics for non-alcoholic steatohepatitis (NASH), today announced acceptance of four abstracts for oral presentation at the European Association for the Study of the Liver's (EASL) International Liver Congress, including a late-breaker presentation of data from the Phase 3 MAESTRO-NAFLD-1 trial, as well as other resmetirom clinical development program updates. The Company also reported financial results for the first quarter of 2022, including the completion of a $250 million term loan facility to support resmetirom clinical and commercial development objectives and position Madrigal for a potential first-to-market launch in NASH. The company drew $50 million from the facility at closing and has the ability to draw a further $200 million under the agreement.

Paul Friedman, M.D., Chief Executive Officer of Madrigal, stated, "The MAESTRO-NAFLD-1 data as described below have reinforced our confidence in the safety and potential efficacy of resmetirom in treating non-cirrhotic NASH with significant fibrosis. We look forward to sharing detailed MAESTRO-NAFLD-1 results in a late-breaking presentation at EASL followed by topline results from the MAESTRO-NASH biopsy study in Q4. Based on the totality of efficacy data generated thus far in our clinical development program, we believe resmetirom can both address the underlying drivers of NASH in the liver and also reduce the level of fibrosis that is associated with progression to more advanced disease."

Dr. Friedman added, "The term loan facility we are announcing today strengthens Madrigal's balance sheet, providing an additional source of funding that can be drawn at the appropriate times to meet our operational needs and support our strategic priorities, including a new MAESTRO study and the ramp-up for the potential launch of resmetirom in the U.S."

Becky Taub, M.D., Chief Medical Officer and President of Research & Development of Madrigal, stated, "We are planning to expand our NASH development program by initiating a second study in the next few months to complement the clinical outcomes portion of MAESTRO-NASH; this second study, MAESTRO-NASH Outcomes, will non-invasively examine liver-related outcomes (decompensation events) in patients with early NASH cirrhosis. In contrast, MAESTRO-NASH relies primarily on serial liver biopsy to measure progression to cirrhosis. Resmetirom has been studied in over 180 patients with well-compensated NASH cirrhosis in an open-label arm of MAESTRO-NAFLD-1. The safety and efficacy results that will be presented at EASL are supportive of a potential for benefit in this population. A positive outcome in this study, in a group of patients with the highest unmet need, has the potential to significantly broaden the label for resmetirom and increase the commercial opportunity. Furthermore, it is expected to accelerate the path to full approval and enhance the statistical power to assess benefit in patients with non-cirrhotic NASH. The addition of MAESTRO-NASH Outcomes does not alter our timeline for the subpart H NDA submission in non-cirrhotic NASH that is based on the results of the liver biopsy portion of MAESTRO-NASH."

Dr. Taub added, "As we have continued to gain confidence that we will achieve both the NASH resolution as well as the fibrosis improvement endpoints in the MAESTRO-NASH biopsy study we are moving one point fibrosis reduction up the hierarchy to a primary endpoint along with NASH resolution. While we expect to achieve both endpoints, dual primaries allow for a successful outcome of the study that can be filed for subpart H approval if either the NASH resolution or one point fibrosis reduction liver biopsy endpoint is met."

Stephen Harrison, M.D., Medical Director for Pinnacle Clinical Research, San Antonio, Texas, Visiting Professor of Hepatology, Oxford University, and Principal Investigator of the MAESTRO studies commented, "There is an urgent need for NASH treatments that can prevent progression to hepatic decompensation in patients at the early stages of NASH cirrhosis, but few late-stage development programs have focused on this population. The MAESTRO-NASH Outcomes study will help us determine if resmetirom can benefit patients with more advanced disease and achieve the endpoints that are valued most by healthcare providers, regulators, payers and, most importantly, patients."

Clinical Program Updates

Late-Breaking Presentation and Multiple Oral Presentations at EASL
Multiple resmetirom abstracts have been accepted at EASL's International Liver Congress taking place June 22-26 in London:

