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As filed with the Securities and Exchange Commission on July 14, 2017

Registration No. 333-

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

FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

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 Number)

Four Tower Bridge
200 Barr Harbor Drive, Suite 400
West Conshohocken, Pennsylvania 19428
(484) 380-9263
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Marc R. Schneebaum
Chief Financial Officer
Madrigal Pharmaceuticals, Inc.
Four Tower Bridge
200 Barr Harbor Drive, Suite 400
West Conshohocken, Pennsylvania 19428
(484) 380-9263
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Michael L. Lawhead, Esq.
Stradling Yocca Carlson & Rauth, P.C.
660 Newport Center Drive, Suite 1600
Newport Beach, California 92660
(949) 725-4000

Approximate date of commencement of proposed sale to public:

From time to time after this Registration Statement becomes effective.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. o

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. o

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. o

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a 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 o	Accelerated filer o	Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company ☒ Emerging growth company o

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 7(a)(2)(B) of Securities Act. o

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Number of shares to be registered(1)	Proposed maximum offering price per share(2)	Proposed maximum aggregate offering price(2)	Amount of registration fee
Common stock, $0.0001 par value per share	328,300	$15.50	$5,087,009	$589.58

(1) Pursuant to Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), the shares being registered hereunder include such indeterminate number of shares of common stock as may be issuable with respect to the shares being registered hereunder as a result of stock splits, stock dividends, or similar transactions.

(2) Estimated solely for the purpose of calculating the registration fee pursuant to Rules 457(c) of the Securities Act based on a price of $15.50, which was the average of the high and low sales prices of the common stock, as reported on the Nasdaq Global Market on July 12, 2017.

The Registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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The information in this prospectus is not complete and may be changed. The selling stockholders may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

PRELIMINARY PROSPECTUS
SUBJECT TO COMPLETION, DATED JULY 14, 2017

328,300 Shares

MADRIGAL PHARMACEUTICALS, INC.

Common Stock

This prospectus relates to the disposition of up to 328,300 shares of Madrigal Pharmaceuticals, Inc., or Madrigal, common stock by the selling stockholders listed in this prospectus or their permitted transferees. The shares of common stock being offered by the selling stockholders were originally issued in a private placement to selling stockholders completed on June 23, 2017.

All of the shares offered hereby are being sold by the selling stockholders named in this prospectus, or their permitted transferees, and Madrigal will not receive any proceeds from sales of these securities. Madrigal will bear the costs and fees of the registration of the shares, and the selling stockholders will bear all commissions and discounts, if any, attributable to the sales of the shares.

The prices at which the selling stockholders or their permitted transferees may dispose of their Madrigal shares will be determined by the selling stockholders at the time of sale and may be at the prevailing market price for the shares, at prices related to such market price, at varying prices determined at the time of sale, or at negotiated prices. Information regarding the selling stockholders and the times and manner in which they may offer and sell the shares or interests therein under this prospectus is provided under "Selling Stockholders" and "Plan of Distribution" in this prospectus. The selling stockholders may resell the common stock to or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions.

You should carefully read this prospectus and any prospectus supplement, as well as the documents incorporated by reference or deemed to be incorporated by reference into this prospectus and any prospectus supplement, before you invest in our common stock.

Our common stock is listed on the NASDAQ Global Market and traded under the symbol "MDGL." On July 13, 2017, the last reported sale price for our common stock on the NASDAQ Global Market was $15.35 per share.

INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD CAREFULLY CONSIDER THE SECTION OF THIS PROSPECTUS ENTITLED "RISK FACTORS" BEGINNING ON PAGE 25 OF THIS PROSPECTUS BEFORE YOU INVEST IN OUR SECURITIES.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is , 2017.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a "shelf" registration process. Under this shelf registration process, selling stockholders may from time to time sell the shares of common stock described in this prospectus in one or more offerings.

All references to "Madrigal," "Company," "we," "our" or "us" refer solely to Madrigal Pharmaceuticals, Inc. References to "selling stockholders" refer to those stockholders listed under the "Selling Stockholders" section of this prospectus, who may sell shares from time to time as described in this prospectus.

We may add, update or change any of the information contained in this prospectus or in any accompanying prospectus supplement we may authorize to be delivered to you. To the extent there is a conflict between the information contained in this prospectus and any accompanying prospectus supplement, you should rely on the information in the prospectus supplement. This prospectus, together with any accompanying prospectus supplement, includes all material information relating to this offering.

No dealer, salesperson or other person has been authorized to give any information or to make any representations other than those contained or incorporated by reference in this prospectus or any accompanying prospectus supplement in connection with the offer made by this prospectus or any accompanying prospectus supplement. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or any accompanying prospectus supplement as if we had authorized it.

This prospectus and any accompanying prospectus supplement does not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor does this prospectus and any accompanying prospectus supplement constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

You should not assume that the information contained in this prospectus and any accompanying prospectus supplement is correct on any date after their respective dates, even though this prospectus or any prospectus supplement may be delivered or securities may be sold on a later date.

Investing in our securities involves a high degree of risk. You should carefully consider the section entitled "Risk Factors" in this prospectus and any accompanying prospectus supplement before you invest in our securities.

You should also carefully read the additional information described in the sections entitled "Incorporation of Certain Documents by Reference" and "Where You Can Find More Information" before you invest in our securities.

SPECIAL NOTE REGARDING FORWARD-LOOKING INFORMATION

This prospectus, any accompanying prospectus supplement, and the documents we incorporate by reference in this prospectus and any accompanying prospectus supplement contain forward-looking statements within the meaning of the federal securities laws, which statements are subject to substantial risks and uncertainties. These forward-looking statements are intended to qualify for the safe harbor from liability established by the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical fact are forward-looking statements. We have attempted to identify forward-looking statements by using words such as "may," "believe," "will," "could," "project," "anticipate," "expect," "estimate," "should," "continue," "potential," "plan," "forecasts," "goal," "seek," "intend," other forms of these words or similar words or expressions or the negative thereof.

In particular, this prospectus, any accompanying prospectus supplement, and the documents we incorporate by reference in this prospectus and any accompanying prospectus supplement, contain forward-looking statements relating to, among other things:

- Anticipated or estimated future results, including the risks and uncertainties associated with our future operating performance and financial position;
- 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 related to our ability to accomplish our business development objectives and realize the anticipated benefit of any such transactions; and
- Assumptions underlying any of the foregoing.

We have based our forward-looking statements on our expectations and projections about trends affecting our business and industry and other future events. Although we do not make forward-looking statements unless we believe we have a reasonable basis for doing so, we cannot guarantee their accuracy. Forward-looking statements are subject to substantial risks and uncertainties that could cause our future business, financial condition, results of operations or performance, to differ materially from our historical results or those expressed or implied in any forward-looking statement. Some of the risks and uncertainties that may cause actual results to differ from those expressed or implied in the forward-looking statements are described in the section entitled "Risk Factors" in this prospectus and in any accompanying prospectus supplement, as well as in our other filings with the SEC. In addition, actual results may differ as a result of additional risks and uncertainties of which we are currently unaware or which we do not currently view as material to our business. For these reasons, investors are cautioned not to place undue reliance on any forward-looking statements.

You should read this prospectus in its entirety, together with any accompanying prospectus supplement, the documents that we file as exhibits to the registration statement of which this prospectus is a part, and the documents that we incorporate by reference into this prospectus and any accompanying prospectus supplement, with the understanding that our future results may be materially different from what we currently expect. The forward-looking statements we make speak only as of the date on which they are made. We expressly disclaim any intent or obligation to update any forward-looking statements after the date hereof to conform such statements to actual results or to changes in our opinions or expectations, except as required by applicable law or the rules of The NASDAQ Stock Market, LLC. If we do update or correct any forward-looking statements, investors should not conclude that we will make additional updates or corrections.

