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**Filed Pursuant to Rule 424(b)(5)**

**Registration No. 333-206135**

**PROSPECTUS SUPPLEMENT**

(To Prospectus dated October 16, 2015)

1,506,025 Shares



Common Stock



We are selling 1,506,025 shares of our common stock in this offering.

Our common stock trades on The Nasdaq Global Market under the trading symbol "MDGL". On December 18, 2017, the last reported sale price of our common stock on The Nasdaq Global Market was $84.04 per share.

*Investing in our common stock involves a high degree of risk. You should carefully consider the risks described under the heading "Risk Factors" beginning on page S-8 of this prospectus supplement before buying shares of our common stock.*

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  | Per Share |  | Total |
| Public offering price | | $83.00 | | $125,000,075 | |
| Underwriting discounts and commissions | | $4.98 | | $7,500,005(1) | |
| Proceeds, before expenses, to us | | $78.02 | | $117,500,071 | |
|  |  |  |  |  |  |

1. We have agreed to reimburse the underwriters for certain expenses in connection with the offering and have paid certain other amounts to one of the underwriters. See "Underwriting."

We have agreed to reimburse the underwriters for certain expenses in connection with this offering. See "Underwriting".

The underwriters have the option to purchase up to 225,904 additional shares of our common stock at the public offering price, less the underwriting discounts and commissions payable by us, within 30 days from the date of this prospectus supplement.

The underwriters are offering the common stock as set forth under "Underwriting". The underwriters expect to deliver the shares against payment therefor in New York, New York on or about December 21, 2017.

|  |  |  |
| --- | --- | --- |
| **Goldman Sachs & Co. LLC** | | **Evercore ISI** |
| **JMP Securities** | **Roth Capital Partners** | **H.C. Wainwright & Co.** |
|  | The date of this prospectus supplement is December 18, 2017 | |
|  |  |  |



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**ABOUT THIS PROSPECTUS SUPPLEMENT**

This document is part of a registration statement that was filed with the Securities and Exchange Commission, or the SEC, using a "shelf" registration process and consists of two parts. The first part is the prospectus supplement, including the documents incorporated by reference herein, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference therein, provides more general information. In general, when we refer only to the prospectus, we are referring to both parts of this document combined. Before you invest, you should carefully read this prospectus supplement, the accompanying prospectus, all information incorporated by reference herein and therein, as well as the additional information described under the heading "Where You Can Find More Information." These documents contain information you should carefully consider when deciding whether to invest in our common stock.

This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent there is a conflict between the information contained in this prospectus supplement and the accompanying prospectus, you should rely on information contained in this prospectus supplement, provided that if any statement in, or incorporated by reference into, one of these documents is inconsistent with a statement in another document having a later date, the statement in the document having the later date modifies or supersedes the earlier statement. Any statement so modified will be deemed to constitute a part of this prospectus only as so modified, and any statement so superseded will be deemed not to constitute a part of this prospectus.

You should rely only on the information contained in this prospectus supplement, the accompanying prospectus, any document incorporated by reference herein or therein, or any free writing prospectuses we may provide to you in connection with this offering. Neither we nor any of the sales agents has authorized anyone to provide you with any different information. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may provide to you. The information contained in this prospectus supplement, the accompanying prospectus, and in the documents incorporated by reference herein or therein is accurate only as of the date such information is presented. Our business, financial condition, results of operations and prospects may have changed since that date.

This prospectus supplement and the accompanying prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the shares of common stock to which it relates, nor do this prospectus supplement and the accompanying prospectus 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.

Unless otherwise indicated, information contained in or incorporated by reference into this prospectus concerning our industry and the markets in which we operate, including market opportunity, market position and competitive landscape, is based on information from our management's estimates, as well as from industry publications, surveys and studies conducted by third parties. Management estimates are derived from publicly available information, our knowledge of our industry, and assumptions based on such information and knowledge, which we believe to be reasonable. In addition, while we believe that information contained in the industry publications, surveys and studies has been obtained from reliable sources, the accuracy and completeness of such information is not guaranteed, and we have not independently verified any of the data contained in these third-party sources.

This prospectus supplement and the accompanying prospectus, and any documents incorporated by reference herein or therein, include statements that are based on various assumptions and estimates that are subject to numerous known and unknown risks and

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uncertainties. Some of these risks and uncertainties are described under the heading "Risk Factors" beginning on page S-8 of this prospectus supplement and in the section titled "Risk Factors" in our most recent Annual Report on Form 10-K, and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2017, which are incorporated by reference into the prospectus. These and other important factors could cause our future results to be materially different from the results expected as a result of, or implied by, these assumptions and estimates. You should read the information contained in this prospectus supplement and the accompanying prospectus, and the documents incorporated by reference herein and therein, completely and with the understanding that future results may be materially different and worse from what we expect. See the information included under the heading "Special Note Regarding Forward-Looking Statements."

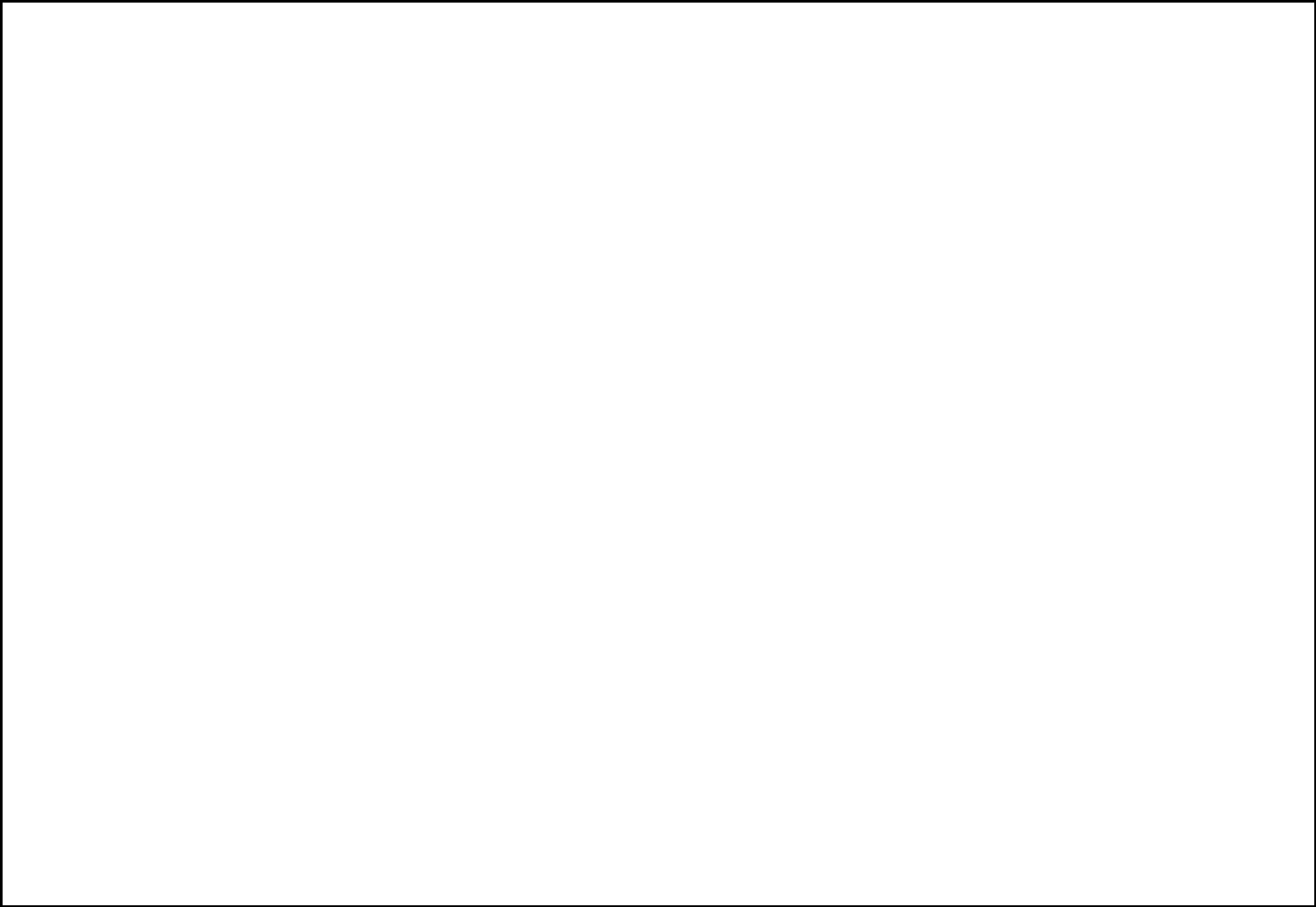
We note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreement, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Unless otherwise indicated or the context otherwise requires, the terms "Company," "Madrigal Pharmaceuticals," "we," "us" and "our" refer to Madrigal Pharmaceuticals, Inc., a Delaware corporation, and its predecessors and consolidated subsidiaries.

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**PROSPECTUS SUPPLEMENT SUMMARY**

*This summary highlights information contained elsewhere in this prospectus supplement and the accompanying prospectus and in the documents we incorporate by reference. This summary does not contain all of the information that you should consider before deciding to invest in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the "Risk factors" section contained in this prospectus supplement and our consolidated financial statements and the related notes and the other documents incorporated by reference herein.*

**Overview**

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of innovative therapeutic candidates for the treatment of cardiovascular, metabolic and liver diseases. Our lead product candidate, MGL-3196, is a proprietary, liver-directed, selective thyroid hormone receptor-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.

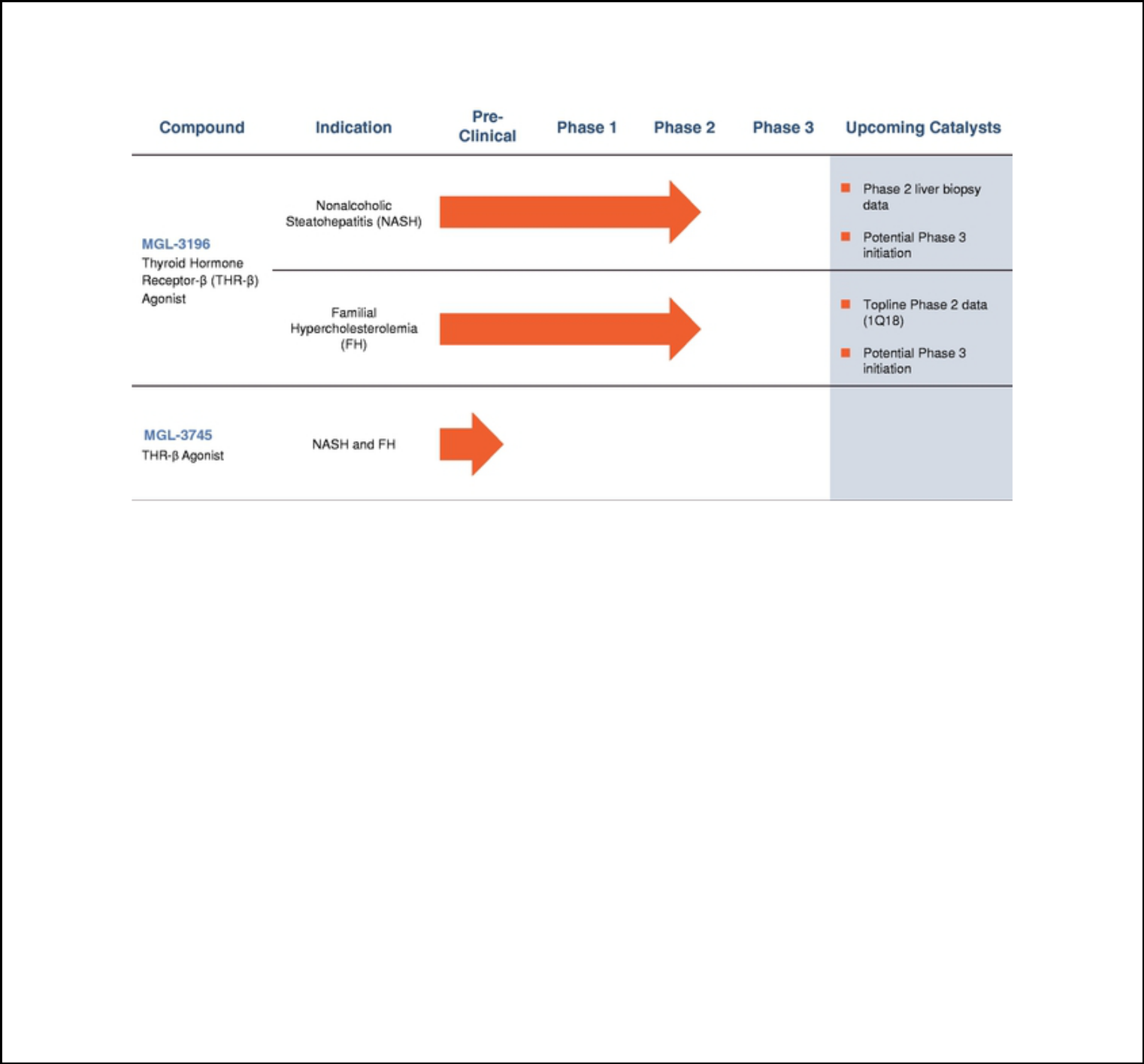
We believe that MGL-3196 is a first-in-class, highly selective, liver-directed THR-ß agonist. We are developing MGL-3196 for NASH and we have initiated a Phase 2 clinical trial in this indication. We are also developing MGL-3196 for dyslipidemia, particularly genetic dyslipidemias such as familial hypercholesterolemia, 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.

