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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2017

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission file number: 001-33277

MADRIGAL PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**04-3508648**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
Four Tower Bridge 200 Barr Harbor Drive, Suite 400 West Conshohocken, Pennsylvania	**19428**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(484) 380-9263**

Securities registered pursuant to Section 12(b) of the Exchange Act:

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.0001 Par Value Per Share	The NASDAQ Stock Market LLC

Securities registered pursuant to Section 12(g) of the Exchange Act: **None.**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐	Accelerated filer ☒	Non-accelerated filer ☐ (Do not check if a smaller reporting company)	Smaller reporting company ☒ Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate), computed by reference to the price at which the common stock was last sold on June 30, 2017, the last business day of the registrant's most recently completed second fiscal quarter, was $84,557,382.

As of March 8, 2018 the registrant had 14,227,634 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

The following documents (or parts thereof) are incorporated by reference into the following parts of this Annual Report on Form 10-K: Certain information required in Part III of this Annual Report on Form 10-K is incorporated from the registrant's Proxy Statement for the 2018 Annual Meeting of Stockholders.

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Item 1. Business

Except for the historical information contained herein, the matters set forth in this Annual Report on Form 10-K, including statements regarding our plans, potential opportunities, financial or other expectations, projections, objectives, milestones, strategies, market growth, timelines, legal matters, product pipeline, clinical studies, product development and the potential benefits of our products under development are forward-looking statements within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from the anticipated or estimated future results, including the risks and uncertainties associated with our future operating performance and financial position, the market demand for and acceptance of our products, research, development and commercialization of new products, obtaining and maintaining regulatory approvals, including, but not limited to potential regulatory delays or rejections, risks associated with meeting the objectives of clinical studies, including, but not limited to, delays or failures in enrollment, and the occurrence of adverse safety events, risks relating to our ability to accomplish our business development objectives, and realize the anticipated benefit of any such transactions, and other risks set forth below under Item 1A. "Risk Factors" and other documents subsequently filed with or furnished to the Securities and Exchange Commission, or the SEC. These forward-looking statements are based on current information that may change and you are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this Annual Report on Form 10-K. All forward-looking statements are qualified in their entirety by this cautionary statement, and we undertake no obligation to revise or update any forward-looking statement to reflect events or circumstances after the date hereof.

References in this report to Madrigal, the Company, we, our and us refer to Madrigal Pharmaceuticals, Inc. "Madrigal" is a registered trademark of Madrigal Pharmaceuticals, Inc. in the U.S. and/or other countries. Other trademarks or service marks appearing in this report may be trademarks or service marks of other owners.

Executive Overview

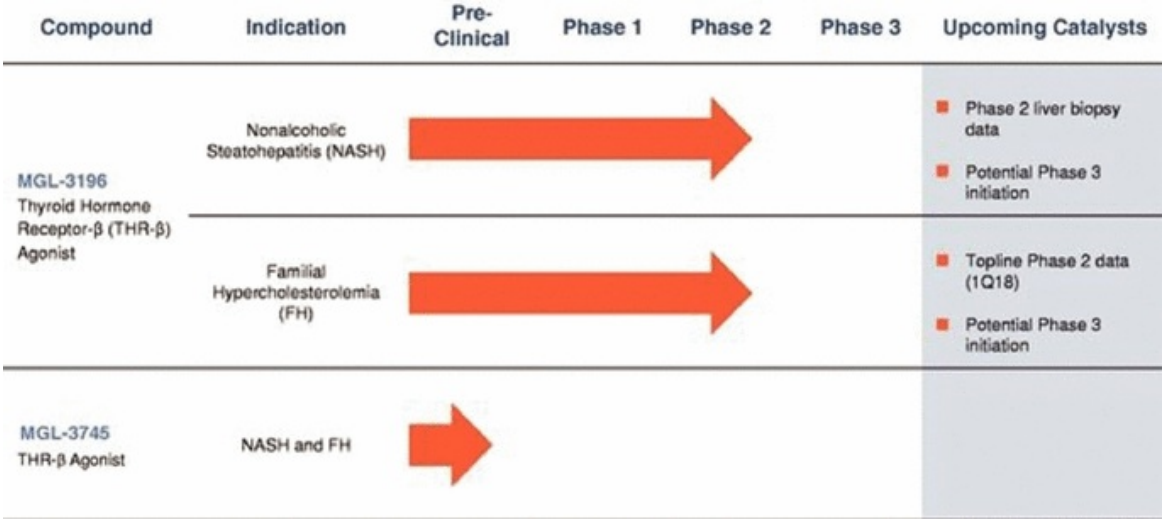
We are a clinical-stage biopharmaceutical company focused on the development and commercialization of innovative therapeutic candidates for the treatment of cardiovascular, metabolic, and liver diseases. Our lead product candidate, MGL-3196, is a proprietary, liver-directed, selective thyroid hormone receptor-β, or THR-β, agonist that can potentially be used to treat a number of disease states with high unmet medical need. THR-β is known to regulate cholesterol and triglyceride metabolism, which we believe suggests potential therapeutic benefits for patients suffering from hypercholesterolemia, genetic dyslipidemias, and diseases resulting from accumulation of fat in liver tissue, such as non-alcoholic steatohepatitis, or NASH. Based on scientific publications in human and animal studies, we believe that human NASH livers have a deficiency in THR-β activity that leads to features of NASH including fatty liver, inflammation and fibrosis, and that treatment with MGL-3196 may potentially replace this hormone deficiency and be an effective NASH treatment.

We believe that MGL-3196 is a first-in-class, highly selective, liver-directed THR-β agonist. To date, MGL-3196 has been studied in six completed Phase 1 trials and two Phase 2 trials, in a total of 183 subjects and 241 patients, respectively. We are developing MGL-3196 as a once-daily oral pill. We have enrolled 125 patients in a Phase 2 NASH clinical trial, and are nearing completion of this 36-week trial. We achieved the 12-week primary endpoint for this NASH trial and reported the results in December 2017. We are also developing MGL-3196 for dyslipidemia, including genetic dyslipidemias such as familial hypercholesterolemia, or FH. We have enrolled 116 patients and completed a Phase 2 clinical trial in heterozygous FH, or HeFH, patients. We achieved the 12-week primary endpoint for this HeFH trial and reported the results in February 2018. In the completed trials to date MGL-3196 appeared to be safe and well-tolerated. These trials included a single ascending dose trial, a multiple

ascending dose trial, two drug interaction trials with statins, a multiple dose mass balance study, and a single dose relative bioavailability study of tablet formulations versus capsule formulation.

In the multiple ascending dose Phase 1 clinical trial in healthy volunteers with mildly elevated low-density lipoprotein cholesterol, or LDL-C, the administration of MGL-3196 in once daily doses of up to 200 mg per day for 14 days demonstrated statistically significant reductions of LDL-C, apolipoprotein B, or ApoB, and non-high density lipoprotein cholesterol, or non-HDL-C, of up to 30%, and a reduction of triglycerides, or TGs, of up to 60%. Increased levels of LDL-C, commonly known as "bad cholesterol," ApoB and non-HDL-C are each strongly associated with increased risk of heart disease. The lipid parameter reductions observed with MGL-3196 treatment occurred rapidly in the trial, becoming apparent within the first few days of dosing.

The following chart summarizes the status of our product candidate development programs for MGL-3196 and MGL-3745, a preclinical compound which has similar thyroid receptor selectivity to MGL-3196 and is thus a potential backup compound for MGL-3196:



Recent Developments

MGL-3196 Phase 2 Clinical Trial in NASH

In December 2017, we announced top-line 12-week results from our Phase 2 clinical trial in NASH. In this trial, MGL-3196 demonstrated statistically significant results for the primary endpoint with a statistically significant 36.6% reduction in hepatic fat versus 9.6% reduction for placebo ($p<0.0001$)as measured by magnetic resonance imaging proton density fat fraction, or MRI-PDFF, a non-invasive imaging test, at 12 weeks. Recent published data have shown a high correlation of the reduction of liver fat of 30% or more as measured by MRI-PDFF to improvement in NASH on liver biopsy.

Statistically significant reductions in alanine aminotransferase, or ALT, and aspartate aminotransferase, or AST, were observed in MGL-3196 treated patients; greater reductions in ALT and AST, statistically significant relative to placebo, were observed in the pre-specified group with relatively higher MGL-3196 drug levels. In drug-treated patients relative to placebo patients, statistically significant improvements were also seen in multiple secondary endpoints considered to be potentially clinically relevant in patients with NASH including LDL-C, TGs, ApoB, and lipoprotein(a), or Lp(a).

MGL-3196 has been well-tolerated with mostly mild adverse events, or AEs, and a few moderate AEs, the numbers of which are balanced between placebo and drug-treatment groups. There are no adverse effects of MGL-3196 on safety laboratory or vital sign parameters. There were three serious AEs in the study, all considered unrelated to MGL-3196.

The on-going Phase 2 clinical trial in NASH remains blinded. Safety, efficacy of NASH resolution by biopsy, and repeat MRI-PDFF will be assessed at 36 weeks. Multiple inflammatory and fibrosis serum biomarkers at 12 and 36 weeks are being and will be assessed, respectively.

MGL-3196 Phase 2 Clinical Trial in HeFH

In February 2018, we announced top-line results from our Phase 2 clinical trial in HeFH. In this trial, patients treated with MGL-3196 (placebo corrected) achieved highly significant ($p< 0.0001$) LDL-C lowering of 18.8%, and 21% LDL-C lowering in those patients receiving an optimal dose of MGL-3196. LDL-C lowering was 28.5% in patients treated with MGL-3196 as compared to placebo in a prespecified group of patients who did not tolerate high intensity statin doses. Highly significant ($p<0.0001$) and numerically similar results were observed with ApoB. Highly significant ($p<0.0001$) TG (25-31%), apolipoprotein CIII, and Lp(a) lowering (25-40%) were observed in all patients treated with MGL-3196 and certain prespecified subgroups, irrespective of statin treatment.

MGL-3196 has been well-tolerated with mostly mild AEs and some moderate AEs, the numbers of which are balanced between placebo and drug-treatment groups. Fewer than seven percent of patients did not complete the study, and patients who discontinued for AEs, all mild to moderate, were balanced between drug-treated and placebo patients. There were two serious AEs in the study, both considered unrelated to treatment, one in a placebo and one in a drug-treated patient.

Lead Product Candidate—MGL-3196

Active thyroid hormone, known as T3, interacts with two nuclear receptors, THR-α, which is the predominant receptor expressed in most human tissues, including heart and bone, and THR-β, which has more restricted tissue expression, and is the predominant receptor responsible for metabolic actions in the liver, including both cholesterol- and TG-lowering. Selective activation of the THR-β receptor in liver tissue is believed to favorably affect cholesterol and lipoprotein levels via multiple mechanisms, which may be complementary to those of other lipid-lowering therapies such as statin drugs. We believe that these characteristics of THR-β activation by MGL-3196 will in turn lead to clinically meaningful reductions in LDL-C, and plasma and liver TGs.

We believe that MGL-3196 is the first selective small molecule THR-β agonist compound. MGL-3196, along with other THR-β-selective small molecules, such as MGL-3745, a potential backup compound to MGL-3196, was discovered at Hoffmann-La Roche, or Roche, in Nutley, New Jersey, by utilizing a novel functional assay that, unlike a simple receptor binding assay, assessed the functional activity of compounds which interacted with thyroid hormone receptors. In a published study by us and Roche in the Journal of Medicinal Chemistry using this functional assay, MGL-3196 was shown to be highly selective for the THR-β receptor, with almost no effect on THR-α, unlike other compounds purported in published studies to be β-selective based on binding affinity, but which were shown to equally activate THR-α and THR-β in the novel functional assay.

We believe that the β-selectivity and liver-targeting properties of MGL-3196 are critically important for MGL-3196's beneficial metabolic actions in the liver, and enable avoidance of safety issues associated with THR-α activation by thyroid hormone and/or less selective THR agonists in tissues such as heart and bone. In a variety of preclinical animal model studies, MGL-3196 showed enhanced safety relative to T3 or other thyroid agonists. In animal models, MGL-3196 demonstrated cholesterol lowering, liver TG lowering, and reduction of markers of NASH-related liver inflammation and fibrosis at drug levels similar to those that lowered LDL-C in human clinical trials, providing data

to support the advancement of MGL-3196 into NASH and FH clinical trials. In chronic animal toxicology studies in dogs and rats, no effects on bone or cartilage histology were seen at any MGL-3196 dose in either species.

We believe that MGL-3196 may be the first product candidate in development for NASH or FH that selectively targets the THR-β pathway and has shown a lack of liver enzyme elevations in Phase 1 and 2 clinical studies as well as an absence of bone and cartilage histologic findings in chronic animal toxicology studies.

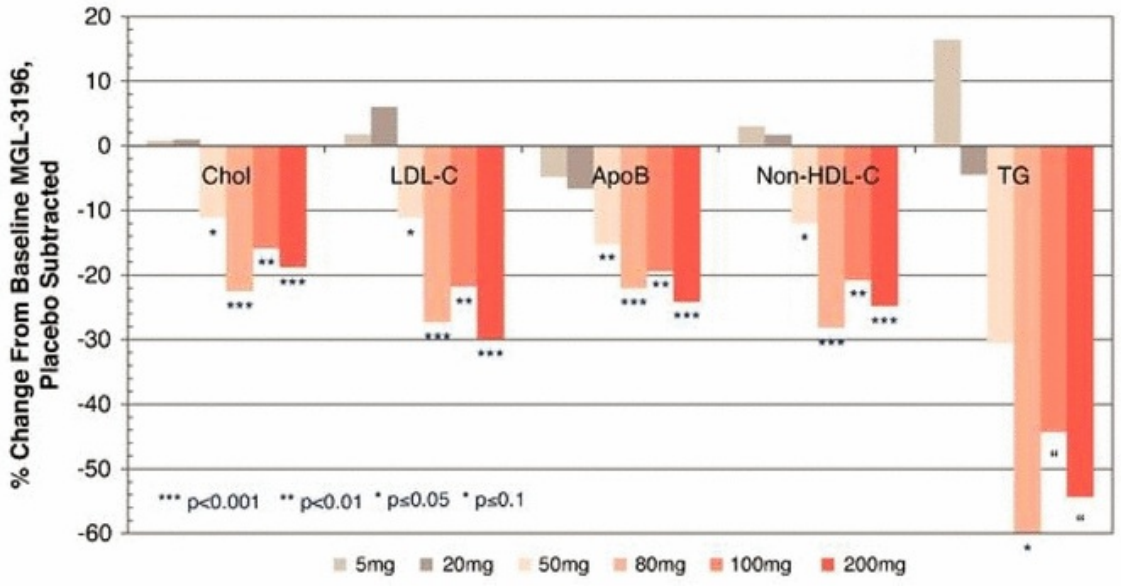
MGL-3196 Clinical and Non-Clinical Development Program

To date, we have completed a series of Phase 1 and 2 clinical studies, Phase 2-enabling preclinical good laboratory practice, or GLP, toxicology studies, and drug manufacturing studies to support further clinical development, including active pharmaceutical ingredient, or API, manufacturing and drug product development studies, drug metabolism studies, acute, subchronic and chronic animal toxicology studies, and other safety pharmacology and toxicology studies.

We have completed Phase 1 studies with MGL-3196 in a total of 183 subjects to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamic effects of MGL-3196. Our Phase 1 studies included randomized, placebo-controlled, double-blind, single and 14-day multiple-dose escalation studies, drug-interaction studies with statins, a study using radiolabeled MGL-3196, and a study of table verses capsule formulation of MGL-3196. In Phase 1 studies, MGL-3196 appeared safe and was well-tolerated at all doses tested. The results of these studies suggest that MGL-3196 has pharmacokinetic properties suitable for once-daily oral dosing.

In the multiple ascending dose study, lipid parameters were assessed as initial markers of MGL-3196 pharmacodynamic activity (Atherosclerosis 230:373-380, 2013). As illustrated in the figure below, daily doses of MGL-3196 ranging from 50 to 200 mg showed highly statistically significant reductions relative to placebo of up to 30% for LDL-C (range, p=.05-<0.0001), 28% for non-HDL-C (range, p =0.027-p<0.0001) and 24% for ApoB (range, p =0.008-0.0004), and statistical trends of up to 60% reduction in TG (range, p =0.13-0.016). The near maximal lipid effects were observed at a MGL-3196 dose of 80 mg once-daily. MGL-3196 was well-tolerated at all doses, with no dose-related adverse events or liver enzyme, electrocardiography or vital-sign changes. At the highest dose of MGL-3196 (200 mg), there was a reversible reduction of 20% in the level of a precursor hormone to T3, free T4, which was significantly different from placebo ($p < 0.0001$) that may be explained by increased liver metabolism of free T4. There was no change in thyrotropin, a pituitary hormone that regulates the level and production of thyroid hormone by the thyroid gland or T3, or other evidence of central thyroid axis dysfunction at any dose of MGL-3196.

Change in Lipids After 14 Days



Change from Baseline (CFB) by mean % CFB calculated for each individual subject 24 h after 14th dose; baseline value obtained just prior to first dose; ApoB, apolipoprotein B; Chal, total cholesterol; LDL-C, LDL cholesterol directly measured; Non-HDL-C, non-HDL cholesterol; TG, triglycerides (median %CFB).

While we are encouraged by these results, they are based on a small number of patients in early-stage clinical trials and are not necessarily predictive of results in later-stage clinical trials with larger and more diverse patient populations. In addition, the FDA typically requires sponsors of lipid-lowering product candidates to conduct drug-drug interaction studies with statins because statins may have increased safety risks when administered together with other drug therapies that affect their pharmacokinetic profile. We have completed two clinical drug interaction studies of MGL-3196 and three commonly used statins in 39 normal healthy volunteers, which showed MGL-3196 to have a favorable safety profile and to be well-tolerated. We have initiated a Phase 2 clinical trial in NASH including patients taking low dose statins. We reached our top-line analysis of the primary endpoint for the Phase 2 clinical trial in NASH in December 2017. We have also completed a 12 week Phase 2 clinical trial in HeFH including patients taking high dose statins that is fully enrolled (116 patients). In February 2018, we announced positive results from the 12 week Phase 2 clinical trial in HeFH.

The randomized, double-blind, placebo-controlled, multi-center NASH Phase 2 clinical trial 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 placebo (N=41) or MGL-3196 (N=84) with twice as many patients receiving MGL-3196 as placebo. The starting dose in MGL-3196-treated patients was 80 mg once a day. The study employed an adaptive dosing design whereby, in a blinded fashion, the dose could be adjusted by small amounts (i.e. 20 mg up or down) or remain at 80 mg in each MGL-3196-treated patient based on a pharmacokinetic analysis of drug level performed in each patient at 2 weeks.

The primary endpoint of the study is the reduction of liver fat at 12 weeks compared with baseline (relative change), assessed by MRI-PDFF, with efficacy confirmed at the end of the trial (36 weeks) by repeat MRI-PDFF and conventional liver biopsy to examine histological evidence for the resolution of

NASH. A total of 116 patients completed the 12 week MRI-PDFF; the nine discontinuations were balanced between placebo and drug treated; two of the nine discontinuations were AE-related.

Other secondary endpoints include changes in clinically relevant biomarkers at 12 and 36 weeks, improvement in fibrosis by at least one stage with no worsening of steatohepatitis, and safety and tolerability. We expect results at 36-weeks in the second quarter of 2018. In this trial, MGL-3196 demonstrated statistically significant results for the primary endpoint, the percent change in hepatic fat versus placebo as measured by MRI-PDFF, a non-invasive imaging test. Recent published data have shown a high correlation of the reduction of liver fat of 30% or more as measured by MRI-PDFF to improvement in NASH on liver biopsy.

	ALL MGL-3196	HIGH MGL-3196**	Placebo
Numbers of patients	78	44	38
Relative change in MRI-PDFF (% change from baseline, median)			
Significance relative to placebo	–36.3% p<0.0001	–42.0% p<0.0001	–9.6%
Percentage of patients attaining □30% liver fat reduction			
Significance relative to placebo	60.3% p<0.0001	75.0% p<0.0001	18.4%

** Prespecified group of patients (44/78) with relatively higher MGL-3196 drug levels

Statistically significant reductions in ALT and AST were observed in MGL-3196 treated patients; greater reductions in ALT and AST, statistically significant relative to placebo, were observed in the prespecified group of 44/78 patients with relatively higher MGL-3196 drug levels. In drug-treated relative to placebo patients, statistically significant improvements were also seen in multiple secondary endpoints considered to be potentially clinically relevant in patients with NASH including LDL-C, TGs, ApoB, and Lp(a).

MGL-3196 has been well-tolerated with mostly mild AEs, and a few moderate AEs, the numbers of which are balanced between placebo and drug-treatment groups. There are no adverse effects of MGL-3196 on safety laboratory or vital sign parameters. There have been three serious adverse effects in the study, all considered unrelated to MGL-3196.

The on-going Phase 2 clinical trial remains blinded. Safety, efficacy of NASH resolution by biopsy, and repeat MRI-PDFF will be assessed at 36 weeks. Multiple inflammatory and fibrosis serum biomarkers at 12 and 36 weeks are being and will be assessed.

Our Strategy

Our goal is to become a leading biopharmaceutical company developing and commercializing innovative liver-directed, β-selective thyroid hormone receptor agonists for the treatment of cardio-metabolic and liver disease, fibrosis and inflammation. A key element is building a multi-therapy NASH focused company. To achieve our goal, we plan to:

- ***Complete clinical development and seek regulatory approval of MGL-3196 in NASH.*** We reported data for the primary endpoint from our Phase 2 study in NASH in December 2017. NASH is a disease driven by the growing epidemic of obesity, with a significant unmet need for approved therapies that are effective and well tolerated. We believe MGL-3196 is an excellent candidate for the chronic treatment of NASH due to its safety profile and first-in-class dual mechanism of action targeting fibrosis-generating cells.

- ***Establish commercial capabilities to market MGL-3196 as a leading treatment for NASH.*** If approved, we may choose either to establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize MGL-3196, or to collaborate

with one or more third parties to accomplish these tasks. Patients with NASH are primarily managed by a concentrated group of liver specialists in the United States and Europe. We believe this will enable us to launch MGL-3196 in NASH in a cost-effective, targeted manner.

- ***Grow our pipeline through additional indications for MGL-3196 including orphan indications.*** We believe that MGL-3196 has the potential to be an effective treatment for other disease indications that are rare diseases or may be designated rare diseases, including HoFH and severe HeFH, and we plan to pursue orphan drug designation where possible.

Target Indications

Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis

Overview and Market Opportunity

NASH is a serious inflammatory form of nonalcoholic fatty liver disease, or NAFLD. NAFLD has become the most common liver disease in the United States and other developed countries and is characterized by an accumulation of fat in the liver with no other apparent causes. The rising worldwide prevalence of obesity-related disorders has contributed to a rapid increase in the global prevalence of NASH and NAFLD. In the United States, NAFLD is estimated to affect approximately 27% to 34% of the population, or an estimated 86 million to 108 million people, and approximately 10% to 20% of those will progress from NAFLD to NASH. Current estimates place NASH prevalence at approximately 9 million to 15 million people in the United States, or three percent to five percent of the population, with similar prevalence in Europe and Asia. The prevalence of NASH is also increasing in developing regions due to the adoption of a more sedentary lifestyle and a diet consisting of processed foods with high fat and fructose content.