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

PROSPECTUS SUMMARY

The following is a summary of what we believe to be the most important aspects of our business and the offering of our common stock under this prospectus. Please read the additional information in the sections entitled "Incorporation of Certain Documents by Reference" and "Where You Can Find More Information."

References 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.

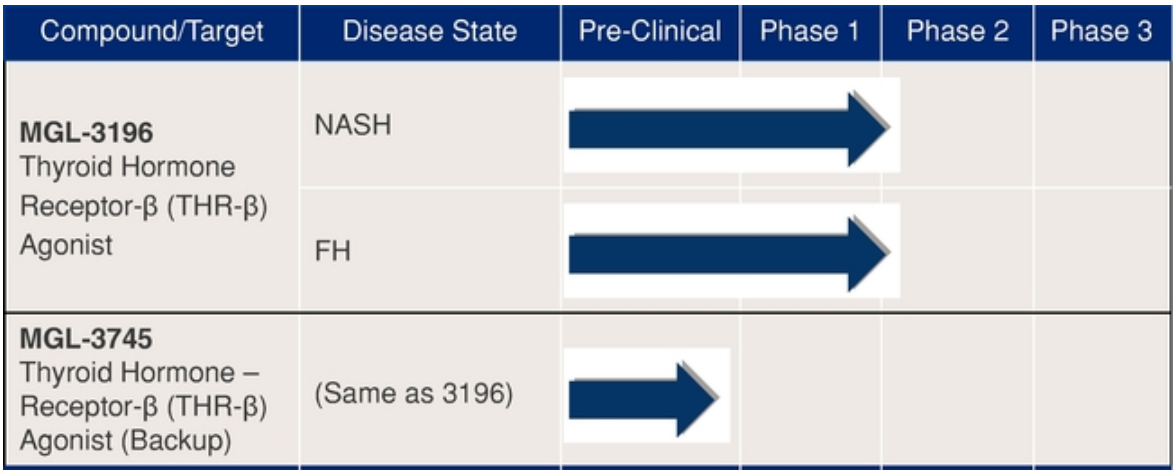
Executive Overview

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-ß, or THR-ß, agonist that can potentially be used to treat a number of disease states with high unmet medical need. THR-ß 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-ß 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-ß agonist. We are developing MGL-3196 for 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 initiated a Phase 2 clinical trial in heterozygous FH, or HeFH, patients and we are planning to conduct a proof-of-concept clinical trial in homozygous FH, or HoFH, patients. MGL-3196 is a once-daily oral pill that has been studied in four completed Phase 1 trials in a total of 129 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, and two drug interaction trials with statins.

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 TG, 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:



On July 22, 2016, we completed the merger with Synta Pharmaceuticals Corp., or the Merger, which provided $42.6 million in cash, cash equivalents and marketable securities.

Lead Product Candidate—MGL-3196

Active thyroid hormone, known as T3, interacts with two nuclear receptors, thyroid hormone receptor-alpha (THR-a), which is the predominant receptor expressed in most human tissues, including heart and bone, and thyroid hormone receptor-beta (THR-ß), 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-ß 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-ß activation by MGL-3196 will in turn lead to clinically meaningful reductions in LDL-C, plasma and liver TGs.

We believe that MGL-3196 is the first selective small molecule THR- ß agonist compound. MGL-3196, along with other THR-ß-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-ß receptor, with almost no effect on THR-a, unlike other compounds purported in published studies to be ß-selective based on binding affinity, but which were shown to equally activate THR-a and THR-ß in the novel functional assay.

We believe that the ß-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-a 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 triglyceride 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-ß pathway and has shown a lack of liver enzyme elevations in Phase 1 clinical studies as well as an absence of bone and cartilage histologic findings in chronic animal toxicology studies.

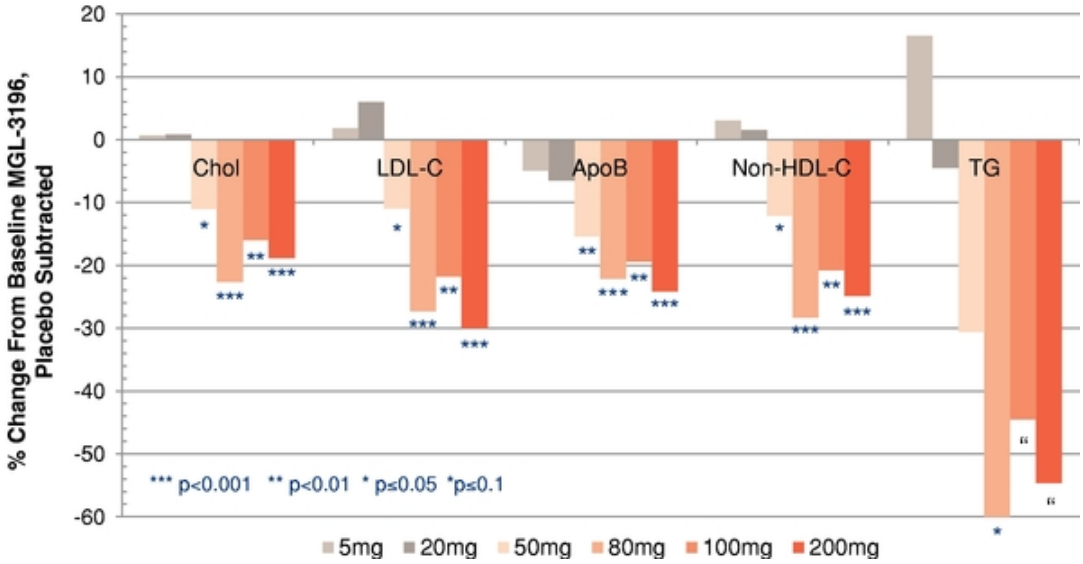
MGL-3196 Clinical and Non-Clinical Development Program

To date, we have completed a series of Phase 1 clinical studies, Phase 2-enabling preclinical GLP toxicology studies, and drug manufacturing studies to support further clinical development, including 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 129 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, as well as a drug-interaction study in healthy volunteers. 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 24h after 14th dose; baseline value obtained just prior to first dose; ApoB, apolipoprotein B; Chol, 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 3 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 study in NASH including patients taking low dose statins. We have also initiated a Phase 2 clinical study in HeFH including patients taking high dose statins.

Our Strategy

Our goal is to become a leading biopharmaceutical company developing and commercializing innovative liver-directed, ß-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 plan to report data for the primary endpoint from our Phase 2 study in NASH by the end of 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 3% to 5% 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 5 to 10 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.