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

**Recent Developments**

We recently announced top-line results from our Phase 2 clinical trial in NASH. In this trial, MGL-3196 demonstrated statistically significant results for the primary endpoint, the percent change in hepatic fat versus placebo as measured by MRI-PDFF, a non-invasive imaging test, at 12 weeks. Recent published data have shown a high correlation of the reduction of liver fat of 30% or more as measured by MRI-PDFF to improvement in NASH on liver biopsy.

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

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

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

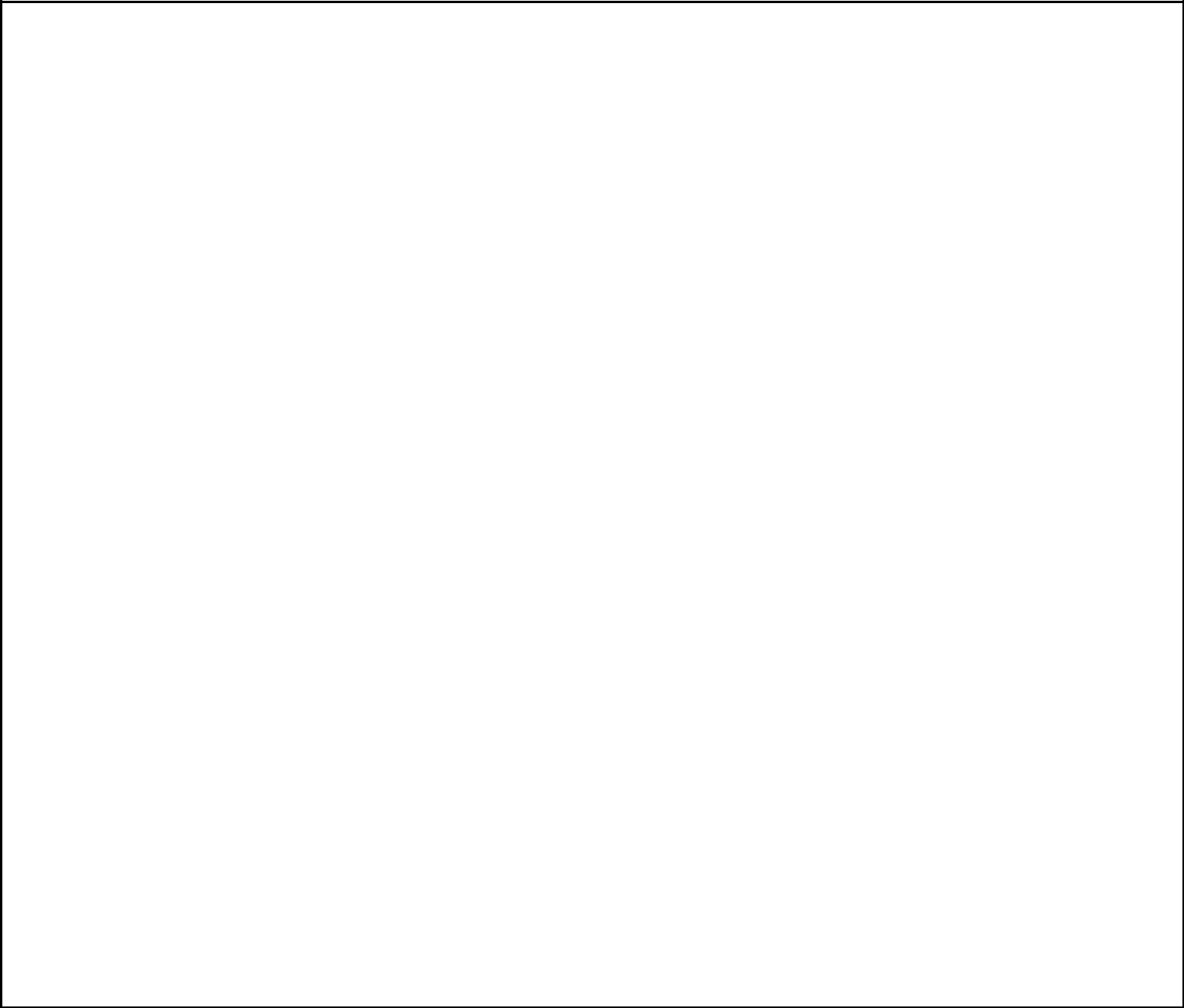
**Our Strategy**

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-

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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 have reported data for theprimary endpoint from our Phase 2 study in NASH in December 2017. NASH is a disease driven by the growing epidemic of obesity, with a significant unmet need for approved therapies that are effective and well tolerated. We believe MGL-3196 is an excellent candidate for the chronic treatment of NASH due to its safety profile and first-in-class dual mechanism of action targeting fibrosis-generating cells.
* ***Establish commercial capabilities to market MGL-3196 as a leading treatment for NASH.*** If approved, we may chooseeither 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.

**Market Opportunity in NASH**

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.

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.

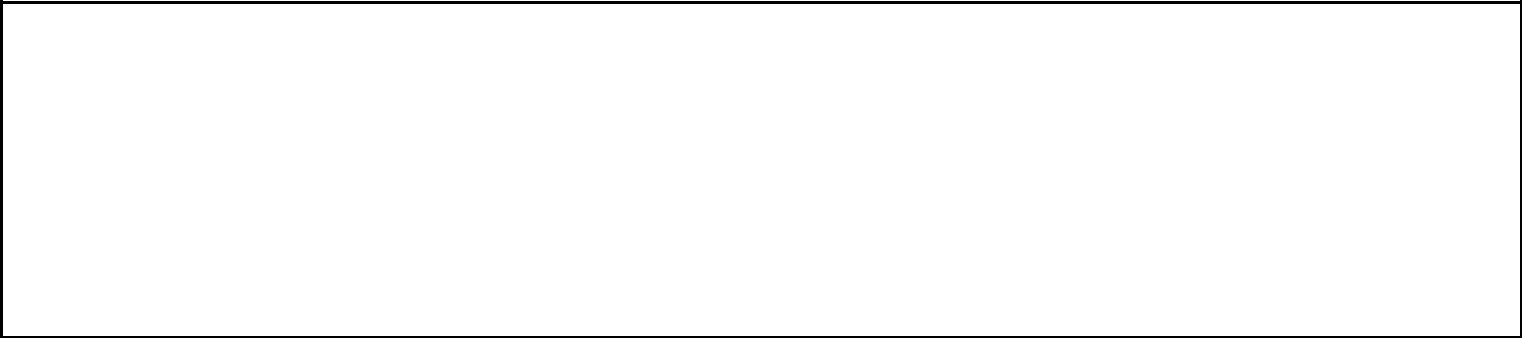
**General Information**

We were incorporated in Delaware in September 2011. On July 22, 2016, Synta Pharmaceuticals Corp., or Synta, completed its business combination with Madrigal

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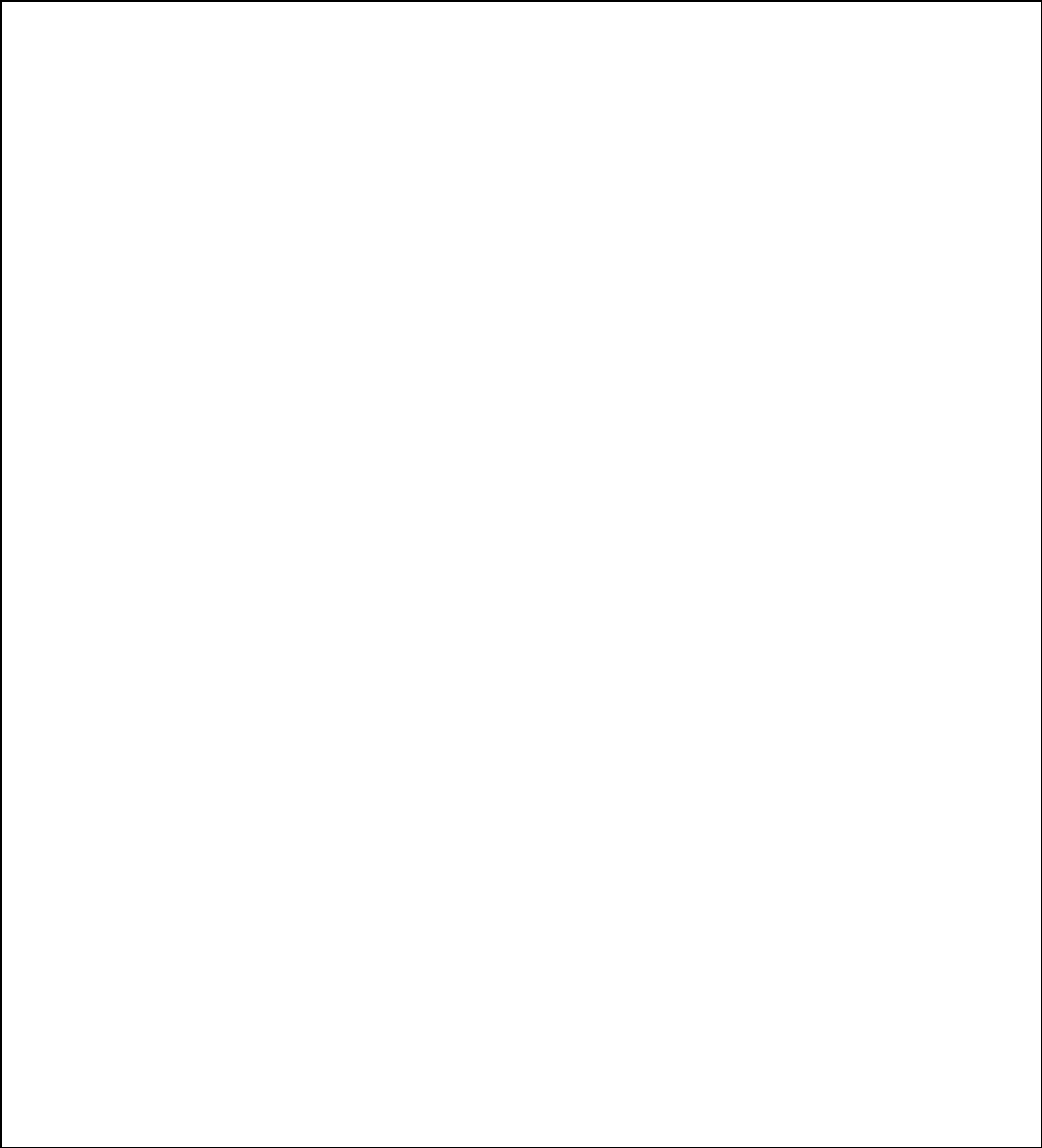


Pharmaceuticals, Inc., a privately-held Delaware corporation, or Private Madrigal, in accordance with the terms of an Agreement and Plan of Merger and Reorganization, dated as of April 13, 2016, whereby a wholly-owned subsidiary of Synta merged with and into Private Madrigal, or the Merger, with Private Madrigal surviving the Merger as a wholly-owned subsidiary of Synta. Following the Merger, Synta changed its name to "Madrigal Pharmaceuticals, Inc.", and our business became the business conducted by Private Madrigal prior to the Merger. In addition, the Merger provided us with $42.6 million in cash, cash equivalents and marketable securities. 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.

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**The Offering**

*The following summary contains basic information about our common stock and the offering and is not intended to be complete. It does not contain all of the information that may be important to you. For a more complete understanding of our common stock, you should read the section entitled "Description of Capital Stock."*

|  |  |  |
| --- | --- | --- |
| **Issuer** | | Madrigal Pharmaceuticals, Inc. |
| **Common stock offered by us** | | 1,506,025 shares. We have also granted the |
|  |  | underwriters a 30-day option to purchase up to |
|  |  | 225,904 additional shares. |
| **Common stock to be outstanding after this** | | 14,001,730 shares (or 14,227,634 shares if the |
| **offering**(1) | | underwriters exercise their option to purchase |
|  |  | additional shares in full). |
| **Use of Proceeds** | | We estimate that the net proceeds from this offering |
|  |  | will be approximately $117.5 million based on the sale |
|  |  | of 1,506,025 shares of our common stock offered |
|  |  | hereby (or approximately $135.1 million if the |
|  |  | underwriters exercise their option to purchase |
|  |  | 225,904 additional shares in full), at the public |
|  |  | offering price of $83.00 per share, after deducting |
|  |  | estimated underwriting discounts and commissions. |
|  |  | We intend to use the net proceeds from this offering, |
|  |  | if any, for general corporate purposes, including, |
|  |  | without limitation, research and development |
|  |  | expenditures, clinical trial expenditures, manufacture |
|  |  | and supply of drug substance and drug products, |
|  |  | acquisitions of new technologies, capital expenditures |
|  |  | and working capital. See "Use of Proceeds" beginning |
|  |  | on page S-59 of this prospectus. |
| **Nasdaq Global Market Symbol** | | MDGL |
| **Risk Factors** | | Your investment in our common stock involves |
|  |  | substantial risks. You should read carefully the "Risk |
|  |  | Factors" included and incorporated by reference in |
|  |  | this prospectus, including the risk factors incorporated |
|  |  | by reference from our filings with the SEC. |
|  |  |  |

1. The common stock outstanding after the offering is based on approximately 12,495,705 shares of our common stock outstanding as of September 30, 2017 and excludes the following:
   * 1,969,797 shares of common stock issuable upon conversion of our Series A Convertible Preferred Stock outstanding as of September 30, 2017;
   * 991,711 shares of our common stock issuable upon the exercise of options outstanding as of September 30, 2017, having a weighted average exercise price of $11.96 per share; and
   * an aggregate of 1,443,561 shares of our common stock reserved for future issuance as of September 30, 2017 under our 2015 Stock Plan.

