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MIRNA THERAPEUTICS, INC. Index to Financial Statements

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Confidential Draft Submission Amendment No. 4 submitted to the Securities and Exchange Commission on July 15, 2015.
This draft registration statement has not been filed publicly with the Securities and Exchange Commission and all information contained herein remains confidential.

Registration No. 333-

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

AMENDMENT NO. 4 TO
FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

Mirna Therapeutics, Inc.
(Exact name of Registrant as specified in its charter)

Delaware	**2834**	**26-1824804**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

2150 Woodward Street, Suite 100
Austin, TX 78744
(512) 901-0900
(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Paul Lammers, M.D., M.Sc.
President & Chief Executive Officer
Mirna Therapeutics, Inc.
2150 Woodward Street, Suite 100
Austin, TX 78744
(512) 901-0900
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Alan C. Mendelson, Esq. **Mark V. Roeder, Esq.** **Latham & Watkins LLP** **140 Scott Drive** **Menlo Park, CA 94025** **Telephone: (650) 328-4600** **Facsimile: (650) 463-2600**	**Scott D. Elliott, Esq.** **Patrick O'Brien, Esq.** **Ropes & Gray LLP** **3 Embarcadero Center** **San Francisco, CA 94111** **Telephone: (415) 315-6300** **Facsimile: (415) 315-6350**

Approximate date of commencement of proposed sale to the public:
As soon as practicable after the effective date of this Registration Statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. o

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

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

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

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

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

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Proposed maximum aggregate offering price(1)	Amount of registration fee(1)
Common Stock, $0.001 par value per share	$	$

(1) Estimated solely for the purpose of calculating the amount of the registration fee in accordance with Rule 457(o) under the Securities Act of 1933, as amended. Includes shares that the underwriters have the option to purchase.

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

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Subject to completion, dated , 2015

PRELIMINARY PROSPECTUS

Shares

MIRNA THERAPEUTICS™

Common Stock

Mirna Therapeutics, Inc. is offering shares of common stock. This is our initial public offering and no public market currently exists for our shares. We have applied to list our common stock on The NASDAQ Global Market under the symbol "MIRN." We expect that the initial public offering price will be between $ and $ per share.

We are an "emerging growth company" as that term is defined under the federal securities laws and, as such, may elect to comply with certain reduced public company reporting requirements for this and future filings.

Investing in our common stock involves a high degree of risk. Before buying any shares, you should read carefully the discussion of the material risks of investing in our common stock under the heading "Risk Factors" starting on page 11 of this prospectus.

	Per share	Total
Public offering price	$	$
Underwriting discounts(1)	$	$
Proceeds, before expenses, to Mirna Therapeutics, Inc.	$	$

(1) See "Underwriting" for additional information regarding total underwriting compensation.

We have granted the underwriters the right to purchase up to additional shares of common stock. The underwriters can exercise this right at any time within 30 days after the date of this prospectus.

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 underwriters expect to deliver the shares of common stock to investors on or about , 2015.

Citigroup **Leerink Partners**

The date of this prospectus is , 2015.

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We are responsible for the information contained in this prospectus. Neither we nor the underwriters have authorized anyone to provide you with information that is different from that contained in this prospectus or in any free writing prospectus we may authorize to be delivered or made available to you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are offering to sell shares of common stock and seeking offers to buy shares of common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date on the front of this prospectus, regardless of the time of delivery of this prospectus or any sale of shares of our common stock.

Until , 2015 (the 25th day after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

Market, Industry and Other Data

This prospectus also contains estimates, projections and other information concerning our industry, our business and the markets for oncology therapeutics, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to the sources from which this data are derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph are derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

Trademarks

Our logo used in this prospectus is subject to a trademark that is owned by us. This prospectus also includes trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this prospectus may appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the right of the applicable licensor to these trademarks and tradenames.

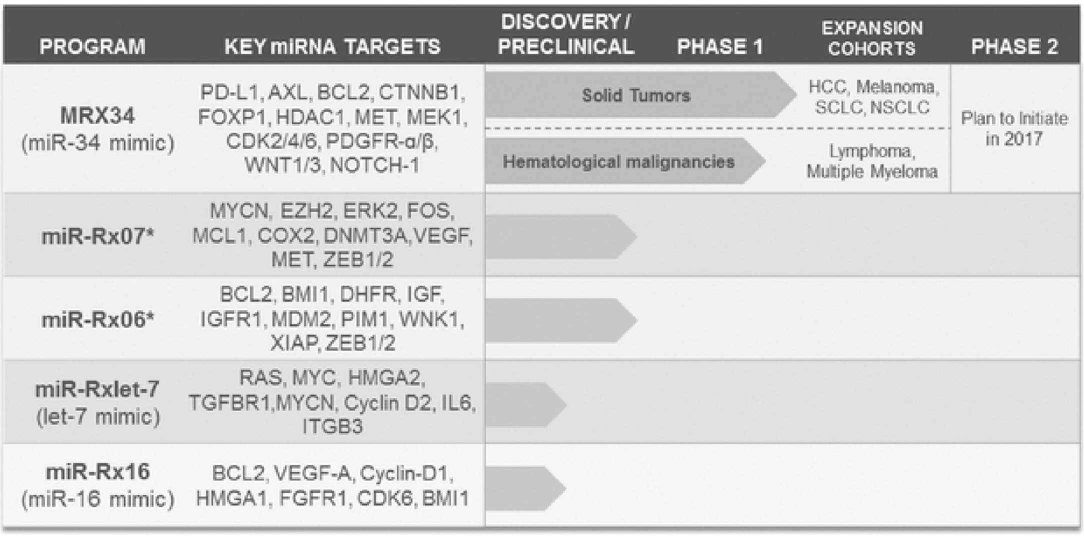
Prospectus Summary

This summary highlights information contained in other parts of this prospectus. Because it is only a summary, it does not contain all of the information that you should consider before investing in shares of our common stock and it is qualified in its entirety by, and should be read in conjunction with, the more detailed information appearing elsewhere in this prospectus. You should read the entire prospectus carefully, especially "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and the notes related thereto, before deciding to buy shares of our common stock. Unless the context requires otherwise, references in this prospectus to "Mirna," "we," "us" and "our" refer to Mirna Therapeutics, Inc.

Overview

We are a clinical-stage biopharmaceutical company developing a broad pipeline of microRNA-based oncology therapeutics. microRNAs are naturally occurring, short ribonucleic acid, or RNA, molecules, or oligonucleotides, that play a critical role in regulating key biological pathways. Misexpression of even a single microRNA can contribute to disease development and tumor suppressor microRNAs are commonly reduced in cancer. Our scientists and others at leading academic institutions have identified numerous tumor suppressor microRNAs that play key roles in preventing normal cells from becoming cancerous and facilitating proper cancer immunosurveillance. We are developing mimics of naturally occurring microRNAs that are designed to restore this tumor suppressor activity and aid appropriate tumor immune response. This approach is known as microRNA replacement therapy. Our lead product candidate, MRX34, a mimic of naturally occurring microRNA-34 (miR-34) encapsulated in a liposomal nanoparticle formulation, is the first microRNA mimic to enter clinical development and has shown preliminary clinical evidence of anti-tumor activity as a single agent in our ongoing Phase 1 clinical trial. miR-34 is one of the most widely published microRNAs and considered key regulator of oncogenic pathways. We plan to develop MRX34 as a monotherapy and in combination with other therapeutic modalities, such as targeted therapies and immuno-oncology agents. We believe that microRNA mimics represent a new paradigm in cancer therapy and have the potential to create a new, important class of effective cancer drugs, that can potentially be used alone or in combination with other cancer therapeutics.

We are developing a pipeline of tumor suppressor microRNA mimics, as shown in the following chart.



* Undisclosed microRNA

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Our tumor suppressor microRNA mimics are designed to impede the development of cancer by regulating the expression of multiple important oncogenes across key oncogenic pathways, whose inappropriate activation can lead to the transformation of normal cells into immortalized cancer cells. For example, we believe that th impressive anti-cancer activity of the miR-34 mimic in preclinical pharmacology studies is derived from its capacity to regulate more than 30 oncogenes, whereas many existing cancer therapies target only one or two oncogenes or pathways. The potential capacity to simultaneously affect multiple pathways and processes that ar critical to cancer cell viability may make mimics of tumor suppressor microRNAs potent anti-cancer agents and less susceptible to drug resistance.

MRX34 is a potential first in class, first in clinic microRNA mimic which is currently in an ongoing Phase 1 study. Dose escalation in the Phase 1 clinical trial is expected to be completed by the end of 2015 and we plan to complete enrollment of several expansion cohorts and have multiple study data read-outs in different tumor types by the end of 2016.

In addition to evaluating the safety, tolerability, and pharmacokinetic profile of MRX34, an important goal of our ongoing Phase 1 clinical trial is to establish proof of concept of microRNA replacement therapy in patients with primary liver cancer or advanced solid tumors. Our focus on hepatocellular carcinoma, or HCC, i based on the fact that liposomal nanoparticle formulations have a tendency to deliver their payload to the liver, and the high unmet medical need in this tumor type. Fo example, sorafenib (Nexavar®), the only approved drug for unresectable primary liver cancer, has only shown a 2% objective response rate. Additionally, we have also demonstrated meaningful results with MRX34 in multiple mouse models of primary liver cancer, including a study in which MRX34 demonstrated improved survival over sorafenib. To date we have observed tumor shrinkage greater than 30% in two patients with Stage IV cancer: one patient with a confirmed partial response in primary liver cancer metastasized to the lung, and a confirmed partial response in a melanoma patient with disseminated disease.

During the course of our Phase 1 clinical trial, the patient population was expanded to also include patients with hematological malignancies, based on the observation that specific lymphomas and leukemias are characterized by low levels of miR-34, and biodistribution data that supports high delivery to bone marrow an malignant lymphocytes. During the trial, we have observed dose-dependent MRX34 delivery and activity in normal white blood cells of patients and we aim to demonstrate delivery to tumors when patient biopsies become available during our expansion cohorts.

We are led by a management team with extensive experience in the biopharmaceutical industry. Members of our management team have played key roles at prio companies, including Bristol-Myers Squibb Company, Pfizer Inc., Reata Pharmaceuticals, Inc. and EMD Serono, Inc. Our principal investors are funds managed by Sofinnova Ventures, New Enterprise Associates, Pfizer Venture Investments, Eastern Capital, Baxalta, Sante Ventures, Morningside Ventures, and Celgene. As of March 31, 2015, we had $40.1 million in cash and cash equivalents.

microRNAs: A Unique Class in the RNA Therapeutics Space

The landscape of RNA-based therapeutic technologies has rapidly expanded over the past few years, mostly due to advances in the delivery of these molecules to their intended targets. These new delivery technologies have enabled the use of microRNA mimics, which we believe provide stronger therapeutic activity than other RNA-based approaches. Since tumor suppressor microRNAs are natural molecules expressed in normal tissues and cells, we also believe that undesired, or so-called "off-target," side effects are less likely to be associated with our microRNA mimic approach.

While other companies in the field of microRNA have focused primarily on inhibiting overexpressed microRNAs by antagonists known as anti-miRs or AntagomiRs, we have focused on introducing microRNAs that are under-expressed in disease through the use of microRNA mimics. This is in part due to what we believe is stronger therapeutic activity of microRNA mimics compared to anti-miRs or AntagomiRs. Within the group of companies in the microRNA space, we are the first company to clinically employ microRNA mimics.

microRNAs are misexpressed in a broad range of diseases including cancer, obesity, cardiovascular diseases, neurodegenerative diseases and viral infections. We believe that microRNA-based therapies have the potential to become a new class of drugs with broad therapeutic application due to their ability to modulate multiple disease pathways, target specificity which minimizes off-target effects, and their potential to work synergistically with other currently marketed drugs.

MRX34: Our Lead Product Candidate

We are the first to establish clinical proof-of-concept for a microRNA-based replacement therapy for cancer. Our lead microRNA-mimic product candidate, MRX34, is the potential first in a new class of promising cancer drugs, and has shown evidence of anti-tumor activity in a patient with metastasized hepatocellular carcinoma and a patient with advanced melanoma in our ongoing Phase 1 clinical trial. Once the dose-escalation phase in the ongoing Phase 1 trial has been completed, we intend to enroll additional patients across various tumor-specific expansion cohorts, including primary liver cancer, melanoma, small cell and non-sma cell lung cancer, lymphoma and multiple myeloma. We expect to complete these expansion cohorts and have multiple study data read-outs by end of 2016. After consultation with the Food and Drug Administration, or FDA, on study results and recommended clinical development program going forward, we intend to initiate a Phase 2 clinical trial program in early 2017.

MRX34 is a double-stranded RNA mimic of the tumor suppressor microRNA, miR-34, encapsulated in a liposomal nanoparticle formulation called SMARTICLES®. miR-34 inhibits multiple oncogenic pathways as well as stimulates anti-tumor immune response to induce cancer cell death. We performed cell culture studies that revealed that introducing a mimic of miR-34 into cancer cell lines derived from patients with liver, lung, colon, pancreatic and breast cancers results in significant reductions in cell proliferation. In various preclinical studies, miR-34 also inhibited formation of cancer stem cells, which are believed to contribute to the development, metastasis and therapeutic resistance of tumors. Studies performed at other laboratories have indicated that increasing miR-34 levels also inhibit the proliferation of cancer cells derived from patients with malignant melanoma, B-cell lymphoma and multiple myeloma.

MRX34 features an innovative liposomal formulation called SMARTICLES, which is used to deliver our miR-34 mimic to cancer cells. We selected SMARTICLES based on a number of identified efficacy and safety parameters during a comprehensive evaluation of more than 10 preclinical or clinical stage lipid- and polymer-based nanoparticle delivery technologies. Based on head-to-head preclinical comparisons and signs of clinical activity, we believe that the SMARTICLE technology currently offers the best combination of delivery and tolerability for our miRNA mimics.

In April 2013, we initiated a multi-center, open label dose escalation Phase 1 clinical trial during which we evaluated two different dosing schedules for MRX34 as a single agent in multiple advanced solid tumors and various types of hematological malignancies. To date, 97 patients have been enrolled in the ongoing MRX34 Phase 1 clinical trial at five clinical trial sites in the US and three sites in Korea. Primary objectives of the Phase 1 clinical trial are to establish the maximum tolerated dose and an appropriate dose for expansion cohorts and future Phase 2 clinical trials. To date:

- 47 patients have been treated on a twice weekly, or BIW, schedule for three weeks in 28-day cycles until the maximum tolerated dose of MRX34 was found to be 110 mg/m^2 among patients with solid cancers.

- The other 50 patients have been or are being treated daily for five days, or QD × 5, in 21-day cycles. We have not yet determined the maximum tolerated dose of MRX34 with this dosing schedule. Current dose levels are 70 mg/m^2 for primary liver cancer patients, 93 mg/m^2 for other solid tumors, and 110 mg/m^2 for hematological malignancies.

Based on observations from the two dosing schedules, we believe the QD × 5 dosing schedule has certain advantages over the BIW schedule such as better safety and tolerability, which we believe may in turn lead to improved efficacy. Therefore, the QD × 5 dosing schedule has been selected for all new patients enrolling in the Phase 1 clinical trial.

Secondary objectives of the clinical trial are to assess the safety, tolerability and pharmacokinetic profile of MRX34 after intravenous dosing as well as to assess any biological and clinical activity. The most common adverse events observed to date with MRX34 are similar to those observed with marketed liposomal drug formulations and have been manageable with interventions commonly used by oncologists. Biological activity has been demonstrated by dose-dependent down-regulation of target oncogenes of miR-34 and up-regulation of p21, a tumor suppressor induced by miR-34 in normal white blood cells from patients treated with MRX34. Signs of clinical activity have been demonstrated by the observation of confirmed partial responses in one patient with primary metastasized liver cancer and one patient with advanced melanoma per independent radiology review using RECIST (Response Evaluation Criteria in Solid Tumors) criteria.

Once the dose-escalation phase in the QD × 5 dose schedule cohort has been completed, and a recommended dose for the expansion cohorts has been determined we intend to enroll approximately 100 additional patients across different tumor-specific expansion cohorts, including primary liver cancer, melanoma, small cell and non-small cell lung cancer, lymphoma and multiple myeloma. We expect to complete these expansion cohorts and have multiple study data read-outs by the end of 2016. After consultation with the Food and Drug Administration, or FDA, on study results and recommended clinical development program going forward, we intend to initiate a Phase 2 clinical trial program in early 2017.

We have identified multiple tumor suppressor microRNAs that, like miR-34, have demonstrated the ability to inhibit cancer cell proliferation and tumor growth i preclinical studies. Each tumor suppressor miRNA regulates a unique set of genes and oncogenic pathways that we believe will enable the development of multiple therapeutic candidates either as monotherapies or as combination therapies. We plan to initiate a Phase 1 trial for our second therapeutic candidate in 2016.

We intend to continue building on our technology platform, comprised of intellectual property, proprietary methods and knowhow in the field of microRNA, and also to successfully expand and defend our position as a leader in the field of microRNA. We are pursuing or have been granted therapeutic use patent claims related t several tumor suppressor microRNAs, as well as composition of matter claims for multiple chemistries and structures that are, or may be used in or contemplated for use with, our therapeutic microRNA mimics, including miR-34. We have an exclusive license to the patent estate covering the SMARTICLES liposomal delivery technology for four of our product pipeline candidates, including miR-34, and could be broadened to include other tumor suppressor microRNAs. We believe our strong intellectual property position can be used to support internal development as well as out-licensing opportunities.

Our Strategy

Key elements of our strategy are as follows:

- *Advance our lead product candidate, MRX34, through clinical development.*

- *Identify biomarkers to support therapeutic product candidates.*

- *Expand our clinical development program to additional microRNAs.*
- *Expand our intellectual property position.*
- *Leverage partnership opportunities.*

Risks Associated with Our Business

- We have incurred significant losses since inception. We anticipate that we will continue to incur significant losses for the foreseeable future, and if we are unable to achieve and sustain profitability, the market value of our common stock will likely decline. We will also need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or terminate our product development, other operations or commercialization efforts.
- The approach we are taking to discover and develop novel therapeutics using microRNA is unproven and may never lead to marketable products.
- We are heavily dependent on the success of our lead product candidate, MRX34, which is in Phase 1 clinical development. If we are not successful in discovering, developing and commercializing additional product candidates, our ability to expand our business and achieve our strategic objectives would be impaired.
- Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results. Even if a product candidate does obtain regulatory approval, that product candidate may never achieve market acceptance or commercial success.
- We rely on third parties to conduct some of our nonclinical and all of our clinical trials as well as on single source third-party contract manufacturing organizations to manufacture and supply MRX34 and other product candidates for us. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may face delays in the development and commercialization of our product candidates.
- If we are unable to obtain and maintain sufficient patent protection for our product candidates, or if the scope of the patent protection is not sufficientl broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our produ candidates may be adversely affected.
- The patent rights of third parties may have an adverse effect on our business and may impact our ability to successfully commercialize one or more of our product candidates.
- We will need to increase the size of our organization, and we may experience difficulties in managing growth.

Our Corporate Information

We were incorporated in late 2007 under the laws of Delaware and were maintained as a wholly-owned subsidiary of our former parent company, Asuragen, Inc. until the end of 2009 when we became an independent entity. Our principal executive offices are located at 2150 Woodward St., Austin, TX 78744 and our telephone number is (512) 901-0900. Our website address is www.mirnarx.com. The information contained on, or that can be accessed through, our website is not part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

We are an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We will remain an emerging growth company until the earlier of the last day of the fiscal year following the fifth anniversary of the completion of this offering, the last day of the fiscal year in which we have total annual gross revenue of at least $1.0 billion, the date on which we are deemed to be a large accelerated filer (this means the market value of our common stock that is held by non-affiliates exceeds $700 million at the end of the second quarter of that fiscal year), or the date on which we have issued more than $1.0 billion in nonconvertible debt securities during the prior three-year period. An emerging growth company may take advantage of specified reduced reporting requirements and is relieved of certain other significant requirements that are otherwise generally applicable to public companies. As an emerging growth company,

- we will avail ourselves of the exemption from the requirement to obtain an attestation and report from our auditors on the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act of 2002;
- we will provide less extensive disclosure about our executive compensation arrangements; and
- we will not require shareholder non-binding advisory votes on executive compensation or golden parachute arrangements.

However, we are choosing to "opt out" of the extended transition periods available under the JOBS Act for complying with new or revised accounting standards. The decision to opt out of the extended transition periods under the JOBS Act is irrevocable.

The Offering

Issuer	Mirna Therapeutics, Inc.
Common stock we are offering	shares
Common stock to be outstanding after the offering	shares
Option to purchase additional shares	shares
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $ million, or approximately $ million if the underwriters exercise the option to purchase additional shares in full, at an assumed initial public offerin price of $ per share, the midpoint of the range set forth on the cover page of this prospectus, after deducting the underwriting discounts and commission and estimated offering expenses payable by us. At March 31, 2015, we had cas and cash equivalents of $40.1 million. We currently estimate that we will use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows: approximately $53.0 to $65.0 million to fund clinical development expenses for our lead program, MRX34, which includes approximately $13.0 to $17.0 million to complete the Phase 1 clinical trial, including expansion cohorts on multiple indications and/or changes in protoco approximately $14.0 to $18.0 million to initiate the Phase 2 clinical trial for an indication still to be determined, and approximately $26.0 to $30.0 million to fund preclinical and clinical studies for the use of MRX34 in additional indications or in combination with standard of care drugs; and approximately $21.0 to $27.0 million to fund preclinical and clinical studies for a second product candidate using another to be determined mimic product. The remainder of the net proceeds from this offering, together with our existing cas and cash equivalents, will be used for preclinical studies, working capital and other general corporate purposes, which may include selection and developme of our pursuit of our other research and discovery efforts, expenditures on intellectual property and the acquisition or in-license of other products, produc candidates or technologies. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of and results from preclinical testing or clinical trials, as well as any collaborations that we may enter into with third parties fo our product candidates, and any unforeseen cash needs. See "Use of Proceeds" on page 66 for a more complete description of the intended use of proceeds from this offering.
Risk factors	See "Risk Factors" beginning on page 11 and other information included in thi prospectus for a discussion of factors that you should consider carefully before deciding to invest in our common stock.
Symbol on The NASDAQ Global Market	"MIRN"

The number of shares of common stock to be outstanding after this offering is based on 143,459,827 shares of common stock outstanding at March 31, 2015, and excludes the following:

- 8,354,031 shares of common stock issuable upon the exercise of outstanding stock options at March 31, 2015 having a weighted-average exercise price of $0.34 per share;
- 6,221,749 shares of common stock reserved for issuance pursuant to future awards under our 2008 Long Term Incentive Plan, as amended, at March 31, 2015, which will become available for issuance under our 2015 Equity Incentive Award Plan after consummation of this offering;
- shares of common stock reserved for issuance pursuant to future awards under our 2015 Equity Incentive Award Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan, which will become effective immediately prior to the consummation of this offering; and
- shares of common stock issuable to the holders of Series C convertible preferred stock and Series D convertible preferred stock under the terms of our certificate of incorporation as a result of the accruing paid-in-kind dividend in connection with the conversion of all shares of Series C convertible preferred stock and Series D convertible preferred stock into shares of common stock immediately prior to the consummation of this offering.

Unless otherwise indicated, the number of shares of our common stock described above gives effect to:

- the conversion of all 142,085,100 shares of our convertible preferred stock into an aggregate of 142,085,100 shares of common stock immediately prior to the consummation of this offering;
- the adoption of our amended and restated certificate of incorporation and amended and restated bylaws immediately prior to the consummation of this offering; and
- except as otherwise indicated, the assumption there will be no exercise of the underwriters' over-allotment option.

We refer to our Series A, Series B, Series B-1, Series C and Series D convertible preferred stock collectively as "convertible preferred stock" for financial reporting purposes and in the financial tables included in this prospectus, as more fully explained in Note 7 to our financial statements. In other parts of this prospectus, we refer to our Series A, Series B, Series B-1, Series C and Series D convertible preferred stock collectively as "preferred stock."

Summary Financial Data

The following tables set forth a summary of our historical financial data at, and for the period ended on, the dates indicated. The statement of operations data for the years ended December 31, 2012, 2013 and 2014 are derived from our audited financial statements included elsewhere in this prospectus. The statement of operations data for the three months ended March 31, 2014 and 2015 and balance sheet data as of March 31, 2015 have been derived from our unaudited financial statements included elsewhere in this prospectus. Our unaudited financial statements are prepared on the same basis as our audited financial statements. You should read these data together with our audited financial statements and related notes appearing elsewhere in this prospectus and the information under the captions "Selecte Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." Our historical results are not necessarily indicative o our future results, and results for the three months ended March 31, 2015 are not necessarily indicative of results to be expected for the full year ending December 31, 2015.