In addition to the accumulation of fat in the liver, NASH is characterized by inflammation and cellular damage with or without fibrosis, the first stage of liver scarring, which may ultimately progress to cirrhosis. NASH is a severe condition that can lead to fibrosis and eventually progress to cirrhosis, portal hypertension, esophageal varices, ascites, liver cancer and liver failure. NASH is strongly associated with cardiovascular disease, or CVD, and the most common cause of death in NASH patients is CVD. Progression to cirrhosis and other late-stage complications can occur within five to ten years after an initial NASH diagnosis. NASH patients with type-2 diabetes have a heightened risk of NASH disease progression. Once the disease advances beyond NASH to such life-threatening conditions as liver cancer and failure, then liver transplantation is the only treatment alternative.

The Centers for Disease Control and Prevention projects the prevalence of obesity to increase from 34% of the United States population to 42% of the United States population by 2030. Driven by this epidemic of obesity, NASH is projected to become the leading cause of liver transplants by 2020. Given the extremely limited availability of organ donors and high transplant costs, NASH patients who require transplantation will place a significant economic burden on the healthcare system. As such, there is a significant unmet medical need for well-tolerated oral treatments for NASH. Because there are currently no therapeutic products approved for the treatment of NASH, the market size is difficult to estimate. However, based on our analysis of multiple market assessments, we estimate that the addressable NASH population is several million patients worldwide, and that NASH could become a multi-billion dollar market able to support multiple approved drug products.

MGL-3196 in NASH

We are developing MGL-3196 for NASH. Based on the scientific literature in human and animal studies, we believe that NASH livers in humans frequently have a deficiency in THR-β activity that leads to features of NASH, including fatty liver, inflammation and fibrosis, and that treatment with MGL-3196 will replace this hormone deficiency and be an effective NASH treatment. We believe that

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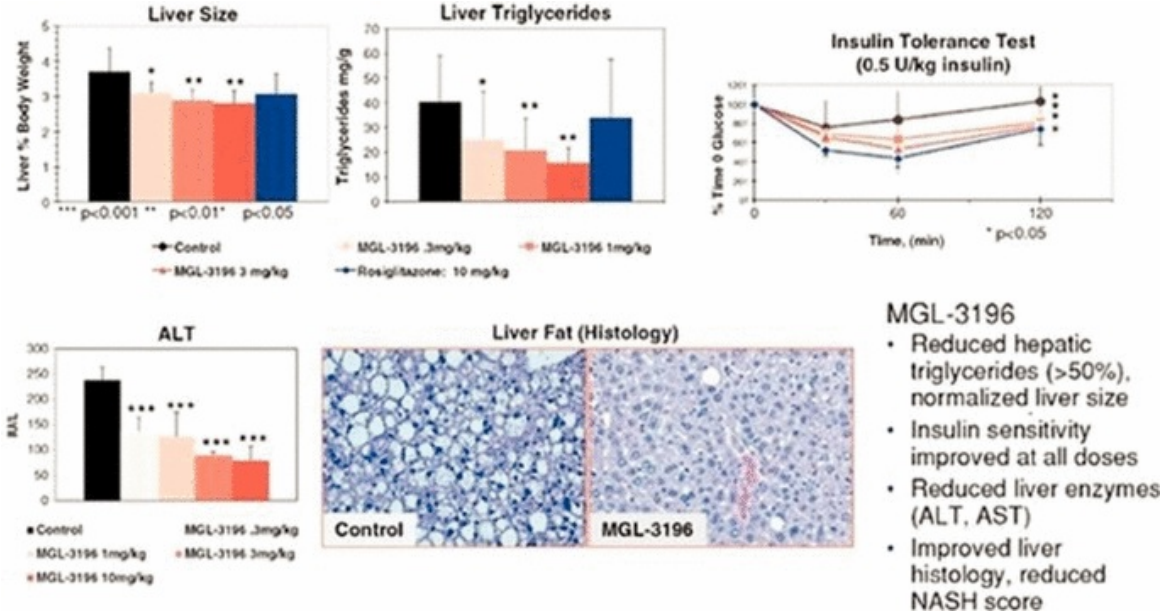
MGL-3196 is an excellent candidate for the chronic treatment of NASH because of its safety and tolerability profile observed to date in healthy subjects, its effects in reducing cardiovascular risk factors such as LDL-C and TGs in early-stage clinical trials, and its multiple beneficial effects in animal models of NASH. CVD is the most common cause of death in patients with NASH. We have completed multiple studies in animal models of metabolic diseases, dyslipidemia and NASH in which MGL-3196 demonstrated a statistically significant reduction in liver TGs, insulin resistance, liver enzymes (which may be elevated in NASH), and markers of inflammation and fibrosis (Figures). The figures below show the beneficial effects of MGL-3196 to reduce these parameters in NASH animal models. We believe that MGL-3196 will treat the underlying lipotoxicity that drives the inflammation and liver cell damage observed in NASH patients, and after the underlying lipotoxicity is treated, NASH-related liver fibrosis will resolve as the liver regenerates.

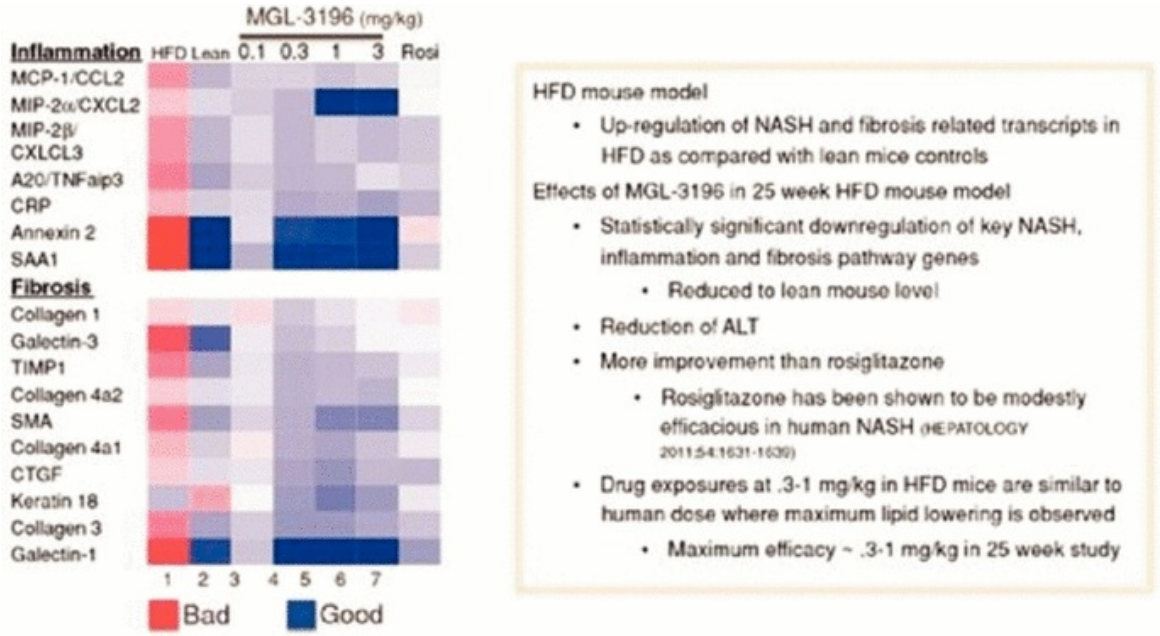
MGL-3196: Preclinical NASH Animal Model Study

Upper panels: 24d study in 17 wk old DIO mice (po, qd) on high fat diet (HFD) 13 wks;
lower panels: 24d study in 40 wk old DIO mice on HFD 35 wks



MGL-3196 Preclinical NASH Animal Model Gene Expression Study

25 week study in DIO, lean control mice and HFD mice treated with 0.1 to 3 mg/kg MGL-3196 or Rosiglitazone (3mg/kg)



"HFD", lane 1 means HFD gene expression normalized to mean Lean; Lanes (2-7) mean gene expression normalized to mean of DIO; "Rosi" (rosiglitazone, 3 mg/kg, 24 weeks); TIMP1 tissue inhibitor metalloproteinase; CTGF connective tissue growth factor; SMA smooth muscle actin; SAA serum amyloid A; CRP C-reactive protein; Red, higher expression; blue decreased expression.

MGL-3196 NASH Phase 2 Clinical Plan

In October 2016, we initiated a Phase 2 proof of concept clinical trial in patients with liver biopsy documented NASH, including those with type-2 diabetes, dyslipidemia and hypertension. In the study we have randomized 125 NASH patients 2:1, MGL-3196 or placebo QD in a double-blind, placebo-controlled, study of once-daily MGL-3196 versus placebo in patients with NASH, including those with type-2 diabetes. Patients are to continue treatment through 36 weeks. The study is being conducted in the United States. The primary endpoint is to evaluate the efficacy of MGL-3196 as measured by the reduction of liver fat at 12 weeks, and the secondary endpoint will be to evaluate the efficacy of MGL-3196 as measured by a reduction of NASH, which will be assessed by liver biopsy, at 36 weeks. Other secondary and exploratory endpoints include safety and tolerability, and effects on serum biomarkers at 12 and 36 weeks, lipid parameters, and biomarker measures of insulin sensitivity. We reached our top-line analysis of the primary endpoint in December 2017, and we expect to reach our top-line analysis of the secondary endpoint (NASH assessment on liver biopsy) in the spring of 2018.

In September 2013, the American Association for the Study of Liver Disease and the FDA conducted a joint workshop focused on trial designs and endpoints in drug and diagnostic development for liver disease secondary to NAFLD, including NASH. In December 2014, the journal Hepatology accepted for publication a manuscript summarizing the workshop output, including potentially acceptable surrogate endpoints for clinical studies supporting the approval of agents for NASH and liver fibrosis. We believe that our Phase 2 NASH study design incorporates surrogate secondary

endpoints consistent with the current FDA requirements for demonstration of efficacy in registrational trials. Following completion of our Phase 2 clinical trial of MGL-3196 in NASH patients we intend to meet with the FDA and other regulatory agencies to discuss a Phase 3 clinical plan for MGL-3196 in NASH. We cannot be certain what efficacy endpoints and other elements the FDA or other regulatory agencies would require for approval of MGL-3196 in NASH. However, currently there are ongoing Phase 3 clinical trials of compounds to treat NASH by other companies in which it is contemplated that accelerated approval of the compounds under FDA subpart H, which provides for accelerated approval of certain new drug products that have been studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit to patients over existing treatments, would be based on the surrogate endpoint of histological evidence of NASH resolution without the worsening of fibrosis. It is expected that these trials would continue after approval to confirm the long term clinical benefit of NASH resolution based on a reduction in patients progressing to cirrhosis and other liver related events.

Familial Hypercholesterolemia

Overview and Market Opportunity

FH is a genetic disorder characterized by aggressive and early onset CVD. In people with FH, genetic mutations make the liver incapable of metabolizing or removing excess LDL-C, causing very high LDL-C levels in the blood. There are two forms of FH: HoFH, a less common condition where mutation is inherited from both parents, and HeFH, a more common condition where mutation is inherited from just one parent. The vast majority of the cholesterol circulating in a person's body is produced by the liver. Cholesterol is a necessary component in the structure and function of human cells. Individuals with FH are unable to recycle this natural supply of cholesterol that their bodies are constantly producing. Therefore, the cholesterol levels of an individual with FH are exceedingly high. Over time, the elevated blood cholesterol can lead to blockages in the arteries of the heart and/or brain. The longer a person experiences high LDL-C, the more likely he or she will be to experience a cardiovascular event (*i.e.*, heart attack or stroke).

HoFH has an estimated worldwide prevalence of 1 in 160,000 to 1 in 1,000,000 and is a life-threatening condition characterized by markedly elevated levels of LDL-C. This is predominantly due to inactivating mutations in the LDL receptor, with onset of atherosclerotic CVD in childhood to early adulthood. HeFH, more common than HoFH, has an estimated worldwide prevalence of 1 in 200 to 1 in 500 and is characterized by early onset CVD in middle age, typically caused by an inactivating mutation in one of the two LDL receptor genes. While HeFH patients have a range of disease severity, we believe approximately 10% of the HeFH population can be characterized as having severe FH, with higher baseline LDL-C levels (>309 mg/dL; 8 mmol/L) than those of a majority of the HeFH population. Despite multiple therapeutics currently available for the treatment of HoFH, including statins, ezetimibe, and newer agents such as lomitapide, mipomersen, and anti-PCSK9 antibodies, we believe that the treatment target goal to reduce LDL-C to recommended levels is rarely achieved. In HeFH, with the recent addition of anti-PCSK9 antibodies to the treatment regimen, we believe that LDL-C target treatment goals (<100 mg/dL; < 70 mg/dL in patients with CVD or diabetes) may be achieved in > 50% of the patients; however, many HeFH patients, particularly those with severe FH or who cannot tolerate treatment with high-dose statins, are not at goal and are in need of additional lipid-lowering therapies beyond current therapeutic approaches. In addition, elevation of Lp(a), a severely atherogenic lipoprotein particle, which is frequently elevated in FH patients, is not effectively lowered by current therapeutic approaches. In 2014, an estimated $16.6 billion was spent on drug therapy in the United States, five major European Union, or EU, markets, and Japan to treat dyslipidemias, according to Datamonitor.

MGL-3196 in FH

We are developing MGL-3196 for FH and potentially other genetic dyslipidemias. We believe that experimental results from various sources, including Madrigal, academic groups and other pharmaceutical companies, support targeting the THR-β pathway as a potential novel approach to lipid-lowering in FH. We believe that MGL-3196 has a unique and complementary lipid-lowering profile that will bring an added benefit to the standard of care treatment of FH patients, particularly those with severe HeFH (~10% of FH patients with high baseline LDL-C, typically >309 mg/dL) and those with HoFH who do not achieve LDL-C target levels with current therapies. Specifically, in preclinical animal studies MGL-3196 lowered LDL-C in a variety of species as a monotherapy and also when dosed in combination with statins. MGL-3196 also showed the potential to lower Lp(a), a severely atherogenic particle that is frequently elevated in patients with FH. A previous THR agonist, eprotirome, demonstrated clinical proof of concept for the THR target in Phase 2 and Phase 3 FH clinical trials by significantly lowering LDL-C and Lp(a) in patients with HeFH who were on standard treatments such as statins and ezetimibe. The development of eprotirome ceased during the Phase 3 FH trial due to liver toxicity observed in the trial as well as eprotirome-induced cartilage damage seen in chronic toxicology studies in dogs. Because of its high level of THR-β selectivity, its liver-targeting properties, and its absence of findings in chronic animal toxicology studies, we believe that MGL-3196 will avoid the toxicity issues of previous THR agonist compounds and may be a beneficial treatment for FH patients.

MGL-3196 FH Phase 2 Clinical Plan

In February 2017, we initiated a Phase 2 clinical trial of MGL-3196 for the treatment of HeFH. In the study we have randomized HeFH patients 2:1, MGL-3196 or placebo QD in double-blind, placebo-controlled fashion. Patients are to continue treatment through 12 weeks. The study is being conducted in Europe. In this 12 week clinical trial, the primary endpoint is to evaluate the efficacy of MGL-3196 as measured by the percent reduction in LDL-C as compared with placebo. Secondary endpoints include safety and tolerability, and evaluate the efficacy of MGL-3196 to reduce a variety of lipid parameters, including non-HDL-C, ApoB, TGs, Lp(a), apoA/B, and lipoprotein particles. In February 2018, we announced positive results from the 12 week Phase 2 clinical trial of MGL-3196 for the treatment of HeFH.

Collaborations

VIA Pharmaceuticals, Inc., or VIA, entered into a research, development and commercialization agreement, or the Roche Agreement, with Roche, on December 18, 2008. We subsequently assumed all of VIA's rights in, to and under, and all of VIA's obligations under, the Roche Agreement pursuant to an asset purchase agreement, dated September 14, 2011. Pursuant to the terms of the Roche Agreement, we, as successor-in-interest to VIA, assumed control of all development and commercialization of MGL-3196 and will hold exclusive worldwide rights for all potential indications. Under the Roche Agreement, Roche exclusively licensed certain patent rights and know-how relating to MGL-3196 in exchange for consideration consisting of an upfront payment, milestone payments, the remainder of which total $10 million and are tied to future commencement of Phase 3 clinical trials and regulatory approval in the United States and Europe of MGL-3196 or any derivative product, and single-digit royalty payments based on net sales of MGL-3196 and any derivative products, subject to certain reductions. In 2011, we commenced Phase 1 clinical trials and subsequently paid Roche a related milestone payment. In October 2016, we commenced a Phase 2 study in NASH and subsequently paid Roche a related milestone payment. Except as described above, we have not achieved any additional product development or regulatory milestones under the Roche Agreement and have generated no net sales of products developed from MGL-3196.

Pursuant to the Roche Agreement, we must use commercially reasonable efforts to conduct clinical and commercial development programs for products containing MGL-3196. If we determine that it is not reasonable to continue clinical trials or other development of MGL-3196, we may elect to cease further development and Roche may terminate the license. If we determine not to pursue the development or commercialization of MGL-3196 in certain jurisdictions, including the United States, Roche may terminate the license for such territories. The Roche Agreement will expire, unless earlier terminated pursuant to other provisions of the agreement, on the last to occur of (i) the expiration of the last valid claim of a licensed patent covering the manufacture, use or sale of products containing MGL-3196, or (ii) ten years after the first sale of a product containing MGL-3196.

Competition

The development and commercialization of new drugs is highly competitive. We will face competition with respect to all product candidates we may develop or commercialize in the future from pharmaceutical and biotechnology companies worldwide. The key factors affecting the success of any approved product will be its efficacy, safety profile, drug interactions, method of administration, pricing, reimbursement and level of promotional activity relative to those of competing drugs.

Our potential competitors may have substantially greater financial, technical, and personnel resources than us. In addition, many of these competitors have significantly greater commercial infrastructures. Our ability to compete successfully will depend largely on our ability to leverage our collective experience in drug discovery, development and commercialization to:

- discover and develop medicines that are differentiated from other products in the market,
- obtain patent and/or proprietary protection for our products and technologies;
- obtain required regulatory approvals;
- obtain a commercial partner;
- commercialize our drugs, if approved; and
- attract and retain high-quality research, development and commercial personnel.

There are currently no therapeutic products approved for the treatment of NASH. There are several commercially available products that are currently used off-label for NASH, such as vitamin E, an antioxidant, insulin sensitizers, such as pioglitazone, anti-hyperlipidemic agents, such as gemfibrozil, pentoxifylline, ursodiol and others. In addition, there are numerous drugs in development for the treatment of NASH. We are aware of several companies that have product candidates in clinical development for the treatment of NASH, including Intercept Pharmaceuticals, Inc., Gilead Sciences, Inc., Galectin Therapeutics, Inc., Allergan plc / Tobira Pharmaceuticals, Inc., Galmed Medical Research Ltd., Genfit Corp., Cirius Therapeutics, Novartis AG, Novo Nordisk A/S, Takeda, Immuron Ltd., Shire plc, Boehringer Ingelheim GmbH, Bristol-Myers Squibb, Pfizer, Inc., Sanofi S.A., NGM Biopharmaceutical, and Conatus Pharmaceuticals Inc., and there are other companies with candidates in earlier stages of development. Given MGL-3196's actions on the underlying biological pathways across the spectrum of early to late stages of NASH, its CV beneficial effects, and its complementary mechanism to other therapies, we believe that MGL-3196 has the potential to be used alone or in combination with some of these potential NASH products.

There are several marketed products, both generic and proprietary, available for the treatment of HoFH and HeFH. We believe that MGL-3196 has the potential to be used in combination with several of these products. Available marketed products include: various statins, Merck's ezetimibe, Aegerion's lomitapide, Ionis' mipomersen, Amgen's evolocumab and Sanofi/Regeneron's alirocumab. In addition, there are multiple drugs in development for the treatment of FH, including Gemphire's gemcabene, Merck's anacetrapib, Esperion's ETC-1002, and drugs at an earlier stage of development. Given

MGL-3196's pleoitropic lipid-lowering actions, its complementary mechanism to statins and other lipid-lowering drugs, and its potential for lowering Lp(a), we believe that MGL-3196 has the potential to be used in combination with the standard of care to treat patients with HoFH and HeFH.

Sales and Marketing

Because we are focused on discovery and development of our product candidates, we currently have no sales, marketing or distribution capabilities in order to commercialize any approved product candidates. If our product candidates are approved, we intend either to establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize our products, or to outsource this function to a third party.

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently rely, and expect to rely, on third-party contract manufacturers, or CMOs, for the manufacture of any product candidates that we may develop for larger-scale preclinical and clinical testing, as well as for commercial quantities of any drug candidates that are approved.

Research and Development

Research and development expenses primarily consist of costs associated with our research activities, including the preclinical and clinical development of our product candidates. Our research and development expenses were $24.4 million for the year ended December 31, 2017 compared to $15.9 million for the same period in 2016. The increase in research and development expenses was primarily due to the advancement of clinical programs to Phase 2 studies, further API manufacturing studies and the continuation of preclinical studies. We expect research and development expenses to increase over time as we advance our clinical and preclinical development programs for MGL-3196.

Intellectual Property

We will be able to protect our technology and products from unauthorized use by third parties only to the extent we are covered by valid and enforceable patents or such knowledge is effectively maintained as trade secrets. Patents and other proprietary rights are thus an essential element of our business. We also rely on trade secrets, know-how, continuing technological innovation and licensing opportunities to develop and maintain our competitive position.

Our success will depend in part on our ability to obtain and maintain patent and other proprietary protection for our current and future product candidates, technology and know-how, to operate without infringing on the proprietary rights of others, and to prevent others from infringing our proprietary rights. We seek to protect our proprietary position by, among other methods, filing United States and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business.

We own, co-own or have exclusive rights to three United States and 69 foreign issued patents and allowed patent applications, and two United States and 25 foreign pending patent applications, relating to composition-of-matter of MGL-3196, including certain dosage forms, and its use in the treatment of key disease indications. Our current patent portfolio covers the United States and certain other jurisdictions worldwide.

Issued United States patents directed to MGL-3196, including certain dosage forms, have statutory expiration dates between 2026 and 2033, excluding any patent term extensions that might be available following the grant of marketing authorizations. Issued patents outside of the United States directed to MGL-3196, including certain dosage forms, have statutory expiration dates between 2026 and 2033. We

have pending patent applications for MGL-3196 that, if issued, would be expected to expire in the United States and in countries outside of the United States between 2026 and 2033, excluding any patent term adjustment that might be available following the grant of the patent and any patent term extensions that might be available following the grant of marketing authorizations.