Except as otherwise noted, we have presented the information in this prospectus supplement assuming no exercise by the underwriters of the option to purchase up to 225,904 additional shares of our common stock in this offering.

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**RISK FACTORS**

*Before making an investment decision, you should carefully consider the risks described below and discussed in the section titled "Risk Factors" in our most recent Annual Report on Form 10-K, as well as the risks, uncertainties and additional information set forth in our SEC reports on Forms 10-K, 10-Q and 8-K and in other documents incorporated by reference in this prospectus. We expect to update these Risk Factors from time to time in the periodic and current reports that we file with the SEC after the date of this prospectus. These updated Risk Factors will be incorporated by reference in this prospectus.*

*Our business, financial condition or results of operations could be materially adversely affected by any of these risks. The trading price of our common stock could decline due to any of these risks, and you may lose all or part of your investment. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business, financial condition results of operations and prospects. Certain statements below are forward-looking statements. See the information included under the heading "Special Note Regarding Forward-Looking Statements."*

**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 September 30, 2017, we had an accumulated deficit of $98.0 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 September 30, 2017, we had cash, cash equivalents and marketable securities of $62.1 million. In the future, we intend to continue to conduct research and development, clinical testing, regulatory compliance and, if MGL-3196 or other future product candidates are approved, sales and marketing activities that, together with anticipated general and administrative expenses, will likely result in us incurring further significant losses for the foreseeable future.

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

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

To date, the sole focus of our product development has been MGL-3196, a liver-directed selective thyroid hormone receptor beta agonist for potential use in non-alcoholic steatohepatitis, or NASH, and FH. Successful continued development and ultimate regulatory approval of MGL-3196 for NASH or genetic dyslipidemias, such as FH, is critical to the future success of our business. We have invested, and will continue to invest, a significant portion of our time and financial resources in

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the clinical development of MGL-3196. We will need to raise sufficient funds to successfully complete our clinical development program for MGL-3196 in NASH and FH. The future regulatory and commercial success of MGL-3196 is subject to a number of risks, including the following:

* we may not have sufficient financial and other resources to complete the necessary clinical trials for MGL-3196, including but not limited to our currently ongoing Phase 2 clinical trials and, later, registrational clinical trials to obtain drug approval;
* the mechanism of action of MGL-3196 is complex and we do not know the degree to which it will translate into a therapeutic benefit, if any, in NASH, FH or any other indication, and we do not know the degree to which the complex mechanism of action may contribute to long term safety issues or adverse events, if any, when MGL-3196 is taken for prolonged periods such as in the treatment of NASH, FH or any other indication;
* we may not be able to obtain adequate evidence from clinical trials of efficacy and safety for MGL-3196 in NASH, FH or any other indication;
* we do not know the degree to which MGL-3196 will be accepted as a therapy by physicians, patients and payors, even if approved;
* in our clinical programs for MGL-3196, we may experience variability in patients, adjustments to clinical trial procedures and the need for additional clinical trial sites, which could delay our clinical trial progress;
* the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory bodies for marketing approval;
* patients in our clinical trials may die or suffer other adverse effects for reasons that may or may not be related to MGL-3196, which could delay or prevent further clinical development;
* the standards implemented by clinical or regulatory agencies may change at any time;
* we cannot be certain what efficacy endpoints FDA or foreign clinical or regulatory agencies may require in a Phase 3 trial of NASH or FH or for approval of our product candidates; we also cannot be certain if we will be able to gain accelerated approval of any of our product candidates based on surrogate endpoints;
* the FDA or foreign clinical or regulatory agencies will likely require efficacy endpoints for Phase 3 clinical trials for the treatment of NASH or FH that differ from the endpoints of our current trials and the results of our Phase 3 trials may not be as favorable as the results we have observed to date in our current trials;
* if we obtain accelerated approval of a product candidate based on a surrogate endpoint, we will likely be required to conduct a post-approval clinical outcomes trial to confirm the clinical benefit of the product candidate and if the post-approval trial is not successful we may not be able to continue marketing the product;
* if approved for NASH, MGL-3196 will likely compete with the off-label use of currently marketed products and other therapies in development that may reach approval for NASH prior to MGL-3196;
* if approved for FH, MGL-3196 will likely compete with currently approved and marketed products and other therapies in development that may reach approval for FH prior to MGL-3196; and
* we may not be able to obtain, maintain or enforce our patents and other intellectual property rights.

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Of the large number of drugs in development in the pharmaceutical industry, only a small percentage results in the submission of a new drug application, or NDA, to the FDA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market MGL-3196, any such approval may be subject to limitations on the indicated uses or patient populations for which we may market the products. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, we may be unable to successfully develop or commercialize MGL-3196. If we or any of our future development partners are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize MGL-3196, we may not be able to generate sufficient revenue to continue our business.

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

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

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

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

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

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

We cannot predict whether we will encounter problems with any of our completed, ongoing or planned clinical trials that will cause us or any regulatory authority to delay, suspend, or terminate those clinical trials or delay the analysis of data derived from them. A number of events, including any of the following, could delay or impede completely the completion of our ongoing and planned clinical trials and negatively affect our ability to obtain regulatory approval for, and to market and sell, a particular product candidate:

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

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

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

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

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

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

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. We may not be able to initiate, continue, or complete clinical trials required by the FDA or foreign regulatory agencies for MGL-3196 if we are unable to locate and enroll a sufficient number of eligible patients to participate in these clinical trials. Patient enrollment, a significant factor in the timing to conduct and complete clinical trials, is affected by many factors, including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials, and clinicians' and patients' perceptions as to the potential advantages and disadvantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. For instance, we are aware that other companies conducting clinical trials in NASH patients have had delays in recruiting patients for their trials. In the proposed clinical trials, patient willingness to undergo a liver biopsy in our NASH trials, and identification of patients willing to participate in our FH trials due to the rarity of the disease, are also risk factors. Potential patients for MGL-3196 may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for our studies.

The FDA typically requires sponsors of lipid-lowering product candidates to conduct drug-drug interaction studies with statins because statins may have increased safety risks when administered together with other drug therapies that affect their pharmacokinetic profile. We have completed two clinical drug interaction studies of MGL-3196 and statins in 129 subjects, which showed MGL-3196 to have a favorable safety profile and to be well-tolerated. We have completed enrollment of a Phase 2 clinical study in NASH including patients taking low dose statins. We have also completed enrollment of a Phase 2 clinical study in HeFH including patients taking high dose statins. In general, drug interactions between MGL-3196 and statins and any other drug that might result in adverse events could delay development in later clinical trials.

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

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

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

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

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

Even if we receive regulatory approval to market a particular product candidate, the manufacturing, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, sampling, and record keeping related to the product will remain subject to extensive regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP, regulations and GCPs, for any clinical trials that we conduct post-approval, all of which may result in significant expense and limit our ability to commercialize such products. In addition, any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a REMS Program as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

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

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

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

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

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

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

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

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

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

Even if any of our product candidates obtain regulatory approval, they may not gain market acceptance among physicians, patients, and third-party payers. Efforts to educate the medical

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community and third-party payers on the benefits of our product candidates may require significant resources and may not be successful. If any of our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenue or any profits from operations. Physicians may decide not to recommend its treatments for a variety of reasons including:

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

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

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

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

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

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

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***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 develops due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative proposals.

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

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

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

* decreased demand for any of our future approved products; S-16



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* 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

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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

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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

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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. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

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

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

We have not obtained orphan designation for any product candidates to date, although we believe some of the potential indications of our product candidates could qualify for orphan drug

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

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

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

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

In addition, we and/or our partners may be subject to patient data privacy and security regulation, including the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective

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implementing regulations, which impose specified requirements relating to the privacy, security and transmission of individually identifiable health information.

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

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

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

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

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

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

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

We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates, and we lack the resources and the capabilities to do so. As a

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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

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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 hold exclusive worldwide rights for all potential indications. Under the license agreement, Roche exclusively licensed certain patent rights and know-how relating to MGL-3196 in exchange for consideration consisting of an upfront payment, milestone payments tied to the achievement of product development and regulatory milestones, and royalty payments based on net sales of products containing MGL-3196 or another licensed product, subject to certain reductions. We must use commercially reasonable efforts to conduct clinical and commercial development programs for products containing MGL-3196. If we determine that it is not reasonable to continue clinical trials or other development of MGL-3196, we may elect to cease further development and Roche may terminate the license. If we determine not to pursue the development or commercialization of MGL-3196 in certain jurisdictions, including the United States, Roche may terminate the license for such territories. The Roche Agreement will expire, unless earlier terminated pursuant to other provisions 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.

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

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

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

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

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

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

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

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

We can provide no assurance that our patent applications or those of our licensors will result in additional patents being issued or that issued patents will afford sufficient protection against competitors with similar technologies, nor can we provide any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. Even issued patents may later be found unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. This failure to properly protect the intellectual property rights relating to our product candidates could have a material adverse effect on our financial condition and results of operations. Composition-of-matter patents on the biological or chemical active pharmaceutical ingredients are generally considered to offer the strongest protection of intellectual property and provide the broadest scope of patent protection for pharmaceutical products, as such patents provide protection without regard to any method of use or any method of manufacturing. While we have licensed rights to issued composition-of-matter patents in the United States and other jurisdictions for MGL-3196, we cannot be certain that the claims in issued composition-of-matter patents will not be found invalid or unenforceable if challenged. We cannot be certain that the claims in owned and licensed patent applications covering our product candidates will be considered patentable by the United States Patent and Trademark Office, or USPTO, and valid by courts in the United States or by the patent offices and

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courts in foreign jurisdictions. Even if we owned and licensed patent applications covering our product candidates, the patents may not be enforced against competitors. For example, a formulation patent will not be enforced against those making and marketing a product that has the same active pharmaceutical ingredient in a different formulation that is not claimed in the formulation patent. Method-of-use patents protect the use of a product for the specified method or for treatment of a particular indication. This type of patent may not be enforced against competitors making and marketing a product that has the same active pharmaceutical ingredient but is used for a method not claimed in the patent. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products "off-label." Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute.

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

* the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process and after a patent has issued. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case;
* patent applications may not result in any patents being issued;
* patents may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
* 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

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not have patent rights, and then use the information learned from such activities to develop competitive products for sale in major commercial markets;

* there may be significant pressure on the United States government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
* countries other than the United States may have patent laws less favorable to patentees than those upheld by United States courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

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

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

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

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

The biotechnology industry has been characterized by frequent litigation regarding patent and other intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. As the biotechnology industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained in secrecy until the application is published, we may be unaware of third party patents that may be infringed by commercialization of

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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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

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any of our other product candidates which we are pursuing or may choose to pursue in the future;

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

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

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

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

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

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

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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 51.1% of our outstanding common stock as of September 30, 2017 and acting together, may have the ability to affect matters submitted to our stockholders for approval. This concentration of ownership may have the effect of delaying, deferring or preventing a strategic transaction, even if such a transaction would benefit other stockholders.

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

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

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

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our

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stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

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

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

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

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

**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.***

As of September 30, 2017, there were 1,969,797 shares of Series A Convertible Preferred stock outstanding, all of which are readily convertible into common stock at the option of the holders. In addition, there are an additional 991,711 shares of our common stock issuable upon the exercise of outstanding stock options. 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 sales or 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.

**Risks Related to This Offering**

***Investors in this offering will pay a much higher price than the book value of our common stock.***

If you purchase common stock in this offering, you will incur an immediate and substantial dilution of $70.73 per share after giving effect to the sale by us of 1,506,025 shares of our common stock offered in this offering at the public offering price of $83.00 per share, and after deducting underwriting discounts and commissions for shares sold in the public offering. See "Dilution." To the extent outstanding options or warrants we have issued are ultimately exercised, you will incur additional dilution. Furthermore, if the underwriters exercise their option to purchase additional shares, you will also incur additional dilution.

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***Our management will have broad discretion over the use of the net proceeds from this offering; you may not agree with how we use the proceeds and the proceeds may not be invested successfully.***

Our management will have broad discretion as to the use of the net proceeds from this offering by us and could use them for purposes other than those contemplated at the time of this offering. Accordingly, you may be relying on the judgment of our management with regard to the use of these net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that the proceeds will be invested in a way that does not yield a favorable, or any, return for us.

***Sales of additional shares of our common stock, including by us or our directors, officers and significant stockholders following expiration or early release of the 90 day lock up, could cause the price of our common stock to decline.***

Sales of substantial amounts of our common stock in the public market, or the availability of such shares for sale, by us or others, including the issuance of common stock upon exercise of outstanding options or upon the conversion of our Series A Convertible Preferred Stock, could adversely affect the price of our common stock. Based on the total number of outstanding shares of our common stock as of September 30, 2017, upon completion of this offering, we will have outstanding 14,001,730 shares of common stock (or 14,227,634 shares of common stock if the underwriters exercise their option to purchase additional shares in full). In connection with this offering, we, our directors and officers and certain of our significant stockholders have entered into lock-up agreements with the underwriters under which we, our directors and officers and significant stockholders have agreed, subject to specific exceptions described in the section titled "Underwriting", not to sell, directly or indirectly, any shares of common stock without the permission of Goldman Sachs & Co. LLC for a period of 90 days following the date of this prospectus. Upon expiration or earlier release of the lock-up, we, our directors or officers or significant stockholders may sell shares into the market, which could adversely affect the market price of shares of our common stock. Sales of a substantial number of such shares upon expiration of the lock-up agreements, the perception that such sales may occur, or early release of these agreements, could cause our market price to fall or make it more difficult for you to sell your common stock at a time and price that you deem appropriate.