	Year Ended December 31,			Three Months Ended March 31,	
	2012	2013	2014	2014	2015
	(in thousands, except share and per share data)			(unaudited)	
Statement of Operations Data:					
Operating expenses:					
Research and development	$ 2,742	$ 4,391	$ 10,545	$ 2,188	$ 3,425
General and administrative	1,562	2,384	3,369	848	854
Write-off of offering expenses	—	—	1,920	—	—
Total operating expenses	4,304	6,775	15,834	3,036	4,279
Other income (expense):					
Change in fair value of option liability	—	339	—	—	—
Gain on extinguishment of note payable	1,001	—	—	—	—
Interest expense	(355)	—	—	—	—
Net loss	$ (3,658)	$ (6,436)	$ (15,834)	$ (3,036)	$ (4,279)
Less: Accretion and dividends on convertible preferred stock	(6,142)	(2,324)	(2,824)	(696)	(1,118)
Net loss attributable to common stockholders	$ (9,800)	$ (8,760)	$ (18,658)	$ (3,732)	$ (5,397)
Net loss per share attributable to common stockholders, basic and diluted	$ (373.52)	$ (293.92)	$ (19.40)	$ (12.08)	$ (4.06)
Common shares used to compute basic and diluted net loss per share attributable to common stockholders	26,237	29,804	961,963	309,017	1,327,688
Pro forma net loss per common share (unaudited)—basic and diluted			$ (0.19)		$ (0.05)
Common shares used to compute pro forma net loss per share (unaudited)—basic and diluted			84,962,729		85,973,836

The table below presents our balance sheet data at March 31, 2015:

- on an actual basis;
- on a pro forma basis to give effect to:
  - the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 142,085,100 shares of common stock immediately prior to the consummation of this offering; and
  - the filing and effectiveness of our amended and restated certificate of incorporation, which will occur immediately prior to the consummation of this offering; and
- on a pro forma as adjusted basis to give further effect to the sale of shares of common stock in this offering at an assumed initial public offering price of $ per share (the midpoint of the range set forth on the cover page of this prospectus), after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

	At March 31, 2015		
	Actual	Pro Forma	Pro Forma As Adjusted(1)
	(in thousands)		
Balance Sheet Data:			
Cash and cash equivalents	$ 40,130	$ 40,130	
Total assets	40,547	40,547	
Total liabilities	2,277	2,277	
Convertible preferred stock	91,464	—	
Common stock	1	143	
Additional paid-in capital	—	91,322	
Accumulated deficit	(53,195)	(53,195)	
Total stockholders' (deficit) equity	(53,194)	38,270	

(1) Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share, the midpoint of the range set forth on the cover page of this prospectus, would increase (decrease) each of pro forma as adjusted additional paid-in capital and stockholders' equity by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. We may also increase or decrease the number of shares we are offering. An increase (decrease) of 1,000,000 in the number of shares we are offering would increase (decrease) each of pro forma as adjusted additional paid-in capital, stockholders' equity and total capitalization by approximately $ million, assuming the assumed initial public offering price per share, as set forth on the cover page of this prospectus, remains the same.

Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this prospectus and any related free writing prospectus, including our financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

Risks Related to Our Limited Operating History, Financial Position and Capital Requirements

We have incurred significant losses since inception. We anticipate that we will continue to incur significant losses for the foreseeable future, and if we are unable to achieve and sustain profitability, the market value of our common stock will likely decline.

We are a clinical-stage biopharmaceutical company with a limited operating history. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We have not generated any product revenues and we do not expect to generate any product revenues for the foreseeable future. We have incurred losses in each year since our founding in 2007 and we expect to continue to incur significant operating losses for the foreseeable future. The amount of future losses is uncertain. All of our product candidates are in development, and none has been approved for sale. We have devoted substantially all of our efforts to research and development, including our preclinical and nonclinical development activities, and expect that it will be many years, if ever, before we have a product candidate ready for commercialization. To date, we have derived all of our funding from our collaboration with our former parent company, Asuragen, Inc., or Asuragen, private placements of preferred stock and government grants for research and development. Our net losses for the years ended December 31, 2012, 2013 and 2014 were $3.7 million, $6.4 million and $15.8 million, respectively, and $4.3 million for the three months ended March 31, 2015. Since inception, we have incurred net losses leading to an accumulated deficit of approximately $53.2 million as of March 31, 2015.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future as we continue our Phase 1 clinical trial of our lead product candidate, MRX34, pursue development of MRX34 for additional indications, conduct research and development of other product candidates and pursue marketing approval for MRX34 in the future. If we obtain marketing approval of MRX34, we also expect to incur significant sales, marketing, distribution and manufacturing expenses. Even after obtaining such marketing approval, our products may never gain sufficient market acceptance and adequate market share. If we fail to succeed in any of these activities or our product candidates fail to demonstrate safety and efficacy in clinical trials, do not gain regulatory approval or do not achieve significant market acceptance following regulatory approval and commercialization, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. If we are unable to achieve and sustain profitability, the market value of our common stock will likely decline. Because of the numerous risks and uncertainties associated with developing biopharmaceutical products, we are unable to predict the extent of any future losses or whether we will become profitable.

Our short operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are a clinical-stage biopharmaceutical company that was founded in 2007 and did not exist as a standalone company until 2009. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring and developing our technology, identifying and evaluating potential product candidates and delivery technologies, undertaking nonclinical studies, filing an Investigational New Drug, or IND, application with the U.S. Food and Drug Administration, or FDA, and conducting the Phase 1 clinical trial of our most advanced product candidate, MRX34. Except for MRX34, all of our product candidates are still in preclinical development. We have not yet demonstrated our ability to initiate clinical trials for product candidates other than MRX34, or successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial scale medicine, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Typically, it takes several years to develop one new product candidate from the time it is discovered to when it is available for treating patients. Consequently, any predictions about our future success or viability, or any evaluation of our business or prospects, may not be as accurate as they could be if we had a longer operating history. In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown challenges. We will need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or terminate our product development, other operations or commercialization efforts.

Developing biopharmaceutical products, including conducting preclinical and nonclinical studies and clinical trials, is an expensive and highly uncertain process that takes years to complete. Our expenses will increase substantially as we continue our Phase 1 clinical trial of our lead product candidate, MRX34, pursue development of MRX34 for additional indications, and conduct research and development of our other product candidates. Additional clinical trials, including one or more late-stage pivotal trials, will be required to obtain potential marketing approval for MRX34, and the costs of any future trials may be more expensive and time consuming than our current trial. If we obtain marketing approval of MRX34, we also expect to incur significant sales, marketing, distribution and outsourced manufacturing expenses.

As of March 31, 2015, we had working capital of $38.1 million and cash and cash equivalents of $40.1 million. Based on our current operating plan, we believe that our available cash and the proceeds from this offering are sufficient to fund our anticipated levels of operation for at least the next 12 months. Our future capital requirements for the period for which we expect our existing resources to support our operations may vary significantly from what we expect. For example, our expenses could increase beyond expectations if we are required by the FDA or comparable foreign regulatory agencies to perform studies and trials in addition to those that we currently anticipate. Our funds following this offering will not be sufficient to obtain marketing approval for MRX34. As a result, we will be required to obtain additional financing in the future, which we may obtain through public or private equity offerings, debt financings, a credit facility, government grants and contracts and/or strategic collaborations. If we are required to secure additional capital, such additional fundraising efforts may divert our management from our day-to-day activities, which may adversely affect our ability to develop and commercialize future product candidates. Additional financing may not be available to us when we need it or it may not be available to us on favorable terms, if at all. If we are unable to obtain adequate financing or form favorable collaborations, when needed, we may have to delay, reduce the scope of or eliminate one or more of our clinical trials, research and development programs or our commercialization efforts, including with respect to MRX34.

Additionally, our future financing requirements will depend on many factors, some of which are beyond our control, including:

- the demonstration of clinical proof-of-concept with our product candidates, including MRX34, in one or more cancer types or other indications;
- the rate of progress and cost of our clinical trials, preclinical and nonclinical studies and other discovery and research and development activities;
- the successful outcome of one or more pivotal clinical trials demonstrating safety and efficacy of our product candidates, including MRX34;
- the timing of, and costs involved in, seeking and obtaining FDA and other regulatory approvals;
- the costs of preparing, filing, prosecuting, maintaining and enforcing any patent claims and other intellectual property rights, including litigation costs and the results of such litigation;
- our ability to practice our technology without infringing the intellectual property rights of third parties;
- our ability to enter into additional collaboration, licensing, government or other arrangements and the terms and timing of such arrangements;
- the potential need to acquire, by acquisition or in-licensing, other products or technologies; and
- the emergence of competing technologies or other adverse market developments.

Future capital requirements will also depend on the extent to which we acquire or invest in additional complementary businesses, products and technologies. We currently have no understandings, commitments or agreements relating to any of these types of transactions.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through public or private equity offerings, debt financings, credit facilities, government grants and contracts and/or strategic collaborations.

To raise capital, we may from time to time issue additional shares of common stock at a discount from the then-current trading price of our common stock. As a result, our common stockholders would experience immediate dilution upon the purchase of any shares of our common stock sold at such discount. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, preferred stock or common stock. Whether or not we issue additional shares of common stock at a discount, any issuance of common stock will, and any issuance of other equity securities, securities convertible into equity securities or options, warrants or other rights to purchase common stock may, result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to decline. New investors could also gain rights, preferences and privileges senior to those of holders of our common stock, which could cause the price of our common stock to decline. Debt securities may also contain covenants that restrict our operational flexibility, impose liens or other restrictions on our assets, restrict our ability to incur additional debt, impose limitations on our ability to acquire, sell or license intellectual property or impose other operating restrictions that could adversely affect our business and could also cause the price of our common stock to decline.

Other than our collaboration with our former parent company, Asuragen, and private placements of preferred stock, the only external source of funds to date has been state and federal government grants for research and development. The grants have been, and any future government grants and contracts we may receive may be, subject to the risks and contingencies set forth below under the risk factor entitled "Reliance on government funding for our programs may add uncertainty to our research and commercialization efforts with respect to those programs that are tied to such funding and may impose requirements that limit our ability to take certain actions, increase the costs of commercialization and production of product candidates developed under those programs and subject us to potential financial penalties, which could materially and adversely affect our business, financial condition and results of operations." Although we apply for government and private contracts and grants, we cannot assure you that we will be successful in obtaining additional grants or contracts in the future for MRX34 or any other product candidates or programs.

Risks Related to Product Development and Commercialization

The approach we are taking to discover and develop novel therapeutics using microRNA is unproven and may never lead to marketable products.

The scientific discoveries that form the basis for our efforts to discover and develop new drugs are relatively recent. To date, neither we nor any other company has received regulatory approval to market therapeutics utilizing microRNA. The scientific evidence to support the feasibility of developing drugs based on these discoveries is both preliminary and limited. Successful development of microRNA-based products by us will require solving a number of issues, including providing suitable methods of stabilizing the microRNA material and delivering it into target cells in the human body. In addition, any compounds that we develop may not demonstrate in patients the chemical and pharmacological properties ascribed to them in laboratory and nonclinical studies, and they may interact with human biological systems in unforeseen, ineffective or even harmful ways. If we do not successfully develop and commercialize product candidates based upon our technological approach, we may not become profitable and the value of our common stock may decline.

Further, the FDA has relatively limited experience with microRNA-based therapeutics. No regulatory authority has granted approval to any person or entity, including us, to market and commercialize microRNA therapeutics, which may increase the complexity, uncertainty and length of the regulatory approval process for our product candidates. If our microRNA technologies prove to be ineffective, unsafe or commercially unviable, our entire pipeline would have little, if any, value, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

Further, our exclusive focus on microRNA technology for developing products as opposed to multiple, more proven technologies for drug development increases the risk associated with our business. If we are not successful in developing a product candidate using microRNA technology, we may not be able to identify and successfully implement an alternative product development strategy.

We are heavily dependent on the success of our lead product candidate, MRX34, which is in Phase 1 clinical development.

We currently have no products approved for sale and have invested a significant portion of our efforts and financial resources in the development of MRX34. The clinical development of MRX34 began in April 2013 with a multi-center Phase 1 clinical trial that is currently enrolling patients with unresectable primary liver cancer or solid cancers. We have also expanded the Phase 1 clinical trial with a separate cohort of patients with hematological malignancies, which may include patients with non-Hodgkin's lymphoma, acute myelogenous leukemia, acute and chronic lymphocytic leukemia, chronic myelogenous leukemia in accelerated or blast phase, multiple myeloma and myelodysplastic syndrome. The primary objectives of the Phase 1 clinical trial, including the hematological malignancy cohort, are to establish the maximum tolerated dose and an appropriate dose for Phase 2 clinical trials. The secondary objectives of the Phase 1 clinical trial are to assess the safety, tolerability and pharmacokinetic profile of MRX34 after intravenous dosing as well as to assess any biological and clinical activity.

Our prospects are substantially dependent on our ability to develop and commercialize MRX34. Our ability to timely develop and effectively commercialize MRX34 will depend on several factors, including the following:

- successful completion of our Phase 1 clinical trial or other clinical trials, which will depend substantially upon the satisfactory performance of third-party contractors;
- successful demonstration of clinical proof-of-concept with MRX34 in one or more Phase 2 clinical trials in one or more cancer types;
- successful outcome of one or more pivotal clinical trials required for regulatory approval demonstrating safety and efficacy of MRX34;
- receipt of marketing approvals for MRX34 from the FDA and similar regulatory authorities outside the United States;
- establishing commercial manufacturing capabilities, for example, by making arrangements with third-party manufacturers;
- successfully launching commercial sales of the product, whether alone or in collaboration with others;
- acceptance of the product by patients, the medical community and third-party payors;
- establishing market share while competing with other therapies;
- a continued acceptable safety and adverse event profile of the product following regulatory approval;
- qualifying for, identifying, registering, maintaining, enforcing and defending intellectual property rights and claims covering the product; and
- manufacturing, marketing, selling and using MRX34 and practicing our technology without infringing the proprietary rights of third parties, or successfully defending against claims alleging such infringement.

If we do not achieve one or more of these factors in a timely manner, or at all, we could experience significant delays or an inability to commercialize MRX34, which would materially and adversely affect our business, financial condition and results of operations.

We have not previously submitted a new drug application, or NDA, to the FDA, or similar drug approval filings to comparable foreign authorities, for any product candidate, and we cannot be certain that any of our product candidates will be successful in clinical trials or receive regulatory approval. Further, our product candidates may not receive regulatory approval even if they are successful in clinical trials. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approvals to market one or more of our product candidates, our revenues will be dependent upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights. If the markets for patient subsets that we are targeting are not as significant as we estimate, we may not generate significant revenues from sales of such products, if approved. Successful development of MRX34 or other product candidates for additional indications will be subject to these same risks.

If we are not successful in discovering, developing and commercializing additional product candidates, our ability to expand our business and achieve our strategic objectives would be impaired.

Although a substantial amount of our efforts will focus on the Phase 1 clinical trial and potential approval of our lead product candidate, MRX34, a key element of our strategy is to discover, develop and potentially commercialize a portfolio of product candidates to treat cancer and other indications. We are seeking to do so through our internal research programs and are exploring, and intend to explore in the future, strategic partnerships for the development of new products. Other than MRX34, all of our other potential product candidates remain in the discovery and preclinical study stages. Research programs to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following:

- the research methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our product candidates obsolete;
- product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- a product candidate may, on further study, be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors.

If we are unsuccessful in identifying and developing additional product candidates, our potential for growth may be impaired.

We may use our financial and human resources to pursue a particular research program or product candidate and fail to capitalize on programs or product candidates that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and human resources, we may forego or delay pursuit of opportunities with certain programs or product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or more profitable market opportunities. Our spending on current and future research and development programs and future product candidates for specific indications may not yield any commercially viable products. We may also enter into strategic alliance agreements to develop and commercialize certain of our programs and potential product candidates in indications with potentially large commercial markets. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic alliance, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

The regulatory approval process is lengthy, expensive and uncertain, and we may be unable to obtain regulatory approval for our drug products under applicable regulatory requirements. The denial or delay of any such approval would delay commercialization of our drug products and adversely impact our ability to generate revenue, our business and our results of operations.

The development, research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products are subject to extensive and evolving regulation by federal, state and local governmental authorities in the United States, principally the FDA, and by foreign regulatory authorities, which regulations differ from country to country. Neither we nor any future collaborator is permitted to market MRX34 or any other product candidate in the United States until we receive regulatory approval of an NDA from the FDA.

Obtaining regulatory approval of an NDA can be a lengthy, expensive and uncertain process. Prior to obtaining approval to commercialize a drug candidate in the United States or abroad, we or our collaborators must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or other foreign regulatory agencies, that such drug candidates are safe and effective for their intended uses. The number of nonclinical studies and clinical trials that will be required for FDA approval varies depending on the drug candidate, the disease or condition that the drug candidate is designed to address, and the regulations applicable to any particular drug candidate. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our drug candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. Administering drug candidates to humans may produce undesirable side effects, which could interrupt, delay or halt clinical trials and result in the FDA or other regulatory authorities denying approval of a drug candidate for any or all indications. The FDA may also require us to conduct additional studies or trials for our product candidates either prior to or post-approval, such as additional drug-drug interaction studies or safety or efficacy studies or trials, or it may object to elements of our clinical development program such as the number of subjects in our current clinical trials from the United States.

We expect the Phase 1 clinical trial for our lead product candidate, MRX34, to be completed by the end of 2016, and our business currently depends substantially on the successful development, regulatory approval and commercialization of MRX34. We currently have no drug products approved for sale, and we may never obtain regulatory approval to commercialize MRX34.

The FDA or any foreign regulatory bodies can delay, limit or deny approval of MRX34 or require us to conduct additional nonclinical or clinical testing or abandon a program for many reasons, including:

- the FDA or the applicable foreign regulatory agency's disagreement with the design or implementation of our clinical trials;
- negative or ambiguous results from our clinical trials or results that may not meet the level of statistical significance required by the FDA or comparable foreign regulatory agencies for approval;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- our inability to demonstrate to the satisfaction of the FDA or the applicable foreign regulatory body that MRX34 is safe and effective for the proposed indication;
- the FDA's or the applicable foreign regulatory agency's disagreement with the interpretation of data from nonclinical studies or clinical trials;
- our inability to demonstrate the clinical and other benefits of MRX34 outweigh any safety or other perceived risks;

- the FDA's or the applicable foreign regulatory agency's requirement for additional nonclinical studies or clinical trials;
- the FDA's or the applicable foreign regulatory agency's disagreement regarding the formulation, labeling and/or the specifications of MRX34;
- the FDA's or the applicable foreign regulatory agency's failure to approve the manufacturing processes or facilities of third-party manufacturers with which we contract; or
- the potential for approval policies or regulations of the FDA or the applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of drugs in development, only a small percentage successfully complete the FDA or other regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market MRX34, which would significantly harm our business, financial condition, results of operations and prospects.

Even if we eventually complete clinical testing and receive approval of an NDA or foreign marketing application for MRX34, the FDA or the applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials, including Phase 4 clinical trials, and/or the implementation of a Risk Evaluation and Mitigation Strategy, or REMS, which may be required to ensure safe use of the drug after approval. The FDA or the applicable foreign regulatory agency also may approve MRX34 for a more limited indication or a narrower patient population than we originally requested, and the FDA or applicable foreign regulatory agency may not approve the labeling that we believe is necessary or desirable for the successful commercialization of MRX34. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of MRX34 and would materially adversely impact our business and prospects.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Furthermore, we rely on contract research organizations, or CROs, and clinical trial sites to ensure the proper and timely conduct of our clinical trials. While we have agreements with our CROs governing their committed activities, and the ability to audit their performance, we have limited influence over their actual performance. Failure or delay can occur at any time during the clinical trial process. Success in nonclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and the results of clinical trials by other parties may not be indicative of the results in trials we may conduct. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in clinical trials, even after promising results in earlier nonclinical or clinical studies. These setbacks have been caused by, among other things, nonclinical findings made while clinical studies were underway and safety or efficacy observations made in clinical studies, including previously unreported adverse events. The results of preclinical, nonclinical and early clinical studies of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical and initial clinical trials. Notwithstanding any potential promising results in earlier studies, we cannot be certain that we will not face similar setbacks. Even if our clinical trials are completed, the results may not be sufficient to obtain regulatory approval for our product candidates.

Although we have an ongoing Phase 1 clinical trial for MRX34 and expect to complete the unresectable primary liver cancer, solid tumors and hematological malignancy cohort portions of the trial by the end of 2016, we may experience delays in our ongoing trial and we cannot be certain that the trial or any other future clinical trials for MRX34 or other product candidates will begin on time, need to be redesigned, enroll an adequate number of patients on time or be completed on schedule, if at all. Clinical trials can be delayed or aborted for a variety of reasons, including delay or failure related to:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical studies;
- obtaining regulatory approval to commence a trial;
- reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining institutional review board, or IRB, or equivalent approval at each site;
- recruiting suitable patients to participate in a trial;
- having patients complete a trial or return for post-treatment follow-up;
- clinical sites deviating from trial protocol or dropping out of a trial;
- addressing patient safety concerns that arise during the course of a trial;
- addressing any conflicts with new or existing laws or regulations;
- adding a sufficient number of clinical trial sites; or
- manufacturing sufficient quantities of product candidate for use in clinical trials.

Patient enrollment is a significant factor in the timing of clinical trials and 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 of the drug being studied in relation to other available therapies, including any new drugs or treatments that may be approved for the indications we are investigating.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Further, conducting clinical trials in foreign countries, as currently do for MRX34, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

If we experience delays in the completion, or termination, of any clinical trial of our product candidates, the commercial prospects of our product candidates may be harmed, and our ability to generate product revenues from any of these product candidates will be delayed or not realized at all. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may significantly harm our business, financial condition and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

If we are required to suspend or discontinue clinical trials due to side effects or other safety risks, or if we are required to conduct studies on the long-term effects associated with the use of MRX34 or other product candidates, our ability to commercialize our product candidates could be adversely affected.

Our clinical trials, including our Phase 1 clinical trial for MRX34, or other trials our strategic partners or CROs may conduct, may be suspended or terminated at any time for a number of safety-related reasons. For example, we may voluntarily suspend or terminate our clinical trials if at any time we believe that our product candidates present an unacceptable safety risk to the clinical trial patients. In addition, IRBs or regulatory agencies may order the temporary discontinuation or termination of our clinical trials at any time if they believe that the clinical trials are not being conducted in accordance with applicable regulatory requirements, including if they present an unacceptable safety risk to patients. Administering any product candidate to humans may produce undesirable side effects. The existence of undesirable side effects resulting from our product candidates could cause us or regulatory authorities, such as the FDA, to interrupt, delay or halt clinical trials of our product candidates and could result in the FDA or other regulatory agencies denying further development or approval of our product candidates for any or all indications.

We have not conducted complete studies on the long-term effects associated with the use of MRX34 or any other product candidate. Studies of these long-term effects may be required for regulatory approval and such requirement would delay our introduction of MRX34 or other product candidates into the market. These studies could also be required at any time after regulatory approval of a product candidate. Absence of long-term data may also limit the approved uses of a product, if any, to short-term use. MRX34 or any other product candidate may prove to be unsafe for human use, which would materially harm our business.

Certain oligonucleotide therapeutics and liposomal drug delivery products have shown injection site reactions, infusion reactions and pro-inflammatory effects and may also lead to impairment of organ function, including kidney or liver function. There is a risk that our current and future product candidates may induce similar adverse events, or require pre- or co-administration of other drugs to minimize such effects, which pre- or co-administration might adversely affect the benefits of our product or add additional side effects to the treatment regimens. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all indications. Drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may significantly harm our business, financial condition, results of operations and prospects significantly.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

As with many pharmaceutical products and product candidates under development, MRX34 or our other potential product candidates may produce undesirable side effects or adverse reactions or events. In the event we or others identify undesirable side effects caused by one of our product candidates, any of the following adverse events could occur:

- we may be required, or we may decide, to halt or delay further clinical development of our product candidates;
- the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all indications; or
- product-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims.

If MRX34 or our other potential product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product;
- we may be required to recall a product or change the way such product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof;
- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- we may be required to implement a REMS or create a Medication Guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of the foregoing events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and result in the loss of significant revenues to us, which would materially and adversely affect our results of operations and business.

Our clinical drug development program may not uncover all possible adverse events that patients who take MRX34 or other product candidates may experience. The number of subjects exposed to MRX34 or other product candidates and the average exposure time in the clinical development program may be inadequate to detect rare adverse events, or chance findings, that may only be detected once the product is administered to more patients and for greater periods of time.

Clinical trials by their nature utilize a sample of the potential patient population. However, with a limited number of subjects and limited duration of exposure, we cannot be fully assured that rare and severe side effects of MRX34 or other product candidates will be uncovered. Such rare and severe side effects may only be uncovered with a significantly larger number of patients exposed to the drug. If such safety problems occur or are identified after MRX34 or another product candidate reaches the market, the FDA may require that we amend the labeling of the product or recall the product, or may even withdraw approval for the product.

