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

August 5, 2021

CONSHOHOCKEN, Pa., Aug. 05, 2021 (GLOBE NEWSWIRE) -- Madrigal Pharmaceuticals, Inc. (NASDAQ:MDGL) reports today its second quarter 2021 financial results and provides a summary of corporate accomplishments.

Paul Friedman, M.D., Chief Executive Officer of Madrigal, stated, “The Madrigal team has made great progress on multiple fronts in the first half of 2021. Importantly, we reached our goal of enrollment to support the 52 week liver biopsy accelerated approval portion of MAESTRO-NASH. Top-line results are expected by the third quarter of 2022 for MAESTRO-NASH and by the end of this year for the non-invasive imaging and biomarker study, MAESTRO-NAFLD-1.”

“We made multiple presentations recently at EASL. In particular, data from the open-label portion of the ongoing MAESTRO-NAFLD-1 Phase 3 clinical trial provide further evidence that treatment with resmetirom for 52 weeks leads to rapid and sustained reductions of liver fat, fibrosis, cell injury and inflammation in non-cirrhotic NASH patients that project favorably on the liver biopsy endpoints in MAESTRO-NASH,” stated Becky Taub, M.D., Chief Medical Officer and President of Research & Development of Madrigal.

Dr. Taub added, “Also during the quarter, the Medical Affairs team at Madrigal continued to engage with the NASH physician and patient advocacy communities that recognize NASH with liver fibrosis as a very large unmet need. Our commercial team’s product launch planning also supports our objective to demonstrate the value of available non-invasive imaging and biomarkers that better diagnose and allow management of patients with NASH, enabling preparation for the planned launch and commercialization of resmetirom.”

Recent Accomplishments
1. Clinical and Medical Affairs

- Positive clinical results presented at the European Association for the Study of the Liver Annual Meeting (EASL), The International Liver Congress™ 2021, further point out the potential therapeutic value of resmetirom in a real-life NASH setting using non-invasive tools (versus serial liver biopsies): [click here to view press release]
    - Oral Plenary Presentation: Reduction in Fibrosis and Steatohepatitis Imaging and Biomarkers in a Phase 3, 52 Week Resmetirom NASH Trial. Presenter: Stephen Harrison [click here to view oral presentation]
    - EASL Poster: Treatment of NASH cirrhotic patients with resmetirom: baseline characteristics and effects on safety, biomarkers and imaging. Presenter: Stephen Harrison [click here to view poster]
    - Madrigal Hosted Symposium: Phase 3 development of resmetirom, a liver-directed thyroid hormone receptor (THR)-β agonist for the treatment of patients with NASH and significant liver fibrosis. Presenters: Vlad Ratziu, Jörn Schattenberg and Stephen Harrison [click here to view slides, click here to view webcast]
- Analysis of patient reported outcome data from the Phase 2 trial of resmetirom revealed that achieving ≥30% relative reduction in hepatic fat was associated with greater improvements in Quality of Life Scores. Improvements in quality of life scores were also observed in those patients with NASH and fibrosis improvement on liver biopsy. The data has recently been published online in Clinical Gastroenterology and Hepatology: Hepatic Fat Reduction Due to Resmetirom in Patients with Nonalcoholic Steatohepatitis is Associated with Improvement of Quality of Life.
- Well over 2,000 patients enrolled in MAESTRO trials that will help support the required safety database for NDA approval. Recent highlights:
    - Enrolled sufficient patients in the Phase 3 clinical trial MAESTRO-NASH to support the planned Subpart H (Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses) submission to the US Food and Drug Administration (FDA). Madrigal will continue to enroll additional patients beyond those required for accelerated approval to provide for the clinical outcomes portion of the MAESTRO-NASH Phase 3 clinical trial.
    - First patients enrolled in Phase 3 MAESTRO-NAFLD Open Label Extension Study (OLE). Patients who complete the first 52-week randomized portion of the study can receive 52 weeks of active treatment with resmetirom. The study is expected to provide both additional long-term safety and tolerability data as well as further efficacy measures documenting reduction of NASH using non-invasive scans and blood chemistries.
- Medical Affairs Outreach:
    - Scientific engagements are occurring at NASH-focused meetings including: EASL, the American Association of Clinical Endocrinology (AACE), the American Association for the Study of Liver Diseases (AASLD), NASH-TAG,

Paris-NASH, the GI Alliance and the Chronic Liver Disease Foundation (CLDF). These activities are intended to build awareness of the evolving clinical data supporting the therapeutic value of resmetirom, improve the medical community's understanding of NASH, identify the unmet needs of NASH patients, and communicate the growing body of clinical evidence regarding the utility of non-invasive tools and techniques to diagnose and monitor NASH patients.