***Tax reform may significantly affect our operations and stockholders.***

The Trump Administration and the U.S. Congress are close to passing substantial revisions to U.S. federal income tax law, and such revisions could significantly impact our company and the tax treatment of our operating results. There is substantial uncertainty around the likelihood, timing and details of any such tax reform being enacted, but any such reform, if enacted, could have a significant impact on our company and its stockholders. Potential investors should consult their tax advisors about such developments, and their potential impact before investing in our securities.

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**BUSINESS**

**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.

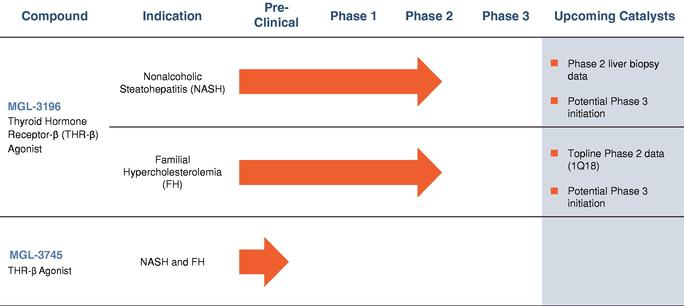
In the multiple ascending dose Phase 1 clinical trial in healthy volunteers with mildly elevated low-density lipoprotein cholesterol, or LDL-C, the administration of MGL-3196 in once daily doses of up to 200 mg per day for 14 days demonstrated statistically significant reductions of LDL-C, apolipoprotein 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.

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



**Recent Developments**

We recently announced top-line results from our Phase 2 clinical trial in NASH. In this trial, MGL-3196 demonstrated statistically significant results for the primary endpoint, the percent change in hepatic fat versus placebo as measured by MRI-PDFF, a non-invasive imaging test at 12 weeks. Recent published data have shown a high correlation of the reduction of liver fat of 30% or more as measured by MRI-PDFF to improvement in NASH on liver biopsy.

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

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

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

**Lead Product Candidate — MGL-3196**

Active thyroid hormone, known as T3, interacts with two nuclear receptors, THR-a, which is the predominant receptor expressed in most human tissues, including heart and bone, and THR-b, 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

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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-b 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-b agonist compound. MGL-3196, along with other THR-b-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 b-selective based on binding affinity, but which were shown to equally activate THR-a and THR-b 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 good laboratory practice, or GLP, toxicology studies, and drug manufacturing studies to support further clinical development, including active pharmaceutical ingredient, or API, manufacturing and drug product development studies, drug metabolism studies, acute, subchronic and chronic animal toxicology studies, and other safety pharmacology and toxicology studies.

We have completed Phase 1 studies with MGL-3196 in a total of 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

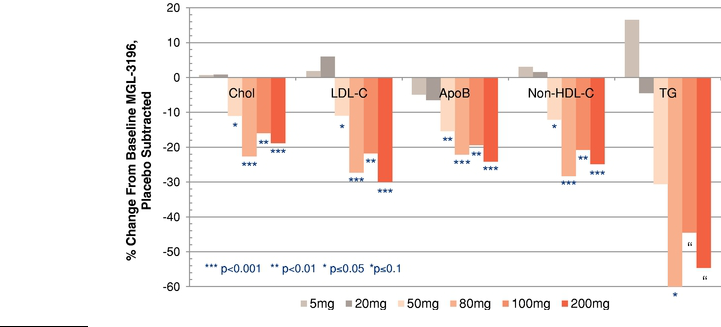
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highest dose of MGL-3196 (200 mg), there was a reversible reduction of 20% in the level of a precursor hormone to T3, free T4, which was significantly different from placebo (p < 0.0001) that may be explained by increased liver metabolism of free T4. 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 24th after 14th dose; baseline value obtained just prior to first dose; ApoB, apolipoprotein B; Chal, total cholesterol; LDL-C, LDL cholesterol directly measured; Non-HDL-C, non-HDL cholesterol; TG, triglycerides (median %CFB)

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

The randomized, double-blind, placebo-controlled, multi-center NASH Phase 2 study enrolled 125 patients 18 years of age and older with liver biopsy-confirmed NASH and included approximately 25 clinical sites in the United States. Patients were randomized to receive either placebo or MGL-3196 with twice as many patients receiving MGL-3196 as placebo. The starting dose in MGL-3196-treated patients was 80 mg once a day. The study employed an adaptive dosing design whereby, in a blinded fashion, the dose could be adjusted by small amounts (i.e. 20 mg up or down) or remain at 80 mg in each MGL-3196-treated patient based on a pharmacokinetic analysis of drug level performed in each patient at

2 weeks.

The primary endpoint of the study is the reduction of liver fat at 12 weeks compared with baseline (relative change), assessed by MRI-PDFF, with efficacy confirmed at the end of the trial

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(36 weeks) by repeat MRI-PDFF and conventional liver biopsy to examine histological evidence for the resolution of NASH. A total of 116 patients completed the 12 week MRI-PDFF; the 9 discontinuations were balanced between placebo and drug treated; 2/9 discontinuations were AE-related.

Other secondary endpoints include changes in clinically relevant biomarkers at 12 and 36 weeks, improvement in fibrosis by at least one stage with no worsening of steatohepatitis, and safety and tolerability. Results at 36-weeks are expected in the second quarter of 2018. In this trial, MGL-3196, a first-in-class, oral, once-daily, liver-directed, thyroid hormone receptor (THR) b -selective agonist, demonstrated statistically significant results for the primary endpoint, the percent change in hepatic fat versus placebo as measured by MRI-PDFF, a non-invasive imaging test. Recent published data have shown a high correlation of the reduction of liver fat of 30% or more as measured by MRI-PDFF to improvement in NASH on liver biopsy.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | ALL MGL- |  |  |  |  |  |
|  |  |  | 3196 |  | HIGH MGL-3196\*\* |  | Placebo |  |
|  | Numbers of patients | | 78 | 44 | | 38 | |  |
| Relative change in MRI-PDFF (% change from baseline, median) | | | –36.3% |  | –42.0% |  |  |  |
|  | Significance relative to placebo | | p<0.0001 |  | p<0.0001 |  | –9.6% | |
|  | Percentage of patients attaining ³30% liver fat reduction Significance | | 60.3% | 75.0% | |  |  |  |
|  | relative to placebo | | p<0.0001 |  | p<0.0001 | 18.4% | | |
|  |  |  |  |  |  |  |  |  |

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

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

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

The on-going study remains blinded. Safety, efficacy of NASH resolution by biopsy, and repeat MRI-PDFF will be assessed at 36 weeks.

Multiple inflammatory and fibrosis serum biomarkers at 12 and 36 weeks are being and will be assessed.

**Our Strategy**

Our goal is to become a leading biopharmaceutical company developing and commercializing innovative liver-directed, 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 have reported data for the primaryendpoint from our Phase 2 study in NASH in December 2017. NASH is a disease driven by the growing epidemic of obesity, with a significant unmet need for approved therapies that are effective and well tolerated. We believe MGL-3196 is an

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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 toestablish 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 hasthe 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

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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.

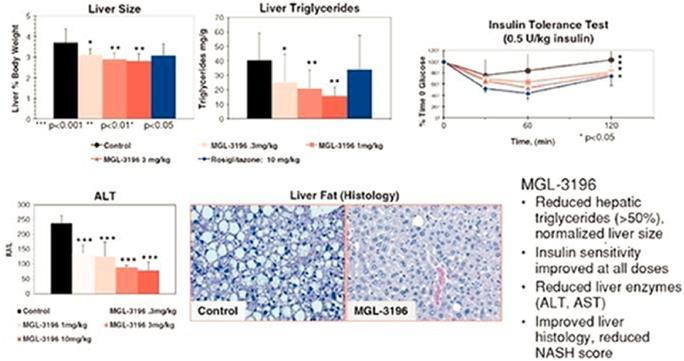
***MGL-3196 in NASH***

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**



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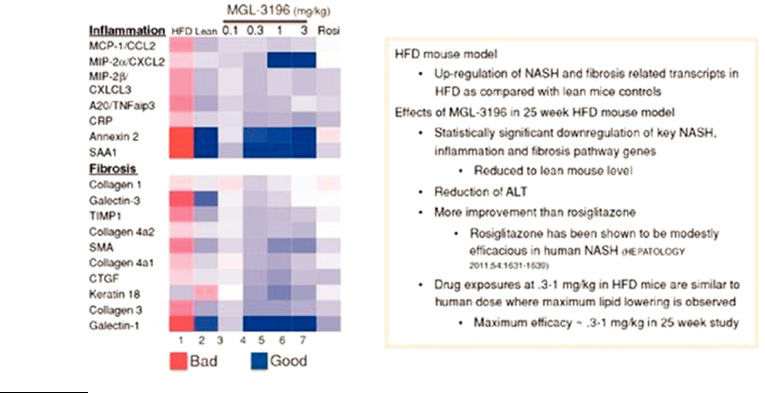


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*MGL-3196 Preclinical NASH Animal Model Gene Expression Study*

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

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

**Familial Hypercholesterolemia**

*Overview and Market Opportunity*

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

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

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*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 have randomized HeFH patients 2:1, MGL-3196 or placebo QD in double-blind, placebo-controlled fashion. Patients are to continue treatment through 12 weeks. The study is being conducted in Europe. In this 12 week clinical trial, the primary endpoint is to evaluate the efficacy of MGL-3196 as measured by the percent reduction in LDL-C as compared with placebo. Secondary endpoints include safety and tolerability, and evaluate the efficacy of MGL-3196 to reduce a variety of lipid parameters, including non-HDL-C, apoB, TGs, Lp(a), apoA/B, and lipoprotein particles. Based on 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 early 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 hold exclusive worldwide rights for all potential indications. Under the license agreement, Roche exclusively licensed certain patent rights and know-how relating to MGL-3196 in exchange for consideration consisting of an upfront payment, milestone payments, the remainder of which total $10 million and are tied to future commencement of Phase 3 clinical trials and regulatory approval in the United States and Europe of MGL-3196 or any derivative product, and single-digit royalty payments based on net sales of MGL-3196 and any derivative products, subject to certain reductions. In 2011, we commenced Phase 1 clinical trials and subsequently paid Roche a related milestone payment. In October 2016, we commenced a Phase 2 study in NASH and subsequently paid Roche a related milestone payment. Except as described above, we have not

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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.

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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, co-own or have exclusive rights to three United States and 69 foreign issued patents and allowed patent applications, and two United States and 25 foreign pending patent applications,

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relating to composition-of-matter of MGL-3196, including certain dosage forms, and its use in the treatment of key disease indications. Our current patent portfolio covers the United States and certain other jurisdictions worldwide.

Issued United States patents directed to MGL-3196, including certain dosage forms, have statutory expiration dates between 2026 and 2033, excluding any patent term extensions that might be available following the grant of marketing authorizations. Issued patents outside of the United States directed to MGL-3196, including certain dosage forms, have statutory expiration dates between 2026 and 2033. We have pending patent applications for MGL-3196 that, if issued, would be expected to expire in the United States and in countries outside of the United States between 2026 and 2033, excluding any patent term adjustment that might be available following the grant of the patent and any patent term extensions that might be available following the grant of marketing authorizations.

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

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

**Orphan Drug Designation**

Some of MGL-3196's target disease indications are rare diseases or may be designated rare diseases, including HoFH and severe HeFH, and we plan to pursue orphan drug designation where possible. If granted, each such designation might provide for regulatory exclusivity for seven years in the United States and ten years in the 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 before it may be legally marketed in the United States, and must be approved by foreign regulatory authorities via various procedures before it can be marketed in the applicable country. The animal and other non-clinical data and the results of human clinical trials performed under an Investigational New Drug application, or IND, and under similar foreign applications will become part of the NDA.

***United States Drug Development Process***

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process,

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approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other things, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters and other types of enforcement-related letters, requesting product recalls, product seizures, changes to the conditions surrounding marketing approval such as labeling changes or changes to a Risk Evaluation and Mitigations Strategies, or REMS, program, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, debarment, restitution, disgorgement of profits, or civil or criminal investigations and penalties. Any agency or judicial enforcement action could have a material adverse effect on us. The process required by the FDA before a drug or biologic may be marketed in the United States generally involves the following:

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

Once a pharmaceutical candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies, to assess the safety and quality of the product. Animal studies must be performed in compliance with FDA's GLP regulations and the U.S. Department of Agriculture's Animal Welfare Act. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. The sponsor will also include a protocol detailing, among other things, the objectives of the first phase of the clinical trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated, if the first phase lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the

30-day time period, places the clinical trial on a clinical hold or a partial clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during studies due to safety concerns or non-compliance, or other reasons.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with good clinical practice regulations. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and progress reports detailing the results of the clinical trials must be submitted at least annually. In addition, timely safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events or animal test results that suggest a

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significant risk to human subjects. An institutional review board, or IRB, at each institution participating in the clinical trial must review and approve each protocol before a clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be provided to each trial subject or his or her legal representative, monitor the study until completed and otherwise comply with IRB regulations. Foreign studies conducted under an IND must meet the same requirements that apply to studies being conducted in the U.S. Data from a foreign study not conducted under an IND may be submitted in support of an NDA if the study was conducted in accordance with GCP and the FDA is able to validate the data.