We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability and costs. If the use or misuse of our product candidates harms patients, or is perceived to harm patients even when such harm is unrelated to our product candidates, our regulatory approvals could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims. If we are unable to obtain adequate insurance or are required to pay for liabilities resulting from a claim excluded from, or beyond the limits of, our insurance coverage, a material liability claim could adversely affect our financial condition.

The use or misuse of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. There is a risk that our product candidates may induce adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. Certain oligonucleotide therapeutics and liposomal drug delivery products have shown injection site reactions, infusion reactions, and pro-inflammatory effects, and may also lead to organ dysfunction, including impairment of kidney or liver function. There is a risk that our future product candidates may induce similar adverse events. Patients with the diseases targeted by our product candidates are often already in severe and advanced stages of disease and have both known and unknown significant pre-existing and potentially life-threatening health risks. During the course of treatment, patients may suffer adverse events, including death, for reasons that may be related to our product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our products, or require us to suspend or abandon our commercialization efforts. Even in a circumstance in which we do not believe that an adverse event is related to our products, the investigation into the circumstance may be time-consuming or inconclusive. These investigations may interrupt our sales efforts, delay our regulatory approval process in other countries, or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations.

Although we have product liability insurance that we feel is appropriate for our stage of development, which covers our clinical trials in the United States, for up to $1 million per occurrence, up to an aggregate limit of $5 million, our insurance may be insufficient to reimburse us for any expenses or losses we may suffer, and we will be required to increase our product liability insurance coverage for our advanced clinical trials that we plan to initiate. We have obtained an additional product liability insurance policy for our planned clinical trials in the Republic of Korea. If and when we obtain marketing approval for product candidates, we intend to expand our insurance coverage to include the sale of commercial products. We do not know whether we will be able to continue to obtain product liability coverage and obtain expanded coverage if we require it, in sufficient amounts to protect us against losses due to liability, on acceptable terms, or at all. We may not have sufficient resources to pay for any liabilities resulting from a claim excluded from, or beyond the limits of, our insurance coverage. Where we have provided indemnities in favor of third parties under our agreements with them, there is also a risk that these third parties could incur liability and bring a claim under such indemnities. An individual may bring a product liability claim against us alleging that one of our product candidates or products causes, or is claimed to have caused, an injury or is found to be unsuitable for consumer use. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. Any product liability claim brought against us, with or without merit, could result in:

- withdrawal of clinical trial volunteers, investigators, patients or trial sites or limitations on approved indications;
- the inability to commercialize, or if commercialized, decreased demand for, our product candidates;
- if commercialized, product recalls, withdrawals or labeling, marketing or promotional restrictions or the need for product modification;
- initiation of investigations by regulators;
- loss of revenues;
- substantial costs of litigation, including monetary awards to patients or other claimants;
- liabilities that substantially exceed our product liability insurance, which we would then be required to pay ourselves;
- an increase in our product liability insurance rates or the inability to maintain insurance coverage in the future on acceptable terms, if at all;
- the diversion of management's attention from our business; and
- damage to our reputation and the reputation of our products and our technology.

Product liability claims may subject us to the foregoing and other risks, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Currently, our product candidates are expensive to produce and are expensive relative to presently-marketed therapeutics targeting similar indications.

To date, our proposed product candidates have only been manufactured at a scale that is adequate to supply our research activities and early-stage clinical trials. As with many companies conducting Phase 1 clinical trials or preclinical studies on product candidates, the current cost of each treatment is expensive relative to presently-marketed therapeutics targeting similar indications. We cannot assure you that we will be able to scale the manufacturing of our products during future clinical trials or commercialization in order to achieve a treatment price that would allow for commercial acceptance. In the event our product candidates cannot be manufactured in sufficient commercial quantities at a competitive price, our future prospects could be significantly impacted and our financial prospects would be materially harmed.

Even if a product candidate does obtain regulatory approval, that product candidate may never achieve market acceptance or commercial success.

Even if we obtain FDA or other regulatory approvals, and are able to launch MRX34 or any other product candidate commercially, the product candidate may not achieve market acceptance among physicians, patients, patient advocacy groups and third-party payors and, ultimately, may not be commercially successful. Market acceptance of any product candidate for which we receive approval depends on a number of factors, including:

- the efficacy and safety of the product candidate as demonstrated in clinical trials;
- the clinical indications for which the product candidate is approved;
- acceptance by physicians, patients, operators of treatment facilities and parties responsible for reimbursement of the product candidate as a safe and effective treatment;

- the potential and perceived advantages of the product candidate, including the cost of treatment and benefits over alternative treatments;
- the safety of the product candidate seen in a broader patient group, including use outside the approved indications;
- the cost of treatment in relation to alternative treatments;
- the availability of adequate reimbursement and pricing by third-party payors and government authorities;
- relative convenience and ease of administration;
- the tolerance of the products by patients, including prevalence and severity of adverse side effects;
- the availability of the product and the ability to meet market demand; and
- the effectiveness of our sales and marketing efforts.

Any failure by MRX34 or any other product candidate that obtains regulatory approval to achieve market acceptance or commercial success would adversely affect our financial results.

Risks Related to Our Reliance on Third Parties

We rely on third parties to conduct some of our nonclinical and all of our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to obtain regulatory approval for or commercialize any of our product candidates.

Although we conduct certain nonclinical studies, we currently do not have the ability to independently conduct nonclinical studies that comply with the regulatory requirements known as good laboratory practice, or GLP, requirements. We also do not currently have the ability to independently conduct any clinical trials. The FDA and regulatory authorities in other jurisdictions require us to comply with regulations and standards, commonly referred to as current good clinical practice, or GCP, requirements for conducting, monitoring, recording and reporting the results of clinical trials, in order to ensure that the data and results are scientifically credible and accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials. We rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct GLP-compliant nonclinical studies and GCP-compliant clinical trials on our product candidates properly and on time. While we will have agreements governing their activities, we control only certain aspects of their activities and have limited influence over their actual performance. The third parties with whom we contract for execution of our GLP nonclinical studies and our GCP clinical trials play a significant role in the conduct of these studies and trials and the subsequent collection and analysis of data. These third parties are not our employees and, except for restrictions imposed by our contracts with such third parties, we have limited ability to control the amount or timing of resources that they devote to our programs. Although we rely on these third parties to conduct our GLP-compliant preclinical and nonclinical studies and GCP-compliant clinical trials, we remain responsible for ensuring that each of our GLP preclinical and nonclinical studies and GCP clinical trials is conducted in accordance with its investigational plan and protocol and applicable laws and regulations, and our reliance on the CROs does not relieve us of our regulatory responsibilities.

Many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. If the third parties conducting our GLP preclinical or nonclinical studies or our clinical trials do not perform their contractual duties or obligations, experience work stoppages, do not meet expected deadlines, terminate their agreements with us or need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to their failure to adhere to our clinical trial protocols or to GCPs, or for any other reason, we may need to enter into new arrangements with alternative third parties. This could be difficult, costly or impossible, and our nonclinical studies or clinical trials may need to be extended, delayed, terminated or repeated. As a result we may not be able to obtain regulatory approval in a timely fashion, or at all, for the applicable product candidate, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

We rely on single source third-party contract manufacturing organizations to manufacture and supply MRX34 and other product candidates for us. If our supplier or manufacturer fails to perform adequately or fulfill our needs, or if these agreements are terminated by the third parties, we may be required to incur significant costs and devote significant efforts to find new suppliers or manufacturers. We may also face delays in the development and commercialization of our product candidates.

We do not currently independently conduct manufacturing activities for our product candidates, including MRX34. We rely upon single source third-party contract manufacturing organizations to manufacture and supply our product candidates. We currently have a relationship with only one supplier, NITTO DENKO Avecia, or Avecia, located in Massachusetts, for clinical supply of the drug substance for our miR-34 mimic. We are actively evaluating and qualifying a second-source supplier of our miR-34 mimic. We expect to complete this process in the second half of 2015. Polymun Scientific Immunbiologische Forschung GmbH, or Polymun, located in Austria, is the exclusive manufacturer of our MRX34 drug products. Further, we rely on our contract manufacturers to manage the supply chain for the raw materials used in the manufacture of the drug substance and drug product.

Any manufacturers of the drug substance and drug product for our product candidates must comply with current good manufacturing practice, or cGMP, requirements enforced by the FDA through its facilities inspection program. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. Manufacturers of our component materials may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. We do not directly control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMPs. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or foreign regulatory agencies, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no direct control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. The FDA or similar foreign regulatory agencies at any time may also implement new standards, or change their interpretation and enforcement of existing standards for manufacture, packaging or testing of products. We have little control over a manufacturer's compliance with these regulations and standards. However, a failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval. If the safety of any product supplied is compromised due to our manufacturer's failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize our products, and we may be held liable for any injuries sustained as a result. In addition, if the FDA or a comparable foreign regulatory agency does not approve our contract manufacturer's facilities for the manufacture of our product candidates or if it withdraws its approval in the future, we may need to find alternative manufacturing facilities, which would negatively impact our ability to develop, obtain regulatory approval for, or market our product candidates, if approved. Any of these factors could cause a delay of clinical trials, regulatory submissions, approvals or commercialization of our product candidates or entail higher costs or impair our reputation.

The manufacture of pharmaceutical products in compliance with cGMP regulations requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, including difficulties with production costs and yields, quality control, including stability of the product candidate and quality assurance testing, or shortages of qualified personnel. If our manufacturers were to encounter any of these difficulties or otherwise fail to comply with their obligations to us or under applicable regulations, our ability to provide study materials in our nonclinical studies and clinical trials would be jeopardized. Any delay or interruption in the supply of nonclinical study or clinical trial materials could delay the completion of our nonclinical studies and clinical trials, increase the costs associated with maintaining our nonclinical study and clinical trial programs and, depending upon the period of delay, require us to conduct nonclinical studies, commence new trials at significant additional expense or terminate the studies and trials completely.

We currently believe that our third party suppliers have the necessary expertise to produce our MRX34 drug substance and drug product in sufficient quantity and of acceptable quality to support our development program through at least Phase 3 clinical trials and possibly through commercialization of MRX34. However, our current agreements with our suppliers do not provide for the entire supply of the drug necessary for additional clinical trials or for full-scale commercialization. In the event that we and our suppliers cannot agree to the terms and conditions for them to provide some or all of our clinical and commercial drug supply needs, or if our suppliers terminate their agreements with us in response to a breach by us or any other reason permitted under our agreements, we would not be able to manufacture the drug on a commercial scale until a qualified alternative supplier is identified, which could also delay the development of, and impair our ability to commercialize, our product candidates. Any supplier would be required to obtain regulatory approval of their manufacturing facilities, processes and quality systems before engaging in the commercial manufacture of a pharmaceutical product. Due to the complexity of the processes used to manufacture pharmaceutical products and product candidates, any potential third-party manufacturer may be unable to continue to pass or initially pass federal, state or international regulatory inspections in a cost-effective manner.

Although we believe that appropriate alternative sources of supply exist for each of our current product candidates, the number of third-party suppliers with the necessary manufacturing and regulatory expertise and facilities is limited, and it could be expensive and take a significant amount of time to arrange for alternative suppliers, which could have a material adverse effect on our business. New suppliers of any drug would be required to qualify under applicable regulatory requirements and would need to have sufficient rights under applicable intellectual property laws to the method of manufacturing such ingredients. Obtaining the necessary FDA approvals or other qualifications under applicable regulatory requirements and ensuring non-infringement of third- party intellectual property rights could result in a significant interruption of supply and could require the new manufacturer to bear significant additional costs which may be passed on to us.

The failure of third-party manufacturers or suppliers to perform adequately or the termination of our arrangements with any of them may negatively and adversely affect our business.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- the inability to meet any product specifications and quality requirements consistently;
- a delay or inability to procure or expand sufficient manufacturing capacity;
- capacity related to the scale-up of manufacturing;
- manufacturing and product quality issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;

- a failure to comply with cGMP and similar foreign standards;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier;
- carrier disruptions or increased costs that are beyond our control;
- the failure of third parties involved in the transportation, storage and distribution of our products, including the failure to deliver products under specified storage conditions and in a timely manner; and
- the possibility that our contract manufacturer, or third parties with access to their facilities, will have access to and may appropriate our trade secrets or other proprietary information.

Any of these events could lead to clinical trial delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future products. Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production.

We may not be able to develop or identify a technology that can effectively deliver our miR-34 mimic or any other of our microRNA-based product candidates to the intended diseased cells or tissues, and any failure in such delivery technology could adversely affect and delay the development of MRX34 and our other product candidates.

In connection with our Phase 1 clinical trial of MRX34, we have used a SMARTICLES liposomal formulation to facilitate delivery to tumors. SMARTICLES has demonstrated successful tumor delivery of our miR-34 mimic in multiple mouse models of liver cancer, but we cannot be certain that the SMARTICLES technology will be capable of delivering adequate levels of our miR-34 mimic to liver tumors in patients to produce a therapeutic response. While we believe SMARTICLES could be used to deliver mimics in additional indications, future clinical testing could reveal that the efficacy of SMARTICLES is limited to delivery to liver cancer cells. While we are continuing to evaluate the use of SMARTICLES in other indications, and additional delivery technologies that might enable us to target other cells with our product candidates, we cannot be certain whether we will be successful in developing such alternative delivery mechanisms. Our failure to effectively deliver any of our product candidates to the intended diseased cells or tissues could adversely affect and delay the development of our product candidates.

We currently have no sales and marketing staff or distribution organization. If we are unable to develop a sales and marketing and distribution capability on our own or through third parties, we will not be successful in commercializing our future products.

We currently have no sales, marketing or distribution capabilities or experience. To achieve commercial success for any approved product candidate, we must either develop a sales, marketing and distribution organization or outsource these functions to third parties. If we rely on third parties for marketing and distributing our approved products, any revenue we receive will depend upon the efforts of third parties, which may not be successful and are only partially within our control and our product revenue may be lower than if we directly marketed or sold our products. If we are unable to enter into arrangements with third parties to sell, market and distribute product candidates for which we have received regulatory approval on acceptable terms or at all, we will need to market these products ourselves. This is likely to be expensive and logistically difficult, as it would require us to build our own sales, marketing and distribution capacity. We have no experience in this area, and if such efforts were necessary, we may not be able to successfully commercialize our future products. If we are not successful in commercializing our future products, either on our own or through third parties, any future product revenue will be materially and adversely affected.

We may attempt to form collaborations in the future with respect to our product candidates, but we may not be able to do so, which may cause us to alter our development and commercialization plans.

We may attempt to form strategic alliances, create joint ventures or collaborations or enter into licensing arrangements with third parties with respect to our programs that we believe will complement or augment our existing business. For example, we may attempt to find a strategic partner for the development and/or commercialization of MRX34. We may face significant competition in seeking appropriate strategic partners, and the negotiation process to secure appropriate terms is time-consuming and complex. We may not be successful in our efforts to establish such a strategic partnership for any product candidates and programs on terms that are acceptable to us, or at all. This may be because our product candidates and programs may be deemed to be at too early of a stage of development for collaborative effort, our research and development pipeline may be viewed as insufficient, the competitive or intellectual property landscape may be viewed as too intense or risky, and/or third parties may not view our product candidates and programs as having sufficient potential for commercialization, including the likelihood of an adequate safety and efficacy profile.

Any delays in identifying suitable collaborators and entering into agreements to develop and/or commercialize our product candidates could delay the development or commercialization of our product candidates, which may reduce their competitiveness even if they reach the market. Absent a collaboration partner, we would need to undertake development and/or commercialization activities at our own expense. If we elect to fund and undertake development and/or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we are unable to do so, we may not be able to develop our product candidates or bring them to market and our business may be materially and adversely affected.

We may be unable to realize the potential benefits of any collaboration.

Even if we are successful in entering into a collaboration with respect to the development and/or commercialization of one or more product candidates, there is no guarantee that the collaboration will be successful. Collaborations may pose a number of risks, including:

- collaborators often have significant discretion in determining the efforts and resources that they will apply to the collaboration, and may not commit sufficient resources to the development, marketing or commercialization of the product or products that are subject to the collaboration;
- collaborators may not perform their obligations as expected;
- any such collaboration may significantly limit our share of potential future profits from the associated program, and may require us to relinquish potentially valuable rights to our current product candidates, potential products or proprietary technologies or grant licenses on terms that are not favorable to us;
- collaborators may cease to devote resources to the development or commercialization of our product candidates if the collaborators view our product candidates as competitive with their own products or product candidates;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the course of development, might cause delays or termination of the development or commercialization of product candidates, and might result in legal proceedings, which would be time-consuming, distracting and expensive;
- collaborators may be impacted by changes in their strategic focus or available funding, or business combinations involving them, which could cause them to divert resources away from the collaboration;

- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;

- the collaborations may not result in us achieving revenues to justify such transactions; and

- collaborations may be terminated and, if terminated, may result in a need for us to raise additional capital to pursue further development or commercialization of the applicable product candidate.

As a result, a collaboration may not result in the successful development or commercialization of our product candidates.

Reliance on government funding for our programs may add uncertainty to our research and commercialization efforts with respect to those programs that are tied to such funding and may impose requirements that limit our ability to take certain actions, increase the costs of commercialization and production of product candidates developed under those programs and subject us to potential financial penalties, which could materially and adversely affect our business, financial condition and results of operations.

During the course of our development of our product candidates, we have been funded in significant part through federal and state grants, including but not limited to the substantial funding we have received from the Texas Emerging Technology Fund and the Cancer Prevention & Research Institute of Texas, or CPRIT. In addition to the funding we have received to date, we have applied and intend to continue to apply for federal and state grants to receive additional funding in the future. Contracts and grants funded by the U.S. government, state governments and their related agencies, including our contracts with the State of Texas pertaining to funds we have already received, include provisions that reflect the government's substantial rights and remedies, many of which are not typically found in commercial contracts, including powers of the government to:

- require repayment of all or a portion of the grant proceeds, in certain cases with interest, in the event we violate certain covenants pertaining to various matters that include any potential relocation outside of the State of Texas, failure to achieve certain milestones or to comply with terms relating to use of grant proceeds, or failure to comply with certain laws;

- terminate agreements, in whole or in part, for any reason or no reason;

- reduce or modify the government's obligations under such agreements without the consent of the other party;

- claim rights, including intellectual property rights, in products and data developed under such agreements;

- audit contract-related costs and fees, including allocated indirect costs;

- suspend the contractor or grantee from receiving new contracts pending resolution of alleged violations of procurement laws or regulations;

- impose U.S. manufacturing requirements for products that embody inventions conceived or first reduced to practice under such agreements;

- impose qualifications for the engagement of manufacturers, suppliers and other contractors as well as other criteria for reimbursements;

- suspend or debar the contractor or grantee from doing future business with the government;

- control and potentially prohibit the export of products;

- pursue criminal or civil remedies under the False Claims Act, False Statements Act and similar remedy provisions specific to government agreements; and

- limit the government's financial liability to amounts appropriated by the U.S. Congress on a fiscal-year basis, thereby leaving some uncertainty about the future availability of funding for a program even after it has been funded for an initial period.

In addition to those powers set forth above, the government funding we may receive could also impose requirements to make payments based upon sales of our products in the future. For example, under the terms of our award from CPRIT, we are required to pay CPRIT a portion of our revenues from sales of certain products by us, or received from our licensees or sublicensees, at a percentage in the low single digits until the aggregate amount of such payments equals a specified multiple of the grant amount, and thereafter at a rate of less than one percent, subject to our right, under certain circumstances, to make a one-time payment in a specified amount to CPRIT to buy out such payment obligations. See "Business—Strategic Partnerships and Collaborations" for a description of the CPRIT agreement, which includes a description of our obligations to make royalty payments.

We may not have the right to prohibit the U.S. government from using certain technologies developed by us, and we may not be able to prohibit third-party companies, including our competitors, from using those technologies in providing products and services to the U.S. government. The U.S. government generally takes the position that it has the right to royalty-free use of technologies that are developed under U.S. government contracts. These and other provisions of government grants may also apply to intellectual property we license now or in the future.

In addition, government contracts and grants normally contain additional requirements that may increase our costs of doing business, reduce our profits, and expose us to liability for failure to comply with these terms and conditions. These requirements include, for example:

- specialized accounting systems unique to government contracts and grants;

- mandatory financial audits and potential liability for price adjustments or recoupment of government funds after such funds have been spent;

- public disclosures of certain contract and grant information, which may enable competitors to gain insights into our research program; and

- mandatory socioeconomic compliance requirements, including labor standards, non-discrimination and affirmative action programs and environmental compliance requirements.

If we fail to maintain compliance with any such requirements that may apply to us now or in the future, we may be subject to potential liability and to termination of our contracts.

Our business involves the use of hazardous materials and we and our third- party manufacturers must comply with environmental laws and regulations, which may be expensive and restrict how we do business.

Our third-party manufacturers' activities and our own activities involve the controlled storage, use and disposal of hazardous materials, including the components of our pharmaceutical product candidates, test samples and reagents, biological materials and other hazardous compounds. We and our manufacturers are subject to federal, state, local and foreign laws and regulations governing the use, generation, manufacture, storage, handling and disposal of these hazardous materials. We currently carry no insurance specifically covering environmental claims relating to the use of hazardous materials. Although we believe that our safety procedures for handling and disposing of these materials and waste products comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental injury or contamination from the use, storage, handling or disposal of hazardous materials. In the event of an accident, state or federal or other applicable authorities may curtail our use of these materials and/or interrupt our business operations. In addition, if an accident or environmental discharge occurs, or if we discover contamination caused by prior operations, including by prior owners and operators of properties we acquire, we could be liable for cleanup obligations, damages and fines. If such unexpected costs are substantial, this could significantly harm our financial condition and results of operations.

Risks Related to Administrative, Organizational and Commercial Operations and Growth

We will need to increase the size of our organization, and we may experience difficulties in managing growth.

As of March 31, 2015, we had 21 employees. We may need to expand our managerial, operational, financial and other resources in order to manage our operations and clinical trials, continue our development activities and commercialize MRX34 or other product candidates. Our management and personnel, systems and facilities currently in place are likely not adequate to support this future growth. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure and give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. Our need to effectively execute our business strategy requires that we:

- manage our Phase 1 clinical trial, which is being conducted at multiple trial sites, as well as manage any other clinical trials in the future;
- manage our internal development efforts effectively while carrying out our contractual obligations to licensors, contractors, government agencies, any future collaborators and other third parties;
- continue to improve our operational, financial and management controls, reporting systems and procedures; and
- identify, recruit, maintain, motivate and integrate additional employees.

If we are unable to expand our managerial, operational, financial and other resources to the extent required to manage our development and commercialization activities, our business will be materially adversely affected.

We face substantial competition and our competitors may discover, develop or commercialize products faster or more successfully than us.

The development and commercialization of new drug products is highly competitive. We face competition from major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, universities and other research institutions worldwide with respect to MRX34 and other product candidates that we may seek to develop or commercialize in the future. Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective or less costly than MRX34 or any other product candidates that we are currently developing or that we may develop, which could render our product candidates obsolete and noncompetitive.

There are a number of pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of the most prevalent form of liver cancer, hepatocellular carcinoma, or HCC. Companies working in this area include Alnylam Pharmaceuticals, Inc., Dicerna Pharmaceuticals, Inc., Isis Pharmaceuticals, Inc., Quark Pharmaceuticals, Inc., Regulus Therapeutics, Inc., Rosetta Genomics Ltd., Silence Therapeutics plc and Tekmira Pharmaceuticals Corporation, or Tekmira, as well as a number of the multinational pharmaceutical companies. Tekmira has announced an ongoing multicenter, single-arm, open-label dose escalation Phase 1/2 study for TKM-PLK1 in HCC. Notably, Bristol Myers Squibb recently presented positive data from an ongoing Phase 1 clinical trial of nivolumab (Opdivo), a PD-1 blocker, demonstrating a 19% response rate. In addition, there are a variety of available therapies marketed for the treatment of liver cancer with which we would expect to compete. Many of the available therapies are well-established and widely accepted by physicians, patients and third-party payors. For example, Nexavar, marketed by Amgen Inc. and Bayer AG, is currently in use for the treatment of HCC. There are also a number of pharmaceuticals and biologics that are marketed or in clinical development for the treatment of solid tumors. The most common treatments for solid tumors are various chemotherapeutic agents, radiation therapy and certain targeted therapies, including monoclonal antibodies such as Avastin®, Erbitux®, Herceptin® and Vectibix®. Small molecules, such as Nexavar, Sutent® and Tarceva®, are also indicated for the treatment of solid tumors.