In addition, pursuant to the Roche Agreement, Roche granted us an exclusive license to certain patents and know-how relating to MGL-3196, including many of the patents and patent applications referred to above. The Roche Agreement imposes various diligence, milestone payment, royalty payment, insurance, indemnification, and other obligations on us.

Our trademarks are protected under the common law and/or by registration in the United States and other countries. We seek to protect our proprietary processes, in part, by confidentiality agreements and invention assignment agreements with our personnel, including consultants and commercial partners. These agreements are designed to protect our proprietary information.

Orphan Drug Designation

Some of MGL-3196's target disease indications are rare diseases or may be designated rare diseases, including HoFH and severe HeFH, and we plan to pursue orphan drug designation where possible. If granted, each such designation might provide for regulatory exclusivity for seven years in the United States and ten years in the EU from the date of product approval for individual indications.

Government Regulation

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and export and import of products such as those we are developing. A new drug must be approved by the FDA through the new drug application, or NDA, process before it may be legally marketed in the United States, and must be approved by foreign regulatory authorities via various procedures before it can be marketed in the applicable country. The animal and other non-clinical data and the results of human clinical trials performed under an Investigational New Drug application, or IND, and under similar foreign applications will become part of the NDA.

United States Drug Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other things, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters and other types of enforcement-related letters, requesting product recalls, product seizures, changes to the conditions surrounding marketing approval such as labeling changes or changes to a Risk Evaluation and Mitigations Strategies, or REMS, program, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, debarment, restitution, disgorgement of profits, or civil or criminal investigations and penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

The process required by the FDA before a drug or biologic may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies according to GLP or other applicable regulations;
- submission to the FDA of an IND which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to Good Clinical Practices, or GCP, to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA;
- completion of registration batches and validation of the manufacturing process to show ability to consistently produce quality batches of product;
- satisfactory completion of a FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current good manufacturing practice, or cGMP, to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

Once a pharmaceutical candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies, to assess the safety and quality of the product. Animal studies must be performed in compliance with FDA's GLP regulations and the U.S. Department of Agriculture's Animal Welfare Act. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. The sponsor will also include a protocol detailing, among other things, the objectives of the first phase of the clinical trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated, if the first phase lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the clinical trial on a clinical hold or a partial clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during studies due to safety concerns or non-compliance, or other reasons.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with good clinical practice regulations. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and progress reports detailing the results of the clinical trials must be submitted at least annually. In addition, timely safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events or animal test results that suggest a significant risk to human subjects. An institutional review board, or IRB, at each institution participating in the clinical trial must review and approve each protocol before a clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be provided to each trial subject or his or her legal representative, monitor the study until completed and otherwise comply with IRB regulations. Foreign studies conducted under an IND must meet the same requirements that apply to studies being conducted in the U.S. Data from a foreign study not conducted under an IND may be submitted in support of an NDA if the study was conducted in accordance with GCP and the FDA is able to validate the data.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- *Phase 1:* The product candidate is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients with the target diseases.

- *Phase 2:* This phase involves studies in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- *Phase 3:* This phase involves trials undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product candidate and provide, if appropriate, an adequate basis for product approval and product labeling.

The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Phase 1, Phase 2, and Phase 3 testing may not be completed successfully within any specified period, if at all. Further, success in either preclinical studies or early-stage clinical trials does not assure success in later-stage clinical trials. Sponsors of all controlled clinical trials, except for Phase 1 trials, are required to submit certain clinical trial information for inclusion in the public clinical trial registry and results data bank maintained by the National Institutes of Health, which are publicly available at http://clinicaltrials.gov.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and FDA to reach agreement on the next phase of development. Sponsors typically use the end of Phase 2 meeting to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support approval of the new drug.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

United States Review and Approval Processes

The results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling, and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of user fees; a waiver of such fees may be obtained under certain limited circumstances. The FDA conducts a preliminary review of all NDAs submitted to ensure that they are sufficiently complete for substantive review before it

accepts them for filing. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA may refer the NDA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. The approval process is lengthy and often difficult, and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data and information. Even if such data and information are submitted, the FDA may ultimately decide that the NDA does not satisfy the regulatory criteria for approval. Data obtained from clinical trials are not always conclusive, and the FDA may interpret data differently than we interpret the same data. The FDA may issue a complete response letter, which generally outlines the deficiencies in the submission and may require additional clinical or other data or impose other conditions that must be met in order to secure final approval of the NDA, or an approval letter following satisfactory completion of all aspects of the review process. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured. In addition, the FDA often will conduct a bioresearch monitoring inspection of the clinical trial sites involved in conducting pivotal studies to ensure data integrity and compliance with applicable GCP requirements.

NDAs receive either standard or priority review. A drug representing a significant improvement in treatment, prevention or diagnosis of disease may receive priority review. Priority review for an NDA for a new molecular entity will be six months from the date that the NDA is filed. The FDA has ten months in which to complete its initial review of a standard new molecular entity NDA. The FDA does not always meet its goal dates and in certain circumstances the goal date may be extended. In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and which provide meaningful therapeutic benefit over existing treatments, may receive accelerated approval. In that situation, the product may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on the basis of an effect on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. Priority review and accelerated approval do not change the standards for approval, but may expedite the approval process.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases, dosages or patient populations, or the indications for use may otherwise be limited, which could restrict the commercial value of the product. In addition, the FDA may require a sponsor to conduct Phase 4 testing which involves clinical trials designed to further assess a drug's safety and effectiveness after NDA approval, and may require testing and surveillance programs to monitor the safety of approved products which have been commercialized.

The Food and Drug Administration Safety and Innovation Act, or FDASIA, which was enacted in 2012, made permanent the Pediatric Research Equity Act, or PREA, which requires a sponsor to conduct pediatric studies for most drugs and biologics, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements thereto must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each

pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug or biologic is ready for approval for use in adults before pediatric studies are complete or that additional safety or effectiveness data needs to be collected before the pediatric studies begin. After April 2013, the FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of our product candidates, some of our United States patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND, and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application, except that the period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension, and the extension must be applied for prior to expiration of the patent and within 60 days of approval. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Pediatric exclusivity is another type of marketing exclusivity available in the United States. The FDASIA made permanent the Best Pharmaceuticals for Children Act, or BPCA, which provides for an additional six months of marketing exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA, or a Written Request. If the Written Request does not include studies in neonates, the FDA is required to include its rationale for not requesting those studies. The FDA may request studies on approved or unapproved indications in separate Written Requests. The issuance of a Written Request does not require the sponsor to undertake the described studies.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years. Orphan drug exclusivity, however, also could block the approval of one of our product candidates for seven years if a competitor obtains approval of the same drug as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease.

The FDA also administers a clinical research grants program, whereby researchers may compete for funding to conduct clinical trials to support the approval of drugs, biologics, medical devices, and medical foods for rare diseases and conditions. A product does not have to be designated as an orphan drug to be eligible for the grant program. An application for an orphan grant should propose one discrete clinical study to facilitate FDA approval of the product for a rare disease or condition. The study may address an unapproved new product or an unapproved new use for a product already on the market.

Fast Track Designation and Accelerated Approval

The FDA is required to facilitate the development, and expedite the review, of drugs that are intended for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for such a disease or condition. Under the fast track program, the sponsor of a new drug candidate may request that the FDA designate the drug candidate for a specific indication as a fast track drug concurrent with, or after, the filing of the IND for the drug candidate. The FDA must determine if the drug candidate qualifies for fast track designation within 60 days of receipt of the sponsor's request.

Under the fast track program, the FDA may designate a drug for fast-track status if it is intended to treat a serious or life-threatening illness and nonclinical or clinical data demonstrate the potential to address an unmet medical need. Similarly, the agency may designate a drug for accelerated approval if it treats a serious condition and generally provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments.

In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions, or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

In FDASIA, Congress encouraged the FDA to utilize innovative and flexible approaches to the assessment of products under accelerated approval. The law required the FDA to issue related draft guidance within a year after the law's enactment and also promulgate confirming regulatory changes. In May 2014, the FDA published a Guidance for Industry entitled, "Expedited Programs for Serious Conditions-Drugs and Biologics" which provides guidance on FDA programs that are intended to facilitate and expedite development and review of new drugs as well as threshold criteria generally applicable to concluding that a drug is a candidate for these expedited development and review programs. In addition to the Fast Track, accelerated approval and priority review programs discussed above, the FDA also provided guidance on a new program for Breakthrough Therapy designation. A request for Breakthrough Therapy designation should be submitted concurrently with, or as an amendment to an IND. The FDA has already granted this designation to over 30 new drugs and has approved several.

Post-Approval Requirements

Once an approval is granted, products are subject to continuing regulation by the FDA. The FDA may withdraw the approval if, among other things, compliance with regulatory standards is not maintained or if safety or efficacy problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. If new safety issues are identified following approval, the FDA may require the NDA sponsor to take certain measures, such as revising the approved labeling to reflect the new safety information, conducting post-market studies or clinical trials to assess the new safety information, and/or implementing or changing a REMS Program to mitigate newly-identified risks. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further FDA review and approval. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws and regulations. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our product candidates. Future inspections by the FDA and other regulatory agencies may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct.

Any drug products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the drug, providing the FDA with updated safety and efficacy information, drug sampling and distribution requirements, complying with certain electronic records and signature requirements, and complying with FDA promotion and advertising requirements. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label.

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations and guidance are often revised or interpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of its products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries or economic areas, such as the 28-member European Union, before we may commence clinical trials or market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Under EU regulatory systems, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure, which is compulsory for medicinal products produced by biotechnology or those medicinal products containing new active substances for specific indications such as the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, viral diseases and designated orphan medicines, and optional for other medicines which are

highly innovative. Under the centralized procedure, a marketing application is submitted to the EMA where it will be evaluated by the Committee for Medicinal Products for Human Use and a favorable opinion typically results in the grant by the European Commission of a single marketing authorization that is valid for all EU member states within 67 days of receipt of the opinion. The initial marketing authorization is valid for five years, but once renewed is usually valid for an unlimited period. The decentralized procedure provides for approval by one or more "concerned" member states based on an assessment of an application performed by one member state, known as the "reference" member state. Under the decentralized approval procedure, an applicant submits an application, or dossier, and related materials to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on all member states.

When conducting clinical trials in the EU, we must adhere to the provisions of the EU Clinical Trials Directive and the laws and regulations of the EU Member States implementing them. These provisions require, among other things, that the prior authorization of an Ethics Committee and the submission and approval of a clinical trial authorization application be obtained in each Member State before commencing a clinical trial in that Member State.

As in the United States, it may be possible in foreign countries to obtain a period of market and/or data exclusivity that would have the effect of postponing the entry into the marketplace of a competitor's generic product. For example, in the EU, if any of our products receive marketing approval in the European Economic Area, or EEA, which is comprised of the 28 member states of the EU plus Norway, Iceland and Liechtenstein, we expect that we will benefit from eight years of data exclusivity and an additional two years of marketing exclusivity. An additional one-year extension of marketing exclusivity is possible if during the data exclusivity period we obtain an authorization for one or more new therapeutic indications that is deemed to bring a significant clinical benefit compared to existing therapies. The data exclusivity period begins on the date of the product's first marketing authorization in the EU and prevents biosimilars from relying on the holder of the marketing authorization for the reference biological medicine's pharmacological, toxicological and clinical data for a period of eight years. After eight years, a biosimilar product application may be submitted and the sponsoring companies may rely on the marketing authorization holder's data. However, a biosimilar medicine cannot launch until 2 years later (or a total of ten years after the first marketing authorization in the EU of the innovator product), or 3 years later (or a total of eleven years after the first marketing authorization in the EU of the innovator product) if the marketing authorization holder obtains marketing authorization for a new indication with significant clinical benefit within the eight year data exclusivity period.

As in the United States, a sponsor may apply for designation of a product as an orphan drug for the treatment of a specific indication in the EU before the application for marketing authorization is made. Orphan drugs in Europe enjoy economic and marketing benefits, including up to ten years of market exclusivity for the approved indication unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan-designated product.

Reimbursement

Significant uncertainty exists regarding the coverage and reimbursement status of products approved by the FDA and other government authorities. In the United States, sales of any products for which we may receive regulatory approval for commercial sale will depend in significant part on the availability and adequacy of coverage and reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other

organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list which might not include all of the FDA-approved products for a particular indication. Moreover, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Third-party payors are increasingly challenging the prices charged for, examining the medical necessity of, and assessing the cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of any products, in addition to the costs required to obtain regulatory approvals. Our drug candidates may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit.

The U.S. government and state legislatures have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, ACA, contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on cost containment measures in the United States has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the United States and generally tend to be significantly lower

Employees

As of March 8, 2018, we had eight full-time employees, including four engaged in research, development, and regulatory activities, and four in executive, general and administrative functions, and multiple part-time consultants.

General Information

We were incorporated in Delaware in September 2011. Our principal executive offices are located at 200 Barr Harbor Drive, Suite 400, West Conshohocken, PA 19428. Our Internet website address is www.madrigalpharma.com. No portion of Madrigal's website is incorporated by reference into this Annual Report on Form 10-K.

We advise you to read this Annual Report on Form 10-K in conjunction with other reports and documents that we file from time to time with the SEC. In particular, please read our definitive proxy statement, which will be filed with the SEC in connection with our 2018 annual meeting of stockholders, our quarterly reports on Form 10-Q and any current reports on Form 8-K that we may file from time to time. You may obtain copies of these reports after the date of this annual report directly from us or from the SEC at the SEC's Public Reference Room at 100 F Street, N.E. Washington, D.C. 20549. In addition, the SEC maintains information for electronic filers (including us) at its website at www.sec.gov. The public may obtain information regarding the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. We make our periodic and current reports available on our internet website, free of charge, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K for the fiscal year ended December 31, 2017, includes "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which statements are subject to considerable risks and uncertainties. Forward-looking statements include all statements that are not statements of historical facts contained in this Annual Report and can be identified by words such as "anticipates," "believes," "seeks," "estimates," "expects," "intends," "may," "plans," "potential," "predicts, "projects," "should," "could," "will," "would" or similar expressions and the negatives of those expressions. In particular, forward looking statements contained in this Annual Report relate to, among other things, our future or assumed financial condition, results of operations, business forecasts and plans, strategic plans and objectives, product development plans, recent accounting pronouncements and capital needs and financing plans. We caution you that the foregoing list may not include all of the forward-looking statements made in this Annual Report.

Forward-looking statements represent our management's current beliefs and assumptions based on information currently available. Forward-looking statements involve numerous known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. We discuss these risks and uncertainties in greater detail in the section entitled "Risk Factors" in Part I, Item 1A of this Annual Report, as well as in our other filings with the SEC. You should read this Annual Report, and the other documents that we have filed with the SEC, with the understanding that our actual future results may be materially different from the results expressed or implied by these forward-looking statements.

Moreover, we operate in an evolving environment. New risks and uncertainties emerge from time to time and it is not possible for our management to predict all risks and uncertainties, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual future results to be materially different from those expressed or implied by any forward-looking statements.

Except as required by applicable law or the rules of the NASDAQ Stock Market, or NASDAQ, we assume no obligation to update any forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

We qualify all of our forward-looking statements by these cautionary statements.

Item 1A. Risk Factors

You should carefully consider the risks described below, together with all of the other information included in or incorporated by reference into this report, before making an investment decision. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we do not currently believe are important to an investor may also harm our business. If any of the events, contingencies, circumstances or conditions described in the following risks actually occur, our business, financial condition or our results of operations could be seriously harmed. If that happens, the trading price of our common stock could decline and you may lose part or all of the value of any of our shares held by you.

Risks Related to Our Business

We have limited operating history, we have incurred significant operating losses since inception and we expect to incur significant operating losses for the foreseeable future. We may never become profitable or, if achieved, be able to sustain profitability.

We have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future as we continue our clinical trial and development programs for MGL-3196 and other future product candidates. As of December 31, 2017, we had an accumulated deficit of $106.5 million. Losses have principally resulted from costs incurred in our preclinical and clinical trials, research and development programs and from our general and administrative expenses. As of December 31, 2017, we had cash, cash equivalents and marketable securities of $191.5 million. In the future, we intend to continue to conduct research and development, clinical testing, regulatory compliance and, if MGL-3196 or other future product candidates are approved, sales and marketing activities that, together with anticipated general and administrative expenses, will likely result in us incurring further significant losses for the foreseeable future.

We currently generate no revenue from product sales, and we may never be able to commercialize MGL-3196 or other future product candidates. We do not currently have the required approvals to market MGL-3196 or any other future product candidates, and we may never receive them. We may not be profitable even if we or any of our future development partners succeed in commercializing any of our product candidates. Because of the numerous risks and uncertainties associated with developing and commercializing our product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

Our business depends on the success of MGL-3196, which is still in clinical development and has not completed a pivotal trial. If we are unable to obtain regulatory approval for and successfully commercialize MGL-3196, or we experience significant delays in doing so, our business will be materially harmed.

To date, the sole focus of our product development has been MGL-3196, a liver-directed selective thyroid hormone receptor beta agonist for potential use in non-alcoholic steatohepatitis, or NASH, and FH. Successful continued development and ultimate regulatory approval of MGL-3196 for NASH or genetic dyslipidemias, such as FH, is critical to the future success of our business. We have invested, and will continue to invest, a significant portion of our time and financial resources in the clinical development of MGL-3196. We will need to raise sufficient funds to successfully complete our clinical development program for MGL-3196 in NASH and FH. The future regulatory and commercial success of MGL-3196 is subject to a number of risks, including the following:

- we may not have sufficient financial and other resources to complete the necessary clinical trials for MGL-3196, including, but not limited to, our currently ongoing Phase 2 clinical trials and, later, registrational clinical trials to obtain drug approval;

- the mechanism of action of MGL-3196 is complex and we do not know the degree to which it will translate into a therapeutic benefit, if any, in NASH, FH or any other indication, and we do not know the degree to which the complex mechanism of action may contribute to long term safety issues or adverse events, if any, when MGL-3196 is taken for prolonged periods such as in the treatment of NASH, FH or any other indication;
- we may not be able to obtain adequate evidence from clinical trials of efficacy and safety for MGL-3196 in NASH, FH or any other indication;
- we do not know the degree to which MGL-3196 will be accepted as a therapy by physicians, patients and payors, even if approved;
- in our clinical programs for MGL-3196, we may experience variability in patients, adjustments to clinical trial procedures and the need for additional clinical trial sites, which could delay our clinical trial progress;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory bodies for marketing approval;
- patients in our clinical trials may die or suffer other adverse effects for reasons that may or may not be related to MGL-3196, which could delay or prevent further clinical development;
- the standards implemented by clinical or regulatory agencies may change at any time;
- we cannot be certain what efficacy endpoints FDA or foreign clinical or regulatory agencies may require in a Phase 3 clinical trial of NASH or FH or for approval of our product candidates; we also cannot be certain if we will be able to gain accelerated approval of any of our product candidates based on surrogate endpoints;
- the FDA or foreign clinical or regulatory agencies will likely require efficacy endpoints for Phase 3 clinical trials for the treatment of NASH or FH that differ from the endpoints of our current trials and the results of our Phase 3 clinical trials may not be as favorable as the results we have observed to date in our current trials;
- if we obtain accelerated approval of a product candidate based on a surrogate endpoint, we will likely be required to conduct a post-approval clinical outcomes trial to confirm the clinical benefit of the product candidate and if the post-approval trial is not successful we may not be able to continue marketing the product;
- if approved for NASH, MGL-3196 will likely compete with the off-label use of currently marketed products and other therapies in development that may reach approval for NASH prior to MGL-3196;
- if approved for FH, MGL-3196 will likely compete with currently approved and marketed products and other therapies in development that may reach approval for FH prior to MGL-3196; and
- we may not be able to obtain, maintain or enforce our patents and other intellectual property rights.

Of the large number of drugs in development in the pharmaceutical industry, only a small percentage results in the submission of a new drug application, or NDA, to the FDA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market MGL-3196, any such approval may be subject to limitations on the indicated uses or patient populations for which we may market the products. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, we may be unable to successfully develop or commercialize MGL-3196. If we or any of our future development partners are unable to

develop, or obtain regulatory approval for, or, if approved, successfully commercialize MGL-3196, we may not be able to generate sufficient revenue to continue our business.

Clinical trials are very expensive, time-consuming and difficult to design and implement and involve uncertain outcomes. Furthermore, the results of preclinical studies and early clinical trials are not always predictive of future results. Any product candidate that we advance into clinical trials, including MGL-3196, may not have favorable results in later clinical trials or receive regulatory approval.

Drug development has inherent risk. We will be required to demonstrate through adequate and well-controlled clinical trials that our product candidates are safe and effective, with a favorable benefit-risk profile, for use in our target indications before we can seek regulatory approvals for its commercial sale. Clinical studies are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. Delay or failure can occur at any stage of development, including after commencement of any of our clinical trials. In addition, success in early clinical trials does not mean that later clinical trials will be successful, because later-stage clinical trials may be conducted in broader patient populations and involve different study designs. For instance, our Phase 1 results and our Phase 2 primary endpoint results in NASH may not be predictive of any future Phase 2 results or of results in any Phase 3 clinical trial in NASH. Furthermore, our future trials will need to demonstrate sufficient safety and efficacy in larger patient populations for approval by regulatory authorities. Companies frequently suffer significant setbacks in advanced clinical trials, even after earlier clinical trials have shown promising results, and we cannot be certain that we will not face similar setbacks. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. In addition, only a small percentage of drugs under development result in the submission of an NDA to the FDA and even fewer are approved for commercialization.

We cannot be certain that any of our ongoing or future clinical trials will be successful, and any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications.

Because MGL-3196 has not yet received regulatory approval for any indication, it is difficult to predict the time and cost of development and our ability to successfully complete clinical development and obtain the necessary regulatory approvals for commercialization.

MGL-3196 has not yet received regulatory approval for the treatment of NASH, FH or any other indication, and unexpected problems may arise that could cause us to delay, suspend or terminate our development efforts in any or all indications. Further, MGL-3196 has not yet demonstrated efficacy in patients with NASH or FH, and the long-term safety consequences of a liver-directed thyroid hormone receptor beta agonist are not known. Regulatory approval of new product candidates such as MGL-3196 can be more expensive and take longer than approval for candidates for the treatment of more well-understood diseases with previously approved products.

If clinical trials or regulatory approval processes for our product candidates are prolonged, delayed or suspended, we may be unable to commercialize our product candidates on a timely basis, which would require us to incur additional costs and delay our receipt of any revenue from potential product sales.

We cannot predict whether we will encounter problems with any of our completed, ongoing or planned clinical trials that will cause us or any regulatory authority to delay, suspend, or terminate those clinical trials or delay the analysis of data derived from them. A number of events, including any of the following, could delay or impede completely the completion of our ongoing and planned clinical

trials and negatively affect our ability to obtain regulatory approval for, and to market and sell, a particular product candidate:

- conditions imposed on us by the FDA or other regulatory authorities regarding the scope or design of our clinical trials;
- insufficient supply of our product candidates or other materials necessary to conduct and complete our clinical trials;
- slow enrollment and retention rate of subjects in our clinical trials; and
- serious and unexpected drug-related side effects related to the product candidate being tested.