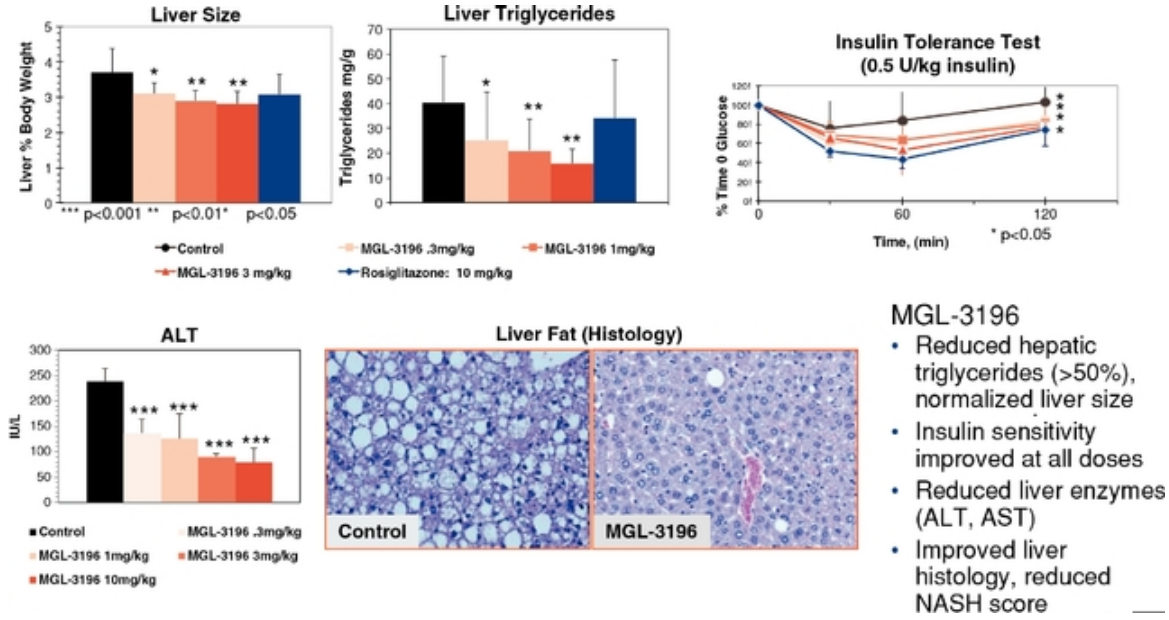
The Centers for Disease Control and Prevention projects the prevalence of obesity to increase from 34% of the United States population to 42% of the United States population by 2030. Driven by this epidemic of obesity, NASH is projected to become the leading cause of liver transplants by 2020. Given 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-ß 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 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.

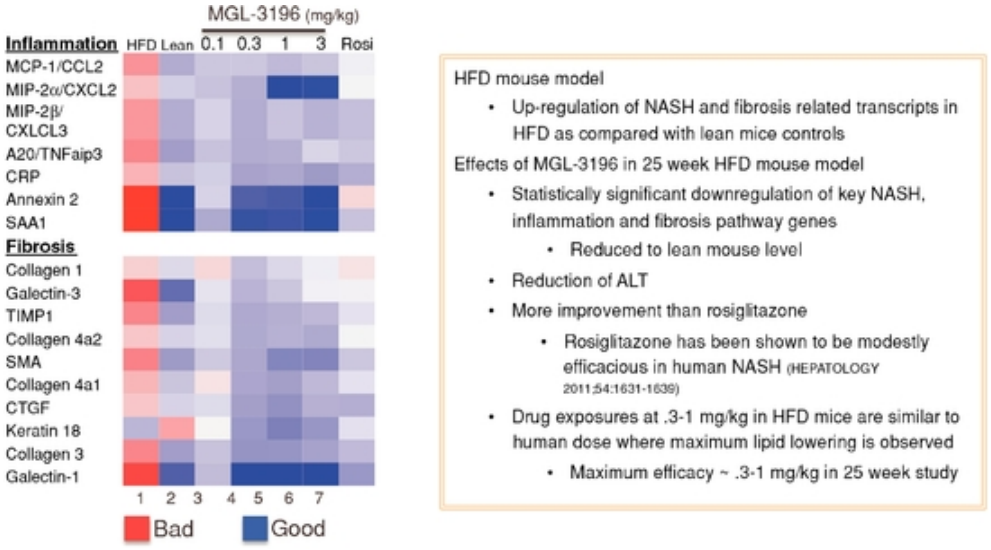
MGL-3196: Preclinical NASH Animal Model Study

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 approximately 117 patients with liver biopsy documented NASH, including those with type-2 diabetes, dyslipidemia and hypertension. In the study we are randomizing 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 expect to reach our top-line analysis of the primary endpoint by late 2017 and our top-line analysis of the secondary endpoint (NASH assessment on liver biopsy) by 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 endpoints consistent with the current FDA requirements for demonstration of efficacy in registrational trials.

Familial Hypercholesterolemia

Overview and Market Opportunity

FH is a genetic disorder characterized by aggressive and early onset of 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 lipoprotein(a), or 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 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-ß 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-ß 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 are randomizing NASH 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. Based on interim efficacy and safety data obtained from this HeFH study, we plan to conduct a proof of concept open-label Phase 2 study of 6-8 patients with HoFH at sites in the United States and Europe. We expect that top-line results of the HeFH clinical trial will be available in late 2017 and top-line results of the HoFH trial will be available in 2018.

Collaborations

VIA Pharmaceuticals, Inc., or VIA, entered into a research, development and commercialization agreement, or the Roche Agreement, with Hoffmann-La Roche Pharmaceutical Company Limited, or 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 own exclusive worldwide rights for all potential indications. Roche assigned all patent rights relating to MGL-3196 to us and granted us an exclusive license to use certain 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 2 and Phase 3 clinical trials and regulatory approval in the United States and Europe of a product developed from MGL-3196, and single-digit royalty payments based on net sales of products developed from MGL-3196, 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., Novartis AG, Novo Nordisk A/S, Takeda, Immuron Ltd., Shire plc, Boehringer Ingelheim GmbH, 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 $15.9 million for the year ended December 31, 2016 compared to $2.4 million for the same period in 2015. The large 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 or have exclusive rights to four 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 and its use in the treatment of key disease indications. Our current patent portfolio broadly covers the United States and other jurisdictions worldwide.

Issued United States patents which cover MGL-3196 will expire 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 will expire between 2026 and 2033. We have pending patent applications for MGL-3196 that, if issued, would 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. 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 European Union 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 and a new biologic must be approved by the FDA through the biologics license application, or BLA, process before it may be legally marketed in the United States. 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 or BLA.

United States Drug Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and in the case of biologics, also under the Public Health Service Act, or PHSA, 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 the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, requesting product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal 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 Good Laboratory Practices 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 to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA or BLA;
- 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 or BLA.

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. 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.

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. 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.

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.

- *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:* Clinical trials are 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 labeling.

The FDA or the sponsor may suspend 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.

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 or BLA 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 or BLA requesting approval to market the product. The submission of an NDA or BLA is subject to the payment of user fees; a waiver of such fees may be obtained under certain limited circumstances. The FDA reviews all NDAs and BLAs 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 or BLA for filing. In this event, the NDA or BLA 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 or BLA 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 or BLA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data and information. Even if such data and information is submitted, the FDA may ultimately decide that the NDA or BLA does not satisfy the 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 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 BLA, 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. The FDA reviews a BLA to determine, among other things whether the product is safe, pure and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency. Before approving an NDA or BLA, the FDA will inspect the facility or facilities where the product is manufactured.

NDAs or BLAs 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 and original BLAs will be six months from the date that the NDA or BLA is filed. In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval and 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 and dosages 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 or BLA 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, BLAs 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 or BLA, plus the time between the submission date of an NDA or BLA 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. 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.

Biologics Price Competition and Innovation Act of 2009

On March 23, 2010, President Obama signed into law the Patient Protection and Affordable Care Act which included the Biologics Price Competition and Innovation Act of 2009, or BPCIA. The BPCIA amended the PHSA to create an abbreviated approval pathway for two types of "generic" biologics—biosimilars and interchangeable biologic products, and provides for a twelve-year exclusivity period for the first approved biological product, or reference product, against which a biosimilar or interchangeable application is evaluated; however if pediatric studies are performed and accepted by the FDA, the twelve-year exclusivity period will be extended for an additional six months. A biosimilar

product is defined as one that is highly similar to a reference product notwithstanding minor differences in clinically inactive components and for which there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity and potency of the product. An interchangeable product is a biosimilar product that may be substituted for the reference product without the intervention of the healthcare provider who prescribed the reference product.

