Madrigal Pharmaceuticals Reports 2018 Fourth Quarter and Full Year Financial Results and Highlights

February 27, 2019

CONSHOHOCKEN, Pa., Feb. 27, 2019 (GLOBE NEWSWIRE) -- Madrigal Pharmaceuticals, Inc. (NASDAQ:MDGL) today announced its fourth quarter and full year 2018 financial results and highlights:

“Madrigal made significant progress in 2018 in advancing the development of MGL-3196. We successfully completed Phase 2 studies in both NASH and dyslipidemia and expanded the Madrigal team to meet the demands of our clinical programs,” stated Paul Friedman, M.D., Chief Executive Officer of Madrigal. “In June, we also raised approximately $312 million of net proceeds from a public offering of our common stock, and we believe we have significant financial resources to fund our currently planned Phase 3 programs.”

Becky Taub, M.D., CMO and Executive VP, Research & Development of Madrigal added, “We had a positive end of phase 2 meeting with FDA for our NASH program, and we expect to initiate our Phase 3 clinical trial before the end of the first quarter of 2019. We continue to believe MGL-3196 has the potential to resolve NASH while decreasing cardiovascular risk, through reduction of levels of multiple atherogenic lipids as well as reduction of fat in the liver. Based on this potential cardiovascular risk reducing profile, we also intend to move ahead with our Phase 3 dyslipidemia clinical program later this year.”

Financial Results for the Three Months and Twelve Months Ended December 31, 2018

As of December 31, 2018, Madrigal had cash, cash equivalents and marketable securities of $483.7 million, compared to $191.5 million at December 31, 2017. The increase in cash and marketable securities resulted primarily from the net proceeds of $311.8 million from Madrigal’s public offering of common stock in June 2018, partially offset by cash used in operations of $25.5 million.

Operating expenses were $14.5 million and $40.7 million, respectively, for the three month and twelve month periods ended December 31, 2018, compared to $8.9 million and $32.1 million in the comparable prior year periods.

Research and development expenses for the three month and twelve month periods ended December 31, 2018 were $8.9 million and $25.4 million, respectively, compared to $6.5 million and $24.4 million in the comparable prior year periods. The increases are primarily attributable to increases in non-cash stock compensation, personnel and consulting costs, the effects of which were partially offset by lower clinical costs due to completion of treatment in our Phase 2 clinical studies in 2018.

General and administrative expenses for the three month and twelve month periods ended December 31, 2018 were $5.6 million and $15.3 million, respectively, compared to $2.4 million and $7.7 million in the comparable prior year periods. The increases are due primarily to higher non-cash stock compensation expense from stock option awards.

Interest income for the three month and twelve month periods ended December 31, 2018 was $3.0 million and $7.7 million, respectively, as compared to $216 thousand and $558 thousand in the comparable prior year periods. The change in interest income was due primarily to a higher average principal balance in our investment account in 2018, and increased interest rates.

Clinical Program Summaries for MGL-3196

NASH

Non-alcoholic Steatohepatitis (NASH) is a common liver disease in the United States and worldwide, unrelated to alcohol use, that is characterized by a build-up of fat in the liver, inflammation, damage (ballooning) of hepatocytes and increasing fibrosis. Although people with NASH may feel well and often do not know they have the disease, NASH can lead to permanent damage, including cirrhosis and impaired liver function in a high percentage of patients.

In October 2016, the first patient was treated in the ongoing Phase 2 trial of MGL-3196 for the treatment of NASH. The randomized, double-blind, placebo-controlled, multi-center Phase 2 study enrolled 125 patients 18 years of age and older with liver biopsy-confirmed NASH and included approximately 25 clinical sites in the United States. Patients were randomized to receive either MGL-3196 or placebo in a 2:1 ratio.

The primary endpoint of the study was the reduction of liver fat at 12 weeks compared with baseline (relative change), assessed by MRI-PDFF. Key secondary endpoints at 36 weeks included: reduction in liver fat compared with baseline (relative change), also assessed by MRI-PDFF; a two-point reduction in NAS (NALFD activity score) on biopsy; resolution of NASH on biopsy; and, safety and tolerability based on adverse events and changes in laboratory values.

The primary endpoint of the study at 12 weeks was achieved. Liver fat was reduced by 36.3% in all MGL-3196 treated patients (78) and 42.0% in a pre-specified group of high exposure MGL-3196 treated patients (44/78), as compared with 9.6% median

reduction in liver fat in 38 placebo treated patients. These results were statistically significant ($p<0.0001$) for both MGL-3196 treatment groups. Further, 75% of the high-exposure MGL-3196 treated patients showed liver fat reductions of ≥30%.

