Madrigal Pharmaceuticals Provides Corporate Update and Reports 2021 Third Quarter Financial Results

November 4, 2021

Several abstracts with data from the open-label arm of the Phase 3 MAESTRO-NAFLD-1 study accepted for presentation at AASLD's upcoming The Liver Meeting® 2021

CONSHOHOCKEN, Pa., Nov. 04, 2021 (GLOBE NEWSWIRE) -- Madrigal Pharmaceuticals, Inc. (NASDAQ:MDGL) today provides a summary of corporate accomplishments and reports its third quarter 2021 financial results.

Paul Friedman, M.D., Chief Executive Officer of Madrigal, stated, "Throughout the third quarter, the Madrigal team continued to progress MAESTRO-NASH, the pivotal serial liver biopsy study and a key component of the Phase 3 program for resmetirom for patients with non-alcoholic steatohepatitis, NASH. We remain on track to complete the double-blind portion of our Phase 3 non-invasive imaging and biomarker study, MAESTRO-NAFLD-1, and report topline data by year-end, with additional topline data rollout in early 2022. We will also be presenting additional data from the open-label portion of this study at the American Association for the Study of Liver Diseases (AASLD) The Liver Meeting® on November 12-15th."

Becky Taub, M.D., Chief Medical Officer and President of Research & Development at Madrigal stated, "Data from the recently completed 52 week open-label arm of the MAESTRO-NAFLD-1 study will be presented at AASLD and provides our most informed insights to date regarding the effects of resmetirom in presumed NASH patients, using a variety of non-invasive tests relevant to clinical practice. The double-blinded MAESTRO-NAFLD-1 and MAESTRO NASH studies readouts over the forthcoming months will further inform our understanding of how to identify and monitor NASH patients with significant fibrosis."

Dr. Taub added, "In October, in recognition of Liver Awareness Month, we announced our alliance with the Fatty Liver Foundation, a leading patient advocacy organization focused on the diagnosis, treatment and support of individuals with non-alcoholic fatty liver disease or NAFLD and NASH. Our alliance with the Foundation is in support of their NAFLD Screening Fund and aligns with our commitment to advance the use of non-invasive techniques to improve the diagnosis and staging of NAFLD and NASH and identify people at risk of NASH earlier in the course of their disease."

Several abstracts summarizing data from the open-label arms of the MAESTRO-NAFLD-1 study have been accepted for presentation at AASLD's The Liver Meeting® 2021. Madrigal will host a webcast and conference call on Tuesday, November 16th at 8.00 AM ET to summarize and discuss the data that are being presented.

AASLD Presentations

- *Friday, November 12, 2021*: Late-breaker Poster Presentation (abstract #LP21)

Biomarkers, imaging and safety in resmetirom 52 week non-cirrhotic NASH Phase 3 clinical trial, completed open-label arm of MAESTRO-NAFLD-1

- *Friday November 12, 2021:* Poster Presentation (abstract #1922)
  Liver volume reduction in resmetirom treated non-cirrhotic and cirrhotic NASH patients

- *Friday, November 12, 2021 (1:00-2:00pm EST):* Virtual Product Theatre
  Live presentation by Manal Abdelmalek, MD, Professor of Medicine, Duke University School of Medicine and Mazen Noureddin, MD, Director, Cedars-Sinai Medical Center, Karsh Division of Gastroenterology and Hepatology entitled: NASH with Fibrosis: Updates from the MAESTRO Phase 3 Clinical Program

- *Sunday, November 14, 2021:* Oral Presentation (4:00pm EST) (abstract #118)
  Presentation by Mazen Noureddin, MD, Director, Cedars-Sinai Medical Center, Karsh Division of Gastroenterology and Hepatology entitled: Utilization of the MAST (MRI-PDFF-MRE-AST) score to predict NASH on liver biopsy in MAESTRO-NASH and access response to resmetirom in MAESTRO-NAFLD-1

Leadership Team Expanded

Stephen Dodge, PharmD, MBA, has joined Madrigal as Senior Vice President and Global Head of Medical Affairs. Prior to joining Madrigal, Dr. Dodge was Senior Vice President, Cholestasis Program Head at Intercept Pharmaceuticals. Prior to Intercept, he held a number of leadership positions in medical affairs at Merck, Novo Nordisk and Novartis. His experience includes over 20 new product launches in new therapeutic areas, spanning over 20 years, with 10 years in liver and GI diseases. Dr. Dodge received an MBA from Washington University in St. Louis, his PharmD - Doctor of Pharmacy from the University of The Pacific School of Pharmacy and a B.S., Biology from California State University.