The biosimilar applicant must demonstrate that the product is biosimilar based on data from (i) analytical studies showing that the biosimilar product is highly similar to the reference product; (ii) animal studies (including toxicity); and (iii) one or more clinical studies to demonstrate safety, purity and potency in one or more appropriate conditions of use for which the reference product is approved. In addition, the applicant must show that the biosimilar and reference products have the same mechanism of action for the conditions of use on the label, route of administration, dosage and strength, and the production facility must meet standards designed to assure product safety, purity and potency.

An application for a biosimilar product may not be submitted until four years after the date on which the reference product was first approved. The first approved interchangeable biologic product will be granted an exclusivity period of up to one year after it is first commercially marketed, but the exclusivity period may be shortened under certain circumstances.

The FDA has issued a number of final and draft guidances in order to implement the law. On April 28, 2015, the FDA issued the following three final guidances: "Scientific Considerations in Demonstrating Biosimilarity to a Reference Product," "Quality Considerations in Demonstrating Biosimilarity of a Therapeutic Protein Product to a Reference Product," and "Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009 Guidance for Industry." The draft guidances include "Formal Meetings between the FDA and Biosimilar Biological Product Sponsors or Applicants" issued March 29, 2013, "Clinical Pharmacology Data to Support a Demonstration of Biosimilarity to a Reference Product" issued May 13, 2014, "Reference Product Exclusivity for Biological Products Filed Under Section 351(a) of the PHS Act" issued August 4, 2014, and "Biosimilars: Additional Questions and Answers Regarding Implementation of the Price Competition and Innovation Act of 2009," issued May 12, 2015. The guidance documents provide FDA's current thinking on approaches to demonstrating that a proposed biological product is biosimilar to a reference product. The FDA intends to issue additional guidance documents in the future. Nevertheless, the absence of final guidance documents covering all biosimilars issues does not prevent a sponsor from seeking licensure of a biosimilar under the BPCIA, and the FDA recently approved the first biosimilar application in the United States.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug 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 or BLA. 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 the 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 irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality 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 addition to other benefits such as the ability to use surrogate endpoints and engage in more frequent interactions with the FDA, the FDA may initiate review of sections of a fast track drug's BLA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing an application does not begin until the last section of the BLA is submitted. Additionally, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

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, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if 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. 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. 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 our 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 European Union 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 European Medicines Agency 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 European Union 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 be obtained 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

Sales of pharmaceutical products depend in significant part on the availability of third-party reimbursement. Third-party payors include government healthcare programs, managed care providers, private health insurers and other organizations. These third-party payors are increasingly challenging the price and examining the cost-effectiveness of medical products and services. In addition, significant uncertainty exists as to the reimbursement status of newly approved healthcare products. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. Our product candidates may not be considered cost-effective. It is time consuming and expensive to seek reimbursement from third-party payors. Reimbursement may not be available or sufficient to allow us to sell our products on a competitive and profitable basis.

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 European Union 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 European Union do not follow price structures of the United States and generally tend to be significantly lower.

Employees

As of March 24, 2017, we had eight full-time employees, including five engaged in research, development, and regulatory activities, and three 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 telephone number is (484) 380-9263. Our Internet website address is www.madrigalpharma.com. The contents of our website are not incorporated into, and do not form a part of, this prospectus or the registration statement of which it forms a part.

Reverse Merger

On July 22, 2016, Synta Pharmaceuticals Corp., or Synta, completed its business combination with Private Madrigal (Madrigal Pharmaceuticals, Inc. prior to the consummation of the Merger described herein) 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.

Securities Purchase Agreement

On June 20, 2017, we entered into a Securities Purchase Agreement, or the Securities Purchase Agreement, with a group of institutional accredited investors, or the Investors, which were existing, non-controlling stockholders of ours, and are named on the Schedule of Investors to the Securities Purchase Agreement. Under the terms of the Securities Purchase Agreement, we sold 328,300 shares of our common stock at a price of $15.23 per share, and 1.97 million shares of our Series A Convertible Preferred Stock, or the Series A Preferred Stock, at a price of $15.23 per share. The Series A Preferred Stock is convertible into shares of our common stock at a one-to-one ratio, subject to adjustment as provided in the Securities Purchase Agreement. We consummated the sale under the Securities Purchase Agreement on June 23, 2017.

The offer and sale of the shares were not registered under the Securities Act in reliance on the exemption afforded by Section 4(a)(2) of the Securities Act and Rule 506(b) of Regulation D promulgated thereunder.

Pursuant to the Securities Purchase Agreement, we agreed to file a registration statement registering the resale of the common stock issued to the Investors under the Securities Purchase Agreement within 30 days after the closing of the sale. We also agreed to use our best efforts to have the registration statement declared effective within 90 days after the closing of the sale. The registration statement of which this prospectus is a part has been filed by us in fulfillment of our obligations under the Securities Purchase Agreement.

The Offering

Common stock offered by us	None
Common stock offered by the selling stockholders	Up to 328,300 shares issued pursuant to the Securities Purchase Agreement.
Use of Proceeds	We will not receive any proceeds from the resale by the selling stockholders of the common stock offered by this prospectus.
Risk Factors	Investing in our securities involves a high degree of risk. Before making an investment decision, you should carefully consider all of the information in this prospectus and, in particular, you should evaluate the risk factors identified in this prospectus under "Risk Factors" beginning on page 25.
NASDAQ Global Market Symbol	MDGL

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.

This prospectus and the documents we incorporate by reference in this prospectus contain forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks described in this prospectus and in the documents incorporated by reference in this prospectus. For more information, see "Special Note Regarding Forward-Looking Information."

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, 2016, we had an accumulated deficit of $75.3 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, 2016, we had cash, cash equivalents and marketable securities of $40.5 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. If we are unable to obtain regulatory approval for or successfully commercialize MGL-3196, 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 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;
- the FDA or foreign clinical or regulatory agencies may require efficacy endpoints for a Phase 3 clinical trial for the treatment of NASH or FH that differ from the endpoints of our current or future trials, which may require us to conduct additional clinical trials;
- 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.

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 may not be predictive of any future Phase 2 results. 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. 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 or suspend those clinical trials or delay the analysis of data derived from them. A number of events, including any of the following, could delay 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, 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.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

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. 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 one clinical drug interaction study of MGL-3196 and two statins in 25 normal healthy volunteers, which showed MGL-3196 to have a favorable safety profile and to be well-tolerated. We are currently conducting a second drug-interaction study of MGL-3196 with a third statin. We have initiated a Phase 2 clinical study in NASH including patients taking low dose statins. We have also initiated a Phase 2 clinical study in HeFH including patients taking high dose statins.

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 have other properties that may delay or prevent its regulatory approval or commercialization or limit its commercial potential.

Unacceptable adverse events 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.

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, adverse event reporting, storage, advertising, promotion, and record keeping related to the product will remain subject to extensive regulatory requirements. 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;
- 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.

Our industry is highly competitive, 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.

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. 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 Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, 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 agreement. 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 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 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.

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.

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal healthcare laws, including those commonly referred to as "fraud and abuse" laws, have been applied in recent years to restrict certain marketing practices in the pharmaceutical industry. These laws include, among others, false claims and anti-kickback statutes. 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 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.

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.

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 entail 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 control 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 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 a research, development and commercialization agreement, or the Roche Agreement, with Hoffmann-La Roche Pharmaceutical Company Limited, or 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 will own exclusive worldwide rights for all potential indications. Roche assigned all patent rights relating to MGL-3196 to us and granted us an exclusive license to use certain 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, 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 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.