At 36 weeks, MGL-3196 achieved multiple key secondary endpoints including a sustained highly significant ($p<0.001$) reduction in liver fat compared to placebo as measured by MRI-PDFF; mean relative fat reduction for MGL-3196 was 37% versus 8.9% for placebo. MGL-3196 was associated with a greater percentage of subjects with a 2-point improvement in NAS (56% of 73 patients vs 32% of 34 placebo subjects, $p=0.02$). NASH resolution (NR) was seen in 27% of MGL-3196 compared with 6% of placebo subjects, $p=0.02$. MGL-3196 patients with ≥ 30% fat reduction on Week 12 MRI-PDFF demonstrated a higher percentage of 2-point improvement in NAS (70%, $p=0.001$) and NR (39%, $p=0.001$) compared with placebo, demonstrating a strong relationship between early reduction in liver fat as demonstrated by week 12 MRI-PDFF and NASH improvement on liver biopsy at Week 36. In patients with NASH Resolution, 35% of the MGL-3196 treated patients and no placebo patients had more advanced NASH (baseline NAS ≥5).

At Week 36, MGL-3196 treated patients showed sustained reduction of fibrosis biomarkers. In MGL-3196 patients with NASH resolution, fibrosis also resolved in 50% of patients and was decreased statistically significantly relative to all placebo patients.

There were statistically significant reductions in liver enzymes in MGL-3196 treated patients compared to placebo treated patients; reductions of greater magnitude were achieved with longer duration of MGL-3196 treatment. Statistically significantly more MGL-3196 treated patients than placebo treated patients had normalization of ALT (alanine transaminase).

Similar to week 12, at week 36 there were sustained, statistically significant reductions in low-density lipoprotein cholesterol (LDL-C), triglycerides, ApoB and lipoprotein(a).

MGL-3196 was well tolerated in this trial with mostly mild and a few moderate AEs which were balanced between drug treated and placebo patients. There was an increase in incidence of mild transient diarrhea in MGL-3196-treated, often a single episode, at the start of treatment. Diarrhea incidence was not increased later in the study.

Based on liver enzyme inclusion criteria, some patients are receiving extended treatment beyond 36 weeks for up to 36 additional weeks. All patients in this extension study will receive MGL-3196 and only non-invasive assessments will be made, including serial MRI-PDFF, safety labs, and circulating biomarkers.

Additional information about the study [NCT02912260] can be obtained at www.ClinicalTrials.gov.

Dyslipidemia

Patients with NASH, and its more prevalent precursor, Non-Alcoholic Fatty Liver Disease (NAFLD), are at heightened cardiovascular risk. In fact, patients suffering from these conditions die more frequently from cardiovascular events than from their liver disease. Multiple factors may contribute to this risk, including elevated levels of LDL-C and excess liver fat. Patients with NASH and NAFLD, however, may not undergo a biopsy to confirm a NASH diagnosis until they reach the more advanced stages of fibrosis (F2 – F4). A significant segment of this large group of patients may also suffer from diabetes and metabolic syndrome, and have lipid levels that are above target despite treatment with established therapies. These patients may benefit from therapy to lower their lipid levels, including excess liver fat.

We believe Madrigal's studies to date in patients with NASH and patients with heterozygous familial hypercholesterolemia (HeFH), have demonstrated the pleiotropic activity of MGL-3196 and the potential of the drug to reduce an array of atherogenic lipids, including liver fat, LDL-C, ApoB, triglycerides, ApoCIII, and Lp(a), as well as hs-CRP. As a result, Madrigal intends to focus its development of MGL-3196 for the treatment of patients across the entire NASH and NAFLD spectrum.

HeFH

Heterozygous familial hypercholesterolemia (HeFH), and a much rarer form called homozygous familial hypercholesterolemia (HoFH), are severe genetic dyslipidemias typically caused by inactivating mutations in the LDL receptor. Both forms of FH lead to early onset cardiovascular disease. HeFH, the most common dominantly inherited disease, is present in up to 1 in 200 people; the disease is found in higher frequencies in certain more genetically homogenous populations. Treatments exist for both HeFH and HoFH but many patients (as many as 40 percent of HeFH patients) are not able to reach their cholesterol (LDL-C) reduction goals on these therapies, reflecting the lifetime burden of cholesterol buildup in their bodies. Based on evidence of impressive LDL cholesterol lowering in Phase 1, and data suggesting that MGL-3196 has a mechanism of action that is different from and complementary to statins, Madrigal initiated a Phase 2 proof-of-concept trial in HeFH in February 2017 and enrolled 116 patients.