Commercialization of our product candidates may be delayed by the imposition of additional conditions on our clinical trials by the FDA or any other applicable foreign regulatory authority or the requirement of additional supportive studies by the FDA or such foreign regulatory authority.

We do not know whether our clinical trials will begin as planned, will need to be restructured, will enroll an adequate number of patients on time, or will be completed on schedule, if at all. Delays in the initiation, enrollment or completion of our clinical trials will result in increased development costs for our product candidates, and our financial resources may be insufficient to fund any incremental costs. In addition, if our clinical trials are delayed, our competitors may be able to bring products to market before we do and the commercial viability of our product candidates could be limited.

If we inadvertently fail to comply with foreign regulatory requirements governing human clinical trials and marketing approval for drugs, we could be prevented from selling our drug candidates in foreign markets, which may adversely affect our operating results and financial condition.

The requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement for marketing our drug candidates outside the United States vary greatly from country to country and may require additional testing. We expect that our future clinical development of our drug candidates will involve a number of clinical trials in foreign jurisdictions, particularly in Europe. We have no experience in obtaining foreign regulatory approvals. The time required to obtain approvals outside the United States may differ from that required to obtain FDA approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. Approval by the FDA does not guarantee approval by regulatory authorities in other countries, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other countries or by the FDA. Failure to comply with these regulatory requirements or obtain required approvals could impair our ability to develop foreign markets for our drug candidates and may have a material adverse effect on our results of operations and financial condition.

We depend on enrollment of patients in our clinical trials for our product candidates. If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. We may not be able to initiate, continue, or complete clinical trials required by the FDA or foreign regulatory agencies for MGL-3196 if we are unable to locate and enroll a sufficient number of eligible patients to participate in these clinical trials. Patient enrollment, a significant factor in the timing to conduct and complete clinical trials, is affected by many factors, including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials, and clinicians' and patients' perceptions as to the potential advantages and disadvantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. For instance, we are aware that other companies conducting clinical trials in NASH

patients have had delays in recruiting patients for their trials. In the proposed clinical trials, patient willingness to undergo a liver biopsy in our NASH trials, and identification of patients willing to participate in our FH trials due to the rarity of the disease, are also risk factors. Potential patients for MGL-3196 may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for our studies.

The FDA typically requires sponsors of lipid-lowering product candidates to conduct drug-drug interaction studies with statins because statins may have increased safety risks when administered together with other drug therapies that affect their pharmacokinetic profile. We have completed two Phase 1 clinical drug interaction studies of MGL-3196 and statins in 39 normal healthy volunteers, which showed MGL-3196 to have a favorable safety profile and to be well-tolerated. We have completed enrollment of a Phase 2 clinical trial in NASH including patients taking low dose statins. We have also completed enrollment of a Phase 2 clinical trial in HeFH including patients taking high dose statins. In general, drug interactions between MGL-3196 and statins and any other drug that might result in adverse events could delay development in later clinical trials.

We will be required to identify and enroll a sufficient number of patients for each of our ongoing and planned clinical trials of MGL-3196 for NASH and FH indications, respectively. We also may encounter difficulties in identifying and enrolling NASH patients and FH patients with a stage of disease appropriate for our ongoing or future clinical trials. We may not be able to initiate or continue clinical trials if we are unable to locate a sufficient number of eligible patients to participate in the clinical trials required by the FDA or other foreign regulatory agencies. In addition, the process of finding and diagnosing patients may prove costly. Our inability to enroll a sufficient number of patients for any of our clinical trials would result in significant delays or may require us to abandon one or more clinical trials.

Any product candidate in our current or future clinical trials may cause unacceptable adverse events or side effects or have other properties that may delay or prevent its regulatory approval or commercialization or limit its commercial potential.

Unacceptable adverse events or undesirable side effects caused by any of our product candidates in current or future clinical trials could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications and markets. This in turn could prevent us from completing development of or commercializing the affected product candidate and generating revenue from its sale. If any of our product candidates cause unacceptable adverse events in clinical trials, we may not be able to obtain regulatory approval or commercialize such product candidate.

Occurrence of serious treatment-related side effects could impede subject recruitment and clinical trial enrollment or the ability of enrolled patients to complete the trial, require us to halt the clinical trial, and prevent receipt of regulatory approval from the FDA. They could also adversely affect physician or patient acceptance of our product candidates or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Our product candidates will remain subject to ongoing regulatory review even if they receive marketing approval, and if we fail to comply with continuing regulations, we could lose these approvals and the sale of any approved commercial products could be suspended.

Even if we receive regulatory approval to market a particular product candidate, the manufacturing, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, sampling, and record keeping related to the product will remain subject to extensive regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP, regulations and

GCPs, for any clinical trials that we conduct post-approval, all of which may result in significant expense and limit our ability to commercialize such products. In addition, any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a REMS Program as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

If we fail to comply with the regulatory requirements of the FDA and other applicable domestic and foreign regulatory authorities, or previously unknown problems with any approved product, manufacturer, or manufacturing process are discovered, we could be subject to administrative or judicially imposed sanctions, including:

- restrictions on the products, manufacturers, or manufacturing processes;
- warning letters or untitled letters;
- civil or criminal penalties;
- fines;
- injunctions;
- product seizures or detentions;
- pressure to initiate voluntary product recalls;
- suspension or withdrawal of regulatory approvals; and
- refusal to approve pending applications for marketing approval of new products or supplements to approved applications.

If any of these events occurs, our ability to sell such products may be impaired, and we may incur substantial additional expense to comply with regulatory requirements, which could adversely affect our business, financial condition and results of operations.

We operate in a highly competitive and rapidly changing industry, and our product candidates may become obsolete.

We are engaged in a rapidly evolving field. Competition from other pharmaceutical companies, biotechnology companies and research and academic institutions is intense and likely to increase. Many of those companies and institutions have substantially greater financial, technical and human resources than us. Those companies and institutions also have substantially greater experience in developing products, conducting clinical trials, obtaining regulatory approval and in manufacturing and marketing pharmaceutical products. Our competitors may succeed in obtaining regulatory approval for their products more rapidly than we do. Competitors have developed or are in the process of developing technologies that are, or in the future may be, the basis for competitive products. Some of these competitive products may have an entirely different approach or means of accomplishing the desired therapeutic effect than products being developed by us. Our competitors may succeed in developing products that are more effective and/or cost competitive than those we are developing, or that would render our product candidates less competitive or even obsolete. In addition, one or more of our competitors may achieve product commercialization or patent protection earlier than us, which could materially adversely affect our business.

If the FDA or other applicable regulatory authorities approve generic products that compete with any of our or any of our partners' product candidates, the sales of our product candidates would be adversely affected.

Once an NDA or marketing authorization application outside the United States is approved, the product covered thereby becomes a "listed drug" that can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application in the United States. Agency regulations and other applicable regulations and policies provide incentives to manufacturers to create modified, non-infringing versions of a drug to facilitate the approval of an abbreviated new drug application or other application for generic substitutes in the United States and in nearly every pharmaceutical market around the world. These manufacturers might only be required to conduct a relatively inexpensive study to show that their product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use, or labeling, as our product and that the generic product is bioequivalent to our product, meaning it is absorbed in the body at the same rate and to the same extent as our product. These generic equivalents, which must meet the same quality standards as branded pharmaceuticals, would be significantly less costly than our product to bring to market, and companies that produce generic equivalents are generally able to offer their products at lower prices. Thus, after the introduction of a generic competitor, a significant percentage of the sales of any branded product are typically lost to the generic product. Accordingly, competition from generic equivalents to our product or any of our partners' future products, if any, would materially adversely affect our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made and expect to make in our or any of our partners' product candidates, including MGL-3196.

Competition that our or any of our partners' products may face from generic versions of our products could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in those product candidates.

If physicians and patients do not accept our future products or if the market for indications for which any product candidate is approved is smaller than expected, we may be unable to generate significant revenue, if any.

Even if any of our product candidates obtain regulatory approval, they may not gain market acceptance among physicians, patients, and third-party payers. Efforts to educate the medical community and third-party payers on the benefits of our product candidates may require significant resources and may not be successful. If any of our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenue or any profits from operations. Physicians may decide not to recommend its treatments for a variety of reasons including:

- timing of market introduction of competitive products;
- demonstration of clinical safety and efficacy compared to other products;
- cost-effectiveness;
- limited or no coverage by third-party payers;
- convenience and ease of administration;
- prevalence and severity of adverse side effects;
- restrictions in the label of the drug;
- other potential advantages of alternative treatment methods; and
- ineffective marketing and distribution support of its products.

If any of our product candidates are approved, but fail to achieve market acceptance or such market is smaller than anticipated, we may not be able to generate significant revenue and our business would suffer.

As we evolve from a company that is primarily involved in clinical development to a company that is also involved in commercialization, we may encounter difficulties in expanding our operations successfully.

As we advance our product candidates through clinical trials, we will need to expand our development, regulatory, manufacturing, and marketing and sales capabilities and may need to further contract with third parties to provide these capabilities. As our operations expand, we likely will need to manage additional relationships with such third parties, as well as additional collaborators, distributors, marketers and suppliers.

Maintaining third party relationships for these purposes will impose significant added responsibilities on members of our management and other personnel. We must be able to effectively manage our development efforts; recruit and train sales and marketing personnel, effectively manage our participation in the clinical trials in which our product candidates are involved and improve our managerial, development, operational and finance systems, all of which may impose a strain on our administrative and operational infrastructure.

If we enter into arrangements with third parties to perform sales, marketing or distribution services, any product revenues that we receive, or the profitability of these product revenues to us, are likely to be lower than if we were to market and sell any products that we develop without the involvement of these third parties. In addition, we may not be successful in entering into arrangements with third parties to sell and market our products or in doing so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our products.

The uncertainty associated with pharmaceutical reimbursement and related matters may adversely affect our business.

Market acceptance and sales of any one or more of our product candidates will depend on reimbursement policies and may be affected by future healthcare reform measures in the United States and in foreign jurisdictions. Government authorities and third-party payers, such as private health insurers and health maintenance organizations, decide which drugs they will cover and establish payment levels. We cannot be certain that reimbursement will be available for any of our product candidates. Also, we cannot be certain that reimbursement policies will not reduce the demand for, or the price paid for, our products. If reimbursement is not available or is available on a limited basis, we may not be able to successfully commercialize any product candidates that we develop.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, also called the Medicare Modernization Act, or MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation established Medicare Part D, which expanded Medicare coverage for outpatient prescription drug purchases by the elderly but provided authority for limiting the number of drugs that will be covered in any therapeutic class. The MMA also introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. The United States and several foreign jurisdictions are considering, or have already enacted, a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payers in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access to healthcare. In the United

States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. We expect to experience pricing pressures in connection with the sale of any products that we develop due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative proposals.

In March 2010, the ACA became law in the United States. The goal of ACA is to reduce the cost of healthcare and substantially change the way healthcare is financed by both government and private insurers. While we cannot predict what impact on federal reimbursement policies this legislation will have in general or on our business specifically, the ACA may result in downward pressure on pharmaceutical reimbursement, which could negatively affect market acceptance of, and the price we may charge for, any products we develop that receives regulatory approval. We also cannot predict the impact of ACA on us as many of the ACA reforms require the promulgation of detailed regulations implementing the statutory provisions, which have not yet been fully implemented.

If any product liability lawsuits are successfully brought against us or any of our collaborative partners, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability lawsuits related to the testing of our product candidates in seriously ill patients and will face an even greater risk if product candidates are approved by regulatory authorities and introduced commercially. Product liability claims may be brought against us or our partners by participants enrolled in our clinical trials, patients, healthcare providers or others using, administering or selling any of our future approved products. If we cannot successfully defend ourselves against any such claims, we may incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any of our future approved products;
- injury to our reputation;
- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- significant litigation costs;
- substantial monetary awards to or costly settlements with patients or other claimants;
- product recalls or a change in the indications for which products may be used;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize our product candidates.

If any of our product candidates are approved for commercial sale, we will be highly dependent upon consumer perceptions of us and the safety and quality of our products. We could be adversely affected if we are subject to negative publicity. We could also be adversely affected if any of our products or any similar products distributed by other companies prove to be, or are asserted to be, harmful to patients. Also, because of our dependence upon consumer perceptions, any adverse publicity associated with illness or other adverse effects resulting from patients' use or misuse of our products or any similar products distributed by other companies could have a material adverse impact on our results of operations.

We do not currently hold product liability insurance coverage. Prior to commercialization of our product candidates, we will need to purchase insurance coverage. As a result, we may be unable to maintain or obtain sufficient insurance at a reasonable cost to protect us against losses that could have a material adverse effect on our business. These liabilities could prevent or interfere with our product

development and commercialization efforts. A successful product liability claim or series of claims brought against us, particularly if judgments exceed our insurance coverage, could decrease our cash resources and adversely affect our business, financial condition and results of operations.

Our employees, contractors, vendors and partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, contractors, vendors or partners. Misconduct by these parties could include failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with federal and state healthcare fraud and abuse laws and regulations, to report financial information or data timely, completely or accurately, or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Third-party misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Conduct and Ethics, but it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us resulting from this misconduct and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

We enter into various contracts in the normal course of our business in which we indemnify the other party to the contract. In the event we have to perform under these indemnification provisions, it could have a material adverse effect on our business, financial condition and results of operations.

In the normal course of business, we periodically enter into academic, commercial, service, collaboration, licensing, consulting and other agreements that contain indemnification provisions. With respect to our academic and other research agreements, we typically indemnify the institution and related parties from losses arising from claims relating to the products, processes or services made, used, sold or performed pursuant to the agreements for which we have secured licenses, and from claims arising from our or our potential sublicensees' exercise of rights under the agreements. With respect to our commercial agreements, we indemnify our vendors from any third-party product liability claims that could result from the production, use or consumption of the product, as well as for alleged infringements of any patent or other intellectual property right by a third party.

Should our obligation under an indemnification provision exceed applicable insurance coverage or if we are denied insurance coverage, our business, financial condition and results of operations could be adversely affected. Similarly, if we are relying on a collaborator to indemnify us and the collaborator is denied insurance coverage or the indemnification obligation exceeds the applicable insurance coverage, and if the collaborator does not have other assets available to indemnify us, our business, financial condition and results of operations could be adversely affected.

If we fail to develop and commercialize other product candidates, we may be unable to grow our business.

Although the development and commercialization of MGL-3196 is our primary focus, as part of our longer-term growth strategy, we plan to evaluate the development and commercialization of other therapies related to thyroid hormone, orphan and other diseases. We will evaluate internal opportunities from our compound libraries, and also may choose to in-license or acquire other product

candidates as well as commercial products to treat patients suffering from thyroid hormone, orphan or other disorders with high unmet medical needs and limited treatment options. These other product candidates may require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA and/or applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, be successfully commercialized, be widely accepted in the marketplace, or be more effective than other commercially available alternatives.

If we lose key management personnel, or if we fail to recruit additional highly skilled personnel, our ability to identify, develop and commercialize products will be impaired.

We are highly dependent on principal members of our management team, including our Chief Executive Officer, Paul A. Friedman, M.D., and our Chief Medical Officer, Rebecca Taub, M.D. These executives each have significant pharmaceutical industry experience. The loss of any member of our management team or scientific staff, including Drs. Friedman and Taub, would impair our ability to identify, develop and market new products. Our management and other employees may voluntarily terminate their employment with us at any time. The loss of the services of these or other key personnel, or the inability to attract and retain additional qualified personnel, could result in delays to development or approval, loss of sales and diversion of management resources. In addition, we depend on our ability to attract and retain other highly skilled personnel. Competition for qualified personnel is intense, and the process of hiring and integrating such qualified personnel is often lengthy. We may be unable to recruit such personnel on a timely basis, if at all, which would negatively impact our development and commercialization programs.

Additionally, we do not currently maintain "key person" life insurance on the lives of our executives or any of our employees. This lack of insurance means that we may not receive adequate compensation for the loss of the services of these individuals.

We currently have no marketing, sales or distribution infrastructure with respect to our product candidates. If we are unable to develop our sales, marketing and distribution capabilities on our own or through collaborations with marketing partners, we will not be successful in commercializing our product candidates.

We currently have no marketing, sales or distribution capabilities and have limited sales or marketing experience within our organization. If our product candidate, MGL-3196, is approved, we intend either to establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize MGL-3196, or to outsource this function to a third party. Either of these options would be expensive and time-consuming. Some or all of these costs may be incurred in advance of any approval of MGL-3196. In addition, we may not be able to hire a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we intend to target. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely affect the commercialization of MGL-3196 and other future product candidates.

With respect to our existing and future product candidates, we may choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or as an alternative to our own sales force and distribution systems. To the extent that we enter into co-promotion or other licensing arrangements, our product revenue may be lower than if we directly marketed or sold any approved products. In addition, any revenue we receive will depend in whole or in part upon the efforts of these third parties, which may not be successful and are generally not within our control. If we are unable to enter into these

arrangements on acceptable terms or at all, we may not be able to successfully commercialize any approved products. If we are not successful in commercializing any approved products, either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we may incur significant additional losses.

Even if we obtain FDA approval of MGL-3196 or any other future product candidate, we or our partners may never obtain approval or commercialize our products outside of the United States, which would limit our ability to realize their full market potential.

In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding clinical trial design, safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We and our partners do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we or our partners fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our target market will be reduced and our ability to realize the full market potential of our products will be harmed.

If we do not obtain protection under the Hatch-Waxman Amendments and similar foreign legislation by extending the term of patents covering each of our product candidates, our business may be materially harmed.

Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our United States patents may be eligible for limited patent term extension under Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product may not extend beyond the current patent expiration dates and our competitors may obtain approval to market competing products sooner. As a result, our revenue could be potentially materially reduced. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

We may fail to obtain orphan drug designations from the FDA for our product candidates, as applicable, and even if we obtain such designations, we may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

Our strategy includes filing for orphan drug designation where available for our product candidates. Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug or

biologic intended to treat a rare disease or condition, which is defined as one occurring in a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug or biologic will be recovered from sales in the United States. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including a full NDA, to market the same drug or biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity.

We have not obtained orphan designation for any product candidates to date, although we believe some of the potential indications of our product candidates could qualify for orphan drug designation and the related benefits if approved for such indications and we may file for orphan drug designation with respect to such indications. Even if we obtain such designations, we may not be the first to obtain regulatory approval of a product candidate for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the orphan-designated disease or condition. Further, even if we obtain orphan drug designation exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may receive and be approved for the same condition, and only the first applicant to receive approval will receive the benefits of marketing exclusivity. Even after an orphan-designated product is approved, the FDA can subsequently approve a later drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior if it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process. In addition, while we may seek orphan drug designation for our product candidates, we may never receive such designations. Failure to obtain an orphan drug designation for our product candidates may have a material adverse effect on our business, results of operations and financial condition.

If we or our partners market products in a manner that violates fraud and abuse and other healthcare laws, or if we or our partners violate government price reporting laws, we or our partners may be subject to administrative civil and/or criminal penalties.

Although we do not currently have any products on the market, if we obtain FDA approval for our product candidates, and begin commercializing those products in the United States, our operations may be directly, or indirectly through our prescribers, customers and third-party payors, subject to various U.S. federal and state healthcare laws and regulations. These laws include, among others, the U.S. federal Anti-Kickback Statute and the U.S. federal civil and criminal false claims laws. At such time, if ever, as we or any of our partners market any of our future approved products, it is possible that some of our business activities and/or our partners could be subject to challenge under one or more of these laws.

Federal false claims, false statements and civil monetary penalties laws prohibit, among others, any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, or causing to be made, a false statement to get a false claim paid.

The federal healthcare program Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers, on the one hand, and prescribers, purchasers and formulary managers, on the other. Although there are several statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor.

In addition, we and/or our partners may be subject to patient data privacy and security regulation, including the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, which impose specified requirements relating to the privacy, security and transmission of individually identifiable health information.

Most states also have statutes or regulations similar to these federal laws, which may apply to items such as pharmaceutical products and services reimbursed by private insurers. We and/or our partners may be subject to administrative, civil and criminal sanctions for violations of any of these federal and state laws. Pharmaceutical and other healthcare companies have been prosecuted under these laws for a variety of promotional and marketing activities, such as: providing free trips, free goods, sham consulting fees and grants and other monetary benefits to prescribers; reporting to pricing services inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in off-label promotion; and submitting inflated best price information to the Medicaid Rebate Program to reduce liability for Medicaid rebates.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations.

If the third parties on which we rely for the conduct of our clinical trials and results do not perform our clinical trial activities in accordance with good clinical practices and related regulatory requirements, we may be unable to obtain regulatory approval for or commercialize our product candidates.

We use third-party service providers to conduct and/or oversee the clinical trials of our product candidates and expect to continue to do so for the foreseeable future. We rely heavily on these parties for successful execution of our clinical trials. Nonetheless, we are responsible for confirming that each of our clinical trials is conducted in accordance with FDA requirements and our general investigational plan and protocol.

The FDA requires us and our third-party service providers to comply with regulations and standards, commonly referred to as good clinical practices, or GCP, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate, and that the trial participants are adequately protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. Third parties may not complete activities on schedule or may not conduct our clinical trials in accordance with regulatory or GCP requirements or the respective trial plans and protocols. In addition, third parties may not be able to repeat their past successes in clinical trials. The failure of these third parties to carry out their obligations could delay or prevent the development, approval and commercialization of our product candidates or result in enforcement action against us.

If our relationship with these third-party providers terminates, we may not be able to enter into arrangements with alternative providers or do so on commercially reasonable terms. Switching or adding additional third-party providers involves substantial cost and requires management time and focus, and could delay development and commercialization of our product candidates. Though we intend to carefully manage our relationships with our third-party providers, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a negative impact on our business and financial condition.

We have relied on, and expect to continue to rely on, third-party manufacturers to produce our product candidates.

We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates, and we lack the resources and the capabilities to do so. As a result, we currently rely, and expect to rely for the foreseeable future, on third-party manufacturers to supply our product candidates. Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured our product candidates or products ourselves, including:

- reliance on third-parties for manufacturing process development, regulatory compliance and quality assurance;
- limitations on supply availability resulting from capacity and scheduling constraints of third-parties;
- the possible breach of manufacturing agreements by third-parties because of factors beyond our control; and
- the possible termination or non-renewal of manufacturing agreements by third-parties, at a time that is costly or inconvenient to us.

If we do not maintain our key manufacturing relationships, we may fail to find replacement manufacturers or develop our own manufacturing capabilities, which could delay or impair our ability to obtain regulatory approval for our products and substantially increase our costs or deplete profit margins, if any. If we do find replacement manufacturers, we may not be able to enter into agreements with them on terms and conditions favorable to us and there could be a substantial delay before new facilities could be qualified and registered with the FDA and other foreign regulatory authorities.