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 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 licensing 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 own and have licensed rights to issue 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 from Roche for MGL-3196 is expected to expire in the United States in 2026. Our owned patents and pending patent applications that cover solid form, method of manufacturing, and use 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;
- us and our licensor(s) may not have been the first to make the inventions covered by pending patent applications or issued patents;
- us 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;
- us 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, in which case 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-3916 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 the intellectual property rights, through licenses from third parties and under patents that we 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. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

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 will require substantial future 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 will need to collaborate with a strategic partner or raise significant financing. 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;
- the 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 52.4% of our outstanding common stock as of December 31, 2016 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 by our existing stockholders 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 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.

Risks Related to Stockholders' Sales of Shares, Including Those Issued under the Securities Purchase Agreement

Sales of a significant number of shares of our common stock in the public markets or significant short sales of our common stock, or the perception that such sales could occur, could depress the market price of our common stock and impair our ability to raise capital.

Sales of a substantial number of shares of our common stock or other equity-related securities in the public markets, could depress the market price of our common stock. If there are significant short sales of our stock, the price decline that could result from this activity may cause the share price to decline further, which, in turn, may cause long holders of the common stock to sell their shares, thereby contributing to sales of common stock in the market. Such sales also may impair our ability to raise capital through the sale of additional shares in the future at a time and price that our management deems acceptable, if at all.

We may not be able to maintain effectiveness of the registration statement of which this prospectus forms a part, which could impact the liquidity of our common stock.

Under the terms of the Securities Purchase Agreement with the initial Investors, we are obligated to include the shares of common stock issued under the Securities Purchase Agreement in an effective registration statement. The registration statement of which this prospectus forms a part is intended to satisfy that obligation. We cannot assure you that we will not be required to suspend or cease sales under the registration statement, that the SEC will not issue any stop order to suspend the effectiveness of the registration statement or that, if such a stop order is issued, we will be able to amend the registration statement to respond to the stop order to permit sales to be made under the registration statement in a timely manner or at all. To the extent the registration statement is not effective, the selling stockholders' ability to sell the shares of common stock may be limited, which could (depending on the extent of the selling stockholders' selling activity) have a material adverse effect on the liquidity of our common stock.

USE OF PROCEEDS

All proceeds from the disposition of the common shares covered by this prospectus will go to the selling stockholders. We will not receive any proceeds from the disposition of the common stock by the selling stockholders. See "Plan of Distribution."

The selling stockholders will pay any underwriting discounts and commissions and expenses incurred by the selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholders in disposing of the shares. We will bear the costs, fees and expenses incurred to effect the registration of the shares covered by this prospectus, including all registration and filing fees, Nasdaq listing fees and fees and expenses of counsel and our independent registered public accounting firm.

SELLING STOCKHOLDERS

This prospectus relates to the offering by the selling stockholders of up to 328,300 shares of common stock, comprised of: (i) an aggregate of 98,490 shares of our common stock held by Adage Capital Partners, L.P., which were issued by us on June 23, 2017 pursuant to the Securities Purchase Agreement; (ii) an aggregate of 131,320 shares of our common stock held by Armistice Capital Master Fund Ltd., which were issued by us on June 23, 2017 pursuant to the Securities Purchase Agreement; and (iii) an aggregate of 98,490 shares of our common stock held by Rock Springs Capital Master Fund LP, which were issued by us on June 23, 2017 pursuant to the Securities Purchase Agreement.

The following table sets forth, based on information provided to us by the selling stockholders or known to us, the name of the selling stockholders and the number of shares of our common stock beneficially owned by the selling stockholders before this offering. The number of shares owned are those beneficially owned, as determined under the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under these rules, beneficial ownership includes any shares of common stock as to which a person has sole or shared voting power or investment power and any shares of common stock which the person has the right to acquire within 60 days through the exercise of any option, warrant or right, through conversion of any security or pursuant to the automatic termination of a power of attorney or revocation of a trust, discretionary account or similar arrangement.

None of the selling stockholders has held any position or office or had any other material relationship with us or any of our predecessors or affiliates within the past three years other than as a result of the ownership of our securities. None of the selling stockholders is a broker-dealer or affiliate of a broker-dealer.

The registration of such shares does not necessarily mean, however, that any of these shares will be offered or sold by the selling stockholders. The selling stockholders may from time to time offer and sell all or a portion of their shares in the over-the-counter market, in negotiated transactions, or otherwise, at market prices prevailing at the time of sale or at negotiated prices.

We have assumed all shares of common stock reflected on the table will be sold from time to time in the offering covered by this prospectus. Because the selling stockholders may offer all or any portions of the shares of common stock listed in the table below, no estimate can be given as to the amount of those shares of common stock covered by this prospectus that will be held by the selling stockholders upon the termination of the offering.

SELLING STOCKHOLDERS' TABLE

	Shares Beneficially Owned Prior to Offering		Shares Offered	Shares Beneficially Owned After Offering	
Name of Beneficial Owner	Number	Percent(1)	Number	Number	Percent(1)
Adage Capital Partners, L.P.	600,000	4.8%	98,490	501,510	4.0%
Armistice Capital Master Fund Ltd.	251,320	2.0%	131,320	120,000	1.0%
Rock Springs Capital Master Fund L.P.	538,790	4.3%	98,490	440,300	3.5%
Total	1,390,110	11.1%	328,300	1,061,810	8.5%

(1) Based on 12,495,705 shares of our common stock outstanding on June 30, 2017 (including the outstanding shares of common stock offered by this prospectus).

PLAN OF DISTRIBUTION

We are registering the shares of common stock to permit the resale of these shares of common stock by the selling stockholders from time to time after the date of this prospectus. We will not receive any of the proceeds from the sale by the selling stockholders of the shares of common stock. We will bear all fees and expenses incident to our obligation to register the shares of common stock.

The selling stockholders may sell all or a portion of the shares of common stock beneficially owned by them and offered hereby from time to time directly or through one or more underwriters, broker-dealers or agents. If the shares of common stock are sold through underwriters or broker-dealers, then the selling stockholders will be responsible for underwriting discounts or commissions or agents' commissions. The shares of common stock may be sold in one or more transactions at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale, or at negotiated prices. These sales may be effected in transactions, which may involve crosses or block transactions, by one or more of the following methods:

- on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale;
- in the over-the-counter market;
- in transactions otherwise than on these exchanges or systems or in the over-the-counter market;
- through the writing of options, whether such options are listed on an options exchange or otherwise;
- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales as permitted by applicable law;
- sales pursuant to Rule 144;
- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

If the selling stockholders effect such transactions by selling shares of common stock to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the selling stockholders or commissions from purchasers of the shares of common stock for whom they may act as agent or to whom they may sell as principal (which discounts, concessions or commissions as to particular underwriters, broker-dealers or agents may be in excess of those customary in the types of transactions involved). In connection with sales of the shares of common stock or otherwise, the selling stockholders may enter into hedging transactions with broker-dealers as permitted by applicable law, which may in turn engage in short sales of the shares of common stock in the course of hedging the positions they assume. The selling stockholders may also sell shares of common stock short as permitted by applicable law and deliver shares of common stock covered by this prospectus to close out short positions and to

return borrowed shares in connection with such short sales. The selling stockholders may also loan or pledge shares of common stock to broker-dealers that in turn may sell such shares.