- Late-breaking presentation: "Primary data analyses of MAESTRO-NAFLD-1, a 52 week double-blind placebo-controlled phase 3 clinical trial of resmetirom in patients with NAFLD" [Saturday, June 25 at 3:00 PM. Presenter: Stephen Harrison]
- Oral presentation: "Impact of resmetirom-mediated reductions in liver volume and steatosis compared with placebo on the quantification of fibrosis using second harmonic generation in a serial liver biopsy study" [Thursday, June 23 at 4:00 PM. Presenter: Dean Tai]
- Oral presentation: "Utility of FIB-4 thresholds to identify patients with at-risk F2-F3 NASH based on screening data from a 2000 patient biopsy confirmed cohort of resmetirom Phase 3 clinical trial, MAESTRO-NASH" [Saturday, June 25 at 9:15 AM. Presenter: Jörn Schattenberg]
- Oral presentation: "Biomarkers, imaging and safety in a well-compensated NASH cirrhotic cohort treated with resmetirom, a thyroid hormone receptor beta agonist, for 52 weeks" [Saturday, June 25 at 5:45 PM. Presenter: Stephen Harrison]
- Poster: "A higher Fibrosis-4 (FIB-4) score is associated with higher healthcare costs and hospitalizations in patients with nonalcoholic steatohepatitis" [Presenter: Elliot Tapper]
- Poster: "Retrospective AI-based measurement of NASH histology (AIM-NASH) analysis of biopsies from Phase 2 study of Resmetirom confirms significant treatment-induced changes in histologic features of non-alcoholic steatohepatitis" [Presenter: Janani Iyer]

Additional Phase 3 MAESTRO-NAFLD-1 Data
In January, Madrigal announced that primary and key secondary endpoints from the double-blind, placebo-controlled, 969-patient MAESTRO-NAFLD-1 safety study were achieved; resmetirom was safe and well-tolerated and provided significant reductions in liver fat, LDL-c and other atherogenic lipids vs. placebo.

Similar to what has been reported for the 100 mg open-label arm, patients in the resmetirom 80 mg and 100 mg double-blind arms achieved reductions in ALT ($p=0.002$; <0.0001) relative to placebo. ALT increases ≥3 times the upper limit of normal occurred in 0.61% in the resmetirom 80 mg group, 0.31% in the 100 mg group and 1.6% of patients in the placebo group.

Treatment-emergent adverse events ≥ grade 3 in severity occurred in 7.6% of patients in the resmetirom 80 mg group, 9.0% in the 100 mg group and 9.1% in the placebo group. Withdrawals due to adverse events were 2.4% in the 80 mg group, 2.8% in the 100 mg group and 1.3% in the placebo group. GI-related adverse events (diarrhea, nausea) were increased relative to placebo at the initiation of therapy but not after the first few weeks.

FibroScan CAP (controlled attenuation parameter) scores reflective of hepatic fat were statistically significantly ($p<0.0001$) reduced in resmetirom arms as compared with placebo. FibroScan liver stiffness reductions were similar in the 100 mg open-label and double-blind arms. Responder analyses of FibroScan vibration-controlled transient elastography (VCTE) reduction and % reduction from baseline comparing resmetirom 100 mg open-label and double-blind arms with placebo showed a significant increase in responders in resmetirom treatment arms (~44% averaged across the arms) compared with placebo (25%); magnetic resonance elastography (MRE) responders as measured by kPa reduction were significantly greater in resmetirom-treated groups compared with placebo. Mean reduction in FibroScan VCTE in resmetirom double-blind patients was greater than placebo but not statistically significant.

Detailed results of MAESTRO-NAFLD-1 are under embargo until the late-breaking presentation at EASL.

MAESTRO-NASH Outcomes Study
In the next few months, Madrigal plans to initiate a second NASH outcomes study, MAESTRO-NASH Outcomes, a randomized double-blind placebo-controlled study in approximately 700 patients with early NASH cirrhosis to allow for non-invasive monitoring of progression to liver decompensation events. Several biomarker and imaging techniques will also be employed to assess correlates with disease progression. Ongoing open-label studies of more than 180 patients with well-compensated NASH cirrhosis (MAESTRO-NAFLD-1 open-label arm) support the potential of resmetirom in this patient population.

Previously reported data from the patients with NASH cirrhosis in the open-label arm of MAESTRO-NAFLD-1 demonstrated that resmetirom reduced hepatic fat, liver volume, liver enzymes, fibrosis markers and atherogenic lipids. Madrigal will be presenting additional results from the MAESTRO-NAFLD-1 cirrhosis population in an oral presentation at EASL.

Term Loan Facility to Support Expansion of Clinical Development Program and Resmetirom Launch

Madrigal has secured a $250 million term loan facility with Hercules Capital, Inc. (NYSE: HTGC), a leader in customized specialty financing for life sciences companies. The committed capital strengthens Madrigal's balance sheet, providing an additional source of funding both to support the expanded clinical program and ramp-up for a potential launch of resmetirom in the U.S.