The FDA and other foreign regulatory authorities require manufacturers to register manufacturing facilities. The FDA and corresponding foreign regulators also inspect these facilities to confirm compliance with current good manufacturing practices, or cGMPs. Contract manufacturers may face manufacturing or quality control problems causing drug substance production and shipment delays or a situation where the contractor may not be able to maintain compliance with the applicable cGMP requirements. Any failure to comply with cGMP requirements or other FDA, European Medicines Agency, or EMA, and comparable foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop our product candidates and market our products following approval.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to develop our product candidates and commercialize any products that receive regulatory approval on a timely basis.

We previously identified a material weakness in our internal control over financial reporting and may identify additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls, which may result in material misstatements of our financial statements or cause us to fail to meet our reporting obligations or fail to prevent fraud; and in that case, our stockholders could lose confidence in our financial reporting, which would harm our business and could negatively impact the price of our stock.

Effective internal controls are necessary for us to provide reliable financial reports and prevent fraud. If we fail to maintain an effective system of internal controls, we may be unable to report our financial results accurately or prevent fraud; and, in that case, our stockholders could lose confidence in our financial reporting, which would harm our business and could negatively impact the price of our stock. On March 31, 2017, we filed with the SEC an amendment to our Quarterly Report on Form 10-Q for the quarter ended September 30, 2016 to correct certain errors therein. Management reported a material weakness in our system of internal controls over financial reporting as of September 30, 2016. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. We remediated this material weakness. We cannot assure you that the measures we have taken to date will be sufficient to avoid future material weaknesses. Even when we conclude that our internal control over financial reporting provides reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with U.S. generally accepted accounting principles, or GAAP, because of its inherent limitations, internal control over financial reporting may not prevent or detect fraud or misstatements.

Our reporting obligations as a public company will require significant managerial, operational and financial resources for the foreseeable future. If we fail to maintain the adequacy of our internal control over financial reporting, we may not be able to produce reliable financial reports or help prevent fraud. Our failure to maintain effective internal control over financial reporting could prevent us from filing our periodic reports on a timely basis which could result in the loss of investor confidence in the reliability of our financial statements, harm our business and negatively impact the trading price of our common stock.

Risks Relating to Our Intellectual Property

Our rights to develop and commercialize our product candidates are subject in part to the terms and conditions of a license to MGL-3196 granted to us by Roche.

We entered into the Roche Agreement, with Roche, on December 18, 2008. Pursuant to the terms of the Roche Agreement, we assumed control of all development and commercialization of MGL-3196 and hold exclusive worldwide rights for all potential indications. Under the Roche Agreement, Roche exclusively licensed certain patent rights and know-how relating to MGL-3196 in exchange for consideration consisting of an upfront payment, milestone payments tied to the achievement of product development and regulatory milestones, and royalty payments based on net sales of products containing MGL-3196 or another licensed product, subject to certain reductions. We must use commercially reasonable efforts to conduct clinical and commercial development programs for products containing MGL-3196. If we determine that it is not reasonable to continue clinical trials or other development of MGL-3196, we may elect to cease further development and Roche may terminate the license. If we determine not to pursue the development or commercialization of MGL-3196 in certain jurisdictions, including the United States, Roche may terminate the license for such territories. The Roche Agreement will expire, unless earlier terminated pursuant to other provisions thereof, on the last to occur of (i) the expiration of the last valid claim of a licensed patent covering the manufacture, use or sale of products containing MGL-3196, or (ii) ten years after the first sale of a product containing MGL-3196.

Under the Roche Agreement, Roche controls prosecution of the licensed patent rights, although we have a right to comment.

We do not have, nor have we had, any material disputes with Roche regarding the Roche Agreement. However, if there is any future dispute between us and Roche regarding the parties' rights under the Roche Agreement, our ability to develop and commercialize MGL-3196, or any other product candidate covered by the Roche Agreement, may be materially harmed. Any uncured, material breach under the Roche Agreement could result in our loss of exclusive rights to MGL-3196 and may lead to a complete termination of the Roche Agreement and force us to cease product development efforts for MGL-3196.

We may fail to comply with any of our obligations under agreements pursuant to which we license rights or technology, which could result in the loss of rights or technology that are material to our business.

We may enter into license agreements from time to time. Licensing of intellectual property is important to our business and involves complex legal, business and scientific issues. Disputes may arise regarding intellectual property subject to a license agreement, including but not limited to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by us and our licensors and collaborators; and
- the priority of invention of patented technology.

If disputes over intellectual property and other rights that we have licensed or acquired from third parties prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

Our success depends on our ability to protect our intellectual property and our proprietary technologies.

Our success depends on our ability to protect our intellectual property and our proprietary technologies. Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies, and their uses, as well as our ability to operate without infringing upon the proprietary rights of others.

We can provide no assurance that our patent applications or those of our licensors will result in additional patents being issued or that issued patents will afford sufficient protection against competitors with similar technologies, nor can we provide any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. Even issued patents may later be found unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. This failure to properly protect the intellectual property rights relating to our product candidates could have a material adverse effect on our financial condition and results of operations. Composition-of-matter patents on the biological or chemical active pharmaceutical ingredients are generally considered to offer the strongest protection of intellectual property and provide the broadest scope of patent protection for pharmaceutical products, as such patents provide

protection without regard to any method of use or any method of manufacturing. While we have licensed rights to issued composition-of-matter patents in the United States and other jurisdictions for MGL-3196, we cannot be certain that the claims in issued composition-of-matter patents will not be found invalid or unenforceable if challenged. We cannot be certain that the claims in owned and licensed patent applications covering our product candidates will be considered patentable by the United States Patent and Trademark Office, or USPTO, and valid by courts in the United States or by the patent offices and courts in foreign jurisdictions. Even if we owned and licensed patent applications covering our product candidates, the patents may not be enforced against competitors. For example, a formulation patent will not be enforced against those making and marketing a product that has the same active pharmaceutical ingredient in a different formulation that is not claimed in the formulation patent. Method-of-use patents protect the use of a product for the specified method or for treatment of a particular indication. This type of patent may not be enforced against competitors making and marketing a product that has the same active pharmaceutical ingredient but is used for a method not claimed in the patent. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products "off-label." Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute.

Our licensed composition-of-matter patent licensed from Roche for MGL-3196 is expected to expire in the United States in 2026. Our co-owned patents and pending patent applications that cover our particular solid form, dosage, method of manufacturing, and uses of MGL-3196 to treat various indications are expected to expire in 2033. While patent term adjustments or patent term extensions could result in later expiration dates for each of these patents, there can be no assurances that we will receive any patent adjustments or patent term extensions. The patent application process and patent maintenance and enforcement are subject to numerous risks and uncertainties, and there can be no assurance that we or any of our future development partners will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process and after a patent has issued. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case;
- patent applications may not result in any patents being issued;
- patents may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- we and our licensor(s) may not have been the first to make the inventions covered by pending patent applications or issued patents;
- we and our licensor(s) may not have been the first to file patent applications for our product candidates or the compositions developed, or for their uses;
- others may independently develop identical, similar or alternative products or compositions and uses thereof;
- we and our licensor(s)' disclosures in patent applications may not be sufficient to meet the statutory requirements for patentability;
- others may design around our owned and licensed patent claims to produce competitive products which fall outside of the scope of the patents;

- others may identify prior art or other bases which could invalidate our or licensor(s)' patents;
- our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where us and our licensor(s) do not have patent rights, and then use the information learned from such activities to develop competitive products for sale in major commercial markets;
- there may be significant pressure on the United States government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by United States courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

In addition, we rely on the protection of our trade secrets and proprietary know-how. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors, we cannot provide any assurances that any of these parties would not breach the agreements to disclose any proprietary information, including trade secrets, and we may not be able to obtain adequate remedies for such breaches. Further, third parties may still obtain this information by other means, such as breaches of our physical or computer security systems. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. Moreover, third parties may come upon this or similar information lawfully and independently. We would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. Further, intellectual property rights have limitations and do not necessarily address all potential threats to our competitive position. If any of these events occurs or if we otherwise lose protection for our trade secrets or proprietary know-how, our business may be harmed.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a "first inventor to file" system in which the first inventor to file a patent application will be entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and a patent may become subject to post-grant proceedings including opposition, derivation, reexamination, *inter partes* review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position.

Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.

The biotechnology industry has been characterized by frequent litigation regarding patent and other intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. As the biotechnology industry expands and more patents are issued, the risk increases that

our product candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained in secrecy until the application is published, we may be unaware of third party patents that may be infringed by commercialization of MGL-3196 or our other product candidates. Moreover, because patent applications can take many years to issue, there may be currently-pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, identification of third party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. Any claims of patent infringement asserted by third parties would be time consuming and could likely:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing MGL-3196 for NASH or FH or our other product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis; or
- require us to enter into royalty or licensing agreements.

Although no third party has asserted a claim of patent infringement against us as of the filing date of this report, others may hold proprietary rights that could prevent MGL-3196 or our other product candidates from being marketed. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our product candidate or processes could subject us to potential liability for damages and require us to obtain a license to continue to manufacture or market MGL-3196 or our other product candidates. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. In addition, we cannot be sure that we could redesign our product candidate or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing MGL-3196 or our other product candidates, which could harm our business, financial condition and operating results.

Moreover, we may be subject to a third party preissuance submission of prior art to the USPTO or in addition to interference proceedings, may become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or other post-grant proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court.

If we or any of our future development partners were to initiate legal proceedings against a third party to enforce a patent directed at one of our product candidates, or one of our future product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent

litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement or insufficient written description. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would have a material adverse impact on our business.

Interference proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

We currently have rights to the intellectual property, through licenses from third parties and under patents that we own or co-own, to develop our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license, or use these proprietary rights. For example, our product candidates may require specific formulations to work effectively and efficiently and the rights to these formulations may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes, or other third party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We may collaborate with U.S. and foreign academic institutions and industry collaborators to accelerate our preclinical or clinical research. Typically, these institutions provide us with an option to

negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

If we are unable to successfully obtain rights to required third party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of that program and our business and financial condition could suffer.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to research and develop and to manufacture our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Any of these could impair our competitive position.

In addition, these agreements typically restrict the ability of our advisors, employees, third party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with in the future will usually expect to be granted rights to publish data arising out of such collaboration, provided that we are notified in advance and given the opportunity to delay publication for a limited time period in order for us to secure patent protection of intellectual property rights arising from the collaboration, in addition to the opportunity to remove confidential or trade secret information from any such publication. In the future we may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other

intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

We may not be able to protect our intellectual property rights throughout the world.

While we have licensed from Roche issued composition-of-matter patents directed at MGL-3196 in the United States and other countries, filing, prosecuting and defending patents on MGL-3196 in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries may not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing their inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with MGL-3196, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Risks Related to Our Financial Position and Need for Capital

If we fail to obtain the capital necessary to fund our operations, we will be unable to successfully develop and commercialize MGL-3196 and other future product candidates.

Although we believe that our existing cash and cash equivalents will be sufficient to fund our current operations through at least the next 12 months, we may require additional working capital in order to complete the remaining clinical development for MGL-3196 and our other product candidates through potential regulatory approval and through potential commercialization of these product candidates. In particular, in order to initiate our Phase 3 clinical program for MGL-3196 in NASH, we may need to collaborate with a strategic partner or raise additional working capital. We expect our spending levels to increase in connection with our clinical trials of MGL-3196 as well as other corporate activities. The amount and timing of any expenditure needed to implement our development and commercialization programs will depend on numerous factors, including:

- the type, number, scope, progress, expansion costs, results of and timing of our ongoing or future clinical trials or the need for additional clinical trials of MGL-3196 for NASH and FH or any of our other product candidates which we are pursuing or may choose to pursue in the future;

- the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;
- the costs and timing of obtaining regulatory approval for MGL-3196 for NASH and FH and any of our other product candidates;
- the costs and timing of obtaining or maintaining manufacturing for MGL-3196 for NASH and FH and any of our other product candidates, including commercial manufacturing if any product candidate is approved;
- the costs and timing of establishing sales, marketing and reimbursement capabilities and enhanced internal controls over financial reporting;
- the terms and timing of establishing and maintaining collaborations, license agreements and other partnerships;
- costs associated with any new product candidates that we may develop, in-license or acquire;
- the effect of competing technological and market developments; and
- the costs associated with operating as a public company.

Some of these factors are outside of our control. We do not expect our existing capital resources to be sufficient to enable us to fund the completion of our clinical trials and commercialization of our product candidates. We expect that we will need to raise substantial additional funds in the future.

We have not sold any products, and we do not expect to sell or derive revenue from any product sales for the foreseeable future. We may seek additional funding through future debt and equity financings, as well as potential additional collaborations or strategic partnerships with other companies or through non-dilutive financings. Additional funding may not be available to us on acceptable terms or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. In addition, the issuance of additional shares by us, or the possibility of such issuance, may cause the market price of our shares to decline.

If we are unable to obtain additional funding on a timely basis, we may be unable to complete ongoing and planned clinical trials for MGL-3196 for NASH and FH and any of our other product candidates, and we may be required to significantly curtail some or all of our activities. We also could be required to seek funds through arrangements with collaborative partners or otherwise that may require us to relinquish rights to our product candidates or otherwise agree to terms unfavorable to us.

Our ability to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments may be limited by provisions of the Internal Revenue Code.

Our net operating losses have been fully offset by a valuation allowance due to uncertainties surrounding our ability to realize these tax benefits. Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change" (generally defined as a greater than 50% change (by value) in its equity ownership over a three year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. Similar rules may apply under state tax laws. We have not performed a detailed analysis to determine whether an ownership change under Section 382 of the Code, or similar state provisions, has previously occurred. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset U.S. federal taxable income may become subject to limitations, which could potentially result in increased future tax liability to us and may be substantial.

Risks Relating to Ownership of Our Common Stock

The price of our common stock has been, and may continue to be, volatile.

Historically, the market price of our common stock has fluctuated over a wide range, and it is likely that the price of our common stock will continue to be volatile in the future. The market price of our common stock could be impacted due to a variety of factors, including, in addition to global and industry-wide events:

- the losses we may incur;
- developments in patent or other proprietary rights owned or licensed by us, our collaborative partners or our competitors;
- public concern as to the safety and efficacy of products developed by us or others; and
- litigation.

In addition, due to one or more of the foregoing factors in one or more future quarters, our results of operations may fall below the expectations of securities analysts and investors. In that event, the market price of our common stock could materially decline.

A small number of our stockholders beneficially own a substantial amount of our common stock and have substantial control over us; therefore, your ability to influence corporate matters may be limited.

Certain stockholders affiliated with our officers and directors collectively beneficially own or control approximately 44.9% of our outstanding common stock as of December 31, 2017 and acting together, may have the ability to affect matters submitted to our stockholders for approval. This concentration of ownership may have the effect of delaying, deferring or preventing a strategic transaction, even if such a transaction would benefit other stockholders.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our charter and bylaws may delay or prevent a merger, acquisition or other change of control that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions include a classified board of directors. In addition, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits, with some exceptions, stockholders owning in excess of 15% of our outstanding voting stock from merging or combining with us. Although we believe these provisions together provide for an opportunity to receive higher bids by requiring potential acquirers to negotiate with our board of directors, they would apply even if the offer may be considered beneficial by some stockholders.

Future sales and issuances of our common stock or rights to purchase common stock could result in additional dilution of the percentage ownership of our stockholders and could cause our share price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market by us, by our existing stockholders, or by the holders of our Series A Convertible Preferred Stock upon conversion, or the perception that these sales might occur, could significantly reduce the market price of our common stock and impair our ability to raise adequate capital through the sale of additional equity securities.

We do not anticipate paying cash dividends on our common stock, and accordingly, stockholders must rely on stock appreciation for any return on their investment.

We have never declared or paid any cash dividend on our common stock and do not anticipate paying cash dividends on our common stock in the future. As a result, the only return to stockholders will be appreciation in the price of our common stock, which may never occur. Investors seeking cash dividends should not invest in our common stock.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We lease our approximately 1,000 square-foot corporate headquarters facility located in West Conshohocken, Pennsylvania. We believe our facility is adequate for our current needs. Our lease expires in June 2018. We may need to acquire additional space as our business continues to grow. We continue to evaluate our facility requirements and believe that appropriate space will be available to accommodate our future needs.

Item 3. Legal Proceedings

We are currently not a party to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchase of Equity Securities.

The term "Private Madrigal" refers to Madrigal Pharmaceuticals, Inc. prior to the consummation of the Merger.

Market Information

Our common stock is traded on the NASDAQ stock market under the symbol "MDGL" as of July 25, 2016, the trading date following the consummation of our merger with Private Madrigal. Prior to July 25, 2016, our common stock was traded on the NASDAQ stock market under the symbol "SNTA." The following table sets forth the quarterly high and low sales prices of our common stock. The per share prices for all periods shown reflect a 1-for-35 reverse stock split effected on July 22, 2016:

2016:	High	Low
First Quarter	$ 12.53	$ 5.25
Second Quarter	15.75	7.88
Third Quarter	13.93	6.60
Fourth Quarter	18.24	12.60

2017:	High	Low
First Quarter	$ 16.63	$ 14.78
Second Quarter	17.84	13.09
Third Quarter	49.48	15.15
Fourth Quarter	101.00	38.82

Stockholders

On March 8, 2018, the last reported sale price of our common stock was $130.78 per share as reported by the NASDAQ Stock Market. As of March 8, 2018, there were approximately 40 stockholders of record of the 14,227,634 outstanding shares of our common stock.

Dividends

We have never paid or declared any cash dividends on our common stock. We currently intend to retain all available funds and any future earnings to fund the development and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors and will depend on our financial condition, results of operations, contractual restrictions, capital requirements, and other factors that our board of directors deems relevant.

Unregistered Sales of Securities

We did not sell or issue any equity securities that were not registered under the Securities Act, except as previously disclosed on our Quarterly Reports on Form 10-Q.

Issuer Purchases of Equity Securities

None.

Item 6. Selected Financial Data

Pursuant to Item 10(f) of Regulation S-K, we are not required to disclose this information in this transitional Form 10-K.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The Risk Factors in Part I, Item 1A of this Annual Report on Form 10-K, the audited financial statements and accompanying notes, included elsewhere in this Annual Report on Form 10-K, and this Management's Discussion and Analysis of Financial Condition and Results of Operations should be read together. In addition to historical information, this discussion and analysis contains forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Exchange Act. Operating results are not necessarily indicative of results that may occur for the full fiscal year or any other future period. The term "Synta" refers to Synta Pharmaceuticals Corp. prior to the consummation of the Merger described herein. Unless otherwise indicated, references to the terms "Madrigal," the "Company," "we," "our" and "us" refer to Private Madrigal prior to the consummation of the Merger described herein and Madrigal Pharmaceuticals, Inc. (formerly known as Synta Pharmaceuticals Corp.) upon the consummation of the Merger described herein.

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of innovative therapeutic candidates for the treatment of cardiovascular, metabolic and liver diseases. Our lead product candidate, MGL-3196, is a proprietary, liver-directed, selective thyroid hormone receptor-β, or THR-β, agonist that can potentially be used to treat a number of disease states with high unmet medical need. We are developing MGL-3196 for non-alcoholic steatohepatitis, or NASH and we have initiated a Phase 2 clinical trial in this indication. We are also developing MGL-3196 for dyslipidemia, particularly genetic dyslipidemias such as familial hypercholesterolemia, or FH, including both homozygous and heterozygous forms of the disease. We have completed a Phase 2 clinical trial in heterozygous FH, or HeFH, patients. MGL-3196 is a once-daily oral pill that has been studied in six completed Phase 1 trials in a total of 183 subjects. MGL-3196 appeared to be safe and well-tolerated in these trials, which included a single ascending dose trial, a multiple ascending dose trial, two drug interaction trials with statins, a multiple dose mass balance study, and a single dose relative bioavailability study of tablet formulations versus capsule formulation.

Key Developments

Clinical Trials

In October 2016, we initiated a Phase 2 clinical trial in NASH ([NCT02912260] at www.ClinicalTrials.gov). The randomized, double-blind, placebo-controlled, multi-center Phase 2 study enrolled 125 patients 18 years of age and older with biopsy-confirmed NASH. Patients are randomized to receive either placebo or MGL-3196, twice as many receiving MGL-3196 as placebo. Efficacy will be confirmed at the end of the trial (36 weeks) by repeat Magnetic Resonance Imaging—Proton Density Fat Fraction (MRI-PDFF) and conventional liver biopsy to examine histological evidence for the resolution of NASH. Recent published data show a high correlation of reduction of liver fat measured by MRI-PDFF to NASH scoring on liver biopsy. Other secondary endpoints include changes in clinically relevant biomarkers at 12 and 36 weeks, improvement in fibrosis by at least one stage with no worsening of steatohepatitis, and safety and tolerability. We reached our top-line analysis of the primary endpoint in December 2017, and we expect to reach our top-line analysis of the secondary endpoint (NASH assessment on liver biopsy) by spring of 2018.

In February 2017, we initiated a Phase 2 clinical trial in HeFH ([NCT03038022] at www.ClinicalTrials.gov). The 12-week, randomized, double-blind, placebo-controlled, multi-center Phase 2 clinical trial enrolled 116 patients with HeFH in several European countries. Patients were randomized in a 2:1 ratio to receive either MGL-3196 or placebo, in addition to their current drug regimen (including high dose statins and/or ezetimibe). The primary endpoint of the study was

reduction of LDL cholesterol, with secondary endpoints including reductions in TGs, Lp(a), and ApoB, as well as safety. Lp(a) is a severely atherogenic lipid particle, commonly elevated in familial hypercholesterolemia patients, the levels of which are not adequately reduced by existing lipid lowering therapies. THR-β agonism is one of the few therapeutic approaches that can substantially lower Lp(a). In February 2018, we announced positive results from the 12 week Phase 2 clinical trial in HeFH.

Reverse Merger

On July 22, 2016, Synta completed its business combination with Private Madrigal in accordance with the terms of an Agreement and Plan of Merger and Reorganization, dated as of April 13, 2016, or the Merger Agreement. Pursuant to the Merger Agreement, Synta formed a wholly-owned subsidiary that merged with and into Private Madrigal, with Private Madrigal surviving the merger and becoming a wholly-owned subsidiary of Synta, or the Merger. In connection with, and prior to the consummation of, the Merger, Synta effected a 1-for-35 reverse stock split of its common stock, or the Reverse Stock Split, and, following the Merger, changed its name to "Madrigal Pharmaceuticals, Inc." All shares and per share amounts have been retrospectively adjusted to give effect to the Reverse Stock Split, except as otherwise disclosed. Following the consummation of the Merger, our business became the business conducted by Private Madrigal prior to the consummation of the Merger.