The selling stockholders may pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time pursuant to this prospectus or any amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act, amending, if necessary, the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus. The selling stockholders also may transfer and donate the shares of common stock in other circumstances in which case the transferees, donees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

The selling stockholders and any broker-dealer participating in the distribution of the shares of common stock may be deemed to be "underwriters" within the meaning of the Securities Act, and any commission paid, or any discounts or concessions allowed to, any such broker-dealer may be deemed to be underwriting commissions or discounts under the Securities Act. At the time a particular offering of the shares of common stock is made, a prospectus supplement, if required, will be distributed which will set forth the aggregate amount of shares of common stock being offered and the terms of the offering, including the name or names of any broker-dealers or agents, any discounts, commissions and other terms constituting compensation from the selling stockholders and any discounts, commissions or concessions allowed or reallowed or paid to broker-dealers.

Under the securities laws of some states, the shares of common stock may be sold in such states only through registered or licensed brokers or dealers. In addition, in some states the shares of common stock may not be sold unless such shares have been registered or qualified for sale in such state or an exemption from registration or qualification is available and is complied with.

There can be no assurance that any selling stockholder will sell any or all of the shares of common stock registered pursuant to the registration statement, of which this prospectus forms a part.

The selling stockholders and any other person participating in such distribution will be subject to applicable provisions of the Securities Exchange Act of 1934, as amended, or the Exchange Act and the rules and regulations thereunder, including, without limitation, Regulation M of the Exchange Act, which may limit the timing of purchases and sales of any of the shares of common stock by the selling stockholders and any other participating person. Regulation M may also restrict the ability of any person engaged in the distribution of the shares of common stock to engage in market-making activities with respect to the shares of common stock. All of the foregoing may affect the marketability of the shares of common stock and the ability of any person or entity to engage in market-making activities with respect to the shares of common stock.

We will pay all expenses of the registration of the shares of common stock pursuant to the registration rights agreement, including, without limitation, SEC filing fees and expenses of compliance with state securities or "blue sky" laws; provided, however, that a selling stockholder will pay all underwriting discounts and selling commissions, if any. We will indemnify the initial selling stockholders against liabilities, in accordance with the Securities Purchase Agreement.

Once sold under the registration statement, of which this prospectus forms a part, the shares of common stock will be freely tradable in the hands of persons other than our affiliates.

DESCRIPTION OF CAPITAL STOCK

The following is a summary of all material characteristics of our capital stock as set forth in our restated certificate of incorporation, our restated bylaws and our Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock. The summary does not purport to be complete and is qualified in its entirety by reference to our certificate of incorporation and bylaws, copies of which have been filed as exhibits to our previous SEC filings. For more information, see the sections entitled "Incorporation of Certain Documents by Reference" and "Where You Can Find More Information."

Description of Common Stock

We are authorized to issue 200,000,000 shares of common stock, par value $0.0001 per share. The following summary of certain provisions of our common stock does not purport to be complete. You should refer to our restated certificate of incorporation and our restated bylaws, both of which have been filed with the SEC. The summary below is also qualified by provisions of applicable law.

General

Holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders, and do not have cumulative voting rights. Subject to preferences that may be applicable to any outstanding shares of preferred stock, holders of common stock are entitled to receive ratably such dividends, if any, as may be declared from time to time by our board of directors out of funds legally available for dividend payments. The holders of common stock have no preferences or rights of conversion, exchange, pre-emption or other subscription rights. There are no redemption or sinking fund provisions applicable to the common stock. In the event of any liquidation, dissolution or winding-up of our affairs, holders of common stock will be entitled to share ratably in our assets that are remaining after payment or provision for payment of all of our debts and obligations and after liquidation payments to holders of outstanding shares of preferred stock, if any.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

NASDAQ Global Market

Our common stock is listed for quotation on The NASDAQ Global Market under the symbol "MDGL."

Description of Preferred Stock

We are authorized to issue 5,000,000 shares of preferred stock, par value $0.0001 per share. As of July 23, 2017, we had 1,969,797 shares of preferred stock, designated Series A Convertible Preferred Stock, outstanding held by two stockholders of record. No other shares of our preferred stock were outstanding or designated. The following summary of certain provisions of our preferred stock does not purport to be complete. You should refer to our restated certificate of incorporation, our restated bylaws and our Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock, each of which have been filed with the SEC. The summary below is also qualified by provisions of applicable law.

General

Our board of directors may, without further action by our stockholders, from time to time, direct the issuance of shares of preferred stock in series and may, at the time of issuance, determine the

rights, preferences and limitations of each series, including voting rights, dividend rights and redemption and liquidation preferences. Satisfaction of any dividend preferences of outstanding shares of preferred stock would reduce the amount of funds available for the payment of dividends on shares of our common stock. Holders of shares of preferred stock may be entitled to receive a preference payment in the event of any liquidation, dissolution or winding-up of our company before any payment is made to the holders of shares of our common stock. In some circumstances, the issuance of shares of preferred stock may render more difficult or tend to discourage a merger, tender offer or proxy contest, the assumption of control by a holder of a large block of our securities or the removal of incumbent management. Upon the affirmative vote of our board of directors, without stockholder approval, we may issue shares of preferred stock with voting and conversion rights which could adversely affect the holders of shares of our common stock.

Series A Convertible Preferred Stock

Each share of the Series A Convertible Preferred Stock is convertible into shares of the common stock at any time at the holder's option at a one-to-one ratio, subject to adjustment. The holder, however, will be prohibited from converting shares of the Series A Convertible Preferred Stock into shares of our common stock if, as a result of such conversion, the holder, together with its affiliates, would own more than 4.99% of the shares of our common stock or any other class of any equity security of ours (other than an exempted security) that is registered pursuant to Section 12 of the Securities Exchange Act of 1934, which may be increased or decreased to any other percentage at the holder's election on 61 days' notice delivered to the Company.

Upon our liquidation, dissolution or winding-up, whether voluntary or involuntary, after the satisfaction in full of our debts and the payment of any liquidation preference owed to the holders of shares of our capital stock ranking prior to the Series A Convertible Preferred Stock upon liquidation, the holders of the Series A Convertible Preferred Stock shall participate *pari passu* with the holders of our common stock (on an as-if-converted-to-common-stock basis) in our net assets. Shares of the Series A Convertible Preferred Stock will generally have no voting rights, except as required by law. Shares of the Series A Convertible Preferred Stock will be entitled to receive dividends before shares of any other class or series of our capital stock (other than dividends in the form of our common stock) equal to the dividend payable on each share of our common stock, on an as-converted basis.

Anti-Takeover Provisions of our Certificate of Incorporation and Bylaws

In addition to the board of directors' ability to issue shares of preferred stock, our restated certificate of incorporation and restated bylaws contain other provisions that are intended to enhance the likelihood of continuity and stability in the composition of the board of directors and which may have the effect of delaying, deferring or preventing a future takeover or change in control of our company unless such takeover or change in control is approved by our board of directors.

These provisions, summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Classified board of directors; removal of directors for cause. Our restated certificate of incorporation and restated bylaws provide for our board of directors to be divided into three classes serving staggered terms. At each annual meeting of stockholders, directors elected to succeed those directors whose terms have expired are elected for a three-year term of office. All directors elected to our classified board of directors will serve until the election and qualification of their respective

successors or their earlier resignation or removal. The board of directors is authorized to create new directorships and to fill such positions so created and is permitted to specify the class to which any such new position is assigned. The person filling such position would serve for the term applicable to that class. The board of directors (or its remaining members, even if less than a quorum) is also empowered to fill vacancies on the board of directors occurring for any reason for the remainder of the term of the class of directors in which the vacancy occurred. Members of the board of directors may only be removed for cause and only by the affirmative vote of 80% of our outstanding voting stock. These provisions are likely to increase the time required for stockholders to change the composition of the board of directors. For example, in general, at least two annual meetings will be necessary for stockholders to effect a change in a majority of the members of the board of directors. The provision for a classified board could prevent a party who acquires control of a majority of our outstanding common stock from obtaining control of our board of directors until our second annual stockholders meeting following the date the acquirer obtains the controlling stock interest. The classified board provision could have the effect of discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us and could increase the likelihood that incumbent directors will retain their positions.