2. Launch and Commercial Preparation

- In preparation for the planned U.S. launch of resmetirom, Madrigal is building its commercial resources and infrastructure, as well as developing a comprehensive product launch plan to position resmetirom for success. To date, our market research projects have involved over 1,000 hepatologists, gastroenterologists and endocrinologists as well as payers who together provide prescription coverage for the vast majority of the patients in the U.S. Results from these efforts confirm that (i) NASH patients with significant liver fibrosis (F2/F3) are already being non-invasively identified by physicians, but given the lack of approved treatment options they are looking for effective new medications to manage the disease; and, (ii) the majority of these physicians believe an ideal therapy for NASH patients with significant fibrosis which addresses the underlying pathophysiology of the disease in the liver will slow, halt and/or reverse disease progression.

3. Leadership Team Expanded

- Alex Howarth, appointed Chief Financial Officer of Madrigal, adds important skills to Madrigal's executive team and is responsible for the development of financial and corporate strategy, long-range planning, business development and implementation of financial and operational systems to support Madrigal's continued growth and its transition to a commercial company.

- Robert Waltermire, newly appointed as Chief Pharmaceutical Development Officer of Madrigal within Research and Development with responsibility for all aspects of chemistry, manufacturing and controls (CMC) and commercial product supply.

Financial Results
As of June 30, 2021, Madrigal had cash, cash equivalents and marketable securities of $323.8 million, compared to $284.1 million at December 31, 2020. The increase in cash and marketable securities was due to net proceeds of $130.2 million from sales of common stock via our at-the-market (ATM) program, partially offset by cash used to support operations of $90.3 million.

Operating expenses were $61.7 million and $114.7 million for the three and six month periods ended June 30, 2021, compared to $50.3 million and $88.3 million in the comparable prior year periods.

Research and development expenses for the three and six month periods ended June 30, 2021 were $51.6 million and $97.4 million, compared to $44.7 million and $78.1 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 six month periods ended June 30, 2021 were $10.1 million and $17.3 million, compared to $5.6 million and $10.2 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 six month periods ended June 30, 2021 was $0.1 million and $0.3 million, compared to $1.2 million and $3.1 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 cardio-metabolic and liver 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 MRI-PDFF. 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 magnetic resonance imaging, proton density fat fraction (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 cardio-metabolic and fatty liver 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 in currently in two Phase 3 clinical studies, MAESTRO-NASH and MAESTRO- NAFLD-1, designed to demonstrate multiple benefits across a broad spectrum of NASH (non-alcoholic steatohepatitis) and NAFLD (non-alcoholic fatty liver disease) 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; research and development activities; 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; 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 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 filings 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 Contact:
Laura Morgan, Sam Brown Inc., lauramorgan@sambrown.com, tel +1-951-333-9110
Bob Conrad, Sam Brown Inc., bobconrad@sambrown.com, tel +1-703-980-0997

(Tables Follow)

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Revenues:				
Total revenues	$ -	$ -	$ -	$ -
Operating expenses:				
Research and development	51,632	44,688	97,402	78,088
General and administrative	10,110	5,639	17,319	10,244
Total operating expenses	61,742	50,327	114,721	88,332
Loss from operations	(61,742)	(50,327)	(114,721)	(88,332)
Interest income, net	91	1,204	251	3,074
Other income	-	100	273	100
Net loss	$ (61,651)	$ (49,023)	$ (114,197)	$ (85,158)
Basic and diluted net loss per common share	$ (3.72)	$ (3.18)	$ (7.05)	$ (5.52)
Basic and diluted weighted average number of common shares outstanding	16,571,322	15,433,348	16,207,880	15,431,251

Madrigal Pharmaceuticals, Inc.
Condensed Consolidated Balance Sheets

(in thousands)
(unaudited)

	June 30, 2021	December 31, 2020
Assets		
Cash, cash equivalents and marketable securities	$ 323,846	$ 284,149
Other current assets	2,221	1,014
Other non-current assets	1,888	1,832
Total assets	$ 327,955	$ 286,995
Liabilities and Equity		
Current liabilities	$ 56,710	$ 46,557
Long-term liabilities	594	468
Stockholders' equity	270,651	239,970
Total liabilities and stockholders' equity	$ 327,955	$ 286,995

Source: Madrigal Pharmaceuticals, Inc.