Basis of Presentation

Research and Development Expenses

Research and development expenses primarily consist of costs associated with our research activities, including the preclinical and clinical development of our product candidates. We expense our research and development expenses as incurred. We contract with clinical research organizations to manage our clinical trials under agreed upon budgets for each study, with oversight by our clinical program managers. We account for nonrefundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received. Manufacturing expense includes costs associated with drug formulation development and clinical drug production. We do not track employee and facility related research and development costs by project, as we typically use our employee and infrastructure resources across multiple research and development programs. We believe that the allocation of such costs would be arbitrary and not be meaningful.

Our research and development expenses consist primarily of:

- salaries and related expense, including stock-based compensation;
- external expenses paid to clinical trial sites, contract research organizations, laboratories, database software and consultants that conduct clinical trials;
- expenses related to development and the production of nonclinical and clinical trial supplies, including fees paid to contract manufacturers;
- expenses related to preclinical studies;
- expenses related to compliance with drug development regulatory requirements; and
- other allocated expenses, which include direct and allocated expenses for depreciation of equipment and other supplies.

We expect to continue to incur substantial expenses related to our development activities for the foreseeable future as we conduct our Phase 2 clinical program, manufacturing and toxicology studies. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-

stage clinical trials, additional drug manufacturing requirements, and later stage toxicology studies such as carcinogenicity studies. Our research and development expenses have increased year over year in each of 2016 and 2017 and we expect that our research and development expenses will increase substantially in the future. The process of conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time consuming. The probability of success for each product candidate is affected by numerous factors, including preclinical data, clinical data, competition, manufacturing capability and commercial viability. Accordingly, we may never succeed in achieving marketing approval for any of our product candidates

Completion dates and costs for our clinical development programs as well as our research program can vary significantly for each current and future product candidate and are difficult to predict. As a result, we cannot estimate with any degree of certainty the costs we will incur in connection with the development of our product candidates at this point in time. We expect that we will make determinations as to which programs and product candidates to pursue and how much funding to direct to each program and product candidate on an ongoing basis in response to the scientific success of early research programs, results of ongoing and future clinical trials, our ability to enter into collaborative agreements with respect to programs or potential product candidates, as well as ongoing assessments as to each current or future product candidate's commercial potential.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, benefits and stock-based compensation expenses for employees, management costs, costs associated with obtaining and maintaining our patent portfolio, professional fees for accounting, auditing, consulting and legal services, and allocated overhead expenses.

We expect that our general and administrative expenses may increase in the future as we expand our operating activities, maintain and expand our patent portfolio and incur additional costs associated with being a public company and maintaining compliance with exchange listing and SEC requirements. We expect these potential increases will likely include management costs, legal fees, accounting fees, directors' and officers' liability insurance premiums and expenses associated with investor relations.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements which have been prepared in accordance with GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets and liabilities, and expenses and the disclosure of contingent assets and liabilities at the date of the financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued research and development expenses. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ materially from these estimates under different assumptions or conditions.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development costs are comprised of costs incurred in performing research and development activities, including internal costs (including stock-based compensation), costs for consultants, and other costs associated with the Company's preclinical and clinical programs. In particular, Madrigal has conducted safety studies in animals, optimized and implemented the API manufacturing, and conducted Phase 1 & 2 clinical trials, all of which are considered research and development expenditures.

Stock-Based Compensation

We recognize stock-based compensation expense based on the grant date fair value of stock options granted to employees, officers and directors. We use the Black-Scholes option pricing model to determine the grant date fair value as our management believes it is the most appropriate valuation method for its option grants. The Black-Scholes model requires inputs for risk-free interest rate, dividend yield, volatility and expected lives of the options.

Certain of the employee stock options granted by us are structured to qualify as incentive stock options, or ISOs. Under current tax regulations, we do not receive a tax deduction for the issuance, exercise or disposition of ISOs if the employee meets certain holding requirements. If the employee does not meet the holding requirements, a disqualifying disposition occurs, at which time we may receive a tax deduction. We do not record tax benefits related to ISOs unless and until a disqualifying disposition is reported. In the event of a disqualifying disposition, the entire tax benefit is recorded as a reduction of income tax expense. We have not recognized any income tax benefit for its share-based compensation arrangements due to the fact that we do not believe it is more likely than not it will realize the related deferred tax assets.

Results of Operations

Comparison Years Ended December 31, 2017 and 2016

The following table provides comparative results of operations for the years ended December 31, 2017 and 2016 (in thousands):

	Year Ended December 31,		2017 to 2016 Change	
	2017	2016	$	%
Research and Development Expenses	$ 24,390	$ 15,933	8,457	53%
General and Administrative Expenses	7,672	9,290	(1,618)	(17)%
Interest Expense (Income)	(558)	1,165	(1,723)	(148)%
Other Income	(350)	—	(350)	100%
	$ 31,154	$ 26,388	4,766	18%

Research and Development Expense

Comparison of Years Ended December 31, 2017 and 2016

Our research and development expenses were $24.4 million for the year ended December 31, 2017 compared to $15.9 million for the year ended December 31, 2016. Research and development expenses increased by $8.5 million in the 2017 period due primarily to the expenses incurred to conduct and support the two Phase 2 studies for MGL-3196, which commenced in the fourth quarter of 2016 and the first quarter of 2017, respectively. Our increased research and development expenses include an $8.5 million increase in contract research organization costs directly associated with the two Phase 2 studies. These increases were partially offset by lower stock based compensation expense in 2017, due to the expense incurred in 2016 from the Change in Control Bonus Plan resulting from the Merger. We expect our research and development expenses to increase over time as we advance our clinical and preclinical development.

General and Administrative Expense

Comparison of Years Ended December 31, 2017 and 2016

Our general and administrative expenses were $7.7 million for the year ended December 31, 2017 compared to $9.3 million for the year ended December 31, 2016. General and administrative expenses

decreased by $1.6 million in the 2017 period due primarily to expenses incurred in 2016 from the Merger, including $0.6 million from the Change in Control Bonus Plan and $2.1 million in other cost associated with the Merger. These Merger costs were partially offset by increases in 2017 from increased compensation expense and expenses related to operating as a public company. We believe that our general and administrative expenses may increase over time as we advance our clinical and preclinical development programs for MGL-3196 and continue operating as a public company, both of which will likely result in an increase in our headcount, consulting services, and certain overhead needed to support those efforts.

Interest Expense (Income)

Comparison of Years Ended December 31, 2017 and 2016

Our interest income was $0.6 million for the year ended December 31, 2017 compared to $1.2 million of interest expense for the year ended December 31, 2016. The change in interest expense (income) 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.

Liquidity and Capital Resources

As of December 31, 2017, we had cash, cash equivalents and marketable securities of $191.5 million. To date, we have funded our operations primarily through the issuance of convertible debt, the issuance of shares of common stock and preferred stock, and the proceeds from the Merger. We believe our cash and cash equivalents and marketable securities will be sufficient to fund our operations past one year from the issuance of these financial statements.

Our primary uses of capital are, and we expect will continue to be, funding research efforts and the development of our product candidates, compensation and related expenses, hiring additional staff, including clinical, scientific, operational, financial and management personnel, and costs associated with operating as a public company. We expect to incur substantial expenditures in the foreseeable future for the development and potential commercialization of our product candidates.

We plan to continue to fund losses from operations and capital funding needs through future equity and/or debt financings, as well as potential additional collaborations or strategic partnerships with other companies. The sale of additional equity or convertible debt could result in additional dilution to our stockholders. The incurrence of indebtedness would result in debt service obligations and could result in operating and financing covenants that would restrict our operations. We can provide no assurance that financing will be available in the amounts we need or on terms acceptable to us, if at all. If we are not able to secure adequate additional funding we may be forced to delay, make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, and/or suspend or curtail planned programs. Any of these actions could materially harm our business.

Cash Flows

The following table provides a summary of our net cash flow activity (in thousands):

	Year Ended December 31,	
	2017	2016
Net cash used in operating activities	$ (22,317)	$ (17,608)
Net cash used or provided by investing activities	(22,006)	21,993
Net cash provided by financing activities	173,805	14,454
Net increase in cash and cash equivalents	$ 129,482	$ 18,839

Comparison of Years Ended December 31, 2017 and 2016

Net cash used in operating activities was $22.3 million for the year ended December 31, 2017 compared to $17.6 million for the year ended December 31, 2016. The use of cash in these periods resulted primarily from our losses from operations, as adjusted for non-cash charges for stock-based compensation, and changes in our working capital accounts.

Net cash used by investing activities was $22.0 million for the year ended December 31, 2017 compared to $22.0 million provided by investing activities for the year ended December 31, 2016. Net cash used by investing activities for the 2017 consisted of $70.2 million of purchases of marketable securities for our investment portfolio, partially offset by $48.3 million from sales and maturities of marketable securities. Net cash provided by investing activities for 2016 consisted primarily of $5.8 million in cash provided from the merger, and a net increase of $15.4 million from the sales and maturities in our investment portfolio.

Net cash provided by financing activities was $173.8 million for the year ended December 31, 2017 compared to $14.5 million for the year ended December 31, 2016. Net cash provided by financing activities for 2017 consisted of net proceeds from sales of common and preferred stock under the October 2015 Sales Agreement, June 2017 Offering, and December 2017 Registered Offering. Net cash provided by financing activities for 2016 consisted of net proceeds from the issuance of related party convertible notes and net proceeds from the sale of common stock under the October 2015 Sales Agreement.

Contractual Obligations

Pursuant to Item 10(f) of Regulation S-K, we are not required to disclose this information in this transitional Form 10-K.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements as defined in the rules and regulations of the SEC.

Recent Accounting Pronouncements

Refer to Note 2, "Summary of Significant Accounting Policies," in the accompanying notes to the consolidated financial statements for a discussion of recent accounting pronouncements.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Interest Rate Risk

Our exposure to market risk is confined to our cash, cash equivalents and marketable securities. We regularly review our investments and monitor the financial markets. We invest in high-quality financial instruments, primarily money market funds, U.S. government and agency securities, government-sponsored bond obligations and certain other corporate debt securities, with the effective duration of the portfolio less than twelve months and no security with an effective duration in excess of twenty-four months, which we believe are subject to limited credit risk. We currently do not hedge interest rate exposure. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, we believe that an immediate 10% change in interest rates would not have a material effect on the fair market value of our portfolio. We do not believe that we have any material exposure to interest rate risk or changes in credit ratings arising from our investments.

Capital Market Risk

We currently have no product revenues and depend on funds raised through other sources. One source of funding is through future debt or equity offerings. Our ability to raise funds in this manner depends upon, among other things, capital market forces affecting our stock price.

Item 8. Financial Statements and Supplementary Data.

The information required by this Item 8 is included at the end of this Annual Report on Form 10-K beginning on page F-1.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

On July 22, 2016, our Audit Committee approved the dismissal of Ernst & Young LLP, or E&Y, as our independent registered public accounting firm, effective immediately. The reports of E&Y on our financial statements for each of the two years ended December 31, 2015 and December 31, 2014 did not contain an adverse opinion or a disclaimer of opinion, nor were they qualified or modified as to uncertainty, audit scope or accounting principles. In connection with the audit of our financial statements for each of the two years ended December 31, 2015 and December 31, 2014, and the subsequent interim periods through July 22, 2016, there were no "disagreements" (as that term is defined in Item 304(a)(1)(iv) of Regulation S-K and related instructions) between us and E&Y on any matter of accounting principles or practices, financial statement disclosure or auditing scope or procedures which, if not resolved to the satisfaction of E&Y, would have caused E&Y to make reference to the subject matter of the disagreement in their reports. This disclosure and the response by E&Y were filed on a Current Report on Form 8-K with the SEC on July 22, 2016.

On September 26, 2016, our Audit Committee approved, on our behalf, the engagement of PricewaterhouseCoopers LLP, or PwC, as our independent registered public accounting firm, effective as of September 28, 2016.

Item 9A. Controls and Procedures.

Disclosure Controls and Procedures

We maintain disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). Our disclosure controls and procedures are designed to provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our chief executive officer and chief financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Our chief executive officer and chief financial officer evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this Report. Based on such evaluation, our chief executive officer and chief financial officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2017.

Limitations on the Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable, not absolute, assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs. The design of any disclosure controls and procedures also is based in part upon certain

assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions.

Management's Report On Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act). Internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP. This process includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with GAAP, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2017. In making this assessment, it used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in "Internal Control—Integrated Framework" (2013). Based on its assessment our management concluded that our internal control over financial reporting was effective as of December 31, 2017.

PricewaterhouseCoopers LLP, an independent registered public accounting firm, has audited the effectiveness of our internal control over financial reporting as of December 31, 2017, as stated in its report, which is included herein.

Changes in Internal Control Over Financial Reporting

There have been no changes in our internal control over financial reporting during the quarter ended December 31, 2017 that have materially affected, or are reasonably likely to materially affect our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item will be contained in our definitive proxy statement on Schedule 14A to be filed with the SEC in connection with our 2018 annual meeting of stockholders, or the Proxy Statement, which we expect to file not later than 120 days after the end of our year ended December 31, 2017, and is incorporated in this report by reference.

Item 11. Executive Compensation.

The information required by this item will be contained in our Proxy Statement, which we expect to file not later than 120 days after the end of our year ended December 31, 2017, and is incorporated in this report by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this item will be contained in our Proxy Statement, which we expect to file not later than 120 days after the end of our year ended December 31, 2017, and is incorporated in this report by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this item will be contained in our Proxy Statement, which we expect to file not later than 120 days after the end of our year ended December 31, 2017, and is incorporated in this report by reference.

Item 14. Principal Accountant Fees and Services

The information required by this item will be contained in our Proxy Statement, which we expect to file not later than 120 days after the end of our year ended December 31, 2017, and is incorporated in this report by reference.

PART IV

Item 15. **EXHIBITS AND FINANCIAL STATEMENT SCHEDULES**

Item 15(a) The following documents are filed as part of, or incorporated by reference into, this Annual Report on Form 10-K:

Item 15(a)(1) and (2) The Consolidated Financial Statements beginning on page F-1 are filed as part of this Annual Report on Form 10-K. Other financial statement schedules have been omitted because the information required to be presented in them is not applicable or is shown in the financial statements or related notes.

Item 15(a)(3) We have filed, or incorporated into this Annual Report on Form 10-K by reference, the exhibits listed on the accompanying Exhibit Index.

Item 15(b) See Item 15(a)(3) above.

Item 15(c) See Item 15(a)(2) above.

The following is a list of exhibits filed as part of, or incorporated by reference into, this Annual Report on Form 10-K.

Exhibit Number	Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
1.1	Underwriting Agreement, dated December 18, 2017, by and between the Registrant and Goldman Sachs & Co. LLC as Representative of the Underwriters set forth therein.		Form 8-K (Exhibit 1.1)	12/21/17	001-33277
2.1	Agreement and Plan of Merger and Reorganization, dated April 13, 2016, by and among Synta Pharmaceuticals Corp., the Registrant and Saffron Merger Sub, Inc.		DEFA14A; Form 8-K (Exhibit 2.1)	04/14/16	001-33277
3.1	Restated Certificate of Incorporation of the Registrant.		Form 10-K (Exhibit 3.1)	03/31/17	001-33277
3.2	Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock.		Form 8-K (Exhibit 3.1)	06/21/17	001-33277
3.3	Bylaws of the Registrant, as amended April 13, 2016.		DEFA14A; Form 8-K (Exhibit 3.1)	04/14/16	001-33277
Equity Agreements					
10.1	Sales Agreement, dated October 16, 2015, by and between the Registrant and Cowen and Company, LLC.		Form 8-K (Exhibit 10.1)	10/16/15	001-33277

Exhibit Number	Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
10.2	Securities Purchase Agreement, dated June 20, 2017, by and among the Registrant and the investors party thereto, including the Registration Rights Agreement attached as Exhibit B thereto.		Form 8-K (Exhibit 10.1)	06/21/17	001-33277
	Agreements with Respect to Collaborations, Licenses, Research and Development				
10.3†	Research, Development and Commercialization Agreement, dated December 18, 2008, by and between Hoffmann-La Roche, Inc., F. Hoffmann-La Roche Ltd and the Registrant.		Form 10-Q (Exhibit 10.5)	11/14/16	001-33277
	Equity Compensation Plans				
10.4*	Amended and Restated 2006 Stock Plan.		Form 8-K (Exhibit 10.1)	06/21/10	001-33277
10.5*	Form of Incentive Stock Option Agreement under 2006 Stock Plan.		Form S-1/A (Exhibit 10.2(a))	01/23/07	333-138894
10.6*	Form of Nonqualified Stock Option Agreement under 2006 Stock Plan.		Form S-1/A (Exhibit 10.2(b))	01/23/07	333-138894
10.7*	Form of Restricted Stock Agreement under 2006 Stock Plan.		Form S-1/A (Exhibit 10.2(c))	01/23/07	333-138894
10.8*	Form of Nonqualified Stock Option Agreement for Directors under 2006 Stock Plan.		Form S-1/A (Exhibit 10.2(d))	01/23/07	333-138894
10.9*	Form of Restricted Stock Agreement for Non-Employee Directors under 2006 Stock Plan.		Form S-1/A (Exhibit 10.2(e))	01/23/07	333-138894
10.10*	Amended 2015 Stock Plan		Form 8-K (Exhibit 10.1)	07/05/17	001-33277
10.11*	Form of Incentive Stock Option Agreement under Amended 2015 Stock Plan.		Form 10-K (Exhibit 10.10)	03/31/17	001-33277
10.12*	Form of Nonqualified Stock Option Agreement under Amended 2015 Stock Plan.		Form 10-K (Exhibit 10.11)	03/31/17	001-33277

Exhibit Number	Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
10.13*	Form of Restricted Stock Agreement under Amended 2015 Stock Plan.		Form 10-K (Exhibit 10.12)	03/31/17	001-33277
10.14*	Form of Nonqualified Stock Option Agreement for Directors under Amended 2015 Stock Plan.		Form 10-K (Exhibit 10.13)	03/31/17	001-33277
10.15*	Form of Restricted Stock Unit Agreement under Amended 2015 Stock Plan.		Form 10-Q (Exhibit 10.1)	05/10/16	001-33277
Agreements with Executive Officers and Directors					
10.16*	Non-Qualified Stock Option Agreement, dated February 27, 2008, by and between the Registrant and Keith R. Gollust.		Form 10-K (Exhibit 10.4)	03/20/08	001-33277
10.17*	Letter Agreement, dated January 14, 2003, by and between the Registrant and Wendy E. Rieder.		Form S-1/A (Exhibit 10.18)	12/01/06	333-138894
10.18*	Letter Agreement, dated December 3, 2014, between Synta Pharmaceuticals Corp. and Chen Schor.		Form 8-K (Exhibit 10.1)	12/04/14	001-33277
10.19*	Offer Letter Addendum, dated as of June 9, 2015, by and between the Registrant and Chen Schor.		Form 10-Q (Exhibit 10.3)	08/06/15	001-33277
10.20*	Letter Agreement, dated November 24, 2014, between Synta Pharmaceuticals Corp. and Marc R. Schneebaum		Form 8-K (Exhibit 10.3)	12/04/14	001-33277
10.21*	Form of Severance and Change in Control Agreement between the Registrant and each of Keith S. Ehrlich and Wendy E. Rieder.		Form 10-K (Exhibit 10.31)	03/11/10	001-33277
10.22*	Severance and Change of Control Agreement, dated December 3, 2014, between Synta Pharmaceuticals Corp. and Chen Schor.		Form 8-K (Exhibit 10.2)	12/04/14	001-33277

Exhibit Number	Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
10.23*	Severance and Change of Control Agreement, dated November 24, 2014, between Synta Pharmaceuticals Corp. and Marc R. Schneebaum.		Form 8-K (Exhibit 10.4)	12/04/14	001-33277
10.24*	Form of Indemnification Agreement between the Registrant and certain directors and executive officers.		Form 8-K (Exhibit 10.2)	07/22/16	001-33277
10.25*	Non-Qualified Stock Option Agreement (outside of the Amended and Restated 2006 Stock Plan), dated December 8, 2014, between the Registrant and Marc Schneebaum.		Form 10-K (Exhibit 10.46)	03/12/15	001-33277
10.26*	Letter Agreement, dated April 13, 2016, by and between the Company and Paul A. Friedman, M.D.		Form 8-K (Exhibit 10.3)	07/22/16	001-33277
10.27*	Letter Agreement, dated April 13, 2016, by and between the Company and Rebecca Taub, M.D.		Form 8-K (Exhibit 10.4)	07/22/16	001-33277
16.1	Letter from Ernst & Young LLP dated July 22, 2016		Form 8-K (Exhibit 16.1)	07/22/16	001-33277
21.1	List of Subsidiaries.	X			
23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm.	X			
31.1	Certification of Principal Executive Officer required by Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X			

Exhibit Number	Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X			
32.1**	Certifications of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X			
101.INS	XBRL Instance Document.	X			
101.SCH	XBRL Taxonomy Extension Schema Document.	X			
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.	X			
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.	X			
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.	X			
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.	X			

* Indicates a management contract, compensatory plan or arrangement.

** The certifications attached as Exhibit 32.1 that accompany this Annual Report on Form 10-K are not deemed filed with the SEC and are not to be incorporated by reference into any filing of the registrant under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, regardless of any general incorporation language contained in any filing.

† Confidential portions of these documents have been filed separately with the Securities and Exchange Commission pursuant to a request for confidential treatment.

Item 16. Form 10-K Summary.

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this Report to be signed on its behalf by the undersigned thereunto duly authorized.

MADRIGAL PHARMACEUTICALS INC.

Date: March 13, 2018 By: /s/ PAUL A. FRIEDMAN, M.D.

Paul A. Friedman, M.D.
Chief Executive Officer
(Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each individual whose signature appears below hereby constitutes and appoints Paul A. Friedman, M.D. and Marc R. Schneebaum, and each or either of them, acting individually, as his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Report, and to file the same, with all exhibits thereto and other documents in connection therewith, with the SEC, granting unto said attorney-in-fact and agent, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or any of them, or their or his or her substitutes, may lawfully do or cause to be done or by virtue hereof.

Pursuant to the requirements of the Exchange Act, as amended, this Report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signatures	Title	Date
/s/ PAUL A. FRIEDMAN, M.D. Paul A. Friedman, M.D.	Chairman of the Board of Directors and Chief Executive Officer (Principal Executive Officer)	March 13, 2018
/s/ MARC R. SCHNEEBAUM Marc R. Schneebaum	Chief Financial Officer (Principal Accounting and Financial Officer)	March 13, 2018
/s/ REBECCA TAUB, M.D. Rebecca Taub, M.D.	Director	March 13, 2018
/s/ FRED B. CRAVES, PH.D. Fred B. Craves, Ph.D.	Director	March 13, 2018

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Signatures	Title	Date
/s/ KENNETH M. BATE Kenneth M. Bate	Director	March 13, 2018
/s/ KEITH R. GOLLUST Keith R. Gollust	Director	March 13, 2018
/s/ DAVID MILLIGAN, PH.D. David Milligan, Ph.D.	Director	March 13, 2018
/s/ RICHARD S. LEVY, M.D. Richard S. Levy, M.D.	Director	March 13, 2018

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of
Madrigal Pharmaceuticals, Inc.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of Madrigal Pharmaceuticals, Inc. and its subsidiaries as of December 31, 2017 and 2016, and the related consolidated statements of operations, of comprehensive loss, of stockholders' equity and of cash flows for the years then ended, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2017, based on criteria established in Internal Control—Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016, and the results of their operations and their cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2017, based on criteria established in Internal Control—Integrated Framework (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control Over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ PricewaterhouseCoopers LLP

Philadelphia, Pennsylvania
March 13, 2018

We have served as the Company's auditor since 2016.