Kia Motesharei, PhD, has joined Madrigal as Senior Vice President Business & Corporate Development. Dr. Motesharei's 20 plus years of industry experience includes over 100 business development transactions and corporate strategy initiatives including therapeutic product licensing and alliances, R&D collaborations, commercial product partnerships, royalty financing and M&A activities with companies in the United States, Europe, Japan, China, Latin America and the Middle East. Prior to joining Madrigal, Dr. Motesharei was Chief Business and Strategy Officer at NeuBase Therapeutics. Since 2004, he has held similar positions with Akcea Therapeutics, EMD Serono (Merck KGaA), Dyax Corporation, Genfit, and Activx Biosciences. Dr. Motesharei completed his Postdoctoral training as a National Institutes of Health fellow at The Scripps Research Institute and received his Doctorate degree from UCLA.

Financial Results

As of September 30, 2021, Madrigal had cash, cash equivalents and marketable securities of $299.1 million, compared to $284.1 million at December 31, 2020. The increase in cash and marketable securities was due to net proceeds of $151.2 million from sales of common stock via our at-the-market (ATM) program, partially offset by cash used to support operations of $135.9 million.

Operating expenses were $63.2 million and $177.9 million for the three and nine month periods ended September 30, 2021, compared to $58.8 million and $147.1 million in the comparable prior

year periods.

Research and development expenses for the three and nine month periods ended September 30, 2021 were $54.9 million and $152.3 million, compared to $53.3 million and $131.4 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, 2021 were $8.3 million and $25.6 million, compared to $5.5 million and $15.8 million in the comparable prior year periods. The increase is attributable 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, 2021 was $0.1 million and $0.3 million, compared to $0.8 million and $3.9 million in the comparable prior year periods. The decrease in interest income was due primarily to decreased interest rates.

About Resmetirom
Thyroid hormone, through activation of its β-receptor in hepatocytes, plays a central role in liver function impacting a range of health parameters from levels of serum cholesterol and triglycerides to the pathological buildup of fat in the liver. Thyroid hormone receptor (THR)-β action in the liver is key to proper function of the liver, including regulation of mitochondrial activity such as breakdown of liver fat and control of the level of normal, healthy mitochondria. Patients with NASH have reduced levels of thyroid hormone activity in the liver with resultant impaired hepatic function, in part due to the inflamed state of the liver that causes degradation of thyroid hormone.

To exploit the thyroid hormone receptor (THR)-β pathway for therapeutic purposes in liver and cardio-metabolic diseases, it is important to avoid activity at the THR-α receptor, the predominant systemic receptor for thyroid hormone that is responsible for activity outside the liver including in heart and bone. The lack of selectivity of older thyromimetic compounds, chemically-related toxicities and undesirable distribution in the body led to safety concerns. Madrigal recognized that greater selectivity for thyroid hormone receptor (THR)-β and liver targeting might overcome these challenges and deliver the full therapeutic potential of THR-β agonism. Resmetirom has been shown to be highly selective based on 1) THR-β receptor functional selectivity based on both in vitro and in vivo assays and 2) specific uptake into the liver, its site of action, virtually avoiding any uptake into tissues outside the liver. In short- and long- term human and animal studies, resmetirom has been confirmed to be safe and devoid of activity at the THR-α receptor and without impact on bone or cardiac parameters. Resmetirom does not impact the thyroid axis hormones, including the central thyroid axis. Madrigal believes that resmetirom is the first orally administered, small-molecule, liver-directed, truly β-selective THR agonist.

About the Phase 3 Registration Program for the Treatment of NASH (Non-alcoholic steatohepatitis)
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 targets 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 primary surrogate endpoint on biopsy will be NASH resolution, with at least a 2-point reduction in NAS (NASH Activity Score), and with no worsening of fibrosis. Two key secondary endpoints are liver fibrosis reduction of at least one stage, with no worsening of NASH on liver biopsy, and lowering of LDL-cholesterol [ClinicalTrials.gov/NCT03900429]. Madrigal announced achievement of the planned target enrollment on June 30, 2021.