Under the terms of the loan agreement, $50 million was drawn at closing. Madrigal may also draw an additional $125 million in two separate tranches upon achievement of resmetirom clinical and regulatory milestones. An additional $75 million may be drawn by Madrigal, subject to the approval of Hercules Capital. The loan facility has a floor rate of 7.45% and adjusts with future changes in the prime rate, subject to the floor rate. The loan bears initial interest at a rate of 7.95%. Madrigal will pay interest-only for a period of 30 months, which may be extended to 60 months upon the achievement of certain milestones. The loan matures in

May 2026 and may be extended an additional year upon the achievement of certain milestones.

R. Bryan Jadot, Senior Managing Director and Life Sciences Group Head at Hercules Capital stated, “Hercules is pleased to provide both upfront funding and future potential funding capacity to help Madrigal deliver on its important mission to address a large unmet medical need and improve the lives of people suffering from NASH and liver disease.”

Additional details of the loan agreement will be filed with the Securities and Exchange Commission on a Current Report on Form 8-K.

Financial Results for the Three Months Ended March 31, 2022

As of March 31, 2022, Madrigal had cash, cash equivalents and marketable securities of $220.0 million, compared to $270.3 million at December 31, 2021. The decrease in cash and marketable securities resulted primarily from cash used in operations of $49.9 million.

Operating expenses were $57.6 million for the three month period ended March 31, 2022, compared to $53.0 million in the comparable prior year period.

Research and development expenses for the three month period ended March 31, 2022 were $47.9 million, compared to $45.8 million in the comparable prior year period. 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 month period ended March 31, 2022 were $9.7 million, compared to $7.2 million in the comparable prior year period. The increase in general and administrative expenses for the latest three month period is due primarily to increases in commercial preparation activities, including an increase in headcount.

Interest income for the three month period ended March 31, 2022 was $0.1 million, compared to $0.2 million in the comparable prior year period. The decrease in interest income was due primarily to a lower average principal balance in our investment account in 2022.

Conference Call at 8:00 am EST

Madrigal will hold a conference call and webcast at 8:00 am EST. To access the conference call, please dial (833) 660-2754 for domestic callers or (409) 350-3497 for international callers and reference conference ID: 9765409. To access the live webcast of the call with slides please visit the Investors section of Madrigal’s website or click here. An archived webcast will be available on the Madrigal website after the event.

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

Madrigal is currently conducting two Phase 3 Clinical trials, MAESTRO-NASH and MAESTRO-NAFLD-1, to demonstrate the safety and efficacy of resmetirom for the treatment of NASH.

MAESTRO-NASH is a Phase 3 multi-center, double-blind, randomized, placebo-controlled study of resmetirom in patients with liver biopsy confirmed NASH and was initiated in March 2019. The study targeted enrollment of 900 patients with biopsy-proven NASH (fibrosis stage 2 or 3, at least 450 fibrosis stage 3), randomized 1:1:1 to receive resmetirom 80 mg once a day, 100 mg once a day, or placebo. After 52 weeks of treatment a second biopsy is performed. The dual primary surrogate endpoints on biopsy are NASH resolution, with at least a 2-point reduction in NAS (NASH Activity Score), and with no worsening of fibrosis OR a one point decrease in fibrosis with no worsening of NASH. Either primary endpoint can be achieved for a successful trial outcome. A key secondary endpoint is lowering of LDL-cholesterol. The planned target enrollment was announced as completed on June 30, 2021.

The first 900 patients in the MAESTRO-NASH study will continue on therapy after the initial 52-week treatment period; up to another 1,100 patients are to be added using the same randomization plan. The study is expected to continue 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 Phase 3 multi-center, double-blind, randomized, placebo-controlled study of resmetirom in over 1,200 patients with non-alcoholic fatty liver disease (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 is to evaluate the safety and tolerability of resmetirom. An open-label extension study, MAESTRO-NAFLD-OLE is ongoing.

Patients in the 52-week blinded phase of MAESTRO-NAFLD-1 were randomized 1:1:1:1 to receive resmetirom 80 mg once a day, 100 mg once a day, placebo or a 100 mg resmetirom 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 non-invasive techniques. Using non-invasive 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. These key secondary endpoints included LDL-cholesterol, apolipoprotein B and

triglyceride (TG) 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 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 for the treatment of NASH.

About Madrigal Pharmaceuticals

Madrigal Pharmaceuticals, Inc. (Nasdaq: MDGL) is a clinical-stage biopharmaceutical company pursuing novel therapeutics for non-alcoholic 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 that is designed to target key underlying causes of NASH in the liver. Resmetirom is currently being evaluated in two Phase 3 clinical studies, MAESTRO-NASH and MAESTRO-NAFLD-1, designed to demonstrate multiple benefits in patients with NASH. For more information, visit www.madrigalpharma.com.