MADRIGAL PHARMACEUTICALS, INC.

Consolidated Balance Sheets

(in thousands, except share and per share amounts)

	December 31, 2017	December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	$ 148,627	$ 19,145
Marketable securities	42,900	21,355
Prepaid expenses and other current assets	485	707
Total current assets	192,012	41,207
Property and equipment, net	301	3
Total assets	$ 192,313	$ 41,210
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,929	$ 762
Accrued expenses	8,125	4,038
Total current liabilities	10,054	4,800
Total liabilities	10,054	4,800
Stockholders' equity:		
Preferred stock, par value $0.0001 per share authorized: 5,000,000 shares at December 31, 2017 and December 31, 2016; 1,969,797 and no shares issued and outstanding at December 31, 2017 and December 31, 2016, respectively	—	—
Common stock, par value $0.0001 per share authorized: 200,000,000 at December 31, 2017 and December 31, 2016, respectively; 14,227,634 and 11,951,866 shares issued and outstanding at December 31, 2017 and December 31, 2016, respectively	1	1
Additional paid-in-capital	288,750	111,691
Accumulated other comprehensive income (loss)	(31)	25
Accumulated deficit	(106,461)	(75,307)
Total stockholders' equity	182,259	36,410
Total liabilities and stockholders' equity	$ 192,313	$ 41,210

See accompanying notes to consolidated financial statements.

MADRIGAL PHARMACEUTICALS, INC.

Consolidated Statements of Operations

(in thousands, except share and per share amounts)

	Years Ended December 31,	
	2017	2016
Revenues:		
Total revenues	$ —	$ —
Operating expenses:		
Research and development	24,390	15,933
General and administrative	7,672	9,290
Total operating expenses	32,062	25,223
Loss from operations	(32,062)	(25,223)
Interest expense	—	(1,213)
Interest income	558	48
Other income	350	—
Net loss	$ (31,154)	$ (26,388)
Net loss per common share:		
Basic and diluted net loss per common share	$ (2.54)	$ (5.07)
Basic and diluted weighted average number of common shares outstanding	12,244,939	5,204,644

See accompanying notes to consolidated financial statements.

MADRIGAL PHARMACEUTICALS, INC.

Consolidated Statements of Comprehensive Loss

(in thousands, except share and per share amounts)

	Years Ended December 31,	
	2017	2016
Net Loss	$ (31,154)	$ (26,388)
Other comprehensive income (loss):		
Unrealized gain (loss) on available-for-sale securities	(56)	25
Comprehensive loss	$ (31,210)	$ (26,363)

See accompanying notes to consolidated financial statements.

MADRIGAL PHARMACEUTICALS, INC.

Consolidated Statements of Stockholders' Equity

(in thousands, except share and per share amounts)

	Preferred stock		Common stock		Additional paid-in Capital	Accumulated other comprehensive income (loss)	Accumulated deficit	Total stockholders' equity
	Shares	Amount	Shares	Amount				
Balance at December 31, 2015	—	$ —	176,158	$ —	$ 6	$ —	$ (48,919)	$ (48,913)
Related party debt restructuring	—	—	—	—	11,224	—	—	11,224
Conversion of convertible notes and related accrued interest to common stock	—	—	7,087,186	1	47,592	—	—	47,593
Retirement of restricted stock	—	—	(9,689)	—	—	—	—	—
Acquisition of Synta	—	—	4,029,138	—	38,236	—	—	38,236
Issuance of shares to financial advisors in connection with Merger	—	—	79,101	—	750	—	—	750
Issuance of restricted common shares	—	—	208,255	—	—	—	—	—
Issuance of common shares in equity offerings, net of transaction costs	—	—	381,717	—	5,954	—	—	5,954
Compensation expense related to stock options for services	—	—	—	—	7,929	—	—	7,929
Unrealized loss on marketable securities	—	—	—	—	—	25	—	25
Net loss	—	—	—	—	—	—	(26,388)	(26,388)
Balance at December 31, 2016	—	$ —	11,951,866	$ 1	$ 111,691	$ 25	$ (75,307)	$ 36,410
Issuance of common and preferred shares in equity offerings, net of transaction costs	1,969,797	—	2,275,768	—	173,805	—	—	173,805
Compensation expense related to stock options for services	—	—	—	—	3,254	—	—	3,254
Unrealized loss on marketable securities	—	—	—	—	—	(56)	—	(56)
Net loss	—	—	—	—	—	—	(31,154)	(31,154)
Balance at December 31, 2017	1,969,797	$ —	14,227,634	$ 1	$ 288,750	$ (31)	$ (106,461)	$ 182,259

See accompanying notes to consolidated financial statements.

MADRIGAL PHARMACEUTICALS, INC.

Consolidated Statements of Cash Flows

(in thousands, except share and per share amounts)

	Years Ended December 31,	
	2017	2016
Cash flows from operating activities:		
Net loss	$ (31,154)	$ (26,388)
Adjustments to reconcile net loss to net cash used in operating activities:		
PIK interest expense on convertible promissory notes payable—related parties	—	1,207
Stock-based compensation expense	3,254	7,929
Other share based compensation	—	750
Depreciation and amortization expense	77	—
Changes in operating assets and liabilities:		
Accounts receivable—related parties	—	7
Prepaid expenses and other current assets	502	1,290
Accounts payable	917	(128)
Accrued expense	4,087	(2,281)
Accrued interest—related party	—	6
Net cash used in operating activities	(22,317)	(17,608)
Cash flows from investing activities:		
Cash received from merger transaction	—	5,849
Purchases of marketable securities	(70,211)	(10,697)
Sales and maturities of marketable securities	48,330	26,063
Purchases of property and equipment	(125)	(3)
Net proceeds from the sale of property, equipment and other assets	—	698
Release of restricted cash	—	83
Net cash provided (used) in investing activities	(22,006)	21,993
Cash flows from financing activities:		
Proceeds from issuance of common and preferred stock, net of transaction costs	173,805	5,954
Proceeds from convertible notes—related parties	—	8,500
Net cash provided by financing activities	173,805	14,454
Net increase (decrease) in cash and cash equivalents	129,482	18,839
Cash and cash equivalents at beginning of period	19,145	306
Cash and cash equivalents at end of period	$ 148,627	$ 19,145
Supplemental disclosure of cash flow information:		
Exchange of related party advances payable for convertible notes	—	500
Related party debt restructuring	—	13,680
Purchases of property and equipment in accounts payable at period end	250	—

See accompanying notes to consolidated financial statements.

MADRIGAL PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements

1. Organization, Business and Basis of Presentation

Organization and Business

Madrigal Pharmaceuticals, Inc. (the "Company" or "Madrigal") is a clinical-stage pharmaceutical company developing novel, high-quality, small-molecule drugs addressing major unmet needs in cardiovascular and metabolic diseases. The Company's lead compound, MGL-3196, is being advanced for non-alcoholic steatohepatitis ("NASH"), a liver disease that commonly affects people with metabolic diseases such as obesity and diabetes, and indications in dyslipidemia, particularly genetic dyslipidemias such as familial hypercholesterolemia ("FH"), including both homozygous and heterozygous forms of the disease. The Company initiated a Phase 2 study of MGL-3196 in NASH in October 2016. In February 2017, the Company initiated a Phase 2 study of MGL-3196 in patients with Heterozygous Familial Hypercholesterolemia ("HeFH"). Both Phase 2 studies were fully enrolled in 2017, and the HeFH study was completed in February 2018.

Madrigal was originally incorporated as a private company ("Private Madrigal") on August 19, 2011 and commenced operations in September 2011. On July 22, 2016, Private Madrigal completed a reverse merger (the "Merger") into Synta Pharmaceuticals Corp. ("Synta") (see Note 3). Upon the consummation of the Merger, the historical financial statements of Private Madrigal became the Company's historical financial statements. Accordingly, the historical financial statements of Private Madrigal are included in the comparative prior periods. The Company, or Madrigal, as used in the accompanying notes to the unaudited condensed consolidated financial statements, refers to Private Madrigal prior to the completion of the Merger and Public Madrigal subsequent to the completion of the Merger.

2. Summary of Significant Accounting Policies

Principle of Consolidation

The consolidated financial statements include the financial statements of the Company and its wholly owned subsidiaries. All significant intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect certain reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting periods. The Company bases its estimates on historical experience and various other assumptions that management believes to be reasonable under the circumstances. Changes in estimates are recorded in the period in which they become known. Actual results could differ from those estimates.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less at the date of purchase to be cash equivalents. The Company maintains its cash in bank accounts, the balance of which, at times, exceeds Federal Deposit Insurance Corporation insured limits.

The primary objective of the Company's investment activities is to preserve its capital for the purpose of funding operations and the Company does not enter into investments for trading or

MADRIGAL PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

speculative purposes. The Company's cash is deposited in highly rated financial institutions in the United States. The Company invests in money market funds and high-grade, short-term commercial paper and corporate bonds, which management believes are subject to minimal credit and market risk.

Marketable Securities

Marketable securities consist of investments in high-grade corporate obligations, and government and government agency obligations that are classified as available-for-sale. Since these securities are available to fund current operations they are classified as current assets on the consolidated balance sheets.

The Company adjusts the cost of available-for-sale debt securities for amortization of premiums and accretion of discounts to maturity. The Company includes such amortization and accretion as a component of interest income, net. Realized gains and losses and declines in value, if any, that the Company judges to be other-than-temporary on available-for-sale securities are reported as a component of interest income, net. To determine whether an other-than-temporary impairment exists, the Company considers whether it intends to sell the debt security and, if the Company does not intend to sell the debt security, it considers available evidence to assess whether it is more likely than not that it will be required to sell the security before the recovery of its amortized cost basis. During the years ended December 31, 2017 and 2016, the Company determined it did not have any securities that were other-than-temporarily impaired.

Marketable securities are stated at fair value, including accrued interest, with their unrealized gains and losses included as a component of accumulated other comprehensive income or loss, which is a separate component of stockholders' equity. The fair value of these securities is based on quoted prices and observable inputs on a recurring basis. Realized gains and losses are determined on the specific identification method. During the years ended December 31, 2017 and 2016, the Company did not have any realized gains or losses on marketable securities.

Fair Value of Financial Instruments

The carrying amounts of the Company's financial instruments, which include cash equivalents, and marketable securities, approximate their fair values. The fair value of the Company's financial instruments reflects the amounts that would be received upon sale of an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. The fair value hierarchy has the following three levels:

Level 1—quoted prices in active markets for identical assets and liabilities.

Level 2—observable inputs other than Level 1 inputs. Examples of Level 2 inputs include quoted prices in active markets for similar assets or liabilities and quoted prices for identical assets or liabilities in markets that are not active.

Level 3—unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability.

Financial assets and liabilities are classified in their entirety within the fair value hierarchy based on the lowest level of input that is significant to the fair value measurement. The Company measures the fair value of its marketable securities by taking into consideration valuations obtained from third-

MADRIGAL PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

party pricing sources. The pricing services utilize industry standard valuation models, including both income and market based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker-dealer quotes on the same or similar securities, issuer credit spreads, benchmark securities and other observable inputs. As of December 31, 2017, the Company's financial assets valued based on Level 1 inputs consisted of cash and cash equivalents in a money market fund and its financial assets valued based on Level 2 inputs consisted of high-grade corporate bonds and commercial paper. During the years ended December 31, 2017 and 2016, the Company did not have any transfers of financials assets between Levels 1 and 2. As of December 31, 2017, the Company did not have any financial liabilities that were recorded at fair value on a recurring basis on the balance sheet.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development costs are comprised of costs incurred in performing research and development activities, including internal costs (including stock-based compensation), costs for consultants, and other costs associated with the Company's preclinical and clinical programs. In particular, Madrigal has conducted safety studies in animals, optimized and implemented the API manufacturing, and conducted Phase 1 & 2 clinical trials, all of which are considered research and development expenditures.

Patents

Costs to secure and defend patents are expensed as incurred and are classified as general and administrative expense in the Company's statements of operations. Patent expenses were approximately $176 thousand and $242 thousand for the years ended December 31, 2017 and 2016, respectively.

Stock-Based Compensation

The Company recognizes stock-based compensation expense based on the grant date fair value of stock options granted to employees, officers and directors. The Company uses the Black-Scholes option pricing model to determine the grant date fair value as management believes it is the most appropriate valuation method for its option grants. The Black-Scholes model requires inputs for risk-free interest rate, dividend yield, volatility and expected lives of the options. The expected lives for options granted represent the period of time that options granted are expected to be outstanding. The Company uses the simplified method for determining the expected lives of options. Expected volatility is based upon an industry estimate. The risk-free rate for periods within the expected life of the option is based on the U.S. Treasury yield curve in effect at the time of the grant. The Company estimates the forfeiture rate based on historical data. This analysis is re-evaluated at least annually and the forfeiture rate is adjusted as necessary.

Certain of the employee stock options granted by the Company are structured to qualify as incentive stock options (ISOs). Under current tax regulations, the Company does not receive a tax deduction for the issuance, exercise or disposition of ISOs if the employee meets certain holding requirements. If the employee does not meet the holding requirements, a disqualifying disposition occurs, at which time the Company may receive a tax deduction. The Company does not record tax benefits related to ISOs unless and until a disqualifying disposition is reported. In the event of a disqualifying disposition, the entire tax benefit is recorded as a reduction of income tax expense. The

MADRIGAL PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Company has not recognized any income tax benefit for its share-based compensation arrangements due to the fact that the Company does not believe it is more likely than not it will realize the related deferred tax assets.

Income Taxes

The Company uses the asset and liability method to account for income taxes. Deferred tax assets and liabilities are determined based on the expected future tax consequences of temporary differences between the Company's financial statement carrying amounts and the tax basis of assets and liabilities using enacted tax rates expected to be in effect in the years in which the differences are expected to reverse. The Company currently maintains a 100% valuation allowance on its deferred tax assets.

Comprehensive Loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. Changes in unrealized gains and losses on marketable securities represent the only difference between the Company's net loss and comprehensive loss.

Basic and Diluted Loss Per Common Share

Basic net loss per share is computed using the weighted average number of common shares outstanding during the period, excluding restricted stock that has been issued but is not yet vested. Diluted net loss per common share is computed using the weighted average number of common shares outstanding and the weighted average dilutive potential common shares outstanding using the treasury stock method. However, for the years ended December 31, 2017 and 2016, diluted net loss per share is the same as basic net loss per share as the inclusion of weighted average shares of unvested restricted common stock and common stock issuable upon the exercise of stock options would be anti-dilutive.

The following table summarizes outstanding securities not included in the computation of diluted net loss per common share as their inclusion would be anti-dilutive:

	December 31,	
	2017	2016
Common stock options	976,777	784,011
Unvested restricted common stock	104,127	157,262
Preferred stock	1,969,797	—

Recent Accounting Pronouncements

In May 2017, the Financial Accounting Standards Board (the "FASB") issued Accounting Standards Update ("ASU") No. 2017-09, "Compensation—Stock Compensation (Topic 718): Scope of Modification Accounting," to provide clarity and reduce both diversity in practice, and cost and complexity when a change is made to the terms or conditions of a share-based payment award. For public business entities, ASU 2017-09 is effective for annual and interim reporting periods beginning after December 15, 2017, with early adoption permitted. The update should be applied prospectively to an award modified on or after the adoption date. The Company is currently evaluating the impact this standard may have on its financial statements.

MADRIGAL PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

In March 2016, the Financial Accounting Standards Board (the "FASB") issued Accounting Standards Update ("ASU") No. 2016-09, "Compensation—Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting," which was designed to simplify several aspects of the accounting for share-based payment transactions, including, among other things, guidance related to accounting for income taxes, modification of the criteria for classification of awards as either equity awards or liability awards where an employer withholds shares from an employee's share-based award for tax withholding purposes, and classification on the statement of cash flows of cash payments to a tax authority by an employer that withholds shares from an employee's award for tax withholding purposes. The amendments in this ASU are effective for annual periods beginning after December 15, 2016, and interim periods within those annual periods. The Company adopted ASU No. 2016-09 effective January 1, 2017. There was no significant impact from the adoption of ASU No. 2016-09 because the Company currently maintains a 100% valuation allowance on its deferred tax assets.

In August 2016, the FASB issued ASU No. 2016-15, "Statement of Cash Flows (Topic 230): Clarification of Certain Cash Receipts and Cash Payments." The objective of ASU No. 2016-15 is to eliminate the diversity in practice related to the classification of certain cash receipts and payments in the statement of cash flows, by adding or clarifying guidance on eight specific cash flow issues. For public business entities, ASU 2016-15 is effective for annual and interim reporting periods beginning after December 15, 2017, with early adoption permitted. ASU 2015-16 provides that the amendments in the update should be applied retrospectively to all periods presented, unless deemed impracticable, in which case, prospective application is permitted. The Company is currently evaluating the impact this standard may have on its financial statements.

In January 2016, the FASB issued ASU No. 2016-01, "Financial Instruments—Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities," which amends the guidance in U.S. generally accepted accounting principles on the classification and measurement of financial instruments. Changes to the current guidance primarily affect the accounting for equity investments, financial liabilities under the fair value option, and the presentation and disclosure requirements for financial instruments. In addition, the ASU clarifies guidance related to the valuation allowance assessment when recognizing deferred tax assets resulting from unrealized losses on available-for-sale debt securities. The amendments in this ASU are effective for fiscal years and interim periods beginning after December 15, 2017, and are to be adopted by means of a cumulative-effect adjustment to the balance sheet at the beginning of the first reporting period in which the guidance is effective. Early adoption is not permitted except for the provision to record fair value changes for financial liabilities under the fair value option resulting from instrument-specific credit risk in other comprehensive income. The Company is currently evaluating the impact this standard may have on its financial statements.

3. Reverse Merger

On July 22, 2016, the Company, Synta and Saffron Merger Sub, Inc., a wholly-owned subsidiary of Synta ("Merger Sub"), completed their merger transaction pursuant to which Merger Sub merged with and into the Company with the Company becoming a wholly-owned subsidiary of Synta and the surviving corporation of the merger. Each outstanding share of private Madrigal common stock was converted into 0.1593 shares of common stock of the post-merger combined company. As a result, Synta issued 7.3 million shares of common stock to the stockholders of private Madrigal in exchange for common shares of private Madrigal. For accounting purposes, the Company is considered to be

MADRIGAL PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements (Continued)

3. Reverse Merger (Continued)

acquiring Synta in the merger. The Company was determined to be the accounting acquirer based upon the terms of the Merger Agreement and other factors including: (i) Madrigal security holders own approximately 64% of the voting interests of the combined company immediately following the closing of the merger; (ii) directors appointed by Madrigal hold a majority of board seats in the combined company; and (iii) Madrigal management hold a majority of the key positions in the management of the combined company. As the accounting acquirer, the Company's assets and liabilities continue to be recorded at their historical carrying amounts and the historical operations that will be reflected in the financial statements will be those of the Company.

Immediately prior to the closing of the merger, Synta completed a one-for-35 reverse stock split. Following the reverse stock split and the merger, the post-merger combined company had approximately 11.3 million shares outstanding and the former stockholders of the Company owned approximately 64% of the outstanding capital stock of the post-merger combined company. The impact of the recapitalization of the Company has been retroactively applied to all periods presented.

Upon the closing of the merger transaction, the Company incurred an expense for a success fee of $750 thousand in cash, plus settled $750 thousand for both parties in shares of the post-merger combined company's common stock with a third party financial advisor.

Purchase Price

Pursuant to the Merger Agreement, Synta issued to Madrigal stockholders a number of shares of Synta common stock representing approximately 64% of the outstanding shares of common stock of the combined company. The purchase price, which represents the consideration transferred to Synta stockholders in the reverse merger is calculated based on the number of shares of common stock of the combined company that Synta stockholders will own as of the closing of the merger, which consists of the following:

Number of shares of the combined company to be owned by Synta stockholders(1)	4,032,734
Multiplied by the fair value of Synta common stock(2)	$ 9.48
Purchase price (in thousands)	$ 38,236

(1) Represents the number of shares of common stock of the combined company that Synta stockholders owned as of the closing of the merger pursuant to the Merger Agreement, including restricted stock awards and common stock underlying outstanding restricted stock units attributed to pre-combination services rendered by certain Synta employees and directors. This amount is calculated as 3,937,309 shares of Synta common stock outstanding as of July 22, 2016, including unvested restricted common stock, plus 95,425 shares of Synta common stock issuable pursuant to restricted stock units, net of tax withholdings, that vested immediately upon closing of the merger. The number of shares of common stock Synta issued to Madrigal stockholders was 7,253,655, calculated pursuant to the terms of the Merger Agreement based on Synta's common stock outstanding as of July 22, 2016.

(2) The fair value of Synta common stock used in determining the purchase price was $9.48, which was derived from the $0.2709 per share closing price of Synta common stock on July 21, 2016, the current price at the time of the closing, adjusted for the 1-for-35 reverse stock split.

MADRIGAL PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements (Continued)

3. Reverse Merger (Continued)

Under the acquisition method of accounting, the total purchase price is allocated to the acquired tangible and intangible assets and assumed liabilities of Synta based on their estimated fair values as of the merger closing date. The excess of the purchase price over the fair value of assets acquired and liabilities assumed, if any, is allocated to goodwill. The allocation of the purchase price to the acquired assets and liabilities assumed of Synta based on the fair values as of July 22, 2016 is as follows, including measurement period adjustments since the fair values presented in the Company's Form 10-Q for the quarter ended September 30, 2016 (in thousands):

	July 22, 2016	Measurement period adjustments	July 22 2016 (As adjusted)
Cash, cash equivalents and marketable securities	$ 42,611		$ 42,611
Prepaid expenses and other currents assets	1,715		1,715
Property and equipment, net	482	65	547
Accounts payable, accrued expenses and other liabilities	(7,019)		(7,019)
Term loans and capital lease obligations	(18)		(18)
In-process research and development	150	250	400
Goodwill	315	(315)	—
Net assets acquired	$ 38,236		$ 38,236

The Company's measurement period adjustments were complete as of December 31, 2016. As a result of the measurement period adjustments recorded above, there was no gain or losses on the disposed tangible or intangible assets.

Convertible Promissory Notes-Related Parties

Immediately prior to the consummation of the merger, the September 14, 2011, September 16, 2011 and March 1, 2016 (amended and restated April 13, 2016) convertible note issuances outstanding totaling $47.6 million on July 22, including accrued but unpaid interest, were converted into 7.1 million shares of common stock on a post-split basis of the Company pursuant to their respective amended and restated terms (see Note 6).