The first 900 patients in the MAESTRO-NASH study will continue on therapy after the initial 52-week treatment period; and up to another 1,100 patients are to be added using the same randomization plan and 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 is a 52-week Phase 3 multi-center, double-blind, randomized, placebo-controlled study of resmetirom, and was initiated in December 2019 in patients with non-alcoholic fatty liver disease (NAFLD), presumed NASH. The primary endpoint for this study is to evaluate the safety and tolerability of resmetirom. Completion of enrollment of over 1,200 patients into the study was announced in November 2020. Top-line data from the study is targeted by end of year 2021.

Patients in MAESTRO-NAFLD-1 are randomized 1:1:1 to receive resmetirom 80 mg once a day, 100 mg once a day, or placebo. MAESTRO-NAFLD-1 also includes a 100 mg resmetirom open label arm. 52 week data were presented from the open label arm at The International Liver Congress™ 2021 in June and demonstrated that resmetirom is safe and well-tolerated at 100mg per day [view press release here]. MAESTRO-NAFLD-1 (unlike MAESTRO-NASH), does not include a liver biopsy and represents a “real-life” NASH study. NASH or presumed NASH is documented using historical liver biopsy or non-invasive techniques including FibroScan and magnetic resonance imaging, proton density fat fraction (MRI-PDFF) respectively. Using non-invasive measures, MAESTRO-NAFLD-1 is 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 include LDL-cholesterol, apolipoprotein B and triglyceride (TG) lowering; reduction of liver fat as determined by MRI-PDFF; and reduction of PRO-C3, a NASH fibrosis biomarker. [ClinicalTrials.gov/NCT04197479]. Additional secondary and exploratory endpoints will be assessed including reduction in liver enzymes, FibroScan scores and other fibrosis and inflammatory 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 that target a specific thyroid hormone receptor pathway in the liver, which is a key regulatory mechanism common to a spectrum of fatty liver and cardio-metabolic diseases with high unmet medical need. Madrigal’s lead candidate, resmetirom, is a first-in-class, orally administered, small-molecule, liver-directed, thyroid hormone receptor (THR)-β selective agonist that is currently in two Phase 3 clinical studies, MAESTRO-NASH and MAESTRO-

NAFLD-1, designed to demonstrate multiple benefits in NASH (non-alcoholic steatohepatitis) patients. 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 or presentations of data from our trials; research and development activities; market size 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 or biomarker effects with resmetirom; the 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 measured by non-invasive tests on NASH resolution with fibrosis reduction or improvement; *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 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 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 "allow," "anticipates," "be," "believes," "continue," "could," "demonstrates," "design," "estimates," "expects," "forecasts," "future," "goal," "hopeful," "inform," "intends," "may," "might," "planned", "plans," "positions," "potential," "powers," "predicts," "predictive," "projects," "seeks," "should," "will," "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 than our prior studies; limitations associated with early stage, 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, 2020, as well as in our other filings with the SEC.

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

Media Contacts
Mike Beyer on behalf of Madrigal Pharmaceuticals
Phone: 312-961-2502
Email: mikebeyer@sambrown.com

(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,	
	2021	**2020**	**2021**	**2020**
Revenues:				
Total revenues	$ -	$ -	$ -	$ -
Operating expenses:				
Research and development	54,873	53,292	152,275	131,380
General and administrative	8,287	5,494	25,606	15,738
Total operating expenses	63,160	58,786	177,881	147,118
Loss from operations	(63,160)	(58,786)	(177,881)	(147,118)
Interest income, net	60	823	311	3,897
Other income	-	-	273	100
Net loss	$ (63,100)	$ (57,963)	$ (177,297)	$ (143,121)
Basic and diluted net loss per common share	$ (3.79)	$ (3.75)	$ (10.84)	$ (9.27)
Basic and diluted weighted average number of common shares outstanding	16,639,776	15,448,425	16,353,428	15,437,018

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

	September 30, 2021	December 31, 2020
Assets		
Cash, cash equivalents and marketable securities	$ 299,144	$ 284,149
Other current assets	3,812	1,014
Other non-current assets	1,741	1,832
Total assets	$ 304,697	$ 286,995
Liabilities and Equity		
Current liabilities	$ 69,325	$ 46,557
Long-term liabilities	491	468
Stockholders' equity	234,881	239,970
Total liabilities and stockholders' equity	$ 304,697	$ 286,995

Source: Madrigal Pharmaceuticals, Inc.