Forward Looking Statements

This communication contains "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: our clinical trials, including the anticipated timing of disclosure, presentations of data from, or outcomes from our trials; research and development activities; market size and patient treatment estimates for NASH and NAFLD patients; the timing and results associated with the future development of our lead product candidate, MGL-3196 (resmetirom); our primary and secondary study endpoints for resmetirom and the potential for achieving such endpoints and projections; plans, objectives and timing for making a Subpart H (Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses) submission to FDA; optimal dosing levels for resmetirom; projections regarding potential future NASH resolution, safety, fibrosis treatment, cardiovascular effects, lipid treatment and/or biomarker effects with resmetirom; the potential efficacy and safety of resmetirom for non-cirrhotic NASH patients and cirrhotic NASH patients; ex-U.S. launch/partnering plans; the predictive power of liver fat reduction, as measured by non-invasive tests, on NASH resolution with fibrosis reduction or improvement; the predictive power of liver fat, liver volume changes or MAST scores for NASH and/or NAFLD patients; the effects of resmetirom' s mechanism of action; the achievement of enrollment objectives concerning patient number, safety database and/or timing for our studies; the predictive power of NASH resolution and/or liver fibrosis reduction or improvement with resmetirom using non-invasive tests, including the use of ELF, FibroScan, MRE and/or MRI-PDFF; the ability to develop clinical evidence demonstrating the utility of non-invasive tools and techniques to screen and diagnose NASH and/or NAFLD patients; the predictive power of non-invasive tests generally, including for purposes of diagnosing NASH, monitoring patient response to resmetirom, or recruiting a NASH clinical trial; potential NASH or NAFLD patient risk profile benefits with resmetirom; the potential for resmetirom to become the best-in-class and/or first-to-market treatment option for patients with NASH and liver fibrosis; and our possible or assumed future results of operations and expenses, business strategies and plans, capital needs and financing plans, trends, market sizing, competitive position, industry environment and potential growth opportunities, among other things. 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; and can be identified by terms such as "accelerate," "achieve," "allow," "anticipates," "be," "believes," "can," "continue," "could," "demonstrate," "design," "estimates," "expectation," "expects," "forecasts," "future," "goal," "hopeful," "inform," "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. Although management presently believes that the expectations reflected in such forward-looking statements are reasonable, it can give no assurance that such expectations will prove to be correct and you should be aware that actual results could differ materially from those contained in the forward- looking statements.

Forward-looking statements are subject to a number of risks and uncertainties including, but not limited to: our clinical development of resmetirom; enrollment uncertainties, generally and in relation to COVID-19-related measures that may be continued for an uncertain period of time or implemented; outcomes or trends from competitive studies; future topline data timing or results; the risks of achieving potential benefits in studies that include 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 entitled "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2021, our Quarterly Report on form 10-Q for the Quarter ended March 31, 2022, and in our other filings with the SEC.

Investor Contact
Alex Howarth, Madrigal Pharmaceuticals, Inc., IR@madrigalpharma.com

Media Contacts
Christopher Frates, Madrigal Pharmaceuticals, Inc., media@madrigalpharma.com

(Tables follow)

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

	Three Months Ended March 31,	
	2022	**2021**
Revenues:		
Total revenues	$ -	$ -
Operating expenses:		
Research and development	47,929	45,770
General and administrative	9,658	7,209
Total operating expenses	57,587	52,979
Loss from operations	(57,587)	(52,979)
Interest income, net	69	160
Other income	-	273
Net loss	$ (57,518)	$ (52,546)
Basic and diluted net loss per common share	$ (3.36)	$ (3.32)
Basic and diluted weighted average number of common shares outstanding	17,103,395	15,840,401

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

	March 31, 2022	**December 31, 2021**
Assets		
Cash, cash equivalents and marketable securities	$ 219,953	$ 270,346
Other current assets	1,217	1,338
Other non-current assets	1,492	1,648
Total assets	$ 222,662	$ 273,332
Liabilities and Equity		
Current liabilities	$ 76,635	$ 76,838
Long-term liabilities	283	387
Stockholders' equity	145,744	196,107
Total liabilities and stockholders' equity	$ 222,662	$ 273,332

Madrigal Pharmaceuticals

Source: Madrigal Pharmaceuticals, Inc.