Advance notice provisions for stockholder proposals. Our restated bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors, as well as procedures for including proposed nominations at special meetings at which directors are to be elected. Stockholders at our annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board or by a stockholder who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given to our secretary timely written notice, in proper form, of the stockholder's intention to bring that business before the meeting, and who has complied with the procedures and requirements set forth in the bylaws. Although our bylaws do not give our board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting, our bylaws may have the effect of precluding the conduct of some business at a meeting if the proper procedures are not followed or may discourage or defer a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of us.

Special meetings of stockholders. Special meetings of the stockholders may be called only by our board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors. Stockholders are not permitted to call a special meeting or to require our board of directors to call a special meeting.

No stockholder action by written consent. Our restated certificate of incorporation and restated bylaws do not permit our stockholders to act by written consent. As a result, any action to be effected by our stockholders must be effected at a duly called annual or special meeting of the stockholders.

Super-majority stockholder vote required for certain actions. The Delaware General Corporation Law, or DGCL, provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless the corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our restated certificate of incorporation requires the affirmative vote of the holders of at least 80% of our outstanding voting stock to amend or repeal certain provisions of our restated certificate of incorporation. This 80% stockholder vote would be in addition to any separate class vote that might in the future be required pursuant to the terms of any preferred stock that might then be outstanding. In addition, an 80% vote is also required for any amendment to, or repeal of, our restated bylaws by the

stockholders. Our restated bylaws may be amended or repealed by a vote of a majority of the total number of authorized directors.

Provisions of Delaware Law Governing Business Combinations

We are subject to the "business combination" provisions of Section 203 of the DGCL. In general, such provisions prohibit a publicly held Delaware corporation from engaging in any "business combination" transactions with any "interested stockholder" for a period of three years after the date on which the person became an "interested stockholder," unless:

- prior to such date, the board of directors approved either the "business combination" or the transaction which resulted in the "interested stockholder" obtaining such status; or

- upon consummation of the transaction which resulted in the stockholder becoming an "interested stockholder," the "interested stockholder" owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the "interested stockholder") those shares owned by (a) persons who are directors and also officers and (b) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

- at or subsequent to such time the "business combination" is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least $66^{2}/_{3}\%$ of the outstanding voting stock which is not owned by the "interested stockholder."

A "business combination" is defined to include mergers, asset sales and other transactions resulting in financial benefit to a stockholder. In general, an "interested stockholder" is a person who, together with affiliates and associates, owns 15% or more of a corporation's voting stock or within three years did own 15% or more of a corporation's voting stock. The statute could prohibit or delay mergers or other takeover or change in control attempts with respect to us and, accordingly, may discourage attempts to acquire us.

LEGAL MATTERS

Certain legal matters, including the validity of the issuance of the shares of common stock offered by this prospectus will be passed upon for us by Stradling Yocca Carlson & Rauth, P.C.

EXPERTS

The financial statements as of December 31, 2016 and for the year ended December 31, 2016 incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2016 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

The financial statements as of December 31, 2015 and for the year ended December 31, 2015 incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2016 have been so incorporated in reliance on the report of Friedman LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate" into this prospectus information that we file with the SEC in other documents. This means that we can disclose important information to you by referring to other documents that contain that information. Any information that we incorporate by reference into this prospectus is considered part of this prospectus.

Information contained in this prospectus and information that we file with the SEC in the future and incorporate by reference in this prospectus automatically modifies and supersedes previously filed information, including information in previously filed documents or reports that have been incorporated by reference in this prospectus, to the extent the new information differs from or is inconsistent with the old information. Any information so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

The following documents previously filed by us with the SEC are incorporated in this prospectus by reference:

- Our Annual Report on Form 10-K for the year ended December 31, 2016, filed with the SEC on March 31, 2017;
- Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2017, filed with the SEC on May 11, 2017;
- Our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 28, 2017;
- Our Current Reports on Form 8-K filed with the SEC on March, 31, 2017, June 1, 2017, June 21, 2017, and July 5, 2017; and
- The description of our common stock set forth in the Registration Statement on Form 8-A filed with the SEC on January 1, 2007 (the "Form 8-A"), as well as the description of our common stock set forth on pages 123 through 125 of the Registration Statement on Form S-1, as amended (Registration No. 333-138894), which was originally filed with the SEC on November 22, 2006 (which description is incorporated by reference into the description of our common stock set forth in the Form 8-A), and any other amendment or report filed for the purpose of updating such description.

We also incorporate by reference all documents filed by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date the initial registration statement is initially filed and prior to the termination of this offering, provided that nothing in this prospectus shall be deemed to incorporate portions of documents or information "furnished" and not "filed" with the SEC.

You should rely only on the information incorporated by reference or provided in this prospectus or any accompanying prospectus supplement. We have not authorized anyone to provide you with different information.

You should not assume that the information contained in this prospectus and any accompanying prospectus supplement is correct on any date after their respective dates, even though this prospectus or any prospectus supplement is delivered or securities are sold on a later date.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, upon oral or written request, a copy of any document incorporated by reference at no cost. Requests should be made to:

Marc R. Schneebaum
Chief Financial Officer
Madrigal Pharmaceuticals, Inc.
Four Tower Bridge
200 Barr Harbor Drive, Suite 400
West Conshohocken, Pennsylvania 19428
(484) 380-9263

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read, without charge, and copy the documents we file at the SEC's public reference rooms in Washington, D.C. at 100 F Street, NE, Washington, DC 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference rooms. Our SEC filings are also available to the public at no cost from the SEC's website at http://www.sec.gov.

This prospectus constitutes a part of a registration statement on Form S-3 filed under the Securities Act. As permitted by the SEC's rules, this prospectus and any accompanying prospectus supplement, which form a part of the registration statement, do not contain all the information that is included in the registration statement. You will find additional information about us in the registration statement. Any statements made in this prospectus or any prospectus supplement concerning legal documents are not necessarily complete and you should read the documents that are filed as exhibits to the registration statement or otherwise filed with the SEC for a more complete understanding of the document or matter.

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328,300 Shares

Madrigal Pharmaceuticals, Inc.

Common Stock

PROSPECTUS

, 2017

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION.

The expenses in connection with the issuance and distribution of the securities being registered, other than underwriting discounts and commissions, are estimated below:

SEC registration fee	$	589.58
Legal fees and expenses	$	85,000*
Accounting fees and expenses	$	35,000*
Miscellaneous	$	5,000
Total expenses*	$	125,589.58

* Does not include expense of preparing prospectus supplements and other expenses relating to specific offerings made pursuant to this prospectus.

ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS.