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

* *Phase 1:* The product candidate is initially introduced into healthy human subjects and tested for safety, dosage tolerance,absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients with the target diseases.
* *Phase 2:* This phase involves studies in a limited patient population to identify possible adverse effects and safety risks, topreliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
* *Phase 3:* This phase involved trials undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patientpopulation at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product candidate and provide, if appropriate, an adequate basis for product approval and product labeling.

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

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

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop

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methods for testing the identity, strength, quality and purity of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

***United States Review and Approval Processes***

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

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

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

The Food and Drug Administration Safety and Innovation Act, or FDASIA, which was enacted in 2012, made permanent the Pediatric Research Equity Act, or PREA, which requires a sponsor to conduct pediatric studies for most drugs and biologics, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements thereto must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug or biologic is ready for approval for use in adults before pediatric studies are complete or that additional safety or effectiveness data needs to be collected before the pediatric studies begin. After April 2013, the FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

***Patent Term Restoration and Marketing Exclusivity***

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

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

***Orphan Drug Designation***

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or

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

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

***Fast Track Designation and Accelerated Approval***

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

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

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

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

***Post-Approval Requirements***

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

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

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

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***Foreign Regulation***

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

Under 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 EMA where it will be evaluated by the Committee for Medicinal Products for Human Use and a favorable opinion typically results in the grant by the European Commission of a single marketing authorization that is valid for all 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 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

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marketing authorization in the EU of the innovator product), or 3 years later (or a total of eleven years after the first marketing authorization in the EU of the innovator product) if the marketing authorization holder obtains marketing authorization for a new indication with significant clinical benefit within the eight year data exclusivity period.

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

***Reimbursement***

Significant uncertainty exists regarding the coverage and reimbursement status of products approved by the FDA and other government authorities. In the United States, sales of any products for which we may receive regulatory approval for commercial sale will depend in significant part on the availability and adequacy of coverage and reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list which might not include all of the FDA-approved products for a particular indication. Moreover, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

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

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

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on cost containment measures in the United States has increased and we expect will continue to increase the pressure on pharmaceutical

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pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the 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 December 12, 2017, we had eight full-time employees, including four engaged in research, development, and regulatory activities, and four in executive, general and administrative functions, and multiple part-time consultants.

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**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 supplement, and the documents we incorporate by reference in this 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 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.

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**USE OF PROCEEDS**

The net proceeds from the sale of shares of common stock that we are selling in this offering will be approximately $117.5 million based on the sale of 1,506,025 shares of our common stock offered hereby, or approximately $135.1 million if the underwriters exercise in full their option to purchase up to 225,904 additional shares of common stock, at the public offering price of $83.00 per share, after deducting estimated underwriting discounts and commissions.

We intend to use the net proceeds from this offering, if any, for general corporate purposes, including, without limitation, research and development expenditures, clinical trial expenditures, manufacture and supply of drug substance and drug products, acquisitions of new technologies, capital expenditures and working capital. We may temporarily invest the net proceeds in short-term, interest-bearing instruments or other investment-grade securities. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

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**DILUTION**

If you purchase our common stock in this offering, your interest will be diluted to the extent of the difference between the public offering price per share and the net tangible book value per share of our common stock after this offering. We calculate net tangible book value per share by subtracting our total liabilities from our total tangible assets and dividing the difference by the number of outstanding shares of our common stock.

Our net tangible book value at September 30, 2017 was approximately $54.3 million, or $4.35 per share, based on 12,495,705 shares of our common stock then outstanding. Historical net tangible book value per share is equal to our total tangible assets, less total liabilities, divided by the number of outstanding shares of our common stock. Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering.

After giving effect to the sale by us of 1,506,025 shares of common stock in this offering at the public offering price of $83.00 per share, less

the underwriting discounts and commissions, our pro forma net tangible book value at September 30, 2017 would have been approximately

$171.8 million, or approximately $12.27 per share. This represents an immediate increase in net tangible book value of $7.92 per share to existing

stockholders and an immediate dilution of $70.73 per share to investors in this offering. The following table illustrates this per share dilution:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Public offering price per share |  | $ | | 83.00 |  |
| Historical net tangible book value per share as of September 30, 2017 | $ | 4.35 |  |  |  |
| Increase in net tangible book value per share attributable to new investors |  |  |  |  |  |
| purchasing shares in this offering | $ | 7.92 |  |  |  |
| Pro forma net tangible book value per share after this offering |  |  | $ | 12.27 |  |
| Dilution per share to new investors |  | $ | | 70.73 |  |
|  |  |  |  |  |  |

The above discussion and table are based on approximately 12,495,705 shares of our common stock outstanding as of September 30, 2017 and excludes the following:

* 1,969,797 shares of common stock issuable upon conversion of our Series A Convertible Preferred Stock outstanding as of September 30, 2017;
* 991,711 shares of our common stock issuable upon the exercise of options outstanding as of September 30, 2017, having a weighted average exercise price of $11.96 per share; and
* an aggregate of 1,443,561 shares of our common stock reserved for future issuance as of September 30, 2017 under our 2015 Stock Plan.

In addition, the amounts in the table above assume no exercise by the underwriters of their option to purchase additional shares of our common stock.

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**PRICE RANGE OF COMMON STOCK**

Our common stock is listed on The Nasdaq Global Market under the symbol "MDGL." The following table shows the closing high and low per share sale prices of our common stock for the periods indicated.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | High | |  |  | Low | |
|  | **Year Ending December 31, 2017:** |  |  |  |  |  |  |  |
|  | First Quarter | $ | 16.39 | | $ | | 14.82 |  |
|  | Second Quarter | $ | 17.50 | | $ | | 13.11 |  |
|  | Third Quarter | $ | 46.19 | | $ | | 15.16 |  |
|  | Fourth Quarter (as of December 18, 2017) | $ | 87.18 | | $ | | 39.35 |  |
|  | **Year Ended December 31, 2016:** |  |  |  |  |  |  |  |
|  | First Quarter | $ | 11.90 | | $ | | 6.65 | |
|  | Second Quarter | $ | 15.40 | | $ | | 8.05 | |
|  | Third Quarter | $ | 12.68 | | $ | | 6.89 | |
|  | Fourth Quarter | $ | 17.66 | | $ | | 12.81 |  |
|  | **Year Ended December 31, 2015:** |  |  |  |  |  |  |  |
|  | First Quarter | $ | 100.45 | | $ | | 67.90 |  |
|  | Second Quarter | $ | 106.05 | | $ | | 69.30 |  |
|  | Third Quarter | $ | 79.10 | | $ | | 57.05 |  |
|  | Fourth Quarter | $ | 71.40 | | $ | | 10.85 |  |

On December 18, 2017, the closing price of our common stock on The Nasdaq Global Market was $84.04 per share, and there were 38 holders of record of our common stock.

**DIVIDEND POLICY**

We do not currently anticipate declaring or paying cash dividends on our capital stock in the foreseeable future. We currently intend to retain all of our future earnings, if any, to finance the operation and expansion of our business. Any future determination relating to our dividend policy will be made at the discretion of our board of directors and will depend on a number of factors, including future earnings, capital requirements, future prospects, contractual restrictions and covenants and other factors that our board of directors may deem relevant.

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**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***

As of December 18, 2017, there were 12,495,705 shares of common stock outstanding. 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., whose address is Meidinger Tower, 462 South 4th Street, Louisville, KY 40202 and whose telephone number is (502) 301-6088.

**NASDAQ Global Market**

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

**Dividends**

We have never declared any cash dividends on our common stock and we do not anticipate paying any cash dividends on our common stock in the foreseeable future.

**Description of Preferred Stock**

We are authorized to issue 5,000,000 shares of preferred stock, par value $0.0001 per share. As of December 15, 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

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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.

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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 ourboard 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 proposalsto 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 aresolution 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.

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*No stockholder action by written consent.* Our restated certificate of incorporation and restated bylaws do not permit our stockholders toact 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 theaffirmative 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 662/3% 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.

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**UNDERWRITING**

The Company and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Goldman Sachs & Co. LLC is the representative of the underwriters.

|  |  |  |  |
| --- | --- | --- | --- |
| Underwriters |  | Number of Shares |  |
| Goldman Sachs & Co. LLC | 790,663 | |  |
| Evercore Group L.L.C. | 376,506 | |  |
| JMP Securities LLC | 150,603 | |  |
| Roth Capital Partners, LLC | 112,952 | |  |
| H.C. Wainwright & Co., LLC |  | 75,301 | |
| Total |  | 1,506,025 |  |
|  |  |  |  |

The underwriters are committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

The underwriters have an option to buy up to 225,904 additional shares from us to cover sales by the underwriters of a greater number of shares than the total number set forth in the table above. They may exercise that option for 30 days. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters by the Company.

Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Paid by the Company |  |  | No Exercise |  |  |  | Full Exercise |  |
| Per Share | $ | | 4.98 | | $ | | 4.98 | |
| Total | $ | | 7,500,005 |  | $ | | 8,625,006 |  |

Shares sold by the underwriters to the public will initially be offered at the public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to $2.99 per share from the public offering price. After the initial offering of the shares, the representative may change the offering price and the other selling terms. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

The Company, members of management, the board of directors and certain existing stockholders have agreed with the underwriters, subject to certain exceptions, not to dispose of or hedge any of their common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus supplement continuing through the date 90 days after the date of this prospectus supplement, except with the prior written consent of the representative.

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, stabilizing transactions pursuant to Regulation M of the Securities Act of 1933, and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering, and a short position represents the amount of such sales that have not been covered by subsequent purchases. A "covered short position" is a short

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position that is not greater than the amount of additional shares for which the underwriters' option described above may be exercised. The underwriters may cover any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to cover the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase additional shares pursuant to the option described above. "Naked" short sales are any short sales that create a short position greater than the amount of additional shares for which the option described above may be exercised. The underwriters must cover any such naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representative has repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the Company's stock, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the common stock. As a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. The underwriters are not required to engage in these activities and may end any of these activities at any time. These transactions may be effected on The Nasdaq Global Market, in the over-the-counter market or otherwise.

*European Economic Area*

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relative Member State") an offer to the public of our common shares may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of our common shares may be made at any time under the following exemptions under the Prospectus Directive:

* to any legal entity which is a qualified investor as defined in the Prospectus Directive;
* to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of the Joint Bookrunners for any such offer; or
* in any other circumstances falling within Article 3(2) of the Prospectus Directive;
* provided that no such offer of shares of our common stock shall result in a requirement for the publication by us or any Brazilian placement agent of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to our common shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and our common shares to be offered so as to enable an investor to decide to purchase our common shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression "Prospectus Directive" means Directive 2003/71/EC (as amended, including by Directive 2010/73/EU) and includes any relevant implementing measure in the Relevant Member State.

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This European Economic Area selling restriction is in addition to any other selling restrictions set out below.

*United Kingdom*

In the United Kingdom, this prospectus supplement is only addressed to and directed as qualified investors who are (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order); or (ii) high net worth entities and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). Any investment or investment activity to which this prospectus supplement relates is available only to relevant persons and will only be engaged with relevant persons. Any person who is not a relevant person should not act or relay on this prospectus supplement or any of its contents.

*Canada*

The securities may be sold in Canada only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions, and Ongoing Registrant Obligations. Any resale of the securities must be made in accordance with an exemption form, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this offering memorandum (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

*Hong Kong*

The shares may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32 of the Laws of Hong Kong) ("Companies (Winding Up and Miscellaneous Provisions) Ordinance") or which do not constitute an invitation to the public within the meaning of the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) ("Securities and Futures Ordinance"), or (ii) to "professional investors" as defined in the Securities and Futures Ordinance and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance, and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to

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"professional investors" in Hong Kong as defined in the Securities and Futures Ordinance and any rules made thereunder.

*Singapore*

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor (as defined under Section 4A of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA")) under Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor, the securities (as defined in Section 239(1) of the SFA) of that corporation shall not be transferable for 6 months after that corporation has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer in that corporation's securities pursuant to Section 275(1A) of the SFA, (3) where no consideration is or will be given for the transfer,

1. where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore ("Regulation 32")

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a trust (where the trustee is not an accredited investor (as defined in Section 4A of the SFA)) whose sole purpose is to hold investments and each beneficiary of the trust is an accredited investor, the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferable for 6 months after that trust has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer that is made on terms that such rights or interest are acquired at a consideration of not less than S$200,000 (or its equivalent in a foreign currency) for each transaction (whether such amount is to be paid for in cash or by exchange of securities or other assets), (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32.

*Japan*

The securities have not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948, as amended), or the FIEA. The securities may not be offered or sold, directly or indirectly, in Japan or to or for the benefit of any resident of Japan (including any person resident in Japan or any corporation or other entity organized under the laws of Japan) or to others for reoffering or resale, directly or indirectly, in Japan or to or for the benefit of any resident of Japan, except pursuant to an exemption from the registration requirements of the FIEA and otherwise in compliance with any relevant laws and regulations of Japan.