In this Phase 2 HeFH trial, patients who were not at their LDL-C goal were randomized in a 2:1 ratio to receive either MGL-3196 or placebo, in addition to their current cholesterol lowering regimen, which included approximately 75% taking high intensity statins (20/40 mg rosuvastatin or 80 mg atorvastatin), and about 2/3 of patients also taking ezetimibe. MGL-3196 treated patients (placebo corrected) achieved highly significant ($p< 0.0001$) LDL-C lowering of 18.8%, and 21% LDL-C lowering in those on an optimal dose of MGL-3196. LDL-C lowering was 28.5% in MGL-3196 treated compared to placebo in a prespecified group of patients who did not tolerate high intensity statin doses. Highly significant reductions ($p<0.0001$) relative to placebo were also observed with ApoB, triglycerides (TG) (25-31%), apolipoprotein CIII (Apo CIII) and Lp(a) (25-40%) in all MGL-3196 treated patients and prespecified subgroups, irrespective of statin treatment.

MGL-3196 was well tolerated with primarily mild and some moderate AEs, the numbers of which were balanced between placebo

and drug-treatment groups.

About MGL-3196
Among its many functions in the human body, thyroid hormone, through activation of its beta receptor, plays a central role in controlling lipid metabolism, impacting a range of health parameters from levels of serum cholesterol and triglycerides to the pathological buildup of fat in the liver. Attempts to exploit this pathway for therapeutic purposes in cardio-metabolic and liver diseases have been hampered by the lack of selectivity of older compounds for the thyroid hormone receptor (THR)-β, chemically-related toxicities and undesirable distribution in the body.

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. Madrigal believes that MGL-3196 is the first orally administered, small-molecule, liver- directed, truly β-selective THR agonist. MGL- 3196 has now demonstrated in two Phase 2 double-blind, placebo-controlled trials in NASH and HeFH the potential for a broad array of therapeutically beneficial effects, improving components of both metabolic syndrome, such as insulin resistance and dyslipidemia, and fatty liver disease, including lipotoxicity and inflammation. Based on evidence of these pleiotropic actions, coupled with an excellent safety profile, Madrigal plans to initiate a Phase 3 clinical program in NASH, and a Phase 3 clinical program is dyslipidemia.

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, MGL-3196, is a first-in- class, orally administered, small-molecule, liver-directed, thyroid hormone receptor (THR) β- selective agonist that is currently in Phase 2 development for NASH and dyslipidemia. 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. Such statements contain words such as "expect," "could," "may," "will," "believe," "estimate," "continue," "future," or the negative thereof or comparable terminology and the use of future dates. Forward-looking statements reflect management's current knowledge, assumptions, judgment and expectations regarding future performance or events. Although management believes that the expectations reflected in such statements are reasonable, they 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, the company's clinical development of MGL-3196, the timing and outcomes of clinical studies of MGL- 3196, 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.

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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,	
	2018	**2017**	**2018**	**2017**
Revenues:				
Total revenues	$ -	$ -	$ -	$ -
Operating expenses:				
Research and development	8,871	6,512	25,389	24,390

General and administrative	5,583	2,399	15,293	7,672
Total operating expenses	14,454	8,911	40,682	32,062
Loss from operations	(14,454)	(8,911)	(40,682)	(32,062)
Interest income (expense), net	2,979	216	7,671	558
Other income	-	250	200	350
Net loss	$ (11,475)	$ (8,445)	$ (32,811)	$ (31,154)
Basic and diluted net loss per common share	$ (0.75)	$ (0.67)	$ (2.22)	$ (2.54)
Basic and diluted weighted average number of common shares outstanding	15,348,358	12,597,864	14,796,712	12,244,939

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

	December 31, 2018	December 31, 2017
Assets		
Cash, cash equivalents and marketable securities	$ 483,718	$ 191,527
Other current assets	1,483	485
Other non-current assets	227	301
Total assets	$ 485,428	$ 192,313
Liabilities and Equity		
Current liabilities	$ 8,444	$ 10,054
Long-term liabilities	-	-
Stockholders' equity	476,984	182,259
Total liabilities and stockholders' equity	$ 485,428	$ 192,313

Source: Madrigal Pharmaceuticals, Inc.