



Madrigal Pharmaceuticals Reports 2017 Fourth Quarter and Year-End Financial Results, Reviews Key Corporate Achievements and Provides Clinical Update on MGL-3196

- *MGL-3196 is a first-in-class, oral, once-daily, liver-directed, thyroid hormone receptor (THR) β -selective agonist that is being developed for patients with non-alcoholic steatohepatitis (NASH) and heterozygous familial hypercholesterolemia (HeFH) -*
- *Recently reported positive top-line results from two Phase 2 trials support ongoing development of MGL-3196 as a potential treatment for NASH and HeFH -*
- *Madrigal is in a strong financial position to advance MGL-3196 in both indications -*

CONSHOHOCKEN, Pa., March 13, 2018 -- Madrigal Pharmaceuticals, Inc. (NASDAQ:MDGL) today announced its fourth quarter and year-end 2017 financial results, highlighting a substantial cash position and significant progress for MGL-3196, its lead compound being developed as a treatment for non-alcoholic steatohepatitis (NASH) and heterozygous familial hypercholesterolemia (HeFH).

“Madrigal had a very productive 2017 and 2018 looks to be equally transforming. During the year, we intend to report for the NASH study with MGL-3196, both the full 12-week Phase 2 results as well as the top-line 36-week data, including liver biopsy results. In addition, we expect to report the full Phase 2 results from the HeFH study later in the year. We also intend to meet with representatives from the FDA to discuss our plans for Phase 3,” stated Paul Friedman, M.D., President and Chief Executive Officer of Madrigal. “Importantly, we are well funded to expeditiously advance MGL-3196 forward in NASH and HeFH, and possibly in other dyslipidemic indications.”

Key Accomplishments

- Successfully recruited two double-blind, placebo-controlled Phase 2 clinical trials evaluating MGL-3196 as a treatment for patients with NASH and HeFH.
- Reported that MGL-3196 demonstrated highly statistically significant results for the primary endpoints in both Phase 2 trials.
- Achieved acceptance of an MGL-3196 NASH abstract for a main plenary presentation at the Annual Meeting of the European Association for the Study of the Liver (EASL) during The International Liver Congress™ 2018.

- Raised net proceeds of more than \$170 million through well-supported public offerings of Madrigal stock.

Becky Taub, M.D., CMO and Executive VP, Research & Development of Madrigal stated, "Achieving these highly statistically significant results for the primary endpoints in the ongoing NASH Phase 2 trial and the completed Phase 2 trial in HeFH is very encouraging. Anticipating continued positive data, we're moving ahead with preparations for Phase 3 studies."

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, the reduction of liver fat at 12 weeks compared with baseline (relative change), assessed by magnetic resonance imaging-estimated proton density fat fraction (MRI-PDFF), 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. MGL-3196 was well tolerated with few serious adverse events noted during the 12-week portion of the study, none of which was related to MGL- 3196.

The study is ongoing and remains blinded. Additional efficacy endpoints are being assessed at the end of the 36-week treatment period by repeat MRI-PDFF and conventional liver biopsy to examine histologic evidence for the resolution of and improvement in NASH.

Results of the 36-week endpoints are expected in the second quarter of 2018. In addition, based on liver enzyme inclusion criteria, some patients (blinded as to whether they were on placebo or MGL-3196 in the main 36-week portion of the study) are

receiving extended treatment beyond 36 weeks for up to 36 additional weeks. All patients in the extension study will receive MGL-3196 and only non-invasive assessments will be made, including serial MRI-PDF, safety labs, and circulating biomarkers. Additional information about the study [NCT02912260] can be obtained at www.ClinicalTrials.gov.

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.

Financial Results for the Three Months and Twelve Months Ended December 31, 2017

Operating expenses were \$8.9 million and \$32.1 million for the three month and twelve month periods ended December 31, 2017, respectively, compared to \$7.8 million and \$25.2 million in the comparable prior year periods.

Research and development expenses for the three month and twelve month periods ended December 31, 2017 increased to approximately \$6.5 million and \$24.4 million in

2017, as compared to \$5.5 million and \$15.9 million, respectively, in 2016. The increases are primarily attributable to higher expenses for our clinical and preclinical development programs for MGL-3196, and increased personnel costs, in both the three and twelve month periods ended December 31, 2017, as compared to the same periods in 2016.

General and administrative expenses for the three month period ended December 31, 2017 increased to approximately \$2.4 million from approximately \$2.2 million in the comparable period in 2016, due primarily to higher compensation expenses. General and administrative expenses for the twelve month period ended December 31, 2017 decreased to approximately \$7.7 million from \$9.3 million in the comparable period in 2016, due primarily to expenses incurred in 2016 associated with the Company's merger.

Interest income (expense), net, for the three month and twelve month periods ended December 31, 2017 was \$216 thousand and \$558 thousand, respectively, as compared to \$6 thousand and \$(1.2) million, respectively, for the same periods in 2016. The change in interest income (expense) was due primarily to the conversion of all outstanding promissory notes to equity upon the consummation of the merger in 2016, and a higher average principal balance in our investment account in 2017.

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 demonstrated 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. These pleiotropic actions, coupled with an excellent safety profile, suggest that MGL-3196 could be the preferred treatment option for 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, 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 HeFH. 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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(Tables Follow)

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,	
	2017	2016	2017	2016
Revenues:				
Total revenues	\$ -	\$ -	\$ -	\$ -
Operating expenses:				
Research and development	6,512	5,523	24,390	15,933
General and administrative	2,399	2,232	7,672	9,290
Total operating expenses	8,911	7,755	32,062	25,223
Loss from operations	(8,911)	(7,755)	(32,062)	(25,223)
Interest income (expense), net	216	6	558	(1,165)
Other income	250	-	350	-
Net loss	\$ (8,445)	\$ (7,749)	\$ (31,154)	\$ (26,388)
Basic and diluted net loss per common share	\$ (0.67)	\$ (0.67)	\$ (2.54)	\$ (5.07)
Basic and diluted weighted average number of common shares outstanding	12,597,864	11,509,791	12,244,939	5,204,644

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

	December 31, 2017	December 31, 2016
Assets		
Cash, cash equivalents and marketable securities	\$ 191,527	\$ 40,500
Other current assets	485	707
Other non-current assets	301	3
Total assets	\$ 192,313	\$ 41,210
Liabilities and Equity		
Current liabilities	\$ 10,054	\$ 4,800
Long-term liabilities	-	-
Stockholders' equity	182,259	36,410
Total liabilities and stockholders' equity	\$ 192,313	\$ 41,210