There are also a number of pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of various hematological malignancies. Companies working in this area include Celgene Corporation, Gilead Sciences, Inc., Infinity Pharmaceuticals, Inc., Millennium Pharmaceuticals, Inc., Pharmacylics LLC and ProNAi Therapeutics, Inc., as well as a number of the multinational pharmaceutical companies. In addition, there are a variety of available therapies marketed for the treatment of various hematological malignancies with which we would expect to compete. Many of the available therapies are well-established and widely accepted by physicians, patients and third-party payors. For example, Rituxan®, marketed by F. Hoffmann-La Roche Ltd. and Genentech Inc., is currently in use for the treatment of chronic lymphocytic leukemia and non-Hodgkin's lymphoma, or NHL. In addition, ProNAi Therapeutics, Inc. has an ongoing Phase 2 clinical trial in patients with NHL on their lead therapeutic product, PNT2258. There are also a number of pharmaceuticals and biologics that are marketed or in clinical development for the treatment of various hematologic malignancies. The most common treatments for various hematological malignancies are chemotherapeutic agents, radiation therapy and certain targeted therapies, including monoclonal antibodies such as Gazyva®, Arzerra® and Campath®. Small molecules, such as Imbruvica®, Vizada®, Treanda®, Velcade® and Revlimid® are also indicated for the treatment of various hematological malignancies.

In addition to the competition we face from alternative therapies for the diseases we intend to target with our product candidates, we are also aware of several companies that are also working specifically to develop microRNA therapeutics, including miRagen Therapeutics, Inc., Regulus Therapeutics, Inc. and Santaris Pharma A/S (now Roche). Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations. Insurers and other third-party payors may also encourage the use of generic products. For example, if MRX34 is approved, it may be priced at a significant premium over other competitive products. This may make it difficult for MRX34 or any other future products to compete with these products.

If our competitors obtain marketing approval from the FDA or comparable foreign regulatory authorities for their product candidates more rapidly than us, it could result in our competitors establishing a strong market position before we are able to enter the market.

Many of our competitors have materially greater name recognition and financial, manufacturing, marketing, research and drug development resources than we do. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Large pharmaceutical companies in particular have extensive expertise in preclinical, nonclinical and clinical testing and in obtaining regulatory approvals for drugs. In addition, academic institutions, government agencies, and other public and private organizations conducting research may seek patent protection with respect to potentially competitive products or technologies. These organizations may also establish exclusive collaborative or licensing relationships with our competitors. Failure of MRX34 or other product candidates to effectively compete against established treatment options or in the future with new products currently in development would harm our business, financial condition, results of operations and prospects.

We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as acquisitions of companies, asset purchases, and out-licensing or in-licensing of products, product candidates or technologies. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near- and long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could adversely affect our operations and financial results. For example, these transactions may entail numerous operational and financial risks, including:

- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention in order to develop acquired products, product candidates or technologies;
- incurrence of substantial debt or dilutive issuances of equity securities to pay for acquisitions;
- higher-than-expected acquisition and integration costs;
- write-downs of assets or goodwill or impairment charges;
- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses.

Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks, could have a material adverse effect on our business, financial condition, results of operations and prospects.

We are highly dependent on the services of our President and Chief Executive Officer, Paul Lammers, M.D., M.Sc., and our ability to attract and retain qualified personnel.

We may not be able to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses. Our industry has experienced a high rate of turnover of management and scientific personnel in recent years. If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

We are highly dependent on the principal members of our management and scientific staff. The loss of service of any of our management and key scientific staff could harm our business, particularly our President and Chief Executive Officer, Dr. Lammers. Due to our limited resources, we may not be able to effectively attract and recruit additional qualified personnel. If we are not able to retain our management, particularly our President and Chief Executive Officer, Dr. Lammers, and to attract, on acceptable terms, additional qualified personnel necessary for the continued development of our business, we may not be able to sustain our operations or grow. Although we have executed employment agreements with each member of our current executive management team, including Dr. Lammers, we may not be able to retain their services as expected.

In addition, we have scientific and clinical advisors who assist us in formulating our product development and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us, or may have arrangements with other companies to assist in the development of products that may compete with ours.

Our internal computer systems, or those of our CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data from completed or ongoing clinical trials for any of our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, including the confidential medical information of clinical trial participants, we could incur liability and the further development of our product candidates could be delayed.

Our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in fraudulent or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (i) FDA regulations, including those laws requiring the reporting of true, complete and accurate information to the FDA; (ii) manufacturing standards; (iii) federal and state healthcare fraud and abuse laws and regulations; or (iv) laws that require the true, complete and accurate information or data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, 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. Activities subject to these laws 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. It is not always possible to identify and deter misconduct by our employees and other third parties, 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 be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Requirements associated with being a public company will increase our costs significantly, as well as divert significant company resources and management attention.

Prior to this offering, we have not been subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or the other rules and regulations of the Securities and Exchange Commission, or SEC, or any securities exchange relating to public companies. We are working with our legal, independent accounting and financial advisors to identify those areas in which changes should be made to our financial and management control systems to manage our growth and our obligations as a public company. These areas include corporate governance, corporate control, disclosure controls and procedures and financial reporting and accounting systems. We have made, and will continue to make, changes in these and other areas. However, the expenses that will be required in order to adequately prepare for being a public company could be material, particularly after we cease to be an "emerging growth company." Compliance with the various reporting and other requirements applicable to public companies will also require considerable time and attention of management. In addition, the changes we make may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis.

However, for as long as we remain an "emerging growth company" as defined in the Jumpstart our Business Startups Act, or the JOBS Act, we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies," including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We may take advantage of these reporting exemptions until we are no longer an "emerging growth company." Because the JOBS Act has only recently been enacted, it is not yet clear whether investors will accept the more limited disclosure requirements that we may be entitled to follow while we are an "emerging growth company." If they do not, we may end up electing to comply with disclosure requirements as if we were not an "emerging growth company," in which case we would incur the greater expenses associated with such disclosure requirements.

We will remain an "emerging growth company" for up to five years after the completion of this offering, although if the market value of our common stock that is held by non-affiliates exceeds $700 million as of any June 30 before that time or if we have total annual gross revenues of $1 billion or more during any fiscal year before that time, we would cease to be an "emerging growth company" as of the end of that fiscal year, or if we issue more than $1 billion in non-convertible debt in a three-year period, we would cease to be an "emerging growth company" immediately.

In addition, being a public company could make it more difficult or more costly for us to obtain certain types of insurance, including directors' and officers' liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

If we are not able to implement the requirements of Section 404 of the Sarbanes-Oxley Act of 2002 in a timely manner or with adequate compliance, we may be subject to sanctions by regulatory authorities.

Section 404 of the Sarbanes-Oxley Act of 2002 requires that we evaluate and determine the effectiveness of our internal controls over financial reporting and, beginning with our annual report for fiscal year 2016, provide a management report on the internal control over financial reporting. If we have a material weakness in our internal control over financial reporting, we may not detect errors on a timely basis and our financial statements may be materially misstated. We will be evaluating our internal controls systems to allow management to report on, and eventually allow our independent auditors to attest to, our internal controls. We will be performing the system and process evaluation and testing (and any necessary remediation) required to comply with the management certification and eventual auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002. The aforementioned auditor attestation requirements will not apply to us until we are not an "emerging growth company."

To date, we have never conducted a review of our internal controls for the purpose of providing the reports required by these rules. We cannot be certain as to the timing of completion of our evaluation, testing and remediation actions or the impact of the same on our operations. If we are not able to implement the requirements of Section 404 in a timely manner or with adequate compliance, we may be subject to sanctions or investigation by regulatory authorities, such as the SEC or The NASDAQ Stock Market LLC, or NASDAQ. Any such action could adversely affect our financial results or investors' confidence in us and could cause our stock price to fall. Moreover, if we are not able to comply with the requirements of Section 404 in a timely manner, or if we or our independent registered public accounting firm identifies deficiencies in our internal controls that are deemed to be material weaknesses, we could be subject to sanctions or investigations by the SEC, NASDAQ or other regulatory authorities, which would entail expenditure of additional financial and management resources and could materially adversely affect our stock price. Inferior internal controls could also cause us to fail to meet our reporting obligations or cause investors to lose confidence in our reported financial information, which could have a negative effect on our stock price.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history and do not expect to become profitable in 2015 and may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. We may be unable to use these losses to offset income before such unused losses expire. Under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss, or NOL, carryforwards and other pre-change tax attributes to offset its post-change income may be further limited. We believe that we have experienced at least one ownership change in the past. We may also experience additional ownership changes as a result of subsequent shifts in our stock ownership, including as a result of this offering. Accordingly, our ability to use our pre-change NOL carryforwards to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. For these reasons, we may not be able to utilize any or a material portion of our NOL carryforwards and other tax attributes.

If we seek and obtain approval to commercialize MRX34 outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If MRX34 is approved for commercialization outside the United States, we will likely enter into agreements with third parties to market MRX34 outside the United States. We expect that we will be subject to additional risks related to entering into these international business relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- differing U.S. and foreign drug import and export rules;
- reduced protection for our intellectual property rights in foreign countries;
- existence of third party intellectual property rights of potential relevance to our business;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad or with U.S. regulations that would apply to activities in such foreign jurisdictions, such as the Foreign Corrupt Practices Act;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- potential liability resulting from development work conducted by these distributors; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters.

We or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters could severely disrupt our operations, and have a material adverse effect on our business, financial condition and results of operations. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our enterprise financial systems or manufacturing resource planning and enterprise quality systems, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

Furthermore, certain integral parties in our supply chain are geographically concentrated and operating from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events. Although we believe there to be sufficient alternative suppliers in other geographic locations, if such an event were to affect such existing parties in our supply chain, it could have a material adverse effect on our business.

Risks Related to Intellectual Property

If we are unable to obtain and maintain sufficient patent protection for our technology and product candidates, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our product candidates may be adversely affected.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our technologies.

In particular, our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates. If we do not adequately protect our intellectual property, competitors may be able to use our technologies and erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we file patent applications in the United States and in limited jurisdictions abroad related to our product candidates and compounds in development that may become our product candidates. The patent application and approval process is expensive and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We may also fail to identify patentable aspects of our research and development before it is too late to obtain patent protection.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. This uncertainty includes changes to the patent laws through either legislative action to change statutory patent law or court action that may reinterpret existing law in ways affecting the scope or validity of issued patents. The patent applications that we own or in-license may fail to result in issued patents in the United States or in foreign countries in which we pursue protection with claims that cover our product candidates. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents have issued, or do successfully issue, from patent applications that we own or license, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. For example, patents granted by the European Patent Office (EPO) may be challenged, also known as opposed, by any person within nine months from the publication of their grant. In May 2015, two separate and unidentified parties filed submissions before the EPO opposing a granted European patent related to MRX34, EP2302055 (the '055 Patent), in-licensed to us from Asuragen. We are currently reviewing these submissions and plan to respond to the submissions before the November 2015 EPO response deadline. All of the claims of the '055 Patent remain valid and in force during the opposition proceedings. It is not possible to predict the outcome of the opposition proceedings, for example whether the patent will be maintained, limited in scope or whether the grant may be revoked. If the '055 Patent is ultimately narrowed in scope or revoked during the opposition proceedings, the patent protection afforded by the '055 Patent, and the extent of our exclusivity with respect to commercialization of MRX-34 in Europe could be materially impaired. Even if they are unchallenged, our patents may not adequately protect our product candidates, provide any competitive advantage or prevent others from designing around our claims. If the breadth or strength of protection provided by the patents and patent applications we hold, in-license or pursue with respect to our product candidates is threatened or insufficient, it could dissuade companies from collaborating with us to develop, or undermine our ability to commercialize our product candidates and could have a material adverse effect on our business, financial condition, results of operations and prospects.

Currently, our patent portfolio includes at least 10 issued U.S. patents and over 80 pending U.S. and foreign applications that we own, co-own, or have in-licensed from third parties, primarily focused on various aspects of microRNA therapeutics, including various microRNA mimics, and methods of use as microRNA related therapies. Within our patent portfolio, we are the sole owner of multiple U.S. and foreign patent applications related to microRNA therapies, including chemically modified versions of miR-34 not currently used in MRX34 (U.S. Patent No. 8,586,727) and other microRNAs mimics that are possible candidates for future product development as microRNA therapeutics. Further, our patent portfolio includes U.S. 7,960,359 and U.S. 8,563,708, both of which are related to miR-34 and are in-licensed from Asuragen. Specifically, U.S. 7,960,359 is related to use of a miR-34a mimic, for example MRX34, for reducing cell viability of human lung cancer cells, human cancerous T cells, human prostate cancer cells or human skin cancer cells. This patent is expected to expire in 2025. See "Business—Intellectual Property—Our Patent Portfolio" for a more detailed description of the patents we own or license covering our product candidates.

If the patent applications we hold or have in-licensed with respect to our programs or product candidates fail to issue, if their breadth or strength of protection is threatened, if we abandon or allow owned or in-licensed patents or patent applications that we are responsible for prosecuting to lapse, or if our owned and in-licensed patents and patent applications fail to provide meaningful exclusivity for our product candidates, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize future products. We have multiple pending patent applications relating to our product candidates. We cannot offer any assurances about which, if any, patents will issue, the breadth of the claims of any such patent, should it issue, or whether any issued patents will be found invalid and/or unenforceable, will be interpreted narrowly or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop.

Almost all of our patents and patent applications are entitled to effective filing dates prior to March 16, 2013. For U.S. patent applications in which patent claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party, for example a competitor, or instituted by the U.S. Patent and Trademark Office, or the USPTO, to determine who was the first to invent any of the subject matter covered by those patent claims. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our participation in an interference proceeding may fail and, even if successful, may result in substantial costs and distract our management.

Further, if we encounter delays in our clinical trials or achieving regulatory approvals, the period of time during which we could market any of our product candidates under patent protection, if approved, would be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to our product candidates. Furthermore, an interference proceeding can be provoked by a third party or instituted by the U.S. Patent and Trademark Office, or USPTO, to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. In addition, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however the life of a patent, and the protection it affords, is limited. Even if we obtain patents that cover the manufacture, use and/or sale of our product candidates and such patents are not successfully challenged by any third parties, once the patent life has expired for a product, we may be open to competition from generic medications.

We may not be successful in obtaining or maintaining necessary rights to product components and processes for our development pipeline through acquisitions and in-licenses.

Presently we have rights to certain intellectual property through licenses from third parties and under patents that we own or co-own, related to a subset of the known microRNA targets. Because our programs may involve a range of microRNA targets and specific formulations of microRNA mimics directed to such targets, including targets and formulations that may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or otherwise gain the right to use these proprietary rights. We may be unable to acquire or in-license any necessary or desirable third-party intellectual property rights on reasonable terms, or at all. 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 now or in the future. 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. If we are unable to successfully obtain rights to required third-party intellectual property rights, including rights related to our lead product candidate, our business, financial condition and prospects for growth could suffer.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that may not be patentable or that we elect not to patent, processes for which patents may be difficult to obtain or enforce, and any other elements of our product candidates discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect. We seek to protect our proprietary data and processes, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and collaborators, and any other third parties that have access to our proprietary know-how, information or technology, for example, third parties involved in our clinical trials. Although we expect all of our employees, consultants, advisors and any third parties who have access to our proprietary knowhow, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed, and we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all.

We also seek to preserve the integrity and confidentiality of our data, trade secrets and knowhow by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. Moreover, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the intellectual property related to our technologies to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, financial condition and results of operations.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or the USPTO.

If we or one of our licensing partners initiated legal proceedings against a third party to enforce a patent covering the manufacture, use or sale, or other aspects of one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include ex parte re-examination, inter partes review, post grant review and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our product candidates. 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, our patent counsel 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 our product candidates. Similarly, the outcome following administrative review of a patent that we own or license, such as via a reexamination or opposition proceeding before the USPTO or a foreign body, is unpredictable. If a third party were to prevail, we could lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business.

If we are sued for infringing the patent rights or misappropriating the trade secrets of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our product candidates and use our proprietary technology without infringing the patent rights of third parties. Numerous third-party U.S. and non-U.S. issued patents and pending applications exist in the area of microRNA. We are aware of certain U.S. and foreign patents and pending patent applications owned by our competitors or other third parties that cover certain miR-34 mimics and therapeutic uses thereof. We are currently monitoring these patents and patent applications. We have and we may in the future pursue available proceedings in the U.S. and foreign patent offices to challenge the validity of these patents and patent applications. In addition or alternatively, we may consider whether to seek to negotiate a license of rights to technology covered by one or more of such patents and patent applications. If any patents or patent applications cover our product candidates or technologies, we may not be free to manufacture or market our product candidates as planned, absent such a license, which may not be available to us on commercially reasonable terms, or at all. For example, in 2013 we launched opposition proceedings against a granted European patent related to miR-34a. Following oral arguments, the European Patent Office upheld the patent. We are currently evaluating all options as we believe the patent was issued erroneously.

It is also possible that we have failed to identify relevant third-party patents or applications. For example, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Moreover, it is difficult for industry participants, including us, to identify all third-party patent rights that may be relevant to our product candidates and technologies because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of a current or future product candidate, or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our products or the use of our products.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding patent rights with respect to our technology or products candidates, including interferences, oppositions and *inter partes* review proceedings before the USPTO and corresponding foreign patent offices. We also monitor patent prosecution activities and pending applications of competitors and potential competitors in our field in order to identify third party patent rights that could pose a potential threat to our freedom to operate in the market with respect to our product candidates, once commercialized. We are currently pursuing and may in the future pursue available administrative proceedings in the U.S. or foreign patent offices to challenge third party patent rights that could adversely impact our ability to commercialize one or more of our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our current or future product candidates may be subject to claims of infringement of the patent rights of third parties, who may assert infringement claims against us based on existing or future patent rights. Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates and third parties could allege that our technology infringes such claims. Further, because patent applications can take many years to issue, third parties may have currently pending patent applications which may later result in issued patents that our product candidates may infringe, or which such third parties claim are infringed by the use of our technologies. The outcome of patent litigation is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid, and we may not be able to do this. Proving that a patent is invalid is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on us. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe a third party's patent rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

Parties making claims against us for infringement of their patent rights may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we could be required to redesign our infringing products or obtain a license from such third party to continue developing and commercializing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms, or at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. It may be impossible to redesign our products and technology, or it may require substantial time and monetary expenditure, which could force us to cease commercialization of one or more of our product candidates, or some of our business operations, which could materially harm our business. In addition, in any such proceeding, we may be required to pay substantial damages, including treble damages and attorneys' fees in the event we are found liable for willful infringement.

We may be involved in lawsuits or administrative proceedings to protect or enforce our intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors may infringe or we may believe that they infringe patents that we own or license. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid or is unenforceable, or may refuse to stop the other party in such infringement proceeding from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly, and could put any of our patent applications at risk of not yielding an issued patent. Litigation is uncertain, and we cannot predict whether we would be successful in any such litigation.

Interference proceedings provoked by third parties or brought by the USPTO or any foreign patent authority may be necessary to determine the priority of inventions with respect to our patents or patent applications. 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, if any license is offered at all. Litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees.

We may not be able to prevent misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States. 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. In addition, there could 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 substantial adverse effect on the price of our common stock.

Legal actions to enforce patent rights or other intellectual property rights that we own or license can be expensive and may involve the diversion of significant management time. In addition, these legal actions could be unsuccessful and could also result in the invalidation of our patents or a finding that they are unenforceable. Moreover, third parties may be able to successfully design around our patents using pre-existing technology, by developing new technology or by using similar technology that is outside the scope of our patents. We may or may not choose to pursue litigation against those that have infringed on our patents, or used them without authorization, due to the associated expense and time commitment of monitoring these activities. If we fail to protect or to enforce our intellectual property rights successfully, our competitive position could suffer, which could harm our results of operations.

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

Filing, prosecuting and defending patents on all of our product candidates throughout the world would be prohibitively expensive, and our patent rights in some countries outside the United States can be less extensive than those in the United States. The requirements for patentability may differ in certain countries, particularly developing countries. For example, unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed therapeutic. In addition, the laws of some foreign countries do 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 our 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.

As part of ordinary course prosecution and maintenance activities, we determine whether to seek patent protection outside the United States and in which countries. This also applies to patents we have acquired or in-licensed from third parties. In some cases this means that we, or our predecessors in interest or licensors of patents within our portfolio, have sought patent protection in a limited number of countries for patents covering our product candidates, including for patents providing coverage for MRX34. Competitors may use our technologies in jurisdictions where we have not pursued and obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and, even in jurisdictions where we have or are able to obtain issued patents, our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so 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 cost 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. In addition, certain countries in Europe and certain developing countries, including India and China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we may have limited remedies if our patents are infringed or if we are compelled to grant a license to our patents to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities.

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 own or license. Moreover, patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

The patent protection and patent prosecution for some of our product candidates may be dependent on our third party licensors.

While we normally seek to obtain the right to control the filing, prosecution, maintenance, defense and enforcement of the patents and patent applications that we in-license relating to our product candidates, there may be times when such activities for patents that relate to our product candidates are controlled by our licensors. For example, we do not have the first right to prosecute, maintain, defend, or enforce the patent rights licensed to us relating to the SMARTICLES technology under our agreement with Marina Biotech, Inc., or Marina. Although we may retain the right to consult on such filing, prosecution, maintenance, defense, and enforcement activities, our overall ability to influence such activities is limited. Further, while we seek to have rights to take action to defend our in-licensed patents and patent applications from third-party challenges in the event that our licensors determine not to, we may not be aware of any such potential threats to the intellectual property rights we in-license, or we may be unsuccessful in protecting such intellectual property rights if we respond to any such challenges by third parties.

If these licensors or any of our future licensors fail to appropriately file, prosecute, maintain, defend or enforce our in-licensed patents and patent applications covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products.

If we breach any of the agreements under which we license patent rights to use, develop and commercialize our product candidates or our technologies from third parties or, in certain cases, we fail to meet certain development deadlines, we could lose license rights that are important to our business.

We are a party to a number of license agreements under which we are granted rights to intellectual property that are important to our business and we expect that we may need to enter into additional license agreements in the future. These include our exclusive cross-license agreement with Asuragen, our exclusive licenses from Yale University, or Yale, Marina Biotech, or Marina, and the University of Zurich, and our non-exclusive license from Merck & Co, or Merck.

Our existing license agreements, except our cross-license agreement with Asuragen, generally impose, and we expect that future license agreements will impose on us, various development, regulatory and/or commercial diligence obligations, and financial obligations, such as payment of milestones and/or royalties. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we may not be able to market products covered by the license. Our business could suffer, for example, if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. See "Business—Strategic Partnerships and Collaborations" for a description of our license agreements, which sets forth the material terms and obligations, including a description of the termination provisions, under our agreements with Asuragen, Yale, Marina, the University of Zurich, and Merck.

We license the technology related to SMARTICLES from Marina Biotech, or Marina. Our license with Marina imposes various development, regulatory, commercial diligence, financial, and other obligations. If we fail to comply with our obligations under the agreement with Marina, or otherwise materially breach the agreement with Marina, and fail to remedy such failure or cure such breach, Marina may have the right to terminate the license. The loss of the license from Marina would affect a portion of the patent portfolio for MRX34, which would adversely affect our ability to proceed with any development or potential commercialization of MRX34, and could subject us to claims of patent infringement by Marina if MRX34 is covered by the affected patents.

As we have done previously, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we cannot provide any assurances that third-party patents do not exist that might be enforced against our current product candidates or future products in the absence of such a license. We may fail to obtain any of these licenses on commercially reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations; and
- the ownership of inventions and knowhow resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we have licensed arise, we would expect to exercise all rights and remedies available to us, including seeking to cure any breach by us, and otherwise seek to preserve our rights under the patents licensed to us. However, we may not be able to do so in a timely manner, at an acceptable cost or at all. Generally, the loss of any one of our current licenses, or any other license we may acquire in the future, could prevent or impair our ability to successfully develop and commercialize the affected product candidates and thus materially harm our business, prospects, financial condition and results of operations.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, provide a barrier to entry against our competitors or potential competitors, or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The following examples are illustrative:

- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of the patents that we own or license;
- we or our licensors or collaborators might not have been the first to make the inventions covered by an issued patent or pending patent application that we own or license;
- we or our licensors or collaborators might not have been the first to file patent applications covering an invention;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing or misappropriating our intellectual property rights;
- pending patent applications that we own or license may not lead to issued patents;
- issued patents that we own or license may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop or in-license additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, results of operations and prospects.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We were previously involved in discussions with Yale University, or Yale, regarding the inventorship and ownership of certain patents and patent applications licensed to us by Asuragen. An independent third party expert was engaged to determine the inventorship and the ownership of patents and patent applications potentially subject to Yale and Asuragen co-ownership. This determination confirmed Asuragen's sole ownership of the patents and patent applications where co-ownership had been under consideration and resulted in a determination that Yale should be removed as a co-owner of one of the pending patent applications, an action we are currently undertaking.