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The Company estimates that its share of the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately $500,000. The underwriters have agreed to reimburse the Company for certain expenses in connection with the offering.

The Company has agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act of

1933.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to the issuer and to persons and entities with relationships with the issuer, for which they received or will receive customary fees and expenses including $350,000 paid to JMP Securities LLC in July, 2017 in its capacity as the Company's financial advisor.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to assets, securities and/or instruments of the issuer (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with the issuer. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

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**LEGAL MATTERS**

Certain legal matters will be passed upon for us by Stradling Yocca Carlson & Rauth, P.C., Newport Beach, California. Certain legal matters will be passed upon for the underwriters by Ropes & Gray LLP, Boston, Massachusetts.

**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 consolidated financial statements for the year ended December 31, 2015, incorporated in this prospectus by reference from the Company's Annual Report on Form 10-K for the year ended December 31, 2016 has been audited by Friedman LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference. Such financial statements and financial statement schedule have been so incorporated in reliance upon the reports of such firm given upon their authority as experts in accounting and auditing.

**WHERE YOU CAN FIND MORE INFORMATION**

This prospectus is part of a registration statement on Form S-3 that we filed with the SEC registering the securities that may be offered and sold hereunder. The registration statement, including exhibits thereto, contains additional relevant information about us and these securities that, as permitted by the rules and regulations of the SEC, we have not included in this prospectus. A copy of the registration statement can be obtained at the address set forth below. You should read the registration statement for further information about us and these securities.

We file annual, quarterly and special reports, proxy statements and other information with the SEC under the Exchange Act. You may read and copy this information at the following SEC location:

Public Reference Room

100 F Street, N.E.

Washington, D.C. 20549

You may obtain information on the operation of the Public Reference Room by calling the SEC at (800) SEC-0330. The SEC also maintains a web site that contains reports, proxy statements, information statements and other information about issuers, like Madrigal Pharmaceuticals, Inc., who file electronically with the SEC. The address of that web site is www.sec.gov.

In addition, our common stock is listed on The Nasdaq Global Market and similar information concerning us can be inspected and copied at the offices of The Nasdaq Stock Market, One Liberty Plaza, 165 Broadway, New York, NY 10006.

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**INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE**

This prospectus is part of a registration statement on Form S-3 filed by us with the SEC. This prospectus does not contain all of the information set forth in the registration statement, certain parts of which are omitted in accordance with the rules and regulations of the SEC. For further information about us and the securities offered by this prospectus, we refer you to the registration statement and its exhibits and schedules which may be obtained as described herein.

The SEC allows us to "incorporate by reference" information into this prospectus. This means that we can disclose important information about us and our financial condition to you by referring you to another document filed separately with the SEC. The information incorporated by reference is considered to be part of this prospectus. This prospectus incorporates by reference the documents listed below that we have previously filed with the SEC:

* Our Annual Report on Form 10-K for the fiscal year ended December 31, 2016, as filed with the SEC on March 31, 2017;
* Our Definitive Proxy Statement on Schedule 14A, as filed with the SEC on April 28, 2017;
* Our Quarterly Reports on Form 10-Q for the fiscal quarter ended March 31, 2017, as filed with the SEC on May 11, 2017, for the fiscal quarter ended June 30, 2017, as filed with the SEC on August 10, 2017, and for the fiscal quarter ended September 30, 2017, as filed with the SEC on November 9, 2017;
* Our Current Reports on Form 8-K, as filed with the SEC on March 31, 2017, June 1, 2017, June 21, 2017, and July 5, 2017;
* 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 into this prospectus all documents filed by us with the SEC pursuant to Sections 12(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of any offering of securities made by this prospectus. Nothing in this prospectus shall be deemed to incorporate information furnished but not filed with the SEC (including without limitation, information furnished under Item 2.02 or Item 7.01 of Form 8-K, and any exhibits relating to such information).

Any statement contained in this prospectus or in a document incorporated or deemed to be incorporated by reference in this prospectus shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained herein or in the applicable prospectus supplement or in any other subsequently filed document which also is or is deemed to be incorporated by reference modifies or supersedes the statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

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You may request a copy of the filings incorporated herein by reference, including exhibits to such documents that are specifically incorporated by reference, at no cost, by writing or calling us at the following address or telephone number:

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

Statements contained in this prospectus as to the contents of any contract or other documents are not necessarily complete, and in each instance investors are referred to the copy of the contract or other document filed as an exhibit to the registration statement, each such statement being qualified in all respects by such reference and the exhibits and schedules thereto.

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**PROSPECTUS**

**SYNTA PHARMACEUTICALS CORP.**

**$300,000,000**

**COMMON STOCK**

**PREFERRED STOCK**

**DEBT SECURITIES**

**WARRANTS**

**RIGHTS**

**PURCHASE CONTRACTS**

**UNITS**



This prospectus will allow us to issue, from time to time at prices and on terms to be determined at or prior to the time of the offering, up to $300,000,000 of any combination of the securities described in this prospectus, either individually or in units. We may also offer common stock or preferred stock upon conversion of or exchange for the debt securities; common stock upon conversion of or exchange for the preferred stock; common stock, preferred stock or debt securities upon the exercise of warrants, rights or performance of purchase contracts; or any combination of these securities upon the performance of purchase contracts.

This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide you with the specific terms of any offering in one or more supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus and any prospectus supplement, as well as any documents incorporated by reference into this prospectus or any prospectus supplement, carefully before you invest.

Our securities may be sold directly by us to you, through agents designated from time to time or to or through underwriters or dealers. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus and in the applicable prospectus supplement. If any underwriters or agents are involved in the sale of our securities with respect to which this prospectus is being delivered, the names of such underwriters or agents and any applicable fees, commissions or discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds that we expect to receive from such sale will also be set forth in a prospectus supplement.



Our common stock is listed on The NASDAQ Global Market under the symbol "SNTA." On October 15, 2015, the last reported sale price of our common stock was $2.04 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on The NASDAQ Global Market or any securities market or other securities exchange of the securities covered by the prospectus supplement. Prospective purchasers of our securities are urged to obtain current information as to the market prices of our securities, where applicable.



**Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks that we have described on page 3 of this prospectus under the caption "Risk Factors." We may include specific risk factors in supplements to this prospectus under the caption "Risk Factors." This prospectus may not be used to sell our securities unless accompanied by a prospectus supplement.**



**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.**



The date of this prospectus is October 16, 2015.



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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 SEC, utilizing a "shelf" registration process. Under this shelf registration process, we may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants, rights or purchase contracts to purchase any of such securities, either individually or in units, in one or more offerings, with a total value of up to $300,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering.

This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits. The prospectus supplement may also add, update or change information contained or incorporated by reference in this prospectus. However, no prospectus supplement will offer a security that is not registered and described in this prospectus at the time of its effectiveness. This prospectus, together with the applicable prospectus supplements and the documents incorporated by reference into this prospectus, includes all material information relating to the offering of securities under this prospectus. You should carefully read this prospectus, the applicable prospectus supplement, the information and documents incorporated herein by reference and the additional information under the heading "Where You Can Find More Information" before making an investment decision.

You should rely only on the information we have provided or incorporated by reference in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained or incorporated by reference in this prospectus. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus or any prospectus supplement is accurate only as of the date on the front of the document and that any information we have incorporated herein by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any sale of a security.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

This prospectus may not be used to consummate sales of our securities, unless it is accompanied by a prospectus supplement. To the extent there are inconsistencies between any prospectus supplement, this prospectus and any documents incorporated by reference, the document with the most recent date will control.

Unless the context otherwise requires, "Synta," "the Company," "we," "us," "our" and similar terms refer to Synta Pharmaceuticals Corp. and our subsidiaries.

Our trademarks include, without limitation, Synta Pharmaceuticals, our corporate logo and the GALAXY trial. Other service marks, trademarks and trade names contained in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference herein and therein are the property of their respective owners.



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**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 securities under this prospectus. We urge you to read this entire prospectus, including the more detailed consolidated financial statements, notes to the consolidated financial statements and other information incorporated by reference from our other filings with the SEC or included in any applicable prospectus supplement. Investing in our securities involves risks. Therefore, carefully consider the risk factors set forth in any prospectus supplements and in our most recent annual and quarterly filings with the SEC, as well as other information in this prospectus and any prospectus supplements and the documents incorporated by reference herein or therein, before purchasing our securities. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities.*

**About Synta Pharmaceuticals Corp.**

We are an innovative, agile biopharmaceutical company focused on research, development and commercialization of novel oncology medicines that have the potential to change the lives of cancer patients. Our lead oncology drug candidate, ganetespib, a novel heat shock protein 90 (Hsp90) inhibitor, is currently being evaluated in several large randomized clinical trials including GALAXY-2, a pivotal Phase 3 trial in non-small cell lung cancer (NSCLC), as well as breast cancer, ovarian cancer and acute myeloid leukemia (AML). We are also evaluating several candidates from our proprietary Hsp90 inhibitor Drug Conjugate program (HDC Program), which leverages the preferential accumulation of Hsp90 inhibitors in tumors to selectively deliver a wide array of anti-cancer payloads. Our first clinical candidate from our HDC Program, STA-12-8666, is undergoing testing to enable the filing of an investigational new drug application (IND). Preclinical evaluation of additional HDC candidates is ongoing. We also have an additional clinical-stage oncology candidate: elesclomol, a mitochondrial metabolism inhibitor.

We believe that the broad clinical and commercial potential of our drug candidates, together with our operational capabilities and additional competitive advantages, provide us with multiple, sustainable growth opportunities. Our capabilities and advantages include: our intellectual property portfolio; the full ownership of all commercial rights in all geographic regions to our programs; our ability to integrate discovery, translational, and clinical research to optimize our development programs and further strengthen our intellectual property position; our operational experience in effectively managing large-scale, global clinical programs; our strong network of relationships with leading investigators and medical centers; our proprietary chemical compound library and the strength of our drug discovery platform; and the skills, talent, and degree of industry experience of our employees.

**Additional Information**

We commenced operations in July 2001. In September 2002, we acquired Principia Associates, Inc., which had previously acquired Shionogi BioResearch Corp., a U.S.-based drug discovery subsidiary of the Japanese pharmaceutical company, Shionogi & Co., Ltd. In this acquisition, we acquired a unique chemical compound library, an integrated set of drug discovery capabilities, and a pipeline of preclinical and research programs. Since 2002, we have been advancing these programs into later stages of development, discovering and developing additional drug candidates and expanding our management and scientific teams and capabilities to support more advanced stages of drug development and commercialization.

Our principal executive offices are located at 45 Hartwell Avenue, Lexington, Massachusetts 02421, and our telephone number is (781) 274-8200. Our website address is *www.syntapharma.com*. The information contained on our website is not incorporated by reference into, and does not form any part of, this prospectus. We have included our website address as a factual reference and do not intend it to

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be an active link to our website. Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports, are available free of charge through the "Investors—SEC Filings" section of our website as soon as reasonably practicable after such materials have been electronically filed with, or furnished to, the SEC.

**Offerings Under This Prospectus**

Under this prospectus, we may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants, rights or purchase contracts to purchase any of such securities, either individually or in units, with a total value of up to $300,000,000, from time to time at prices and on terms to be determined by market conditions at the time of the offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

* designation or classification;
* aggregate principal amount or aggregate offering price;
* maturity, if applicable;
* rates and times of payment of interest or dividends, if any;
* redemption, conversion or sinking fund terms, if any;
* voting or other rights, if any; and
* conversion or exercise prices, if any.

The prospectus supplement also may add, update or change information contained in this prospectus or in documents we have incorporated by reference into this prospectus. However, no prospectus supplement will offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We may sell the securities directly to investors or to or through agents, underwriters or dealers. We, and our agents or underwriters, reserve the right to accept or reject all or part of any proposed purchase of securities. If we offer securities through agents or underwriters, we will include in the applicable prospectus supplement:

* the names of those agents or underwriters;
* applicable fees, discounts and commissions to be paid to them;
* details regarding over-allotment options, if any; and
* the net proceeds to us.

**This prospectus may not be used to consummate a sale of any securities unless it is accompanied by a prospectus supplement.**

**RISK FACTORS**

Investing in our securities involves significant risk. The prospectus supplement applicable to each offering of our securities may contain a discussion of the risks applicable to an investment in Synta. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading "Risk Factors" in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under the heading "Risk Factors" included in our most recent

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annual report on Form 10-K, as revised or supplemented by our subsequent quarterly reports on Form 10-Q or our current reports on Form 8-K on file with the SEC, all of which are incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations.

**RATIO OF EARNINGS TO FIXED CHARGES**

Any time debt securities are offered pursuant to this prospectus, we will provide a table setting forth our ratio of earnings to fixed charges on a historical basis in the applicable prospectus supplement, if required.

**SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS**

The SEC encourages companies to disclose forward-looking information so that investors can better understand a company's future prospects and make informed investment decisions. This prospectus and the documents we have filed with the SEC that are incorporated herein by reference contain such "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995.