Our restated certificate of incorporation, as amended, and restated bylaws provide that each person who was or is made a party or is threatened to be made a party to or is otherwise involved (including, without limitation, as a witness) in any action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that he or she is or was a director or an officer of Madrigal Pharmaceuticals, Inc., or is or was serving at our request as a director, officer, or trustee of another corporation, or of a partnership, joint venture, trust or other enterprise, including service with respect to an employee benefit plan, whether the basis of such proceeding is alleged action in an official capacity as a director, officer or trustee or in any other capacity while serving as a director, officer or trustee, shall be indemnified and held harmless by us to the fullest extent authorized by the Delaware General Corporation Law against all expense, liability and loss (including attorneys' fees, judgments, fines, ERISA excise taxes or penalties and amounts paid in settlement) reasonably incurred or suffered by such. Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to our directors, officers or persons controlling us pursuant to the foregoing provisions, we have been informed that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Section 145 of the Delaware General Corporation Law permits a corporation to indemnify any director or officer of the corporation against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with any action, suit or proceeding brought by reason of the fact that such person is or was a director or officer of the corporation, if such person acted in good faith and in a manner that he or she reasonably believed to be in, or not opposed to, the best interests of the corporation, and, with respect to any criminal action or proceeding, if he or she had no reason to believe his or her conduct was unlawful. In a derivative action, (*i.e.*, one brought by or on behalf of the corporation), indemnification may be provided only for expenses actually and reasonably incurred by any director or officer in connection with the defense or settlement of such an action or suit if such person acted in good faith and in a manner that he or she reasonably believed to be in, or not opposed to, the best interests of the corporation, except that no indemnification shall be provided if such person shall have been adjudged to be liable to the corporation, unless and only to the extent that the court in which the action or suit was brought shall determine that the defendant is fairly and reasonably entitled to indemnity for such expenses despite such adjudication of liability.

Pursuant to Section 102(b)(7) of the Delaware General Corporation Law, Article Ninth of our restated certificate of incorporation eliminates the liability of a director to us or our stockholders for monetary damages for a breach of fiduciary duty as a director, except for liabilities arising:

- from any breach of the director's duty of loyalty to us or our stockholders;
- from acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law;
- under Section 174 of the Delaware General Corporation Law; and
- from any transaction from which the director derived an improper personal benefit.

We carry insurance policies insuring our directors and officers against certain liabilities that they may incur in their capacity as directors and officers. In addition, we have entered into indemnification agreements with our directors and officers.

Any underwriting agreements that we may enter into will likely provide for the indemnification of us, our controlling persons, our directors and certain of our officers by the underwriters against certain liabilities, including liabilities under the Securities Act.

ITEM 16. EXHIBITS.

Exhibit No.	Description
3.1	Restated Certificate of Incorporation of the Registrant (incorporated herein by reference to Exhibit 3.1 to the Registrant's Annual Report on Form 10-K, filed March 31, 2017).
3.2	Bylaws of the Registrant, as amended April 13, 2016 (incorporated herein by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed April 14, 2016).
5.1	Opinion of Legal Counsel±
23.1	Consent of Friedman LLP±
23.2	Consent of PricewaterhouseCoopers LLP±
23.3	Consent of Legal Counsel (included in Exhibit 5.1)±
24.1	Power of Attorney (included on the signature page of this registration statement)±

± Filed herewith.

ITEM 17. UNDERTAKINGS.

The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of this registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in this registration statement. Notwithstanding the foregoing, any increase or decrease in the volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in this registration statement or any material change to such information in this registration statement;

provided, however, that paragraphs (i), (ii) and (iii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5) or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to

the securities in the registration statement to which the prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

(iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and

(iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(6) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(7) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of West Conshohocken, Pennsylvania, on July 14, 2017.

MADRIGAL PHARMACEUTICALS, INC.

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

Paul A. Friedman, M.D.
Chief Executive Officer

Each person whose signature appears below constitutes and appoints Paul A. Friedman, M.D. and Marc R. Schneebaum, and either of them, as his or her true and lawful attorneys-in-fact and agents, 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 (including post-effective amendments) and supplements to this registration statement (or any other registration statement for the same offering that is effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933, as amended) and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact and agents, or his or her substitute or substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

Name	Title	Date
/s/ PAUL A. FRIEDMAN, M.D. Paul A. Friedman, M.D.	Chief Executive Officer and Chairman of the Board (Principal Executive Officer)	July 14, 2017
/s/ MARC R. SCHNEEBAUM Marc R. Schneebaum	Chief Financial Officer (Principal Financial and Accounting Officer)	July 14, 2017
/s/ KENNETH M. BATE Kenneth M. Bate	Director	July 14, 2017
/s/ FRED B. CRAVES, PH.D. Fred B. Craves, Ph.D.	Director	July 14, 2017
/s/ KEITH R. GOLLUST Keith R. Gollust	Director	July 14, 2017

Name	Title	Date
/s/ RICHARD S. LEVY, M.D. Richard S. Levy, M.D.	Director	July 14, 2017
/s/ DAVID MILLIGAN, PH.D. David Milligan, Ph.D.	Director	July 14, 2017
/s/ REBECCA TAUB, M.D. Rebecca Taub, M.D.	Chief Medical Officer, Executive Vice President, Research & Development and Director	July 14, 2017

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Exhibit 5.1

July 14, 2017

Madrigal Pharmaceuticals, Inc.
200 Barr Harbor Drive, Suite 400
West Conshohocken, Pennsylvania 19428

RE: Registration Statement on Form S-3 for the Registration of 328,300 shares of common stock of Madrigal Pharmaceuticals, Inc.

Ladies and Gentlemen:

We have acted as counsel to Madrigal Pharmaceuticals, Inc., a Delaware corporation (the "Company"), in connection with the filing of a Registration Statement on Form S-3 (the "Registration Statement") under the Securities Act of 1933, as amended (the "Act"), with the Securities and Exchange Commission (the "SEC"). The Registration Statement relates to the proposed sale of up to 328,300 shares (the "Shares") of common stock, $0.0001 par value per share (the "Common Stock") of the Company by the parties listed as selling stockholders. All of the Shares are being registered on behalf of certain stockholders of the Company.

In connection with this opinion letter, we have examined the Registration Statement and originals, or copies certified or otherwise identified to our satisfaction, of the Restated Certificate of Incorporation of the Company as filed with the Secretary of State of the State of Delaware, the Bylaws of the Company and the minutes of meetings of the Board of Directors of the Company as provided to us by the Company and such other documents, records and other instruments as we have deemed appropriate for purposes of the opinion set forth herein.

We have assumed the genuineness of all signatures, the legal capacity of all natural persons, the authenticity of the documents submitted to us as originals, the conformity with the originals of all documents submitted to us as certified, facsimile or photostatic copies and the authenticity of the originals of all documents submitted to us as copies. We have not made any independent investigation.

Based upon the foregoing, we are of the opinion that the Shares have been duly authorized by the Company and are validly issued, fully paid and non-assessable.

The opinions expressed herein are limited to the laws of the Delaware General Corporation Law and the federal laws of the United States of America.

We hereby consent to the use of this opinion as Exhibit 5.1 to the Registration Statement and to the reference to us under the caption "Legal Matters" in the prospectus included in the Registration Statement. In giving such consent, we do not hereby admit that we are acting within the category of persons whose consent is required under Section 7 of the Act or the rules or regulations of the SEC thereunder.

Very truly yours,

/s/ Stradling Yocca Carlson & Rauth, P.C.

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Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of our report dated April 12, 2016, except for Note 13, as to which date is March 17, 2017, relating to the Madrigal Pharmaceuticals, Inc. financial statements as of December 31, 2015 and for the year then ended, which includes an explanatory paragraph as to the Company's ability to continue as a going concern and appears in Madrigal Pharmaceuticals, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2016.

We also consent to the reference to our firm under the caption "Experts" in this Registration Statement.

/s/ Friedman LLP

East Hanover, New Jersey
July 14, 2017

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Exhibit 23.2

Consent of Independent Registered Public Accounting Firm

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of our report dated March 31, 2017 relating to the financial statements, which appears in Madrigal Pharmaceuticals, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2016. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ PricewaterhouseCoopers LLP

Philadelphia, Pennsylvania

July 14, 2017

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