Although we seek to protect our ownership of our patents and other intellectual property by ensuring that our agreements with our employees and certain collaborators and other third parties with whom we do business include provisions requiring, for instance, such parties to assign rights in inventions to us, we may be subject to claims that former or current employees, collaborators or other third parties have an ownership interest in our patents, in-licensed patents or other intellectual property. In some situations, our confidentiality agreements may conflict with, or be subject to, the rights of third parties with whom our employees, consultants, or advisors have previous employment or consulting relationships, and further, many of our consultants are currently retained by other biotechnology or pharmaceutical companies, including our competitors or potential competitors, and may be subject to conflicting obligations to these third parties. To the extent that our employees, consultants or contractors use any intellectual property owned by third parties in their work for us, disputes may arise as to the ownership of rights in any related or resulting know-how and inventions, arising, for example, from such conflicting obligations of consultants, employees or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent prosecution process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or patent applications will be due to be paid to the USPTO and various patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ reputable law firms and other professionals and rely on such third parties to effect payment of these fees with respect to the USPTO and non-U.S. patent agencies with respect to the patents and patent applications we own, and we rely upon our licensors to effect payment of these fees with respect to the patents and patent applications that we in-license. Even if we do not control prosecution and maintenance of our in-licensed patents, we may be responsible for reimbursing our licensors for some or all of the costs associated with such activities. If we fail to make timely payment to our licensors for such fees, our licensors may have the right to terminate the affected license, in which event we would not be able to market products covered by the license. We also employ reputable law firms and other professionals to help us comply with the various documentary and other procedural requirements with respect to the patents and patent applications that we own. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products, and 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.

As is the case with other biotechnology companies, our success is heavily dependent on patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. Some of our patent claims may be affected by the recent U.S. Supreme Court decision in *Association for Molecular Pathology v. Myriad Genetics*. In *Myriad*, the Supreme Court held that unmodified isolated fragments of genomic sequences, such as the DNA constituting the BRCA1 and BRCA2 genes, are not eligible for patent protection because they constitute a product of nature. The exact boundaries of the Supreme Court's decision remain unclear as the Supreme Court did not address other types of nucleic acids, such as isolated microRNAs. Nevertheless, our patent portfolio contains claims of various types and scope, including chemically modified mimics, such as in MRX34, as well as methods of medical treatment. In our view, the presence of varying claims in our patent portfolio significantly reduces, but does not eliminate, our exposure to potential validity challenges under *Myriad* or future judicial decisions. However, it is not yet clear what, if any, impact this recent Supreme Court decision or future decisions will have on the operation of our business.

For our U.S. patent applications containing a claim not entitled to priority before March 16, 2013, there is a greater level of uncertainty in the patent law. 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. The USPTO has promulgated regulations and developed procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, did not come into effect until March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

An important change introduced by the Leahy-Smith Act is that, as of March 16, 2013, the United States transitioned to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Furthermore, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our technology and the prior art allow our technology to be patentable over the prior art. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our patents or patent applications.

Among some of the other changes introduced by the Leahy-Smith Act are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal court necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action.

We may be subject to claims that our employees or consultants or independent contractors have wrongfully used or disclosed confidential information or trade secrets of third parties or that our employees or consultants have wrongfully used or disclosed alleged trade secrets of former or other employers.

Many of our employees, independent contractors and consultants, including our senior management, have been previously employed or retained by other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and independent contractors do not use the proprietary information or know-how of third parties in their work for us, and do not perform work for us that is in conflict with their obligations to another employer or any other entity, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise improperly used or disclosed confidential information, including trade secrets or other proprietary information, of a former employer or other third parties. We may also be subject to claims that an employee, advisor, consultant, or independent contractor performed work for us that conflicts with that person's obligations to a third party, such as an employer, and thus, that the third party has an ownership interest in the intellectual property arising out of work performed for us. We are not aware of any threatened or pending claims related to these matters, but in the future litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable personnel or intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property disputes could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and/or management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the market price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of our marketing exclusivity for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, if any, one of the U.S. patents covering each of such approved product(s) or the use thereof may be eligible for up to five years of patent term restoration under the Hatch-Waxman Act. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA approved product. Patent term extension also may be available in certain foreign countries upon regulatory approval of our product candidates. Nevertheless, we may not be granted patent term extension either in the United States or in any foreign country because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request. In addition, if a patent we wish to extend is owned by another party and licensed to us, we may need to obtain approval and cooperation from our licensor to request the extension.

If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

Risks Related to Government Regulation

Even if we receive regulatory approval for a product candidate, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and subject us to penalties if we fail to comply with applicable regulatory requirements.

Once regulatory approval has been granted, the approved product and its manufacturer are subject to continual review by the FDA and/or non-U.S. regulatory authorities. Any regulatory approval that we receive for our product candidates may be subject to limitations on the indicated uses for which the product may be marketed or contain requirements for potentially costly post- marketing follow-up studies to monitor the safety and efficacy of the product. In addition, if the FDA and/or non-U.S. regulatory authorities approve any of our product candidates, we will be subject to extensive and ongoing regulatory requirements by the FDA and other regulatory authorities with regard to the labeling, packaging, adverse event reporting, storage, sampling, advertising, promotion and recordkeeping for our products. Manufacturers of our products are required to comply with cGMP regulations, which include requirements related to quality control and quality assurance as well as the corresponding maintenance of records and documentation. Further, regulatory authorities must approve these manufacturing facilities before they can be used to manufacture our products, and these facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control. We will also be required to report certain adverse reactions and production problems, if any, to the FDA, and to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote our products for indications or uses for which they do not have FDA approval.

If we, any current or future collaborator or a regulatory authority discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory authority may impose restrictions on that product, such collaborator, the manufacturer or us, including requiring withdrawal of the product from the market or suspension of manufacturing. If we, our product candidates or the manufacturing facilities for our product candidates fail to comply with regulatory requirements of the FDA and/or other non-U.S. regulatory authorities, we could be subject to administrative or judicially imposed sanctions, including:

- warning letters;
- civil or criminal penalties;
- injunctions;
- suspension of or withdrawal of regulatory approval;
- total or partial suspension of any ongoing clinical trials or of production;

- voluntary or mandatory product recalls and publicity requirements;
- refusal to approve pending applications for marketing approval of new products or supplements to approved applications filed by us;
- restrictions on operations, including costly new manufacturing requirements; or
- seizure or detention of our products or import bans.

The regulatory requirements and policies may change and additional government regulations may be enacted for which we may also be required to comply. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or in other countries. Any new regulations or revisions or reinterpretations of existing regulations may impose additional costs or lengthen review times of our product candidates. In addition, if we or any current or future collaborator are not able to maintain regulatory compliance, we or such collaborator, as applicable, will not be permitted to market our future products and our business will suffer.

The availability of adequate third-party coverage and reimbursement for newly approved products is uncertain, and failure to obtain adequate coverage and reimbursement from third-party payors could impede our ability to market any future products we may develop and could limit our ability to generate revenue.

There is significant uncertainty related to the third-party payor coverage and reimbursement of newly approved medical products. The commercial success of our future products in both domestic and international markets depends on whether such third-party coverage and reimbursement are available for our future products. Governmental payors, including Medicare and Medicaid, health maintenance organizations and other third-party payors are increasingly attempting to manage their healthcare expenditures and challenging the prices charged for medical products and services by limiting both coverage and the level of reimbursement of new drugs and biologics and, as a result, they may not cover or provide adequate reimbursement for our future products. These payors may not view our future products as cost-effective, and coverage and reimbursement may not be available to our customers, may be limited to certain indications or may not be sufficient to allow our future products to be marketed on a competitive basis. Third-party payors are exerting increasing influence on decisions regarding the use of, and coverage and reimbursement levels for, particular treatments. Cost-control initiatives could cause us to decrease the price we might establish for our products candidates, which could result in lower than anticipated product revenues. If we decrease the prices for our product candidates because of competitive pressures or if governmental and other third-party payors do not provide adequate coverage or reimbursement, our prospects for revenue and profitability will suffer.

If we fail to comply or are found to have failed to comply with FDA and other regulations related to the promotion of our products for unapproved uses, we could be subject to criminal penalties, substantial fines or other sanctions and damage awards.

The regulations relating to the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA and other government agencies. If we receive marketing approval for MRX34 or other product candidates, we will be restricted from promoting the products for uses outside of the approved labeling. However, physicians may nevertheless prescribe products to their patients in a manner that is inconsistent with the approved label. We intend to implement compliance and training programs designed to ensure that our sales and marketing practices comply with applicable regulations. Notwithstanding these programs, the FDA or other government agencies may allege or find that our practices constitute prohibited promotion of our products for unapproved uses. We also cannot be sure that our employees will comply with company policies and applicable regulations regarding the promotion of products for unapproved uses.

Over the past several years, a significant number of pharmaceutical and biotechnology companies have been the target of inquiries and investigations by various federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice and various U.S. Attorneys' Offices, the Office of Inspector General of the Department of Health and Human Services, the FDA, the Federal Trade Commission and various state Attorneys General offices. These investigations have included claims asserting alleged violations of various federal and state laws and regulations, including antitrust laws, the Food, Drug and Cosmetic Act, the False Claims Act, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of products for unapproved uses, pricing and reimbursement from government programs such as the Medicare and Medicaid programs. Many of these investigations originate as "qui tam" actions, commonly referred to as "whistleblower suits," under the False Claims Act, often brought by current or former employees. Under the False Claims Act, any individual can bring a claim on behalf of the government alleging that a person or entity has presented a false claim, or caused a false claim to be submitted, to the government for payment. In a qui tam suit, the government must decide whether to intervene and prosecute the case. If it declines, the individual may pursue the case alone. The person bringing a qui tam suit is entitled to a share of any recovery or settlement, up to a certain cap; the relator's share depends on the extent of the relator's involvement in the case and whether the government intervenes.

If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a qui tam suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

If approved, MRX34 or any future products may cause or contribute to adverse medical events that we are required to report to regulatory agencies, and if we fail to do so we could be subject to sanctions that would materially harm our business.

If we are successful in commercializing MRX34 or any other products, FDA and foreign regulatory agency regulations require that we report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We may fail to report adverse events we become aware of within the prescribed timeframe. We may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our products. If we fail to comply with our reporting obligations, the FDA or a foreign regulatory agency could take action, including criminal prosecution, the imposition of civil monetary penalties, seizure of our products or delay in approval of future products. Through the first 26 months of our Phase 1 clinical trial, most patients treated with MRX34 experienced at least one adverse event, with fever, chills, fatigue, thrombocytopenia, diarrhea, back pain, nausea, vomiting, anorexia, headache, elevation of liver enzymes, decreased albumin, hyponatremia, hyperglycemia, lymphopenia and neutropenia being the most commonly reported. Among the 47 patients in the BIW dosing cohorts, the serious adverse events determined to be related to MRX34 treatment occurring in more than one patient were fever, fatigue, dehydration and elevation of liver enzymes, each of which occurred in two patients. For the 50 patients in the QD x 5 schedule, the serious adverse events determined to be related to MRX34 treatment occurring in more than one patient were bleeding at the site of silent or asymptomatic brain metastasis, elevation of liver enzymes and thrombocytopenia, each of which occurred in two patients. These adverse events associated with MRX34 are generally manageable or preventable with standard interventions or tests used by oncologists, such as administering other medications that prevent or reduce side effects, temporary slowing of infusions, delaying or stopping dosing, or using magnetic resonance imaging, or MRI, to detect silent brain metastases. Of the 29 patients with primary liver cancer treated with escalating doses of MRX34, one patient receiving a 70 mg/m^2 dose in BIW schedule achieved confirmed partial response. This patient is one of the 11 patients with primary liver cancer enrolled from the Korean sites. The one melanoma patient enrolled in the study to date, enrolled into the 110 mg/m^2 dose cohort on the QD x 5 schedule, achieved a confirmed partial response after four cycles of MRX34 treatment. See "Business—MRX34: Our Lead Product Candidate" for a more detailed description of the adverse events experienced during the course of the MRX34 clinical development program.

Failure to obtain regulatory approvals in foreign jurisdictions will prevent us from marketing our product candidates internationally.

We may seek a distribution and marketing collaborator for MRX34 or other product candidates. In order to market our product candidates in the European Economic Area, or EEA (which is comprised of the 28 Member States of the EU plus Norway, Iceland and Liechtenstein), and many other foreign jurisdictions, we or any such collaborator must obtain separate regulatory approvals. More concretely, in the EEA, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

- The Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use of the European Medicines Agency, or EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member State through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

Under these two procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

We have had limited interactions with foreign regulatory authorities, and the approval procedures vary among countries and can involve additional clinical testing, and the time required to obtain approval may differ from that required to obtain FDA approval. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one or more foreign regulatory authorities does not ensure approval by regulatory authorities in other foreign countries or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We or may not obtain foreign regulatory approvals on a timely basis, if at all. We may not be able to file for regulatory approvals and even if we file, we may not receive necessary approvals to commercialize our product candidates in any market.

Healthcare reform measures could hinder or prevent our product candidates' commercial success.

In the United States, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could affect our future revenues and profitability and the future revenues and profitability of our potential customers. Federal and state lawmakers regularly propose and, at times, enact legislation that results in significant changes to the healthcare system, some of which are intended to contain or reduce the costs of medical products and services. For example, in March 2010, the President signed one of the most significant healthcare reform measures in decades, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act. It contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse measures, all of which will impact existing government healthcare programs and will result in the development of new programs. The Affordable Care Act, among other things:

- imposes a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs";
- increases the minimum level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1%;
- addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- requires collection of rebates for drugs paid by Medicaid managed care organizations;
- requires manufacturers to participate in a coverage gap discount program, under which they must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and
- mandates a further shift in the burden of Medicaid payments to the states.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. On August 2, 2011, the President signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee did not achieve its targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reductions to several government programs. These reductions include aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments, will remain in effect through 2024 unless additional Congressional action is taken. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There likely will continue to be legislative and regulatory proposals at the federal and state levels directed at containing or lowering the cost of health care. We cannot predict the initiatives that may be adopted in the future or their full impact. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of health care may adversely affect:

- our ability to set a price we believe is fair for our products;
- our ability to generate revenues and achieve or maintain profitability; and
- the availability of capital.

In light of widely publicized events concerning the safety risk of certain drug products, regulatory authorities, members of Congress, the Governmental Accounting Office, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the withdrawal of drug products, revisions to drug labeling that further limit use of the drug products and establishment of risk management programs that may, for instance, restrict distribution of drug products. The increased attention to drug safety issues may result in a more cautious approach by the FDA to clinical trials and the drug approval process. Data from clinical trials may receive greater scrutiny with respect to safety, which may make the FDA or other regulatory authorities more likely to terminate clinical trials before completion, or require longer or additional clinical trials that may result in substantial additional expense and a delay or failure in obtaining approval or approval for a more limited indication than originally sought. In, addition, because of the serious public health risks of high profile adverse safety events with certain products, the FDA may require, as a condition of approval, costly risk management programs which may include safety surveillance, restricted distribution and use, patient education, enhanced labeling, special packaging or labeling, expedited reporting of certain adverse events, preapproval of promotional materials and restrictions on direct-to-consumer advertising.

If we fail to comply with healthcare regulations, we could face substantial penalties and our business, results of operations and financial condition could be adversely affected.

Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. We could be subject to healthcare fraud and abuse and patient privacy regulation by both the federal government and the states in which we conduct our business. The regulations that may affect our ability to operate include, without limitation:

- the federal Anti-Kickback Statute, which prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the federal False Claims Act, which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, false claims, or knowingly using false statements, to obtain payment from the federal government, and which may apply to entities that provide coding and billing advice to customers;
- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback

Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;

- the federal Physician Payment Sunshine Act, which requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the government information related to payments or other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and requires applicable manufacturers and group purchasing organizations to report annually to the government ownership and investment interests held by the physicians described above and their immediate family members and payments or other "transfers of value" to such physician owners (manufacturers are required to submit reports to the government by the 90th day of each calendar year);

- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information; and

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our financial results. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud and abuse laws may prove costly.

Risks Related to Our Common Stock and This Offering

The price of our common stock may be volatile, and you may not be able to resell your shares at or above the initial public offering price.

The initial public offering price for the shares of our common stock sold in this offering has been determined by negotiation between the underwriters and us. This price may not reflect the market price of our common stock following this offering. You may be unable to sell your shares of common stock at or above the initial public offering price due to fluctuations in the market price of our common stock. Factors that could cause volatility in the market price of our common stock include, but are not limited to:

- ability to commercialize or obtain regulatory approval for our product candidates, or delays in commercializing or obtaining regulatory approval;

- results from, or any delays in, preclinical or nonclinical testing or clinical trial programs relating to our product candidates, including the Phase 1 clinical trial for MRX34;
- any need to suspend or discontinue clinical trials due to side effects or other safety risks, or any need to conduct studies on the long-term effects associated with the use of our product candidates;
- manufacturing issues related to our product candidates for clinical trials or future products for commercialization;
- commercial success and market acceptance of our product candidates following regulatory approval;
- undesirable side effects caused by product candidates after they have entered the market;
- ability to discover, develop and commercialize additional product candidates;
- announcements relating to collaborations that we may enter into with respect to the development or commercialization of our product candidates;
- announcements relating to the receipt, modification or termination of government contracts or grants;
- success of our competitors in discovering, developing or commercializing products;
- strategic transactions undertaken by us;
- additions or departures of key personnel;
- product liability claims related to our clinical trials or product candidates;
- prevailing economic conditions;
- business disruptions caused by earthquakes or other natural disasters;
- disputes concerning our intellectual property or other proprietary rights;
- FDA or other U.S. or foreign regulatory actions affecting us or our industry;
- healthcare reform measures in the United States;
- sales of our common stock by our officers, directors or significant stockholders;
- future sales or issuances of equity or debt securities by us;
- fluctuations in our quarterly operating results; and
- the issuance of new or changed securities analysts' reports or recommendations regarding us.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that have been often unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our management would be diverted from the operation of our business.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Based on the beneficial ownership of our common stock as of March 31, 2015, after this offering, our officers and directors, together with holders of 5% or more of our outstanding common stock before this offering and their respective affiliates, will beneficially own approximately % of our common stock (assuming no exercise of the underwriters' option to purchase additional shares of common stock). Accordingly, these stockholders will continue to have significant influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets or any other significant corporate transaction. The interests of these stockholders may not be the same as or may even conflict with your interests. For example, these stockholders could delay or prevent a change of control of our company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

We are an "emerging growth company" and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act, and may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies" including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, Section 102 of the JOBS Act also provides that an "emerging growth company" can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. An "emerging growth company" can therefore delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. However, we are choosing to "opt out" of such extended transition period, and as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies. Section 107 of the JOBS Act provides that our decision to opt out of the extended transition period for complying with new or revised accounting standards is irrevocable.

Future sales of our common stock or securities convertible or exchangeable for our common stock may depress our stock price.

If our existing stockholders or holders of our options sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after the lock-up and legal restrictions on resale discussed in this prospectus lapse, the trading price of our common stock could decline. The perception in the market that these sales may occur could also cause the trading price of our common stock to decline. Based on 143,459,827 shares of common stock outstanding as of March 31, 2015, upon the completion of this offering, we will have outstanding a total of shares of common stock, assuming no exercise of the underwriters' option to purchase additional shares of common stock. Of these shares, only the shares of common stock sold by us in this offering, plus any shares sold upon exercise of the underwriters' option to purchase additional shares of common stock, will be freely tradable without restriction, unless held by our affiliates, in the public market immediately following this offering.

A total of shares of common stock are not subject to lock-up agreement with the underwriters and therefore will be eligible for sale in the public market 90 days after the date of this prospectus. After the lock-up agreements expire, shares of common stock will be eligible for sale in the public market, subject to volume limitations under Rule 144 under the Securities Act, with respect to shares held by directors, executive officers and other affiliates. The underwriters may, however, in their sole discretion, permit our officers, directors and other stockholders and the holders of our outstanding options who are subject to the lock-up agreements to sell shares prior to the expiration of the lock-up agreements. Sales of these shares, or perceptions that they will be sold, could cause the trading price of our common stock to decline.

In addition, based on the number of shares subject to outstanding awards under our 2008 Long Term Incentive Plan, or 2008 Plan, or available for issuance thereunder, as of March 31, 2015, and including the initial reserves under our 2015 Equity Incentive Award Plan, or 2015 Plan, shares of common stock that are either subject to outstanding options, outstanding but subject to vesting, or reserved for future issuance under the 2008 Plan or 2015 Plan will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. We also plan to file a registration statement permitting certain shares of common stock issued in the future pursuant to the 2008 Plan and 2015 Plan to be freely resold by plan participants in the public market, subject to the lock-up agreements, applicable vesting schedules and, for shares held by directors, executive officers and other affiliates, volume limitations under Rule 144 under the Securities Act. The 2015 Plan also contains provisions for the annual increase of the number of shares reserved for issuance under such plans, as described elsewhere in this prospectus, which shares we also intend to register. If the shares we may issue from time to time under the 2008 Plan or 2015 Plan are sold, or if it is perceived that they will be sold, by the award recipient in the public market, the trading price of our common stock could decline.

Certain holders of 142,085,100 shares of our common stock at March 31, 2015 will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to the lock-up agreements described above. See "Description of Capital Stock—Registration Rights." Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Sales of such shares could also cause the trading price of our common stock to decline.

If there is no viable public market for our common stock, you may not be able to sell your shares at or above the initial public offering price.

Prior to this offering, there has been no public market for our common stock, and there can be no assurance that a regular trading market will develop and continue after this offering or that the market price of our common stock will not decline below the initial public offering price. The initial public offering price was determined through negotiations between us and the underwriters and may not be indicative of the market price of our common stock following this offering. Among the factors considered in such negotiations were prevailing market conditions, certain of our financial information, market valuations of other companies that we and the underwriters believe to be comparable to us, estimates of our business potential, the present state of our development and other factors deemed relevant. See "Underwriting" for additional information.

Investors in this offering will suffer immediate and substantial dilution of their investment.

If you purchase common stock in this offering, you will pay more for your shares than our pro forma as adjusted net tangible book value per share. Based upon an assumed initial public offering price of $ per share, the midpoint of the range on the cover page of this prospectus, you will incur immediate and substantial dilution of $ per share, representing the difference between our assumed initial public offering price and our pro forma as adjusted net tangible book value per share. Based upon the assumed initial public offering price of $ per share, purchasers of common stock in this offering will have contributed approximately % of the aggregate purchase price paid by all purchasers of our stock but will own only approximately % of our common stock outstanding after this offering. For information on how the foregoing amounts were calculated, see "Dilution."

To the extent outstanding stock options are exercised, there will be further dilution to new investors.

We issued options in the past to acquire common stock at prices significantly below the initial offering price. As of March 31, 2015, there were 8,354,031 shares of common stock subject to outstanding options with a weighted-average exercise price of $0.34 per share. To the extent that these outstanding options are ultimately exercised, you will incur further dilution, and our stock price may decline.

Our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expenses related to our product candidates or future development programs;
- if MRX34 or any other product candidate receives regulatory approval, the level of underlying demand for these product candidates;
- addition or termination of clinical trials or funding support;
- receipt, modification or termination of government contracts or grants, and the timing of payments we receive under these arrangements;
- our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements;
- any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved; and
- regulatory developments affecting our product candidates or those of our competitors.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

We will have broad discretion in the use of the net proceeds of this offering and may not use them effectively.

We discuss our plan for the use of the net proceeds of this offering in the sections entitled "Use of Proceeds" and "Business." However, within the scope of our plan, and in light of the various risks to our business that are set forth in this section, our management will have broad discretion over the use of the net proceeds from this offering. Because of the number and variability of factors that will determine our use of such proceeds, you may not agree with how we allocate or spend the proceeds from this offering. We may pursue collaborations or clinical trials that do not result in an increase in the market value of our common shares and that may increase our losses. Our failure to allocate and spend the net proceeds from this offering effectively would have a material adverse effect on our business, financial condition and results of operations. Until the net proceeds are used, they may be placed in investments that do not produce significant investment returns or that may lose value.

Provisions of our charter documents or Delaware law could delay or prevent an acquisition of our company, even if the acquisition would be beneficial to our stockholders, and could make it more difficult for you to change management.

Provisions in our amended and restated certificate of incorporation and our amended and restated bylaws that will become effective upon the closing of this offering may discourage, delay or prevent a merger, acquisition or other change in control that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. In addition, these provisions may frustrate or prevent any attempt by our stockholders to replace or remove our current management by making it more difficult to replace or remove our board of directors. These provisions include:

- a classified board of directors so that not all directors are elected at one time;
- a prohibition on stockholder action through written consent;
- no cumulative voting in the election of directors;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director;
- a requirement that special meetings of stockholders be called only by the board of directors, the chairman of the board of directors, the chief executive officer or, in the absence of a chief executive officer, the president;
- an advance notice requirement for stockholder proposals and nominations;
- the authority of our board of directors to issue preferred stock with such terms as our board of directors may determine; and
- a requirement of approval of not less than $66^{2}/_{3}\%$ of all outstanding shares of our capital stock entitled to vote to amend any bylaws by stockholder action, or to amend specific provisions of our certificate of incorporation.

In addition, Delaware law prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person who, together with its affiliates, owns or within the last three years has owned 15% or more of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. Accordingly, Delaware law may discourage, delay or prevent a change in control of our company. Furthermore, our amended and restated certificate of incorporation will specify that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving actions brought against us by stockholders. We believe this provision benefits us by providing increased consistency in the application of Delaware law by chancellors particularly experienced in resolving corporate disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. However, the provision may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in such action.