Such statements in connection with any discussion of future operations or financial performance are identified by the use of words such as "may," "anticipate," "estimate," "expect," "project," "intend," "plan," "believe," and other words and terms of similar meaning. Such statements are based on management's expectations and are subject to certain factors, risks and uncertainties that may cause actual results, outcome of events, timing and performance to differ materially from those expressed or implied by such statements. These risks and uncertainties include, but are not limited to, the risk that we may be unable to develop and achieve commercial success for our drug candidates; the risk that we may be unable to discover drugs that are safer and more efficacious than our competitors; the risk that we may be unable to establish and maintain manufacturing arrangements for our products; the possibility of delays in the research and development necessary to select drug development candidates and delays in clinical trials; the risk that clinical trials may not result in marketable products; the risk that we may be unable to successfully finance and secure regulatory approval of and market our drug candidates, or that clinical trials will not be completed on the timelines we have estimated; uncertainties about our ability to obtain new corporate collaborations and acquire new technologies on satisfactory terms, if at all; the development of competing products; the risk that we may be unable to protect our proprietary technologies; the risk of patent-infringement claims; risks of new, changing and competitive technologies and regulations in the United States and internationally; and other factors detailed under the heading "Risk Factors" in this prospectus as updated and supplemented by the discussion of risks and uncertainties under "Risk Factors" contained in any supplements to this prospectus and in our most recent annual report on Form 10-K, as revised or supplemented by our subsequent quarterly reports on Form 10-Q or our current reports on Form 8-K, as well as any amendments thereto, as filed with the SEC and which are incorporated herein by reference. The information contained in this document is believed to be current as of the date of this document. We do not intend to update any of the forward-looking statements after the date of this document to conform these statements to actual results or to changes in our expectations, except as required by law.

In light of these assumptions, risks and uncertainties, the results and events discussed in the forward-looking statements contained in this prospectus or in any document incorporated herein by reference might not occur. Investors are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date of this prospectus or the date of the document incorporated by reference in this prospectus. We are not under any obligation, and we expressly disclaim any obligation, to update or alter any forward-looking statements, whether as a result of new

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information, future events or otherwise. All subsequent forward-looking statements attributable to us or to any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

**USE OF PROCEEDS**

We cannot assure you that we will receive any proceeds in connection with securities which may be offered pursuant to this prospectus. Unless otherwise indicated in the applicable prospectus supplement, we intend to use any net proceeds from the sale of securities under this prospectus for our operations and for other general corporate purposes, including, but not limited to, repayment or refinancing of existing indebtedness or other corporate borrowings, working capital, intellectual property protection and enforcement, capital expenditures, investments, acquisitions or collaborations, repurchases and redemption of our securities, research and development and product development. We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds, if any, we receive in connection with securities offered pursuant to this prospectus for any purpose. Pending application of the net proceeds as described above, we may initially invest the net proceeds in short-term, investment-grade, interest-bearing securities or apply them to the reduction of short-term indebtedness.

**PLAN OF DISTRIBUTION**

We may offer securities under this prospectus from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities (1) through underwriters or dealers, (2) through agents or (3) directly to one or more purchasers, or through a combination of such methods. We may distribute the securities from time to time in one or more transactions at:

* a fixed price or prices, which may be changed from time to time;
* market prices prevailing at the time of sale;
* prices related to the prevailing market prices; or
* negotiated prices.

We may directly solicit offers to purchase the securities being offered by this prospectus. We may also designate agents to solicit offers to purchase the securities from time to time. We will name in a prospectus supplement any underwriter or agent involved in the offer or sale of the securities.

If we utilize a dealer in the sale of the securities being offered by this prospectus, we will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If we utilize an underwriter in the sale of the securities being offered by this prospectus, we will execute an underwriting agreement with the underwriter at the time of sale, and we will provide the name of any underwriter in the prospectus supplement which the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we, or the purchasers of the securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and the underwriter may compensate those dealers in the form of discounts, concessions or commissions.

With respect to underwritten public offerings, negotiated transactions and block trades, we will provide in the applicable prospectus supplement information regarding any compensation we pay to underwriters, dealers or agents in connection with the offering of the securities, and any discounts,

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concessions or commissions allowed by underwriters to participating dealers. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act of 1933, as amended, or the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

* the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and
* if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Shares of our common stock sold pursuant to the registration statement of which this prospectus is a part will be authorized for quotation and trading on The NASDAQ Global Market. The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on The NASDAQ Global Market or any securities market or other securities exchange of the securities covered by the prospectus supplement. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

In order to facilitate the offering of the securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than we sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing the applicable security in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if the securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

In compliance with the guidelines of the Financial Industry Regulatory Authority, Inc., or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

The underwriters, dealers and agents may engage in other transactions with us, or perform other services for us, in the ordinary course of their business.

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**DESCRIPTION OF COMMON STOCK**

We are authorized to issue 200,000,000 shares of common stock, par value $0.0001 per share. On August 3, 2015, we had 136,442,378 shares of common stock outstanding and approximately 50 stockholders of record.

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 are included as exhibits to the registration statement of which this prospectus is a part. 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. All shares of common stock outstanding as of the date of this prospectus and, upon issuance and sale, all shares of common stock that we may offer pursuant to this prospectus, will be fully paid and nonassessable. 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 "SNTA."

**DESCRIPTION OF PREFERRED STOCK**

We are authorized to issue 5,000,000 shares of preferred stock, par value $0.0001 per share. As of August 3, 2015, no 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 and our restated bylaws, both of which are included as exhibits to the registration statement of which this prospectus is a part. 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

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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.

If we offer a specific series of preferred stock under this prospectus, we will describe the terms of the preferred stock in the prospectus supplement for such offering and will file a copy of the certificate establishing the terms of the preferred stock with the SEC. To the extent required, this description will include:

* the title and stated value;
* the number of shares offered, the liquidation preference, if any, per share and the purchase price;
* the dividend rate(s), period(s) and/or payment date(s), or method(s) of calculation for such dividends;
* whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
* the procedures for any auction and remarketing, if any;
* the provisions for a sinking fund, if any;
* the provisions for redemption, if applicable;
* any listing of the preferred stock on any securities exchange or market;
* whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price (or how it will be calculated) and conversion period;
* whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price (or how it will be calculated) and exchange period;
* voting rights, if any, of the preferred stock;
* a discussion of any material and/or special U.S. federal income tax considerations applicable to the preferred stock;
* the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the affairs of Synta; and
* any material limitations on issuance of any class or series of preferred stock ranking pari passu with or senior to the series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of Synta.

**Transfer Agent and Registrar**

The transfer agent and registrar for our preferred stock will be set forth in the applicable prospectus supplement.

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**DESCRIPTION OF DEBT SECURITIES**

The following description, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus. While the terms we have summarized below will apply generally to any future debt securities we may offer pursuant to this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. If we so indicate in a prospectus supplement, the terms of any debt securities offered under such prospectus supplement may differ from the terms we describe below, and to the extent the terms set forth in a prospectus supplement differ from the terms described below, the terms set forth in the prospectus supplement shall control.

We may sell from time to time, in one or more offerings under this prospectus, debt securities, which may be senior or subordinated. We will issue any such senior debt securities under a senior indenture that we will enter into with a trustee to be named in the senior indenture. We will issue any such subordinated debt securities under a subordinated indenture, which we will enter into with a trustee to be named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement, of which this prospectus is a part. We use the term "indentures" to refer to either the senior indenture or the subordinated indenture, as applicable. The indentures will be qualified under the Trust Indenture Act of 1939, as in effect on the date of the indenture. We use the term "debenture trustee" to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all the provisions of the indenture applicable to a particular series of debt securities.

**General**

Each indenture provides that debt securities may be issued from time to time in one or more series and may be denominated and payable in foreign currencies or units based on or relating to foreign currencies. Neither indenture limits the amount of debt securities that may be issued thereunder, and each indenture provides that the specific terms of any series of debt securities shall be set forth in, or determined pursuant to, an authorizing resolution and/or a supplemental indenture, if any, relating to such series.

We will describe in each prospectus supplement the following terms relating to a series of debt securities:

* the title or designation;
* the aggregate principal amount and any limit on the amount that may be issued;
* the currency or units based on or relating to currencies in which debt securities of such series are denominated and the currency or units in which principal or interest or both will or may be payable;
* whether we will issue the series of debt securities in global form, the terms of any global securities and who the depositary will be;
* the maturity date and the date or dates on which principal will be payable;
* the interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the date or dates interest will be payable and the record dates for interest payment dates or the method for determining such dates;

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* whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
* the terms of the subordination of any series of subordinated debt;
* the place or places where payments will be payable;
* our right, if any, to defer payment of interest and the maximum length of any such deferral period;
* the date, if any, after which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional redemption provisions;
* the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities;
* whether the indenture will restrict our ability to pay dividends, or will require us to maintain any asset ratios or reserves;
* whether we will be restricted from incurring any additional indebtedness;
* a discussion on any material or special U.S. federal income tax considerations applicable to a series of debt securities;
* the denominations in which we will issue the series of debt securities, if other than denominations of $1,000 and any integral multiple thereof; and
* any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities.

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

**Conversion or Exchange Rights**

We will set forth in the prospectus supplement the terms, if any, on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

**Consolidation, Merger or Sale; No Protection in Event of a Change of Control or Highly Leveraged Transaction**

The indentures do not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate.

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions that may afford holders of the debt securities protection in the event we have a change of control or in the event of a highly leveraged transaction (whether or not such transaction results in a change of control), which could adversely affect holders of debt securities.

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**Events of Default Under the Indenture**

The following are events of default under the indentures with respect to any series of debt securities that we may issue:

* if we fail to pay interest when due and our failure continues for 90 days and the time for payment has not been extended or deferred;
* if we fail to pay the principal, or premium, if any, when due and the time for payment has not been extended or delayed;
* if we fail to observe or perform any other covenant set forth in the debt securities of such series or the applicable indentures, other than a covenant specifically relating to and for the benefit of holders of another series of debt securities, and our failure continues for 90 days after we receive written notice from the debenture trustee or holders of not less than a majority in aggregate principal amount of the outstanding debt securities of the applicable series; and
* if specified events of bankruptcy, insolvency or reorganization occur as to us.

No event of default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an event of default with respect to any other series of debt securities. The occurrence of an event of default may constitute an event of default under any bank credit agreements we may have in existence from time to time. In addition, the occurrence of certain events of default or an acceleration under the indenture may constitute an event of default under certain of our other indebtedness outstanding from time to time.

If an event of default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than a majority in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the debenture trustee if given by the holders), declare to be due and payable immediately the principal (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) of and premium and accrued and unpaid interest, if any, on all debt securities of that series. Before a judgment or decree for payment of the money due has been obtained with respect to debt securities of any series, the holders of a majority in principal amount of the outstanding debt securities of that series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) may rescind and annul the acceleration if all events of default, other than the non-payment of accelerated principal, premium, if any, and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the applicable indenture (including payments or deposits in respect of principal, premium or interest that had become due other than as a result of such acceleration). We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the debenture trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the debenture trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the debenture trustee, or exercising any trust or power conferred on the debenture trustee, with respect to the debt securities of that series, provided that:

* the direction so given by the holder is not in conflict with any law or the applicable indenture; and 11



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* subject to its duties under the Trust Indenture Act, the debenture trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will only have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies if:

* the holder previously has given written notice to the debenture trustee of a continuing event of default with respect to that series;
* the holders of at least a majority in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the debenture trustee to institute the proceeding as trustee; and
* the debenture trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series (or at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) other conflicting directions within 60 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the applicable debenture trustee regarding our compliance with specified covenants in the applicable indenture.

**Modification of Indenture; Waiver**

The debenture trustee and we may change the applicable indenture without the consent of any holders with respect to specific matters, including:

* to fix any ambiguity, defect or inconsistency in the indenture; and
* to change anything that does not materially adversely affect the interests of any holder of debt securities of any series issued pursuant to such indenture.

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the debenture trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) that is affected. However, the debenture trustee and we may make the following changes only with the consent of each holder of any outstanding debt securities affected:

* extending the fixed maturity of the series of debt securities;
* reducing the principal amount, reducing the rate of or extending the time of payment of interest, or any premium payable upon the redemption of any debt securities;
* reducing the principal amount of discount securities payable upon acceleration of maturity;
* making the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security; or
* reducing the percentage of debt securities, the holders of which are required to consent to any amendment or waiver.

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series (or, at a meeting of holders of such series at which a quorum

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is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series or in respect of a covenant or provision, which cannot be modified or amended without the consent of the holder of each outstanding debt security of the series affected; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration.

**Discharge**

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for obligations

to:

* register the transfer or exchange of debt securities of the series;
* replace stolen, lost or mutilated debt securities of the series;
* maintain paying agencies;
* hold monies for payment in trust;
* compensate and indemnify the trustee; and
* appoint any successor trustee.

In order to exercise our rights to be discharged with respect to a series, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, the premium, if any, and interest on, the debt securities of the series on the dates payments are due.

**Form, Exchange, and Transfer**

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of $1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depositary named by us and identified in a prospectus supplement with respect to that series.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange or in the applicable indenture, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

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We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

* issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
* register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

**Information Concerning the Debenture Trustee**

The debenture trustee, other than during the occurrence and continuance of an event of default under the applicable indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the debenture trustee under such indenture must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the debenture trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

**Payment and Paying Agents**

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, will we make interest payments by check which we will mail to the holder. Unless we otherwise indicate in a prospectus supplement, we will designate the corporate trust office of the debenture trustee in the City of New York as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the debenture trustee for the payment of the principal of or any premium or interest on any debt securities which remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the security thereafter may look only to us for payment thereof.