Bonus Plan Awards

Pursuant to the terms of the Change in Control Bonus Plan, the participants therein received 0.6 million shares of common stock of the Company from certain former stockholders of the Company in connection with the merger, which represented 7.87% of Madrigal's common shares outstanding at the time of the merger. The Company recorded $5.4 million in stock compensation associated with the transaction (see Note 9).

Stock Based Compensation

Following the consummation of the merger, the Company issued a combined 208,255 shares of restricted common stock and 557,386 stock options to purchase shares of common stock to the new

MADRIGAL PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements (Continued)

3. Reverse Merger (Continued)

Chief Executive Officer, Chief Medical Officer and Executive Vice President, and Chief Financial Officer and Senior Vice President.

4. Liquidity and Uncertainties

The Company is subject to risks common to development stage companies in the Bio-Pharmaceutical industry including, but not limited to, uncertainty of product development and commercialization, dependence on key personnel, uncertainty of market acceptance of products and product reimbursement, product liability, uncertain protection of proprietary technology, potential inability to raise additional financing necessary for development and commercialization, and compliance with the U.S. Food and Drug Administration and other government regulations.

The Company has incurred losses since inception, including approximately $31.2 million for the year ended December 31, 2017, resulting in an accumulated deficit of approximately $106.5 million and $75.3 million as of December 31, 2017 and 2016, respectively. Management expects to incur losses for the foreseeable future. To date, the Company has funded its operations primarily through the issuance of convertible debt (see Note 6), the proceeds from the Merger on July 22, 2016 (see Note 3), and proceeds from the sales of the Company's common and Series A Convertible Preferred Stock (see Note 8).

The Company believes that its cash, cash equivalents and marketable securities at December 31, 2017 will be sufficient to fund operations past one year from the issuance of these financial statements. To meet its future capital needs, the Company intends to raise additional capital through debt or equity financings, collaborations, partnerships or other strategic transactions. However, there can be no assurance that the Company will be able to complete any such transactions on acceptable terms or otherwise. The inability of the Company to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Company's business, results of operations and financial condition. The Company has the ability to delay certain research activities and related clinical expenses if necessary due to liquidity concerns until a date in which those concerns are relieved.

MADRIGAL PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements (Continued)

5. Cash, Cash Equivalents and Marketable Securities

A summary of cash, cash equivalents and available-for-sale marketable securities held by the Company as of December 31, 2017 and 2016 is as follows (in thousands):

	December 31, 2017			
	Cost	Unrealized gains	Unrealized losses	Fair value
Cash and cash equivalents:				
Cash (Level 1)	$ 2,725	$ —	$ —	$ 2,725
Money market funds (Level 1)	145,902	—	—	145,902
Corporate debt securities due within 3 months of date of purchase (Level 2)	—	—	—	—
Total cash and cash equivalents	148,627	—	—	148,627
Marketable securities:				
Corporate debt securities due within 1 year of date of purchase (Level 2)	42,931	—	(31)	42,900
Total cash, cash equivalents and marketable securities	$ 191,558	$ —	$ (31)	$ 191,527

	December 31, 2016			
	Cost	Unrealized gains	Unrealized losses	Fair value
Cash and cash equivalents:				
Cash (Level 1)	$ 5,651	$ —	$ —	$ 5,651
Money market funds (Level 1)	13,494	—	—	13,494
Corporate debt securities due within 3 months of date of purchase (Level 2)	—	—	—	—
Total cash and cash equivalents	19,145	—	—	19,145
Marketable securities:				
Corporate debt securities due within 1 year of date of purchase (Level 2)	21,330	25	—	21,355
Total cash, cash equivalents and marketable securities	$ 40,475	$ 25	$ —	$ 40,500

6. Convertible Promissory Notes—Related Parties

Prior to the Merger, the Company was financed via issuances of convertible promissory notes, designated as "the September 14, 2011 Notes", "the September 16, 2011 Notes", and "the March 1, 2016 Notes", respectively (collectively "the Notes"). The Notes accrued interest at 8% per annum, compounded monthly, and were collateralized by all assets of the Company.

Effective April 13, 2016, in connection with execution of the Merger Agreement, the Notes were amended and restated, primarily to provide for mandatory conversion upon completion of the Merger. On that same date, the lenders collectively waived all accrued and unpaid interest under all of the convertible notes. The total accrued and waived interest amounted to $13.7 million. The lenders also agreed that no additional interest on these notes would be accrued through the date on which the Merger was consummated or terminated. Also on April 13, 2016, the Company reduced the convertible

MADRIGAL PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements (Continued)

6. Convertible Promissory Notes—Related Parties (Continued)

notes payable by the waived accrued interest less $2.5 million of accrued interest for the period April 14, 2016 through the maturity date of December 31, 2016, as required under Troubled Debt Restructuring accounting guidance. The net waived interest of $11.2 million was recorded as an increase in Additional Paid in Capital ("APIC") at the time of the amendment, as the notes were held by related parties. The remaining $2.5 million of accrued interest was recorded as an increase in APIC upon conversion at the Merger.

During the period March 1, 2016 through the Merger, the lenders provided convertible promissory note financing of $8.5 million in cash. Additionally, on April 13, 2016, one of the lenders exchanged $0.5 million of Advances Payable for an equal amount of convertible promissory notes.

7. Advances Payable—Related Party

On June 29, 2015 and July 30, 2015 a related party agreed to advance the Company a total of $500 thousand to be used for working capital requirements. The advances accrued interest at a rate of four percent (4%) per annum compounded annually. On April 13, 2016, these advances were exchanged for $500 thousand in convertible promissory notes payable and all accrued interest was waived (see Note 6).

8. Stockholders' Equity (Deficit)

Common Stock

Each common stockholder is entitled to one vote for each share of common stock held. The common stock will vote together with all other classes and series of stock of the Company as a single class on all actions to be taken by the Company's stockholders. Each share of common stock is entitled to receive dividends, as and when declared by the Company's board of directors.

The Company has never declared cash dividends on its common stock and does not expect to do so in the foreseeable future.

December 2017 Registered Offering

In December 2017, the Company entered into an underwriting agreement (the "Underwriting Agreement") with Goldman Sachs & Co. LLC, as representative of the several underwriters named therein (the "Underwriters"), relating to an underwritten public offering (the "December 2017 Offering") of 1,731,929 shares of the Company's common stock, including 225,904 shares of the Company's common stock purchased by the Underwriters pursuant to a 30-day option to purchase such additional shares granted therein, at a public offering price of $83.00 per share. The December 2017 Offering resulted in gross proceeds to the Company of approximately $143.8 million, and net proceeds to the Company of approximately $135.7 million, after deducting the Underwriters' discount and other estimated offering expenses payable by the Company. The December 2017 Offering closed on December 21, 2017.

June 2017 Private Placement Offering and its Series A Convertible Preferred Stock

In June 2017, the Company entered into a Securities Purchase Agreement (the "Purchase Agreement)" with a group of institutional accredited investors, who were existing, non-controlling stockholders of the Company, pursuant to which the Company sold securities to the Investors in a

MADRIGAL PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements (Continued)

8. Stockholders' Equity (Deficit) (Continued)

private placement transaction (the "June 2017 Offering"). Under the terms of the Purchase Agreement, the Company sold 328,300 shares of its common stock at a price of $15.23 per share, and 1,969,797 shares of its Series A Convertible Preferred Stock (the "Series A Preferred Stock") at a price of $15.23 per share. The June 2017 Offering resulted in gross proceeds to the Company of approximately $35.0 million, and net proceeds to the Company of approximately $34.9 million. The June 2017 Offering closed on June 23, 2017.

The Series A Preferred Stock has a par value of $0.0001 per share and is convertible into shares of the common stock at a one-to-one ratio, subject to adjustment as provided in the Purchase Agreement. The terms of the Series A Preferred Stock are set forth in the Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock, that the Company filed with the Secretary of State of the State of Delaware on June 21, 2017. Each share of the Series A Preferred Stock is convertible into shares of Common Stock at any time at the holder's option. Upon any liquidation, dissolution or winding-up of the Company, whether voluntary or involuntary, after the satisfaction in full of the debts of the Company and the payment of any liquidation preference owed to the holders of shares of capital stock of the Company ranking prior to the Series A Preferred Stock upon liquidation, the holders of the Series A Preferred Stock shall participate pari passu with the holders of the Common Stock (on an as-if-converted-to-Common-Stock basis) in the net assets of the Company. Shares of the Series A Preferred Stock will generally have no voting rights, except as required by law. Shares of the Series A Preferred Stock will be entitled to receive dividends before shares of any other class or series of capital stock of the Company (other than dividends in the form of the Common Stock) equal to the dividend payable on each share of the Common Stock, on an as-converted basis.

At-The-Market Issuance Sales Agreement

In October 2015, the Company entered into an at-the-market issuance sales agreement (the "October 2015 Sales Agreement"), with Cowen and Company, LLC ("Cowen"), pursuant to which the Company may issue and sell shares of its common stock, having an aggregate offering price of up to $100 million, from time to time, at the Company's option, through Cowen as its sales agent. Sales of common stock through Cowen may be made by any method that is deemed an "at-the-market" offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including by means of ordinary brokers' transactions at market prices, in block transactions or as otherwise agreed by the Company and Cowen. Subject to the terms and conditions of the October 2015 Sales Agreement, Cowen will use commercially reasonable efforts consistent with its normal trading and sales practices to sell the common stock based upon the Company's instructions (including any price, time or size limits or other customary parameters or conditions the Company may impose). The Company is not obligated to make any sales of its common stock under the October 2015 Sales Agreement. Any shares sold will be sold pursuant to an effective shelf registration statement on Form S-3 (file no. 333-206135). The Company will pay Cowen a commission of up to 3% of the gross proceeds. The October 2015 Sales Agreement may be terminated by the Company at any time upon 10 days' notice.

As of December 31, 2017, 597,256 shares have been sold under the October 2015 Sales Agreement for an aggregate of approximately $9.6 million in gross proceeds. Net proceeds to the Company were approximately $9.4 million after deducting commissions and other transactions costs. Of those shares sold, 215,539 were sold in 2017 for an aggregate of approximately $3.5 million in gross proceeds, and $3.4 million in net proceeds. Approximately $90.4 million remained reserved under the Company's shelf

MADRIGAL PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements (Continued)

8. Stockholders' Equity (Deficit) (Continued)

registration statement and the applicable prospectus supplement for possible future issuance under the October 2015 Sales Agreement.

9. Stock-based Compensation

In June 2015, upon obtaining stockholder approval at its annual shareholder meeting, the Company implemented its new 2015 Stock Plan. The 2015 Stock Plan replaced the 2006 Stock Plan which was terminated upon adoption of the 2015 Stock Plan. Shares of common stock reserved for outstanding awards under the 2006 Stock Plan that lapse or are cancelled will be added back to the share reserve available for future awards under the 2015 Stock Plan. The 2015 Stock Plan provides for the grant of incentive stock options, non-statutory stock options, restricted stock and other stock-based compensation awards to employees, officers, directors and consultants of the Company. The administration of the 2015 Stock Plan is under the general supervision of the compensation committee of the board of directors. The exercise price of the stock options is determined by the compensation committee of the board of directors, provided that incentive stock options are granted with an exercise price not less than fair market value of the common stock on the date of grant and expire no later than ten years from the date the option is granted. As of December 31, 2017, the Company had options outstanding to purchase 976,777 shares of its common stock, which includes options outstanding under its 2006 Stock Plan that was terminated in June 2015. As of December 31, 2017, 1,458,495 shares were available for future issuance.

The following table summarizes stock option activity during the twelve months ended December 31, 2017:

	Shares	Weighted average exercise price	Weighted average remaining contractual life (years)	Aggregate intrinsic value (in thousands)
Outstanding at January 1, 2017	784,011	$ 10.70		
Options granted	207,700	16.72		
Options exercised	—	—		
Options cancelled	(14,934)	10.92		
Outstanding at December 31, 2017	976,777	$ 11.97	8.71	$ 78,076
Exercisable at December 31, 2017	396,357	$ 11.37	8.55	$ 31,976

The total cash received by the Company as a result of stock option exercises was $0 in each of the years ended December 31, 2017 and 2016. The weighted-average grant date fair values, based on the Black-Scholes option model, of options granted during the year ended December 31, 2017 and 2016 was $13.30 and $7.50, respectively.

Restricted Common Stock

The Company's share-based compensation plan provides for awards of restricted shares of common stock to employees, officers, directors and consultants to the Company. Restricted stock awards are subject to forfeiture if employment or service terminates during the prescribed retention period. Restricted shares vest over the service period.

MADRIGAL PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements (Continued)

9. Stock-based Compensation (Continued)

The following table summarizes unvested restricted share activity during the year ended December 31, 2017:

	Shares	Weighted average grant date fair value
Outstanding at January 1, 2017	157,262	$ 10.06
Granted	—	—
Forfeited	—	—
Vested	(53,135)	11.27
Outstanding at December 31, 2017	104,127	$ 9.45

Stock-Based Compensation Expense

Stock-based compensation expense during the years ended December 31, 2017 and 2016 was as follows (in thousands):

	Years ended December 31,	
	2017	2016
Stock-based compensation expense by type of award:		
Stock options	$ 2,662	$ 1,782
Restricted stock	592	736
Change in control bonus plan (see note 3)	—	5,411
Total stock-based compensation expense	$ 3,254	$ 7,929
Effect of stock-based compensation expense by line item:		
Research and development	$ 883	$ 5,387
General and administrative	2,371	2,542
Total stock-based compensation expense included in net loss	$ 3,254	$ 7,929

Unrecognized stock-based compensation expense as of December 31, 2017 was as follows (in thousands):

	Unrecognized stock compensation expense	Weighted average remaining period (in years)
Employee stock options	$ 4,628	2.30
Restricted stock	766	1.56
Total	$ 5,394	1.97

MADRIGAL PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements (Continued)

10. Related Party Transactions

Related Party Financing

For the years ended December 31, 2017 and 2016, the Company incurred approximately $0 and $1.2 million, respectively of interest expense to related party lenders which was subsequently waived (see Note 6). This debt was converted to equity at the time of the Merger.

Consulting Agreement

The Company had a consulting agreement with its former Chief Executive Officer ("CEO"), who is also a stockholder of the Company. The consulting agreement automatically renewed monthly unless terminated. The consulting agreement could be terminated upon fifteen (15) day notice by the Company or the CEO. The consultant was paid $0 and $93 thousand, respectively, for the years ended December 31, 2017 and 2016. On July 22, 2016, this consulting agreement was replaced by an employment agreement for the position of Chief Medical Officer ("CMO") upon the completion of the Merger (see Note 3).

11. Commitments and Contingencies

The Company has a Research, Development and Commercialization Agreement with Hoffmann-La Roche ("Roche") which grants the Company a sole and exclusive license to develop, use, sell, offer for sale and import any Licensed Product as defined by the agreement.

The agreement requires future milestone payments to Roche, the remainder of which total $10 million and are earned by the commencement of Phase 3 clinical trials as well as future regulatory approval in the United States and Europe of a product developed from MGL-3916. A single-digit royalty payment range is based on net sales of products developed from MGL-3196, subject to certain reductions. In October 2016 the Company commenced a Phase 2 study in Non-Alcoholic Steatohepatitis (NASH), which triggered a milestone payment under the agreement. Except as described above, the Company has not achieved any additional product development or regulatory milestones to date and has no Licensed Product sales for the quarters ended December 31, 2017 and 2016.

During 2017, the Company has entered into several customary contractual arrangements and letters of intent in preparation for and in support of the Phase 2 clinical trials.

12. Income Taxes

At December 31, 2017, the Company had federal net operating loss ("NOL") carryforwards of approximately $40.4 million and state operating loss carryforwards of approximately $10.0 million, available to reduce future taxable income, which expire between 2031 and 2037. The Company has unused federal research and development carryforwards of approximately $1.7 million which will begin to expire in 2031.

The Internal Revenue Code ("IRC") limits the amounts of NOL carryforwards that a Company may use in any one year in the event of certain cumulative changes in ownership over a three-year period as described in Section 382 of the IRC. Such change in ownership could limit the Company's utilization of the NOL, and could be triggered by subsequent sales of securities by the Company or stockholders. The deferred tax asset related to the NOL reflected on the financial statements could be affected by this limitation. Although a formal analysis has not been completed, the Company has

MADRIGAL PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements (Continued)

12. Income Taxes (Continued)

determined that an ownership change likely occurred for Madrigal during the year ended December 31, 2017. The net operating losses are expected to be subject to an annual limitation; however, none of these NOLs is expected to expire before becoming available to reduce future taxable income.

The Company has analyzed the tax effect of the merger and concluded that an ownership change did take place for IRC 382 purposes. Based on the value of the business, Synta's federal net operating losses and R&D credits are no longer available to be used by the Company. Further, the Company has concluded that the transaction did not trigger an ownership change for Madrigal.

In assessing the realizability of deferred tax assets, management considers whether it is more likely than not that some portion of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which those temporary differences become deductible. As there is no assurance of future taxable income, a full valuation allowance has been established to offset the deferred tax assets. The valuation allowance increased $2.9 million for the year ended December 31, 2017. Changes in the deferred tax asset will be recorded as an income tax benefit or expense on the accompanying statements of operations.

Entities are also required to evaluate, measure, recognize and disclose any uncertain income tax provisions taken on their income tax returns. The Company has analyzed its tax positions and has concluded that as of December 31, 2017 there were no uncertain positions. The 2012 through 2016 tax returns are open to review by the IRS and state taxing authorities. Interest and penalties, if any, as they relate to income taxes assessed, are included in the income tax provision. There was no income tax related interest and penalties included in the income tax provision for 2017.

On December 22, 2017, H.R. 1 (also, known as the Tax Cuts and Jobs Act (the "Act")) was signed into law. Among its numerous changes to the Internal Revenue Code, the Act reduces U.S. federal corporate tax rate from 34% to 21%. As a result, the most significant impact on the Company's consolidated financial statements will be reduction of approximately $9.3 million for the deferred tax assets related to net operating losses and other assets. Such reduction is offset by changes to the Company's valuation allowance. The Company has completed the accounting for the tax impact of the Act as of December 31, 2017 and has recorded no provisional amounts.

MADRIGAL PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements (Continued)

12. Income Taxes (Continued)

Temporary differences that give rise to deferred tax assets and liabilities are as follows (in thousands):

	For the years ended December 31,	
	2017	2016
Deferred Tax Liabilities		
Stock Compensation	$ —	$ 270
Unrealized Gains on Investments	—	13
Total Deferred Tax Liabilities	$ —	$ 283
Deferred Tax Assets		
Charitable Contributions	$ 4	$ 4
Accrued Expenses	421	—
Intangibles	579	997
Stock Compensation	605	—
Unrealized Loss on Investment	9	—
Net Operating Losses	9,229	12,749
Capitalized R&D	8,671	4,226
R&D Credit	1,901	846
Total deferred tax assets before valuation allowance	21,419	18,822
Valuation Allowance	(21,419)	(18,539)
Total deferred tax assets	—	283
Net deferred tax assets	$ —	$ —

Differences between the effective income tax rate and the US statutory rate were as follows (in thousands):

	For the years ended December 31,	
	2017	2016
Tax benefit at U.S. federal statutory rate	$ (10,592)	$ (8,972)
Non-deductible interest expenses	—	410
Stock based compensation	138	407
Transaction Costs	—	256
Effect of tax reform, change in federal tax rate	9,260	—
Other Nondeductible Expenses	1	1
State income taxes benefit before valuation allowance, net of federal benefit	(704)	(1,491)
Increase in domestic valuation allowance	2,880	9,750
Research and development credit	(825)	(390)
Other adjustments	(158)	29
Income tax expense (benefit)	$ —	$ —

MADRIGAL PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements (Continued)

13. Recapitalization

Private Madrigal's historical (pre-merger) common stock, including share and per share amounts, have been retroactively adjusted to reflect the common stock of the post-merger combined company based upon the exchange ratio established in the Merger Agreement as adjusted for the one-for-35 reverse stock split effected by Synta immediately prior to the Merger. As a result, each outstanding share of private Madrigal common stock was exchanged for 0.1593 shares of common stock of the post-merger combined company. The recapitalization of the Company has been retrospectively applied to pre-merger share values.

Exhibit 21.1

SUBSIDIARIES OF MADRIGAL PHARMACEUTICALS, INC.

Synta Securities Corp., a Massachusetts securities corporation

Synta Limited Incorporated, a United Kingdom company

Synta Pharmaceuticals (Bermuda) Ltd., a Bermuda company

Canticle Pharmaceuticals, Inc., a Delaware corporation

QuickLinks

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-3 (No. 333-187242, No. 333-206135, No. 333-219304) and Form S-8 (No. 333-141903, No. 333-152824, No. 333-173862, No. 333-181117, No. 333-187243, No. 333-194477, No. 333-202680, No. 333-206128, No. 333-212615) of Madrigal Pharmaceuticals, Inc. of our report dated March 13, 2018 relating to the financial statements and the effectiveness of internal control over financial reporting, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP

Philadelphia, Pennsylvania
March 13, 2018

QuickLinks

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER PURSUANT TO SECURITIES EXCHANGE ACT RULES 13A-14(a) AND 15D-14(a) AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Paul A. Friedman, M.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Madrigal Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/s/ PAUL A. FRIEDMAN, M.D.

Paul A. Friedman, M.D.
Chief Executive Officer and Chairman of the Board (Principal Executive Officer)
Date: March 13, 2018

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Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER PURSUANT TO SECURITIES EXCHANGE ACT RULES 13A-14(A) AND 15D-14(A) AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Marc R. Schneebaum, certify that:

1. I have reviewed this Annual Report on Form 10-K of Madrigal Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/s/ MARC R. SCHNEEBAUM

Marc R. Schneebaum
Chief Financial Officer (Principal Financial Officer)
Date: March 13, 2018

QuickLinks

Exhibit 32.1

**CERTIFICATIONS PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO SECTION 906
OF THE SARBANES-OXLEY ACT OF 2002**

Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (Subsections (a) and (b) of Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. Section 1350)), each of the undersigned officers of Madrigal Pharmaceuticals, Inc., a Delaware corporation (the "Company"), does hereby certify, to such officer's knowledge, that:

The Annual Report on Form 10-K for the year ended December 31, 2017 (the "Form 10-K") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 13, 2018

/s/ PAUL A. FRIEDMAN, M.D.

Paul A. Friedman, M.D.
Chief Executive Officer and Chairman of the Board
(Principal Executive Officer)

Dated: March 13, 2018

/s/ MARC R. SCHNEEBAUM

Marc R. Schneebaum
Senior Vice President and Chief Financial Officer
(Principal Accounting and Financial Officer)

A signed original of this written statement required by Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. Section 1350), has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request. These certifications accompany the Form 10-K, are not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.

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