Provisions in our charter and other provisions of Delaware law could limit the price that investors are willing to pay in the future for shares of our common stock.

Our employment agreements with our officers may require us to pay severance benefits to any of those persons who are terminated in connection with a change of control of us, which could harm our business, financial condition or results of operations.

Our officers are parties to employment agreements providing for aggregate cash payments of up to approximately $0.8 million at March 31, 2015 for severance and other benefits in the event of a termination of employment in connection with a change of control of us. The payment of these severance benefits could harm our business, financial condition and results of operations. In addition, these potential severance payments may discourage or prevent third parties from seeking a business combination with us.

We do not anticipate paying any cash dividends on our common stock in the foreseeable future; therefore, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

We have never declared or paid cash dividends on our common stock. We do not anticipate paying any cash dividends on our common stock in the foreseeable future. We currently intend to retain all available funds and any future earnings to fund the development and growth of our business. In addition, the terms of any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend, in part, on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts do not currently, and may never, publish research on our company. If no securities or industry analysts commence coverage of our company, the trading price for our common stock would likely be negatively impacted. In the event securities or industry analysts initiate coverage, if one or more of the analysts who cover us downgrade our common stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. In addition, if our operating results fail to meet the forecast of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our common stock could decrease, which might cause our stock price and trading volume to decline.

Changes in, or interpretations of, accounting rules and regulations could result in unfavorable accounting charges or require us to change our compensation policies.

Accounting methods and policies for biopharmaceutical companies, including policies governing revenue recognition, research and development and related expenses and accounting for stock-based compensation, are subject to further review, interpretation and guidance from relevant accounting authorities, including the SEC. Changes to, or interpretations of, accounting methods or policies may require us to reclassify, restate or otherwise change or revise our financial statements, including those contained in this prospectus.

Special Note Regarding Forward-Looking Statements

This prospectus contains forward-looking statements concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our business operations and financial performance and condition. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "predict," "potential," "positioned," "seek," "should," "target," "will," "would" and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the initiation, cost, timing, progress and results of our research and development activities, preclinical and nonclinical studies and future clinical trials;
- our ability to obtain and maintain regulatory approval of our future product candidates, and any related restrictions, limitations and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations;
- our plans to research, develop and commercialize our future product candidates;
- our ability to attract collaborators with development, regulatory and/or commercialization expertise;
- our ability to obtain and maintain intellectual property protection for our current and future product candidates;
- the size and growth potential of the markets for our future product candidates, and our ability to serve those markets;
- our ability to successfully commercialize our product candidates;
- the rate and degree of market acceptance of our product candidates;
- our ability to develop sales and marketing capabilities, whether alone or with potential future collaborators;
- regulatory developments in the United States and foreign countries;
- the performance of our third-party suppliers and manufacturers;
- the success of competing therapies that are or become available;
- our ability to retain key scientific or management personnel;
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act;
- our use of the proceeds from this offering; and
- the accuracy of our estimates regarding expenses, future revenues, capital requirements and need for additional financing.

These forward-looking statements are based on management's current expectations, estimates, forecasts, and projections about our business and the industry in which we operate and management's beliefs and assumptions and are not guarantees of future performance or development and involve known and unknown risks, uncertainties, and other factors that are in some cases beyond our control. As a result, any or all of our forward-looking statements in this prospectus may turn out to be inaccurate. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under "Risk Factors" and elsewhere in this prospectus. Potential investors are urged to consider these factors carefully in evaluating the forward-looking statements. These forward-looking statements speak only as of the date of this prospectus. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future. You should, however, review the factors and risks we describe in the reports we will file from time to time with the SEC after the date of this prospectus. See "Where You Can Find More Information."

Use of Proceeds

We estimate that the net proceeds from the sale of shares of common stock in this offering will be approximately $ million at an assumed initial public offering price of $ per share, the midpoint of the range set forth on the cover page of this prospectus, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their over-allotment option in full, we estimate that net proceeds will be approximately $ million after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share (the midpoint of the price range set forth on the cover page of this prospectus) would increase (decrease) the net proceeds to us from this offering, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. We may also increase or decrease the number of shares we are offering. An increase (decrease) of 1,000,000 in the number of shares we are offering would increase (decrease) the net proceeds to us from this offering, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, by approximately $ million, assuming the assumed initial public offering price stays the same. We do not expect that a change in the offering price or the number of shares by these amounts would have a material effect on our intended uses of the net proceeds from this offering, although it may impact the amount of time prior to which we may need to seek additional capital.

At March 31, 2015, we had cash and cash equivalents of $40.1 million. We currently estimate that we will use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows:

- approximately $53.0-$65.0 million to fund clinical development expenses for our lead program, MRX34, which includes
    - approximately $13.0-$17.0 million to complete the Phase 1 clinical trial, including expansion cohorts on multiple indications and/or changes in protocol,
    - approximately $14.0-$18.0 million to initiate the Phase 2 clinical trial for an indication still to be determined, and
    - approximately $26.0-$30.0 million to fund preclinical and clinical studies for the use of MRX34 in additional indications or in combination with standard of care drugs,
- approximately $21.0-$27.0 million to fund preclinical and clinical studies for a second product candidate using another to be determined mimic product, and
- the remainder for preclinical studies, working capital and other general corporate purposes, which may include selection and development of our pursuit of our other research and discovery efforts, expenditures on intellectual property and the acquisition or in-license of other products, product candidates or technologies.

This expected use of net proceeds from this offering and our existing cash and cash equivalents represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of and results from preclinical testing or clinical trials, as well as any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering. Due to the many variables inherent to the development of our product candidates, we cannot currently predict the stage of development we expect the net proceeds of this offering to enable us to achieve for our clinical studies and product candidates. We have no current agreements, commitments or understandings for any material acquisitions or licenses of any products, businesses or technologies.

Based on our planned use of the net proceeds from this offering and our existing cash and cash equivalents described above, we estimate that such funds will be sufficient to fund operations at least over the next 12 months.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant.

Capitalization

The following table sets forth our capitalization at March 31, 2015:

- on an actual basis;
- on a pro forma basis to give effect to:
  - the conversion of all outstanding shares of our preferred stock into an aggregate of 142,085,100 shares of common stock immediately prior to the consummation of this offering;
  - the filing and effectiveness of our amended and restated certificate of incorporation, which will occur immediately prior to the consummation of this offering; and
  - on a pro forma as adjusted basis to give further effect to the issuance and sale by us of shares of our common stock in this offering at an assumed initial public offering price of $ per share (the midpoint of the range set forth on the cover page of this prospectus), after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this information together with our audited financial statements and related notes appearing elsewhere in this prospectus and the information set forth under the headings "Selected

Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	At March 31, 2015		
	Actual	Pro Forma	Pro Forma As Adjusted
	(unaudited; in thousands, except share and per share data)		
Series A convertible preferred stock, $0.001 par value per share, 3,192,083 shares designated, 3,192,083 shares issued and outstanding, actual; no shares designated, no shares issued and outstanding, pro forma and pro forma as adjusted	$ 6,384	$ —	
Series B convertible preferred stock, $0.001 par value per share, 540,341 shares designated, 540,341 shares issued and outstanding, actual; no shares designated, no shares issued and outstanding, pro forma and pro forma as adjusted	1,500	—	
Series B-1 convertible preferred stock, $0.001 par value per share, 10,914,647 shares designated, 10,914,647 shares issued and outstanding, actual; no shares designated, no shares issued and outstanding, pro forma and pro forma as adjusted	7,498	—	
Series C convertible preferred stock, $0.001 par value per share, 69,353,712 shares designated, 69,353,695 shares issued and outstanding, actual; no shares designated, no shares issued and outstanding, pro forma and pro forma as adjusted	40,591	—	
Series D convertible preferred stock, $0.001 par value per share, 73,649,755 shares designated, 58,084,334 shares issued and outstanding, actual; no shares designated, no shares issued and outstanding, pro forma and pro forma as adjusted	35,491	—	
Stockholders' equity (deficit):			
Preferred stock, $0.001 par value per share; no shares designated, issued and outstanding, actual; shares designated, no shares issued and outstanding, pro forma and pro forma as adjusted	—	—	
Common stock, $0.001 par value per share; 175,100,000 shares authorized; 1,374,727 shares issued and outstanding, actual; 175,100,000 shares authorized, 143,459,827 shares issued and outstanding, pro forma; shares authorized, shares issued and outstanding, pro forma as adjusted	1	143	
Additional paid-in capital	—	91,322	
Accumulated deficit	(53,195)	(53,195)	
Total stockholders' (deficit) equity	(53,194)	38,270	
Total capitalization	$ 38,270	$ 38,270	

Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share, the midpoint of the range set forth on the cover page of this prospectus, would increase (decrease) each of pro forma as adjusted additional paid-in capital, stockholders' equity and total capitalization by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. We may also increase or decrease the number of shares we are offering. An increase (decrease) of 1,000,000 in the number of shares we are offering would increase (decrease) each of pro forma as adjusted additional paid-in capital, stockholders' equity and total capitalization by approximately $ million, assuming the assumed initial public offering price per share, as set forth on the cover page of this prospectus, remains the same. The pro forma as adjusted information is illustrative only, and we will adjust this information based on the actual initial public offering price and other terms of this offering determined at pricing.

The outstanding share information in the table above excludes the following:

- 8,354,031 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of $0.34 per share;
- 6,221,749 shares of common stock reserved for issuance pursuant to future awards under our 2008 Long Term Incentive Plan, as amended, which will become available for issuance under our 2015 Equity Incentive Award Plan after consummation of this offering;
- shares of common stock reserved for issuance pursuant to future awards under our 2015 Equity Incentive Award Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan, which will become effective immediately prior to the consummation of this offering; and
- shares of common stock issuable to the holders of Series C convertible preferred stock and Series D convertible preferred stock under the terms of our certificate of incorporation as a result of the accruing paid-in-kind dividend in connection with the conversion of all shares of Series C convertible preferred stock and Series D convertible preferred stock into shares of common stock immediately prior to the consummation of this offering.

Dilution

If you invest in our common stock, your interest will be diluted to the extent of the difference between the initial public offering price per share of our common stock in this offering and the net tangible book value per share of our common stock after this offering. At March 31, 2015, we had a historical net tangible book value (deficit) of $(53.2) million, or $(38.72) per share of common stock. Our net tangible book value represents total tangible assets less total liabilities and convertible preferred stock, all divided by the number of shares of common stock outstanding on March 31, 2015. Our pro forma net tangible book value at March 31, 2015, before giving effect to this offering, was $38.2 million, or $0.27 per share of our common stock. Pro forma net tangible book value, before the issuance and sale of shares in this offering, gives effect to:

- the conversion of all outstanding shares of our preferred stock into an aggregate of 142,085,100 shares of common stock immediately prior to the consummation of this offering; and

- the filing and effectiveness of our amended and restated certificate of incorporation, which will occur immediately prior to the consummation of this offering.

After giving effect to the sale of shares of common stock in this offering at an assumed initial public offering price of $ per share (the midpoint of the price range set forth on the cover page of this prospectus) and after deducting the underwriting discounts and commissions and estimated offering expenses, our pro forma as adjusted net tangible book value at March 31, 2015 would have been approximately $ million, or $ per share. This represents an immediate increase in pro forma as adjusted net tangible book value of $ per share to existing stockholders and an immediate dilution of $ per share to new investors. The following table illustrates this per share dilution:

Assumed initial public offering price per share		$
Historical net tangible book value per share at March 31, 2015	$ (38.72)	
Pro forma increase in net tangible book value per share	38.99	
Pro forma net tangible book value per share at March 31, 2015	0.27	
Increase in pro forma net tangible book value per share attributable to new investors		
Pro forma as adjusted net tangible book value per share after this offering		
Dilution per share to new investors participating in this offering		$

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) our pro forma as adjusted net tangible book value at March 31, 2015 after this offering by approximately $ million, or approximately $ per share, and would decrease (increase) dilution to investors in this offering by approximately $ per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase (decrease) of 1,000,000 in the number of shares we are offering would increase (decrease) our pro forma as adjusted net tangible book value at March 31, 2015 after this offering by approximately $ million, or approximately $ per share, and would decrease (increase) dilution to investors in this offering by approximately $ per share, assuming the assumed initial public offering price per share remains the same, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. The pro forma as adjusted information is illustrative only, and we will adjust this information based on the actual initial public offering price and other terms of this offering determined at pricing.

If the underwriters fully exercise their over-allotment option, pro forma as adjusted net tangible book value after this offering would increase to approximately $ per share, and there would be an immediate dilution of approximately $ per share to new investors.

To the extent that outstanding options with an exercise price per share that is less than the pro forma as adjusted net tangible book value per share, before giving effect to the issuance and sale of shares in this offering, are exercised, new investors will experience further dilution.

In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

The following table shows, at March 31, 2015, on a pro forma as adjusted basis, after giving effect to the pro forma adjustments described above, the number of shares of common stock purchased from us, the total consideration paid to us and the average price paid per share by existing stockholders and by new investors purchasing common stock in this offering at an assumed initial public offering price of $ per share, before deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders		%	$	%	$
Investors participating in this offering					$
Total		100%	$	100%	

The number of shares of common stock to be outstanding after this offering is based on the number of shares outstanding at March 31, 2015 and excludes the following:

- 8,354,031 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of $0.34 per share;
- 6,221,749 shares of common stock reserved for issuance pursuant to future awards under our 2008 Long Term Incentive Plan, as amended, which will become available for issuance under our 2015 Equity Incentive Award Plan after consummation of this offering;
- shares of common stock reserved for issuance pursuant to future awards under our 2015 Equity Incentive Award Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan, which will become effective immediately prior to the consummation of this offering; and
- shares of common stock issuable to the holders of Series C convertible preferred stock and Series D convertible preferred stock under the terms of our certificate of incorporation as a result of the accruing paid-in-kind dividend in connection with the conversion of all shares of Series C convertible preferred stock and Series D convertible preferred stock into shares of common stock immediately prior to the consummation of this offering.

Selected Financial Data

The following selected statement of operations data for the years ended December 31, 2012, 2013 and 2014, and the selected balance sheet data at December 31, 2013 and 2014 have been derived from our audited financial statements included elsewhere in this prospectus. The balance sheet data at December 31, 2012 have been derived from our audited financial statements not included in this prospectus. The statement of operations data for the three months ended March 31, 2014 and 2015 and balance sheet data as of March 31, 2015 have been derived from our unaudited financial statements included elsewhere in this prospectus. Our unaudited financial statements are prepared on the same basis as our audited financial statements. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period, and results for the three months ended March 31, 2015 are not necessarily indicative of results to be expected for the full year ending December 31, 2015.

The information set forth below should be read in conjunction with the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus and with our financial statements and notes thereto included elsewhere in this prospectus.

	Year Ended December 31,			Three Months Ended March 31,	
	2012	2013	2014	2014	2015
	(in thousands, except share and per share data)			(unaudited)	
Statement of Operations Data:					
Operating expenses:					
Research and development	$ 2,742	$ 4,391	$ 10,545	$ 2,188	$ 3,425
General and administrative	1,562	2,384	3,369	848	854
Write-off of offering expenses	—	—	1,920	—	—
Total operating expenses	4,304	6,775	15,834	3,036	4,279
Other income (expense):					
Change in fair value of option liability	—	339	—	—	—
Gain on extinguishment of note payable	1,001	—	—	—	—
Interest expense	(355)	—	—	—	—
Net loss	$ (3,658)	$ (6,436)	$ (15,834)	$ (3,036)	$ (4,279)
Less: Accretion and dividends on convertible preferred stock	(6,142)	(2,324)	(2,824)	(696)	(1,118)
Net loss attributable to common stockholders	$ (9,800)	$ (8,760)	$ (18,658)	$ (3,732)	$ (5,397)
Net loss per share attributable to common stockholders, basic and diluted	$ (373.52)	$ (293.92)	$ (19.40)	$ (12.08)	$ (4.06)
Common shares used to compute basic and diluted net loss per share attributable to common stockholders	26,237	29,804	961,963	309,017	1,327,688
Pro forma net loss per common share (unaudited)—basic and diluted			$ (0.19)		$ (0.05)
Common shares used to compute pro forma net loss per share (unaudited)—basic and diluted			84,962,729		85,973,836

	At December 31,			At March 31,
	2012	2013	2014	2015
	(in thousands)			(unaudited)
Balance Sheet Data:				
Cash and cash equivalents	$ 13,266	$ 23,182	$ 9,319	$ 40,130
Total assets	13,706	23,684	9,825	40,547
Total liabilities	4,364	1,145	2,499	2,277
Convertible preferred stock	33,710	52,453	55,277	91,464
Common stock	—	—	1	1
Additional paid-in capital	—	890	—	—
Accumulated deficit	(24,368)	(30,804)	(47,952)	(53,195)
Total stockholders' (deficit) equity	(24,368)	(29,914)	(47,951)	(53,194)

Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis of financial condition and results of operations together with the section entitled "Selected Financial Data" and our financial statements and related notes included elsewhere in this prospectus. This discussion and other parts of this prospectus contain forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations and intentions. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the "Risk Factors" section.

Overview

We are a clinical-stage biopharmaceutical company developing a broad pipeline of microRNA-based oncology therapeutics. microRNAs are naturally occurring, short ribonucleic acid, or RNA, molecules, or oligonucleotides, that play a critical role in regulating key biological pathways. Misexpression of even a single microRNA can contribute to disease development and tumor suppressor microRNAs are commonly reduced in cancer. Our scientists and others at leading academic institutions have identified numerous tumor suppressor microRNAs that play key roles in preventing normal cells from becoming cancerous and facilitating proper cancer immunosurveillance. We are developing mimics of naturally occurring microRNAs that are designed to restore this tumor suppressor activity and aid appropriate tumor immune response. This approach is known as microRNA replacement therapy. Our lead product candidate, MRX34, a mimic of naturally occurring microRNA-34 (miR-34) encapsulated in a liposomal nanoparticle formulation, is the first microRNA mimic to enter clinical development and has shown preliminary clinical evidence of anti-tumor activity as a single agent in our ongoing Phase 1 clinical trial. We believe that microRNA mimics represent a new paradigm in cancer therapy and have the potential to create a new, important class of effective cancer drugs, that can potentially be used alone or in combination with other cancer therapeutics. We plan to develop MRX34 as a monotherapy and in combination with other therapeutic modalities, such as targeted therapies and immuno-oncology agents.

We are developing a pipeline of tumor suppressor microRNA mimics. We believe that these mimics have the potential to become promising new oncology therapeutics due to their capacity to regulate many different oncogenes across multiple oncogenic pathways. We believe our technology is supported by a strong intellectual property position, which we continue to expand and strengthen. Our scientists have also discovered functions of microRNAs in numerous diseases other than cancer, which may provide us an opportunity to expand this novel technology into other therapeutic areas of unmet medical need. We believe these microRNAs represent future partnering or diversification opportunities.

We were incorporated in 2007 under the laws of Delaware and were maintained as a wholly-owned subsidiary of our former parent company, Asuragen, Inc., or Asuragen, until the end of 2009, when we became an independent entity.

Our operations have focused on developing our understanding of and capabilities in microRNA biology, identifying potential product candidates, undertaking preclinical studies, initiating and conducting a clinical trial, protecting and enhancing our intellectual property estate and providing general and administrative support for these activities. We have not generated any revenue from product sales and, to date, have funded our operations primarily through the private placement of convertible preferred stock, federal and state government grants and support from our former parent company, Asuragen. From our inception through March 31, 2015, we have raised an aggregate of approximately $95.2 million to fund our operations, of which approximately $83.6 million was from the issuance of preferred stock for cash and assets and approximately $11.6 million was from federal and state grants.

Since our inception, we have incurred significant operating losses. Our net losses were $3.7 million, $6.4 million and $15.8 million for the years ended December 31, 2012, 2013 and 2014, respectively, and $4.3 million for the three months ended March 31, 2015. At March 31, 2015, we had an accumulated deficit of $53.2 million. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and from year to year. We anticipate that our expenses will increase significantly as we conduct clinical trials for MRX34 and other product candidates; manufacture clinical trial materials; continue to discover, validate and develop additional novel product candidates; expand and protect our intellectual property portfolio; and hire additional development and scientific personnel. In addition, upon the consummation of this offering, we expect to incur additional costs associated with operating as a public company.

Financial Operations Overview

Revenue

We have not generated any revenue from product sales or from collaborations. In the future, we may generate revenue from collaborations and licenses. Revenue may fluctuate from period to period, and the timing and extent of any future revenue will depend on our ability to advance our product candidates through the clinical trial process and to obtain regulatory approval and our ability, or our future partners' ability, to commercialize our product candidates.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts, and the development of our product candidates, which include the following:

- employee-related expenses, including salaries, benefits, travel and stock-based compensation;
- external research and development expenses incurred under arrangements with third parties, such as contract research organizations, or CROs, consultants and our scientific advisory board;
- lab supplies, and acquiring, developing and manufacturing preclinical study materials in accordance with Good Laboratory Practices;
- costs of clinical trials, including costs for management, investigator fees and related vendors that provide services for the clinical trials;
- costs to manufacture the drug used in the clinical trials in accordance with Good Manufacturing Practices;
- license and milestone fees;
- development and prosecution of intellectual property; and
- costs of facilities, depreciation and other expenses.

Research and development costs are expensed as incurred. In certain circumstances, we will make nonrefundable advance payments to purchase goods and services for future use pursuant to contractual arrangements. In those instances, we defer and recognize an expense in the period that we receive or consume the goods or services.

Our research and development expenses have been offset by proceeds derived from federal and state grants. These government grants, which have supplemented our research efforts on specific projects, generally provide for reimbursement of approved costs, as defined in the terms of the grant awards. The proceeds from these reimbursement grants are treated as a reduction to the associated expenses as the allowable expenses are incurred.

In August 2010, we received a $10.3 million commercialization award from the State of Texas through The Cancer Prevention Research Institute of Texas, or CPRIT. The CPRIT grant was a three-year award that was funded annually, and funding of the grant was completed in January 2014. At March 31, 2015, all proceeds from this grant had been recognized. We accounted for advances received for the award as deferred grant reimbursement. Under the terms of the award, we are required to pay to CPRIT a portion of our revenues from sales of certain products by us, or received from our licensees or sublicensees, at a percentage in the low single digits until the aggregate amount of such payments equals a specified multiple of the grant amount, and thereafter at a rate of less than one percent, subject to our right, under certain circumstances, to make a one-time payment in a specified amount to CPRIT to buy out such payment obligations.

At March 31, 2015, we had three National Institutes of Health, or NIH, grants ongoing with approximately $173,000 incurred and approximately $652,000 still to be incurred on those grants. Two of the grants, with approximately $428,000 still to be incurred, expire on August 31, 2015.

At any point in time, we typically have various early stage research and drug discovery projects ongoing. Our internal resources, employees and infrastructure are not directly tied to any one research or drug discovery project and are typically deployed across multiple projects. As such, we do not maintain information regarding the costs incurred for these early stage research and drug discovery programs on a project-specific basis. However, we have spent and are currently spending the vast majority of our research and development resources on our lead product candidate, MRX34.

Most of our product development programs are at an early stage, and successful development of future product candidates from these programs is highly uncertain and may not result in approved products. The process of conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time consuming, and we expect our research and development expenses to increase for the foreseeable future as we advance our research programs toward the clinic and initiate and continue clinical trials. The probability of success for each product candidate may be affected by numerous factors, including preclinical data, clinical data, competition, manufacturing capability and commercial viability. We anticipate we will make determinations as to which programs to pursue and how much funding to direct to each program on an ongoing basis in response to the scientific and clinical success of each future product candidate, as well as ongoing assessments as to each future product candidate's commercial potential. Completion dates and completion costs can vary significantly for each future product candidate and are difficult to predict. We will need to raise additional capital and may seek strategic alliances in the future in order to advance the various products in the pipeline and other products that may be developed.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related benefits, including stock-based compensation, related to our executive, finance and support functions. Other general and administrative expenses include allocated facility-related costs not otherwise included in research and development expenses, travel expenses and professional fees for auditing, tax and legal services. We expect that general and administrative expenses will increase in the future as we expand our operating activities and incur additional costs associated with being a publicly-traded company. These increases will likely include legal fees, accounting fees, directors' and officers' liability insurance premiums and fees associated with investor relations.

Critical Accounting Policies and Estimates

This management's discussion and analysis of financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the revenue and expenses incurred during the reported periods. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued expenses, revenue recognition and stock-based compensation. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in the notes to our financial statements appearing in this prospectus, we believe that the following critical accounting policies are most important to understanding and evaluating our reported financial results.

Stock-Based Compensation

We estimate the fair value of our stock-based awards to employees using the Black-Scholes option-pricing model, which requires the input of highly subjective assumptions, including: (1) the expected volatility of our stock; (2) the expected term of the award; (3) the risk-free interest rate; and (4) expected dividends. Due to the lack of a public market for the trading of our common stock and a lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. For these analyses, we have selected companies with comparable characteristics to ours, including enterprise value, risk profiles, position within the industry and historical share price information, sufficient to meet the expected life of the stock-based awards. We compute the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of our stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available. We have estimated the expected life of our employee stock options using the "simplified" method, whereby the expected life equals the average of the vesting term and the original contractual term of the option. The risk-free interest rates for periods within the expected life of the option are based on the U.S. Treasury yield curve in effect during the period the options were granted.