**Governing Law**

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

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**Subordination of Subordinated Debt Securities**

Our obligations pursuant to any subordinated debt securities will be unsecured and will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of senior indebtedness we may incur. It also does not limit us from issuing any other secured or unsecured debt.

**DESCRIPTION OF WARRANTS**

**General**

We may issue warrants to purchase shares of our common stock, preferred stock and/or debt securities in one or more series together with other securities or separately, as described in the applicable prospectus supplement. Below is a description of certain general terms and provisions of the warrants that we may offer. Particular terms of the warrants will be described in the warrant agreements and the prospectus supplement relating to the warrants.

The applicable prospectus supplement will contain, where applicable, the following terms of and other information relating to the warrants:

* the specific designation and aggregate number of, and the price at which we will issue, the warrants;
* the currency or currency units in which the offering price, if any, and the exercise price are payable;
* the designation, amount and terms of the securities purchasable upon exercise of the warrants;
* if applicable, the exercise price for shares of our common stock and the number of shares of common stock to be received upon exercise of the warrants;
* if applicable, the exercise price for shares of our preferred stock, the number of shares of preferred stock to be received upon exercise, and a description of that series of our preferred stock;
* if applicable, the exercise price for our debt securities, the amount of debt securities to be received upon exercise, and a description of that series of debt securities;
* the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
* whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
* any applicable material U.S. federal income tax consequences;
* the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
* the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
* if applicable, the date from and after which the warrants and the common stock, preferred stock and/or debt securities will be separately transferable;

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* if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
* information with respect to book-entry procedures, if any;
* the anti-dilution provisions of the warrants, if any;
* any redemption or call provisions;
* whether the warrants may be sold separately or with other securities as parts of units; and
* any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

**Transfer Agent and Registrar**

The transfer agent and registrar for any warrants will be set forth in the applicable prospectus supplement.

**DESCRIPTION OF RIGHTS**

**General**

We may issue rights to our stockholders to purchase shares of our common stock, preferred stock or the other securities described in this prospectus. We may offer rights separately or together with one or more additional rights, debt securities, preferred stock, common stock, warrants or purchase contracts, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. Each series of rights will be issued under a separate rights agreement to be entered into between us and a bank or trust company, as rights agent. The rights agent will act solely as our agent in connection with the certificates relating to the rights of the series of certificates and will not assume any obligation or relationship of agency or trust for or with any holders of rights certificates or beneficial owners of rights. The following description sets forth certain general terms and provisions of the rights to which any prospectus supplement may relate. The particular terms of the rights to which any prospectus supplement may relate and the extent, if any, to which the general provisions may apply to the rights so offered will be described in the applicable prospectus supplement. To the extent that any particular terms of the rights, rights agreement or rights certificates described in a prospectus supplement differ from any of the terms described below, then the terms described below will be deemed to have been superseded by that prospectus supplement. We encourage you to read the applicable rights agreement and rights certificate for additional information before you decide whether to purchase any of our rights.

We will provide in a prospectus supplement the following terms of the rights being issued:

* the date of determining the stockholders entitled to the rights distribution;
* the aggregate number of shares of common stock, preferred stock or other securities purchasable upon exercise of the rights;
* the exercise price;
* the aggregate number of rights issued;
* whether the rights are transferrable and the date, if any, on and after which the rights may be separately transferred;
* the date on which the right to exercise the rights will commence, and the date on which the right to exercise the rights will expire;
* the method by which holders of rights will be entitled to exercise;

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* the conditions to the completion of the offering, if any;
* the withdrawal, termination and cancellation rights, if any;
* whether there are any backstop or standby purchaser or purchasers and the terms of their commitment, if any;
* whether stockholders are entitled to oversubscription rights, if any;
* any applicable U.S. federal income tax considerations; and
* any other terms of the rights, including terms, procedures and limitations relating to the distribution, exchange and exercise of the rights, as applicable.

Each right will entitle the holder of rights to purchase for cash the principal amount of shares of common stock, preferred stock or other securities at the exercise price provided in the applicable prospectus supplement. Rights may be exercised at any time up to the close of business on the expiration date for the rights provided in the applicable prospectus supplement.

Holders may exercise rights as described in the applicable prospectus supplement. Upon receipt of payment and the rights certificate properly completed and duly executed at the corporate trust office of the rights agent or any other office indicated in the prospectus supplement, we will, as soon as practicable, forward the shares of common stock, preferred stock or other securities, as applicable, purchasable upon exercise of the rights. If less than all of the rights issued in any rights offering are exercised, we may offer any unsubscribed securities directly to persons other than stockholders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby arrangements, as described in the applicable prospectus supplement.

**Rights Agent**

The rights agent for any rights we offer will be set forth in the applicable prospectus supplement.

**DESCRIPTION OF PURCHASE CONTRACTS**

We may issue purchase contracts, including contracts obligating holders to purchase from us, and for us to sell to holders, a specific or variable number of our debt securities, shares of common stock, preferred stock, warrants or rights, or securities of an entity unaffiliated with us, or any combination of the above, at a future date or dates. Alternatively, the purchase contracts may obligate us to purchase from holders, and obligate holders to sell to us, a specific or variable number of our debt securities, shares of common stock, preferred stock, warrants, rights or other property, or any combination of the above. The price of the securities or other property subject to the purchase contracts may be fixed at the time the purchase contracts are issued or may be determined by reference to a specific formula described in the purchase contracts. We may issue purchase contracts separately or as a part of units each consisting of a purchase contract and one or more of our other securities described in this prospectus or securities of third parties, including U.S. Treasury securities, securing the holder's obligations under the purchase contract. The purchase contracts may require us to make periodic payments to holders or vice versa and the payments may be unsecured or pre-funded on some basis. The purchase contracts may require holders to secure the holder's obligations in a manner specified in the applicable prospectus supplement.

The applicable prospectus supplement will describe the terms of any purchase contracts in respect of which this prospectus is being delivered, including, to the extent applicable, the following:

* whether the purchase contracts obligate the holder or us to purchase or sell, or both purchase and sell, the securities subject to purchase under the purchase contract, and the nature and amount of each of those securities, or the method of determining those amounts;

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* whether the purchase contracts are to be prepaid;
* whether the purchase contracts are to be settled by delivery, or by reference or linkage to the value, performance or level of the securities subject to purchase under the purchase contract;
* any acceleration, cancellation, termination or other provisions relating to the settlement of the purchase contracts;
* any applicable U.S. federal income tax considerations; and
* whether the purchase contracts will be issued in fully registered or global form.

The preceding description sets forth certain general terms and provisions of the purchase contracts to which any prospectus supplement may relate. The particular terms of the purchase contracts to which any prospectus supplement may relate and the extent, if any, to which the general provisions may apply to the purchase contracts so offered will be described in the applicable prospectus supplement. To the extent that any particular terms of the purchase contracts described in a prospectus supplement differ from any of the terms described above, then the terms described above will be deemed to have been superseded by that prospectus supplement. We encourage you to read the applicable purchase contract for additional information before you decide whether to purchase any of our purchase contracts.

**DESCRIPTION OF UNITS**

The following description, together with the additional information that we include in any applicable prospectus supplements summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms we have summarized below will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below.

We will incorporate by reference from reports that we file with the SEC, the form of unit agreement that describes the terms of the series of units we are offering, and any supplemental agreements, before the issuance of the related series of units. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the particular series of units that we may offer under this prospectus, as well as any related free writing prospectuses and the complete unit agreement and any supplemental agreements that contain the terms of the units.

**General**

We may issue units consisting of common stock, preferred stock, one or more debt securities, warrants, rights or purchase contacts for the purchase of common stock, preferred stock and/or debt securities in one or more series, in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each security included in the unit. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units being offered, including:

* the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;

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* any provisions of the governing unit agreement that differ from those described below; and
* any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those set forth in any prospectus supplement or as described under "Description of Common Stock," "Description of Preferred Stock," "Description of Debt Securities," "Description of Warrants," "Description of Rights," "Description of Purchase Contracts" and "Description of Units" will apply to each unit, as applicable, and to any common stock, preferred stock, debt security, warrant, right or purchase contract included in each unit, as applicable.

**Unit Agent**

The name and address of the unit agent for any units we offer will be set forth in the applicable prospectus supplement.

**Issuance in Series**

We may issue units in such amounts and in such numerous distinct series as we determine.

**Enforceability of Rights by Holders of Units**

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of the related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

**CERTAIN PROVISIONS OF DELAWARE LAW AND OF THE COMPANY'S CERTIFICATE OF INCORPORATION AND BYLAWS**

**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 ofdirectors to be divided into three classes serving staggered terms. At each annual meeting of stockholders, directors elected to succeed those directors whose terms expire 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

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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 broughtbefore 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 amajority 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 writtenconsent. 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 provides generally that the affirmative vote of amajority 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.

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**Provisions of Delaware Law Governing Business Combinations**

We are subject to the "business combination" provisions of Section 203 of the Delaware General Corporation Law. 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;
* 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 662/3% 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.

**Limitations on Liability and Indemnification of Officers and Directors**

Our restated certificate of incorporation limits the liability of our officers and directors to the fullest extent permitted by the Delaware General Corporation Law, and our restated certificate of incorporation and restated bylaws provide that we will indemnify our officers and directors to the fullest extent permitted by such law. We have also entered into indemnification agreements with our officers and directors and expect to enter into a similar agreement with any new officers and directors.

**LEGAL MATTERS**

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts, will pass upon the validity of the issuance of the securities offered by this prospectus.

**EXPERTS**

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2014, and the effectiveness of our internal control over financial reporting as of December 31, 2014, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

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**WHERE YOU CAN FIND MORE INFORMATION**

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference facilities at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference facilities. SEC filings are also available at the SEC's web site at *http://www.sec.gov.* Our common stock is listed on The NASDAQ Global Market, and you can read and inspect our filings at the offices of the Financial Industry Regulatory Authority at 1735 K Street, Washington, D.C. 20006.

This prospectus is only part of a registration statement on Form S-3 that we have filed with the SEC under the Securities Act of 1933, as amended, and therefore omits certain information contained in the registration statement. We have also filed exhibits and schedules with the registration statement that are excluded from this prospectus, and you should refer to the applicable exhibit or schedule for a complete description of any statement referring to any contract or other document. You may inspect a copy of the registration statement, including the exhibits and schedules, without charge, at the public reference room or obtain a copy from the SEC upon payment of the fees prescribed by the SEC.

We also maintain a website at *www.syntapharma.com*, through which you can access our SEC filings. The information set forth on our website is not part of this prospectus.

**INCORPORATION OF DOCUMENTS BY REFERENCE**

The SEC allows us to "incorporate by reference" information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. We filed a registration statement on Form S-3 under the Securities Act of 1933, as amended, with the SEC with respect to the securities we may offer pursuant to this prospectus. This prospectus omits certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement, including the exhibits, for further information about us and the securities we may offer pursuant to this prospectus. Statements in this prospectus regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in "Where You Can Find More Information." The documents we are incorporating by reference are:

* our Annual Report on Form 10-K for the year ended December 31, 2014 filed on March 12, 2015;
* our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2015 and June 30, 2015 filed on May 7, 2015 and August 6, 2015, respectively;
* our Current Reports on Form 8-K filed on February 5, 2015, March 6, 2015, April 1, 2015, April 6, 2015, April 27, 2015 and June 15, 2015;
* the portions of our Definitive Proxy Statement on Schedule 14A filed on April 30, 2015 that are deemed "filed" with the SEC under the Exchange Act;
* the description of our common stock contained in our Registration Statement on Form 8-A filed on January 26, 2007, including any amendment or report filed for the purpose of updating such description; and

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* all reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the date of this prospectus and prior to the termination or completion of the offering of securities under this prospectus shall be deemed to be incorporated by reference in this prospectus and to be a part hereof from the date of filing such reports and other documents.

The SEC file number for each of the documents listed above is 001-33277.

Any statement contained in this prospectus or in a document incorporated or deemed to be incorporated by reference into this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

You may request, orally or in writing, a copy of any or all of the documents incorporated herein by reference. These documents will be provided to you at no cost, by contacting: Investor Relations, Synta Pharmaceuticals Corp., 45 Hartwell Avenue, Lexington, MA 02421, (781) 274-8200.

You should rely only on information contained in, or incorporated by reference into, this prospectus and any prospectus supplement. We have not authorized anyone to provide you with information different from that contained in this prospectus or incorporated by reference in this prospectus. We are not making offers to sell the securities in any jurisdiction in which such an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make such offer or solicitation.

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1,506,025 Shares



Common Stock



**PROSPECTUS SUPPLEMENT**

**December 18, 2017**



**Goldman Sachs & Co. LLC**

**Evercore ISI**

**JMP Securities**

**Roth Capital Partners**

**H.C. Wainwright & Co.**



**We have not authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement and accompanying prospectus or any free writing prospectus that we or the underwriters provide you in connection with the offering. We take no responsibility for, and cannot provide any assurance as to the reliability of, any other information that others may give you. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information contained in or incorporated by reference in this prospectus supplement and accompanying prospectus is accurate as of any date other than the date on the front of this prospectus supplement.**

**No action is being taken in any jurisdiction outside the United States to permit a public offering of shares of our common stock or possession or distribution of this prospectus supplement in that jurisdiction. Persons who come into possession of this prospectus supplement in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus supplement applicable to that jurisdiction.**