We are also required to estimate forfeitures at the time of grant and revise those estimates in subsequent periods if actual forfeitures differ from estimates. We use historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those awards that are expected to vest. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest.

We have computed the fair value of employee stock options at the date of grant using the following assumptions:

	Year Ended December 31,			Three Months Ended March 31,
	2012	2013	2014	2015
Expected term (years).	4.3 - 6.1	5.6 - 6.1	5.8 - 6.1	5.7 - 6.7
Risk-free interest rate	0.5% - 1.0%	0.9% - 2.0%	1.8% - 2.8%	1.6% - 2.0%
Expected volatility.	80.3% - 85.5%	74.7% - 76.2%	75.3% - 85.4%	80.6% - 84.0%
Expected dividend rate	0.0%	0.0%	0.0%	0.0%

Stock-based compensation expense was allocated as outlined below:

	Year Ended December 31, 2012	2013	2014	Three Months Ended March 31, 2015
	(in thousands)			
Research and development	$ 6	$ 55	$ 110	$ 32
General administrative	18	108	298	102
Total	$ 24	$ 163	$ 408	$ 134

At March 31, 2015, we had $1.3 million of total unrecognized compensation expense, net of related forfeiture estimates. We expect the impact of our stock-based compensation expense for stock options to grow in future periods due to the potential increases in the value of our common stock and headcount.

JOBS Act

Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other companies.

Results of Operations

Comparison of Three Months Ended March 31, 2014 and 2015:

	Three Months Ended March 31, 2014	2015	Dollar Change	% Change
	(in thousands)			
Statement of operations data:				
Operating expenses:				
Research and development, before grant reimbursement	$ 2,190	$ 3,498	$ 1,308	59.7%
Less grant reimbursement	(2)	(73)	(71)	NM*
Research and development	2,188	3,425	1,237	56.5%
General and administrative	848	854	6	0.7%
Net loss	$ (3,036)	$ (4,279)	$ (1,243)	40.9%

* Not Meaningful

Research and Development Expenses

Research and development expenses were $3.4 million for the three months ended March 31, 2015, which was an increase of $1.2 million, or 57%, compared to research and development expenses of approximately $2.2 million for the three months ended March 31, 2014.

Research and development spending, prior to the offset of grant reimbursements, was $3.5 million for the three months ended March 31, 2015, which was an increase of approximately $1.3 million, or 60%, compared to research and development spending, prior to the offset of grant reimbursements, of

$2.2 million for the three months ended March 31, 2014. The increase in the first quarter of 2015 was primarily due to increased clinical trial costs related to our Phase 1 clinical trial, including a higher number of patients, additional investigator sites and additional drug costs related to the increased trial activity, and increased intellectual property costs.

Research and development spending was partially offset by approximately $73,000 of grant reimbursements for the three months ended March 31, 2015, compared to reimbursement of approximately $2,000 for the same period in 2014. The increase was due to a higher volume of work being performed on the research funded by the federal grants.

General and Administrative Expenses

General and administrative expenses were approximately $854,000 for the three months ended March 31, 2015, which was a modest increase of approximately $6,000, or 0.7%, compared to the same period in 2014. The overall expenses remained consistent from quarter to quarter, with an increase in salary and benefits being offset by lower legal, audit and professional costs.

Comparison of Years Ended December 31, 2013 and 2014

	Year Ended December 31, 2013	Year Ended December 31, 2014	Dollar Change	% Change
	(in thousands)			
Statement of operations data:				
Operating expenses:				
Research and development, before grant reimbursement	$ 8,241	$ 10,626	$ 2,385	28.9%
Less grant reimbursement	(3,850)	(81)	3,769	(97.9)%
Research and development	4,391	10,545	6,154	140.2%
General and administrative	2,384	3,369	985	41.3%
Write-off of offering expenses	—	1,920	1,920	NM*
Total operating expenses	6,775	15,834	9,059	133.7%
Other income (expense):				
Change in fair value of option liability	339	—	(339)	(100.0)%
Net loss	$ (6,436)	$ (15,834)	$ (9,398)	146.0%

* Not Meaningful

Research and Development Expenses

Research and development expenses were $10.5 million for the year ended December 31, 2014, which was an increase of $6.2 million, or 140%, compared to research and development expenses of $4.4 million for the year ended December 31, 2013. The net change was due to an increase in overall research and development spending and a significant reduction in grant reimbursement from the prior year.

Research and development spending, prior to offset by grant reimbursement, was $10.6 million for the year ended December 31, 2014, which was an increase of $2.4 million, or 29%, compared to research and development spending of $8.2 million for the year ended December 31, 2013. The increase in research and development spending in 2014 was primarily due to the increased costs for clinical trials. The initiation of our Phase 1 clinical trial was in April 2013. In 2014, the clinical trial costs increased as a result of a full year of clinical trial costs and expansion of testing for additional indications, additional investigator sites, expansion of the trial to overseas locations and a related increase in clinical trial drug costs. The increase was also due to an increase in intellectual property spending. The increases in overall research and development spending were partially offset by lower licensing costs in 2014.

We offset research and development expenses by approximately $81,000 for the year ended December 31, 2014. This was a decrease from the $3.85 million of grant proceeds received for the year ended December 31, 2013 of approximately $3.77 million, or 98%. The reduction in grant reimbursements was due to the completion of the allowable expense provided for by the grant by the Cancer Prevention and Research Institute of Texas, or CPRIT, during the fourth quarter of 2013.

General and Administrative Expenses

General and administrative expenses were $3.4 million for the year ended December 31, 2014, which was an increase of approximately $1.0 million, or 41%, compared to general and administrative expenses of $2.4 million for the year ended December 31, 2013. The increase year over year was due to increases in headcount and the related salaries and benefits, increases in legal and other professional fees, and general overall spending related to increase activities.

Write-off of Offering Expenses

In August 2014, a proposed offering was delayed and the deferred offering costs for that offering, which consisted of direct incremental legal and professional accounting fees related to that offering, in the amount of $1.92 million were expensed.

Change in Fair Value of Option Liability

In October 2012, we completed an initial closing of an offering of Series C convertible preferred stock. The purchasers of the convertible preferred stock in the initial closing received an option to participate in the second closing for the same number of shares and at the same price as the initial closing. At the time of the initial closing, the fair value of this option to participate in the second closing was calculated using an option pricing model, and the effect of this non-cash accounting adjustment was to record an option liability on the balance sheet for the fair value that was calculated. The option liability is marked to fair value at each reporting period and any changes in fair value are recorded in the statement of operations.

When the second closing of the Series C convertible preferred stock was completed in December 2013, we had a one-time non-cash gain on the change in the fair value of the option and the balance of the option liability was reclassified to additional paid-in capital.

Comparison of Years Ended December 31, 2012 and 2013

	Year Ended December 31, 2012	Year Ended December 31, 2013	Dollar Change	% Change
	(in thousands)			
Statement of operations data:				
Operating expenses:				
Research and development, before grant reimbursement	$ 6,380	$ 8,241	$ 1,861	29.2%
Less grant reimbursement	(3,638)	(3,850)	(212)	5.8%
Research and development	2,742	4,391	1,649	60.1%
General and administrative	1,562	2,384	822	52.6%
Total operating expenses	4,304	6,775	2,471	57.4%
Other income (expense):				
Change in fair value of option liability	—	339	339	NA
Gain on extinguishment of note payable	1,001	—	(1,001)	(100.0)%
Interest expense	(355)	—	355	(100.0)%
Net loss	$ (3,658)	$ (6,436)	$ (2,778)	75.9%

Research and Development Expenses

Research and development expenses were $4.4 million for the year ended December 31, 2013, which was an increase of $1.6 million, or 60%, compared to research and development expenses of $2.7 million for the year ended December 31, 2012. The net change was due to an increase in overall research and development spending.

Research and development spending, prior to offset by grant reimbursement, was $8.2 million for the year ended December 31, 2013, which was an increase of $1.9 million, or 29%, compared to research and development spending of $6.4 million for the year ended December 31, 2012. The increase in research and development spending in 2013 was primarily due to the initiation of our Phase 1 clinical trial in April 2013, including the costs of conducting the trial and adding headcount for clinical operations, and additional spending on intellectual property, including a payment of $1.0 million to Marina Biotech, Inc., or Marina. This increase was partially offset by a decrease in spending for clinical trial drug costs and outsourced preclinical studies that had been conducted in 2012 in anticipation of the submission of the Investigational New Drug, or IND, for MRX34 to the Federal Drug Administration, or FDA, in 2013.

We offset research and development expenses by $3.85 million of grant proceeds for the year ended December 31, 2013 and $3.64 million for the same period in 2012, an increase of approximately $212,000, or 6%. In both 2013 and 2012, over 95% of the total grant proceeds recognized by us related to the CPRIT grant. The increase in grant and research proceeds in 2013 was primarily due to the timing of the expenses being incurred that are reimbursed by state and federal grants.

General and Administrative Expenses

General and administrative expenses were $2.4 million for the year ended December 31, 2013, which was an increase of approximately $0.8 million, or 53%, compared to general and administrative expenses of $1.6 million for the year ended December 31, 2012. Prior to 2013, a number of administrative functions had been provided by our former parent company, Asuragen, including accounting and finance, legal, human resources and purchasing, and the costs for these administrative functions were covered by a shared services agreement between us and Asuragen. Beginning in 2013, these administrative functions were transitioned to us, and the additional costs were incurred related to these functions, including additional headcount, new systems, professional fees, outside consultants and transition costs. There were also increases in the costs of audit and tax, legal and stock-based compensation from 2012 to 2013.

Change in Fair Value of Option Liability

In October 2012, we completed an initial closing of an offering of Series C convertible preferred stock. The purchasers of the convertible preferred stock in the initial closing received an option to participate in the second closing for the same number of shares and at the same price as the initial closing. At the time of the initial closing, the fair value of this option to participate in the second closing was calculated using an option pricing model, and the effect of this non-cash accounting adjustment was to record an option liability on the balance sheet for the fair value that was calculated. The option liability is marked to fair value at each reporting period and any changes in fair value are recorded in the statement of operations.

When the second closing of the Series C convertible preferred stock was completed in December 2013, we had a one-time non-cash gain on the change in the fair value of the option and the balance of the option liability was reclassified to additional paid-in capital.

Gain on Extinguishment of Note Payable

In conjunction with a unit investment in 2009 from the Texas Emerging Technology Fund, or the TETF, an economic development affiliate of the State of Texas, we issued a note payable and a warrant to purchase our capital stock. The note payable was initially recorded net of the computed debt discount resulting from the warrant value. In October 2012, the arrangement with the TETF was amended. As part of the amendment, our note with the TETF was deemed satisfied in full and canceled and we were released of all repayment obligations. In conjunction with this release, we recognized a gain on the extinguishment of the note payable and related accrued interest of $1.0 million in 2012.

Interest Expense

Interest expense decreased from $355,000 for the year ended December 31, 2012 to zero for the year ended December 31, 2013 due to the extinguishment of the note payable related to the TETF in October 2012. We did not have any debt obligations outstanding during 2013.

Liquidity and Capital Resources

Liquidity and Capital Expenditures

Since inception, at March 31, 2015, our operations have been financed primarily by net proceeds of $81.2 million from the sales of shares of our convertible preferred stock for cash and assets and $11.6 million from federal and state grants. At March 31, 2015, we had $40.1 million of cash and cash equivalents.

Our primary uses of cash are to fund operating expenses, primarily research and development expenditures. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

We believe that our existing cash and cash equivalents as of March 31, 2015, along with the estimated net proceeds from this offering, will be sufficient to meet our anticipated cash requirements for at least the next 12 months. However, our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially.

Our future capital requirements are difficult to forecast and will depend on many factors, including:

- the initiation, progress, timing and completion of preclinical studies and clinical trials for our lead product and potential product candidates;
- the number and characteristics of product candidates that we pursue;
- the progress, costs and results of our clinical trials;
- the terms and timing of any other strategic alliance, licensing and other arrangements that we may establish;
- the outcome, timing and cost of regulatory approvals;
- delays that may be caused by changing regulatory requirements;
- the costs and timing of hiring new employees to support our continued growth;
- the costs and timing of procuring clinical supplies of our product candidates; and
- the extent to which we acquire or invest in businesses, products or technologies.

The following table shows a summary of our cash flows for the years ended December 31, 2012, 2013 and 2014 and the three months ended March 31, 2014 and 2015.

	Year Ended December 31,			Three Months Ended March 31,	
	2012	2013	2014	2014	2015
		(in thousands)		(unaudited; in thousands)	
Net cash provided by (used in):					
Operating activities	$ (4,520)	$ (6,496)	$ (13,970)	$ (2,980)	$ (4,550)
Investing activities.	—	(7)	(102)	(13)	(5)
Financing activities	16,847	16,419	209	150	35,366
Net increase (decrease)	$ 12,327	$ 9,916	$ (13,863)	$ (2,843)	30,811

Operating Activities

Net cash used in operating activities was $3.0 million and $4.6 million for the three months ended March 31, 2014 and 2015, respectively. The increase in cash used for operating activities of approximately $1.6 million was primarily due to increased salaries, increased spending for clinical trials and intellectual property related expenses, and higher license fees.

Net cash used in operating activities was $14.0 million for the year ended December 31, 2014, compared to net cash used in operations of $6.5 million for the same period in 2013. The increase in 2014 in overall spending in the prior year was primarily due to increased clinical trials related costs, including the higher number of patients, addition of additional sites and related increase in costs of the drug product, and increased spending on intellectual property. The increase was also caused by the lower grant payment from CPRIT, with an annual payment made in 2013.

Investing Activities

The net cash used in investing activities for the periods presented relates entirely to the purchases of property and equipment, primarily computer and lab equipment. For the three months ended March 31, 2014 and 2015, total amounts spent on the purchase of fixed assets were approximately

$13,000 and $5,000, respectively. The amount spent in the years ended December 31, 2013 and 2014 was approximately $7,000 and $102,000, respectively. There were no investing activities in 2012.

Financing Activities

Net cash provided by financing activities was approximately $35.4 million for the three months ended March 31, 2015, which was primarily due to the initial closing of the offering of the our Series D convertible preferred stock. For the three months ended March 31, 2014, approximately $150,000 of net cash provided by financing activities was due to the exercise of stock options.

Net cash provided by financing activities was approximately $209,000 for the year ended December 31, 2014, which was due to the exercise of stock options. For both years ended December 31, 2013 and 2012, the net cash provided by financing activities of $16.4 million and $16.8 million, respectively, was primarily due to the net proceeds from the sale of our Series C convertible preferred stock. The initial funding of the Series C convertible preferred stock was in October 2012 and the second funding was in December 2013.

Contractual Obligations and Commitments

In October 2014, we entered into a sublease agreement and amended an agreement with Asuragen under which we share space with Asuragen and Asuragen provides certain services to us. These services currently include facilities-related services, warehouse services, shipping and receiving and other services. The term of the services agreement expires in August 2016, with commitment for payments remaining under the two agreements totaling approximately $824,000 as of December 31, 2014.

	Payment due by period (in thousands)				
	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
Contractual Obligations:					
Sublease Agreement with Asuragen	$ 148	$ 89	$ 59	$ —	$ —
Services Agreement with Asuragen.	676	389	287	—	—
Total	$ 824	$ 478	$ 346	$ —	$ —

Off-balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the Securities and Exchange Commission.

Quantitative and Qualitative Disclosures about Market Risk

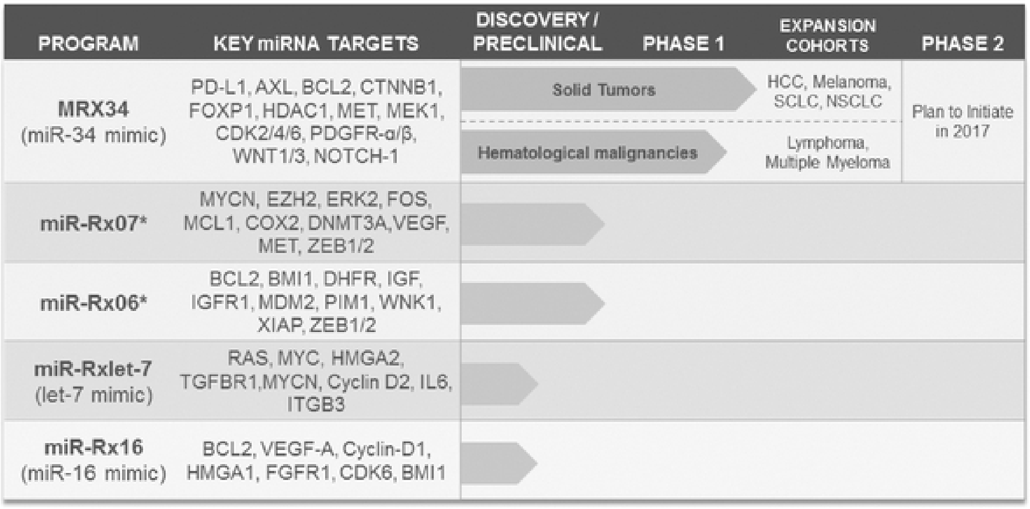
The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. At March 31, 2015, we had cash and cash equivalents of $40.1 million, consisting of interest-bearing money market accounts and prime money market funds. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term maturities of our cash equivalents and the low risk profile of our investments, we do not believe a change in interest rates would have a material effect on the fair market value of our cash equivalents.

Business

Overview

We are a clinical-stage biopharmaceutical company developing a broad pipeline of microRNA-based oncology therapeutics. microRNAs are naturally occurring, short ribonucleic acid, or RNA, molecules, or oligonucleotides, that play a critical role in regulating key biological pathways. Misexpression of even a single microRNA can contribute to disease development and tumor suppressor microRNAs are commonly reduced in cancer. Our scientists and others at leading academic institutions have identified numerous tumor suppressor microRNAs that play key roles in preventing normal cells from becoming cancerous and facilitating proper cancer immunosurveillance. We are developing mimics of naturally occurring microRNAs that are designed to restore this tumor suppressor activity and aid appropriate tumor immune response. This approach is known as microRNA replacement therapy. Our lead product candidate, MRX34, a mimic of naturally occurring microRNA-34 (miR-34) encapsulated in a liposomal nanoparticle formulation, is the first microRNA mimic to enter clinical development and has shown preliminary clinical evidence of anti-tumor activity as a single agent in our ongoing Phase 1 clinical trial. We believe that microRNA mimics represent a new paradigm in cancer therapy and have the potential to create a new, important class of effective cancer drugs that can potentially be used alone or in combination with other cancer therapeutics. We plan to develop MRX34 as a monotherapy and in combination with other therapeutic modalities, such as targeted therapies and immuno-oncology agents.

We are developing a pipeline of tumor suppressor microRNA mimics. Our tumor suppressor microRNA mimics are designed to impede the development of cancer by regulating the expression of multiple important oncogenes across key oncogenic pathways, whose inappropriate activation can lead to the transformation of normal cells into immortalized cancer cells. The potential capacity to simultaneously affect multiple pathways and processes that are critical to cancer cell viability may make mimics of tumor suppressor microRNAs potent anti-cancer agents and less susceptible to drug resistance. We are pursuing or have been granted therapeutic use patent claims related to several tumor suppressor microRNAs as well as composition of matter claims for multiple chemistries and structures that are, or may be used in or are contemplated for use with, our therapeutic microRNA mimics, including miR-34. The following chart provides summary information on the most advanced microRNA mimics in our pipeline:



* Undisclosed microRNA

Our lead product candidate, MRX34, is a miR-34 mimic encapsulated in a liposomal nanoparticle formulation. Our mimic of miR-34 has shown evidence of the potential ability to:

- reduce the proliferation of cultured cancer cells derived from patients with a wide range of malignancies, including liver, lung, colon, pancreatic and breast cancer;
- cause significant tumor regression in multiple mouse models of liver cancer and inhibit tumor growth in mouse models of other cancers;
- reduce the tumor-forming capacity of cancer stem cell populations;
- work in a synergistic manner with different approved cancer therapies to reduce proliferation of cultured cancer cells, and cause significant tumor regression in combination with an approved cancer therapy in an aggressive mouse model of liver cancer; and
- repress Programmed death-ligand 1 (PD-L1) protein expression in tumor tissue in a syngeneic mouse model of lung cancer, leading to an increase in active tumor-infiltrating immune cells (CD8+) and a decrease in so-called exhausted tumor-infiltrating immune cells (CD8+PD1+).

In April 2013, we initiated a multi-center, open label dose escalation Phase 1 clinical trial during which we are evaluating two different dosing schedules for MRX34 as a single agent in multiple advanced solid tumors and various types of hematological malignancies.

To date 97 patients have been enrolled in the ongoing MRX34 Phase 1 clinical trial at five clinical trial sites in the US and three sites in Korea. Primary objectives of the Phase 1 clinical trial are to establish the maximum tolerated dose and an appropriate dose for expansion cohorts and future Phase 2 clinical trials. To date:

- 47 patients have been treated on a twice weekly, or BIW, schedule for three weeks in 28-day cycles until the maximum tolerated dose of MRX34 was found to be 110 mg/m^2 among patients with solid cancers.
- The other 50 patients have been or are being treated daily for five days, or QD × 5, in 21-day cycles. We have not yet determined the maximum tolerated dose of MRX34 with this dosing schedule. Current dose levels are 70 mg/m^2 for primary liver cancer patients, 93 mg/m^2 for other solid tumors, and 110 mg/m^2 for hematological malignancies.

Based on observations from the two dosing schedules, we believe the QD × 5 dosing schedule has certain advantages over the BIW schedule such as better safety and tolerability, which we believe may in turn lead to improved efficacy. Therefore, the QD × 5 dosing schedule has been selected for all new patients enrolling in the Phase 1 clinical trial.

Secondary objectives of the clinical trial are to assess the safety, tolerability and pharmacokinetic profile of MRX34 after intravenous dosing as well as to assess any biological and clinical activity. Observations on these secondary objectives include the following:

- The most common adverse events observed to date with MRX34 are similar to those observed with marketed liposomal drug formulations and have been manageable with interventions commonly used by oncologists.
- Quantitative PCR and Next Generation Sequencing (NGS) analyses have demonstrated dose-dependent accumulation and activity of miR-34 in white blood cells from patients treated with MRX34 in the QD × 5 schedule. Consistent with observations from our preclinical studies, MRX34 dosing resulted on average in an approximately 40% reduction in the levels of multiple miR-34 target genes in white blood cells as well as increased levels of p21, a miR-34 inducible tumor suppressor gene.

- Of the 47 BIW cohort patients, who included patients with primary liver cancer or solid tumors with liver involvement (metastases), 37 patients were evaluable for response, based on availability of baseline and follow-up scans or disease progression as determined by the study investigator. One primary liver cancer patient, still on active study treatment, with a history of hepatitis-B infection and metastases to the lungs enrolled into the 70 mg/m^2 dose cohort on the BIW schedule, and achieved a confirmed partial response after six cycles of treatment per independent radiology review using RECIST (Response Evaluation Criteria in Solid Tumors) criteria. RECIST criteria is the standard method for evaluating solid tumor response in oncology clinical trials. This patient is one of 11 patients with primary liver cancer enrolled to date in Korea. Furthermore, of such 37 patients, six patients showed stable disease varying between two and eight cycles in length, and at different dose levels.

- Of the 50 patients enrolled to date at the same study sites on the QD × 5 dosing schedule, 34 are evaluable for response. One melanoma patient has been treated to date and enrolled in the 110 mg/m^2 QD × 5 dose cohort. This patient, who had progressed on previous treatments, including ipilimumab (Yervoy) and pembrolizumab (Keytruda), achieved a confirmed partial response after four cycles per independent radiology review using RECIST criteria. Furthermore, eight of the 33 patients have shown stable disease of varying duration, between two and 15 cycles of treatment, and at various dose levels; this includes one of two SCLC patients enrolled to date, who started MRX34 on the QD × 5 schedule in the 50 mg/m^2 dose cohort in July 2014 as fourth line therapy after extensive previous therapies, and who has been on MRX34 for 15 consecutive cycles.

- Based on preclinical data and observations of clinical activity to date, our dose expansion studies will focus on specific tumor types, namely, different subtypes of primary liver cancer, melanoma, small and non-small cell lung cancer, lymphoma and multiple myeloma.

Once the dose-escalation phase in the QD × 5 dose schedule cohort has been completed, and a recommended dose for the expansion cohorts has been determined, we intend to enroll approximately 100 additional patients across different tumor-specific expansion cohorts, including primary liver cancer, melanoma, small cell and non-small cell lung cancer, lymphoma and multiple myeloma. We expect to complete these expansion cohorts and have multiple study data read-outs by the end of 2016. After consultation with the FDA on study results and the recommended clinical development program going forward, we intend to initiate a Phase 2 clinical trial program in early 2017.

Our pipeline contains multiple tumor suppressor microRNAs that, like miR-34, have demonstrated the ability to inhibit cancer cell proliferation and tumor growth in preclinical studies by co-regulating the expression of multiple oncogenes. The specific set of genes regulated by each tumor suppressor microRNA as well as the ability to deliver these mimics to the target tissue may determine their potential in treating specific types of cancer, and thus the specific clinical development program for each of our pipeline therapeutic product candidates.

Our microRNA Platform

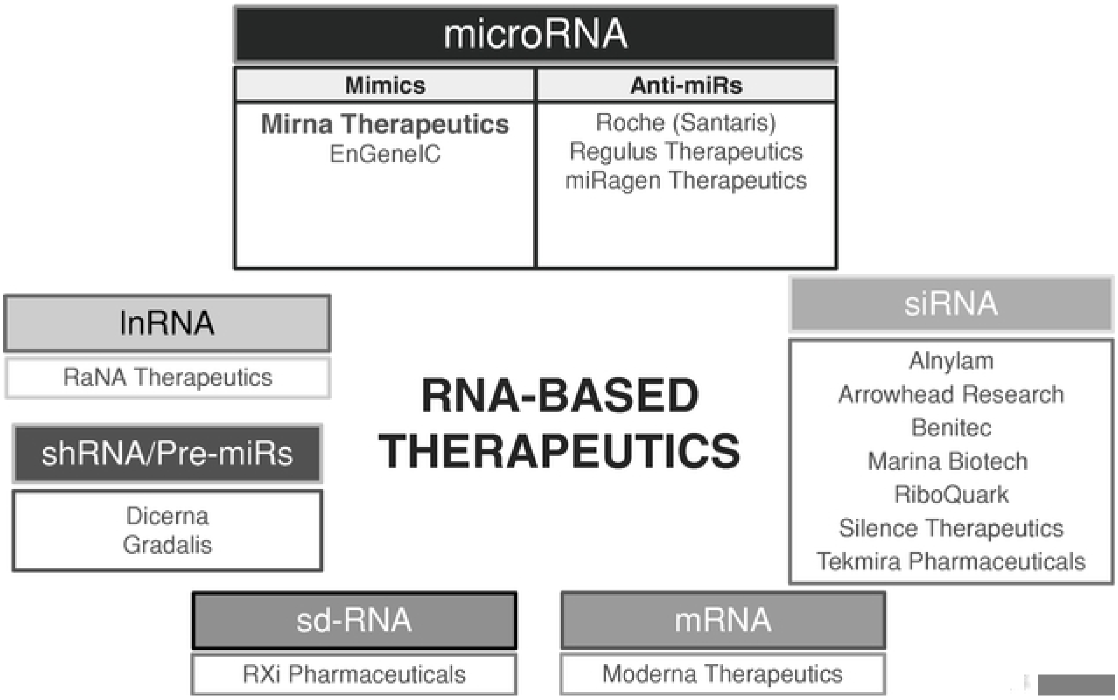
We pioneered the development of therapeutic miRNA mimics that feature two complementary RNA strands that are hybridized to produce a double-stranded RNA. The active strand has a sequence that is identical to a microRNA normally expressed in a cell, while the second, passenger strand is modified to facilitate proper loading of the active strand onto the cytoplasmic protein complex necessary for microRNA function inside the cells. While similar in structure, microRNA mimics are clearly differentiated from small interfering RNAs (siRNAs) through their biological heritage and activity. In contrast to the man-made sequences of siRNAs that target a single gene, microRNA mimics function like naturally occurring microRNAs to orchestrate the expression of many different genes to enable normal cell development and function. Because microRNA mimics have the same functions as the miRNAs that are naturally produced in cells, we believe that they will be unlikely to suffer from the undesired, or so-called "off-target," side effects that are common with siRNAs and other oligonucleotide-based therapies.

We have benefited from the recent expansion of oligonucleotide therapeutic development programs which have produced improved systemic oligonucleotide delivery technologies. We employed a comprehensive evaluation of more than ten of the most compelling preclinical or clinical stage lipid- and polymer-based nanoparticle delivery technologies to select an innovative liposomal technology called SMARTICLES to enable the systemic delivery of our microRNA mimics to cancer cells in patients.

Our early research and discovery work originated in 2002 at Ambion, Inc. and formed the initial basis for our patent portfolio, and later continued at our former parent company, Asuragen, Inc. This pioneering work allowed us to develop deep knowhow and expertise in the science underlying microRNAs and to develop a strong intellectual property position, which we continue to expand and strengthen. While our primary focus has been on the discovery and development of microRNA-based therapies for cancer, our scientists have also discovered functions of microRNAs in numerous diseases other than cancer, which may provide us an opportunity to expand this novel technology into other therapeutic areas of unmet medical need. We believe these microRNAs represent future partnering or diversification opportunities.

microRNAs: A Unique Class in the RNA Therapeutics Space

The landscape of RNA-based therapeutic technologies has rapidly expanded over the past few years, mostly due to advances in the delivery of these molecules to their intended targets. We are aware of several companies that are working specifically to develop RNA therapeutics, which we believe generally fall into the following categories:



While other companies in the field of microRNA have focused primarily on inhibiting overexpressed microRNAs by antagonists known as anti-miRs or AntagomiRs, we have focused on introducing microRNAs that are under-expressed in disease through the use of microRNA mimics. This is in part due to what we believe is stronger therapeutic activity of microRNA mimics compared to anti-miRs or AntagomiRs. Within the group of companies in the microRNA space, we are the first company to clinically employ microRNA mimics. The approach, technological and therapeutic focus and status of lead programs for these microRNA companies are as follows:

Company	microRNA Approach	Technology Focus	Therapeutic Focus	Status of Lead Program
Mirna Therapeutics	microRNA mimics	Replacement of tumor suppressor microRNAs	Cancer	MRX34(miR-34 mimic): 1st microRNA mimic in Phase 1
EnGeneIC	microRNA mimics	Replacement of tumor suppressor microRNAs	Cancer	MesomiR-1 (miR-16 mimic) in Phase 1 for mesothelioma
miRagen Therapeutics	anti-miRs	Inhibition of microRNAs	Cancer, amyotrophic lateral sclerosis (ALS), fibrosis, cardiovascular disease	Preclinical
Regulus Therapeutics	anti-miRs	Inhibition of microRNAs	HCV: kidney fibrosis	RG-101 (anti-miR-122) in Phase 1; RG-012 (anti-miR-21) in Phase 1
Roche(Santaris)	anti-miRs	Inhibition of microRNAs	HCV	Miramersen (anti-miR-122) in Phase 2

We believe that microRNA-based therapies have the potential to become a new class of drugs with broad therapeutic application based on the following:

- **microRNAs are misexpressed in a broad range of diseases.** Comparing the microRNA profiles of diseased and normal adjacent tissues from patients with cancer, obesity, cardiovascular diseases, neurodegenerative diseases, viral infections and a variety of other conditions has revealed consistent alterations in the expression of several microRNAs for each disease. Animal model studies have further revealed that the altered expression of many of these microRNAs contributes to the development of the disease.

- **microRNA therapeutics have the potential to modulate multiple disease pathways.** microRNAs are known to regulate gene networks involved in key biological pathways. Because of this unique attribute, the use of microRNA therapeutics may allow for more effective treatment of complex, multi-factorial diseases, such as cancer, in which multiple disease pathways are affected.

- **Target specificity minimizes off-target effects.** We believe our microRNA mimics regulate the same genes that are regulated by normally-expressed, naturally occurring microRNAs. Because normal cells have high levels of tumor suppressor microRNAs, the human genome has evolved to prevent the microRNAs from regulating the expression of non-target genes. This substantially reduces the likelihood that a microRNA mimic of the same tumor suppressor microRNA will affect the expression of any genes other than those that are targets for the naturally occurring tumor suppressor microRNA. We believe this is a key advantage of microRNA mimics over other targeted oligonucleotide-based therapies, such as antisense and siRNAs.

- **Synergies with other therapies.** In certain complex therapeutic areas, such as cancer, physicians typically treat patients with combination therapies and we believe microRNA-based replacement therapy has the potential to become part of that treatment paradigm. Nonclinical data suggest that microRNA therapeutics and different therapeutic modalities, such as radiation therapy, targeted therapies, or immuno-oncology agents, work synergistically to treat cancer.

The Current Challenges in Cancer and Cancer Therapies

Over the past two decades, cancer drug development has moved from systemic cytotoxic chemotherapy to more targeted therapies, with approximately 1,000 targets discovered and close to

800 drugs in development aimed at specific targets. First-generation targeted therapies have generally produced lower levels of toxicity than systemic cytotoxic therapies with variable efficacy outcomes. Efforts at improving the efficacy of cancer drug targeting have focused on defining subgroups of patients who are most likely to benefit from targeted therapies with the aid of modern molecular diagnostics, on combinations of targeted therapies with complementary mechanisms of action and on combinations of targeted therapies with chemotherapy or biological agents. Harnessing the patients' own immune system to attack cancer has had a long history of disappointments in the past, even though a small percentage of patients have apparently received long-term benefit in tumor control and overall survival. The recent discoveries of checkpoint inhibitors and other immuno-oncology products have resulted in marked improvements in efficacy, especially in long-term tumor control and overall survival. Several immuno-oncology products have been approved for marketing, including ipilimumab (Yervoy®), pembrolizumab (Keytruda®) and nivolumab (Opdivo®). However, only a subset of patients achieve responses to these products when used as a single agent and the development of combinations of these agents has been limited by toxicities.

For the next wave of targeted cancer therapies to produce a measurable improvement over current approaches, we believe it will need to yield drugs that can disrupt multiple oncogenic as well as immuno-oncology pathways. We believe the field of microRNA represents a highly promising area for the development of new cancer agents that can appropriately modulate combinations of oncogenic targets within cancer cells and stimulate patients' own immune system to attack cancer.

By replacing under-expressed tumor suppressor microRNAs to sufficient levels predictably and tolerably, we believe we have the potential to transform the current disease treatment paradigm across a wide variety of cancers provided that the delivery of microRNAs is achieved at sufficient levels. We also believe our microRNA mimics have the mechanistic flexibility to be used as:

- first-line agents in combination with current standards of care, including targeted therapies, immuno-oncology therapies, chemotherapies and/or radiation therapies;
- monotherapies in advanced or refractory patient settings;
- monotherapies in patients who would be intolerant of current standards of care; and
- monotherapies in tumor settings that do not have any approved therapies.

Our Strategy

Our corporate strategy includes the following:

- **Advance our lead product candidate, MRX34, through clinical development.** We are the first to establish clinical proof-of-concept for a microRNA-based replacement therapy for cancer. Our lead microRNA mimic product candidate, MRX34, is the potential first in a new class of promising cancer drugs, and has shown evidence of anti-tumor activity in a patient with metastasized hepatocellular carcinoma and a patient with advanced melanoma in our ongoing Phase 1 clinical trial. Once the dose-escalation phase in the ongoing Phase 1 trial has been completed, we intend to enroll additional patients across various tumor-specific expansion cohorts, including primary liver cancer, melanoma, small cell and non-small cell lung cancer, lymphoma and multiple myeloma. We expect to complete these expansion cohorts and have multiple study data read-outs by the end of 2016. After consultation with the Food and Drug Administration, or FDA, on study results and the recommended clinical development program going forward, we intend to initiate a Phase 2 clinical trial program in early 2017.

- **Identify biomarkers to support therapeutic product candidates.** We believe that biomarkers may be used to monitor microRNA activity and potentially aid in the selection of optimal patient segments in clinical trials. We are using clinical samples supplemented with cell and animal model studies to identify predictive biomarkers that may assist in both demonstrating delivery into and biological activity of miRNA mimics in patient cells, and in selecting patients most likely to benefit from treatment with MRX34 or other product candidates.

- **Expand our clinical development program to additional microRNAs.** Our scientists discovered tumor suppressor microRNAs critical for controlling various cancer processes which has allowed us to build a broad pipeline of tumor suppressor microRNA mimics that we believe to be promising therapeutic product candidates. Developing one or more product candidates in addition to MRX34, either alone or in combination, will allow us to file additional Investigational New Drug, or IND, applications with the FDA or equivalent applications with foreign regulatory agencies, and will also allow us to expand our clinical development program and create new development, commercialization and out-licensing opportunities. We aim to initiate clinical testing of a second product candidate in 2016.

- **Expand our intellectual property position.** We intend to continue building on our technology platform, comprised of intellectual property, proprietary methods and knowhow in the field of microRNA and also to successfully expand and defend our position as a leader in the field of microRNA. We are pursuing or have been granted therapeutic use patent claims related to several tumor suppressor microRNAs, as well as composition of matter claims for multiple chemistries and structures that are, or may be used in or are contemplated for use with, our therapeutic microRNA mimics, including miR-34. We have an exclusive license to the patent estate covering the SMARTICLES liposomal delivery technology for four of our product pipeline candidates, including miR-34, and could be broadened to include other tumor suppressor microRNAs. We believe our strong intellectual property position can be used to support internal development as well as out-licensing opportunities.

- **Leverage partnership opportunities.** The recent successful human application of different RNA therapeutic approaches in early clinical trials has led to increased interest in the field of RNA therapy from large pharmaceutical and biotechnology companies. To date, we have focused on establishing proof-of-concept for MRX34; however, in the future we anticipate that we will explore certain partnership opportunities. These may potentially focus on certain ex-U.S. territories where we do not expect to establish a commercial presence. We may also pursue partnerships to expand our development program for MRX34 in combination with approved or development-stage targeted therapies or immune therapies. In these cases, we anticipate retaining or sharing U.S. commercialization rights. As we progress additional product candidates toward clinical development, we may pursue partnerships for these programs in certain cancer types. We believe our leading position in the clinical development of microRNA-based therapeutics in cancer, coupled with a broad and promising pipeline, positions us well to actively seek such opportunities. Additionally, we have identified microRNAs we believe could have potential therapeutic uses for diseases other than cancer, including in cardiovascular, neurodegenerative and inflammatory diseases and a variety of other conditions. We may seek to partner these potential programs while cancer remains our focus.

Our Approach

microRNA Biology

RNA plays an essential role in the process used by cells to encode and translate genetic information from DNA to proteins. RNA is comprised of subunits called nucleotides and is synthesized from a DNA template by a process known as transcription. Transcription generates different types of RNA, including messenger RNAs that carry the information for proteins in the sequence of their nucleotides. In contrast, microRNAs are short RNAs, or oligonucleotides, that do not code for proteins, but rather ensure that the over 20,000 human protein-encoding genes are produced in the proper cells and at the proper levels by coordinating the production of proteins from messenger RNAs that are produced in each cell. microRNA-encoding genes emerged several hundred million years ago and their presence is believed to be a driving factor in the emergence and diversity of vertebrates in the ecosystem. Without microRNAs, cells and tissues within humans and other vertebrates would not be able to develop or function properly or respond to changes in the internal or external environments.

In humans, each microRNA binds to and regulates the translation of up to several hundred target messenger RNAs. Coordinating the translation of multiple, related genes allows a microRNA to regulate gene networks involved in key biological pathways. Given the importance of microRNAs in coordinating gene expression, it is not surprising that the altered expression of even a single microRNA appears to contribute to a variety of human diseases, including cancer. More than 10 years ago, while working at Ambion, our scientists discovered through extensive microRNA expression and functional assay work that microRNAs are differently expressed in cancer tissue compared to normal adjacent tissue and that several naturally occurring microRNAs function as tumor suppressors by regulating the expression of key oncogenes and preventing the development, progression and dissemination of cancer.

To enable therapeutic application of these tumor suppressor microRNAs, we pioneered technologies for creating RNA molecules that function as natural microRNAs when they enter human cells. These RNA molecules, which we call microRNA mimics, may be used to replace those tumor suppressor microRNAs that are lost, or under-expressed, in cancer cells. We have designed a proprietary, double-stranded microRNA mimic construct for our therapeutic product candidates. The structure of the microRNA mimics we use features two complementary RNA molecules that form a small double-stranded RNA molecule with no overhangs. One strand, the active strand, is an exact copy of the naturally occurring microRNA sequence. The passenger strand is a complement to the active strand with modifications that prevent it from being active in the cytoplasm of the cancer cell, where microRNAs exhibit their cellular function. We have issued patents and pending patent applications on this design, regardless of therapeutic indications, as well as other intellectual property on multiple specific chemistries and structures that may be used in therapeutic microRNA mimics.

Delivery of microRNA Mimics to Target Tissues

Systemic delivery of oligonucleotides, including microRNAs, has been a major challenge, principally due to the fact that these molecules have to overcome multiple barriers after intravenous administration before reaching their ultimate place of action, which is the RNA-induced silencing complex (RISC) in the cytoplasm of cancer cells. Significant hurdles must be overcome at each step:

- binding to plasma proteins and degradation by nucleases in blood;
- excretion through glomerular filtration in the kidney;
- ability to penetrate into the tumor itself; and
- uptake by individual tumor cells and release into cytoplasm.

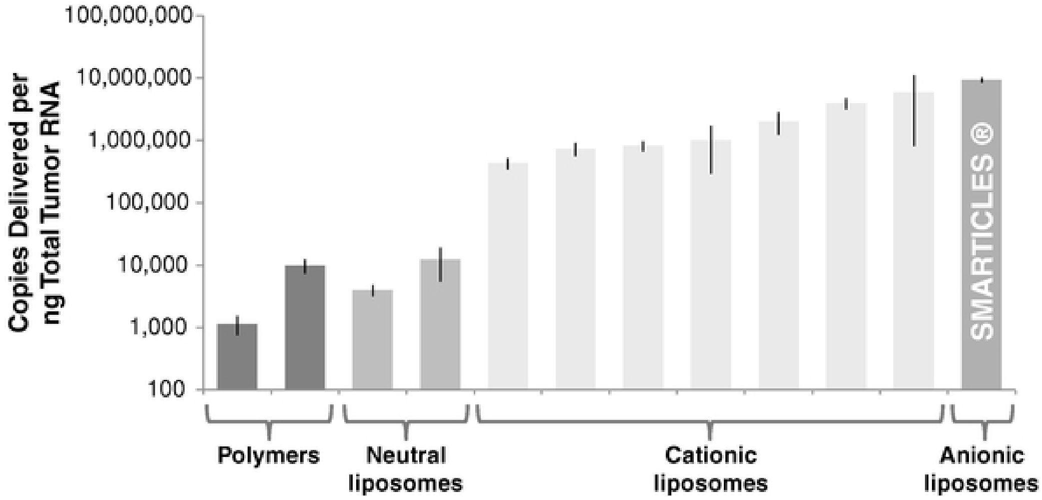
Encapsulation of these oligonucleotides inside delivery nanoparticles overcomes several of these hurdles, and we believe there has been significant progress over the past decade in the design and implementation of novel delivery technologies. Due to the importance of delivery to the success of our product candidates, we have closely monitored progress over the last several years, and will continue to do so going forward. As a result, our team is very focused on, and has become very efficient in, assessing and evaluating new and existing technologies for delivery of our microRNA mimics.

We carried out systematic evaluations of these different proprietary delivery systems under material transfer agreements in conjunction with our microRNA mimics, thereby providing us with formulations of our microRNA compounds for *in vivo* and *ex vivo* testing.

We determined that the SMARTICLES formulation technology, owned by Marina Biotech, Inc., or Marina, had a favorable combination of efficient systemic delivery of miR-34 mimics to solid tumors in mice, a high therapeutic activity of formulated miR-34 in mouse models of cancer, low or no toxicity, and low or no cytokine stimulation in both animal models and an ex vivo human whole blood assay.

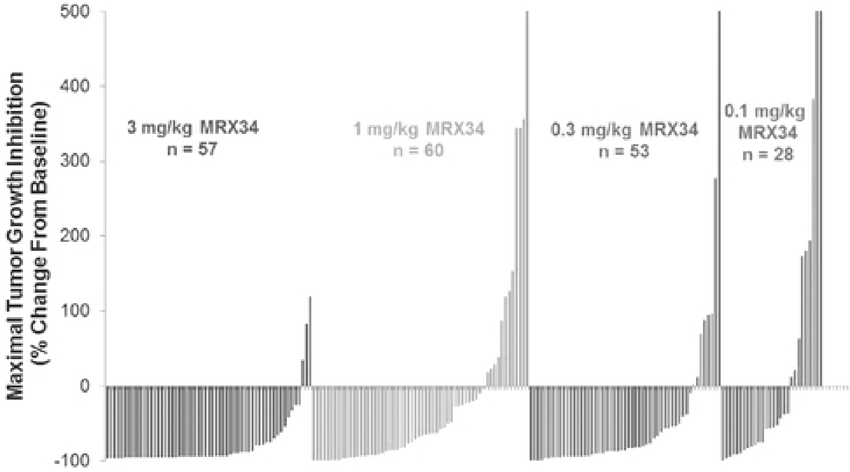
Efficient Systemic Delivery

The SMARTICLES formulation demonstrated key benefits in preclinical studies, including the ability to deliver very high numbers of microRNA mimics to tumors, as shown below.



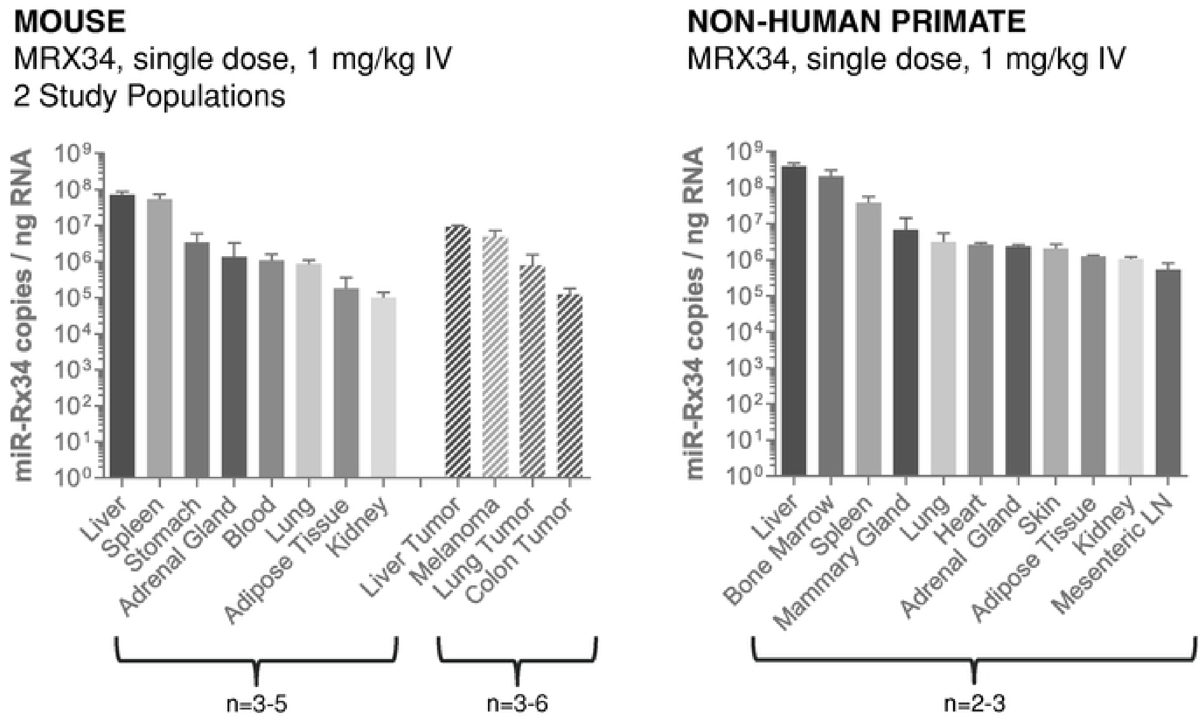
High Therapeutic Efficacy in Mouse Models of Cancer

We observed dramatic efficacy using the SMARTICLES formulation in multiple orthotopic tumor models of liver cancer, including Hep3B, HuH-7, C3A, BN118, and BN124, with full regression in the majority of established liver tumors at different dose levels and with different treatment schedules (see results of mice studies in figure below).



Promising Biodistribution

In addition, the SMARTICLES formulation offers a promising biodistribution pattern after intravenous administration in mice and non-human primates, with delivery of high copy numbers not only to the liver and spleen generally, which is to be expected with liposomal formulations, but also to other highly vascularized tissues, such as lung, adrenal gland, stomach and kidney, and also to bone marrow in non-human primates. As shown in the following figures, the SMARTICLES formulation was found to deliver to both healthy and cancerous cells, with a high number of copies of the miR-34 mimic delivered to tumors located in the liver, lymph nodes (melanoma metastases), lung and colon, as well as to highly vascularized tissues, including adrenal gland and kidney.



This pattern of biodistribution upon intravenous administration is also well documented for other liposomal formulations, with highest levels of delivery to the liver and spleen.

Lack of Cytokine Stimulation

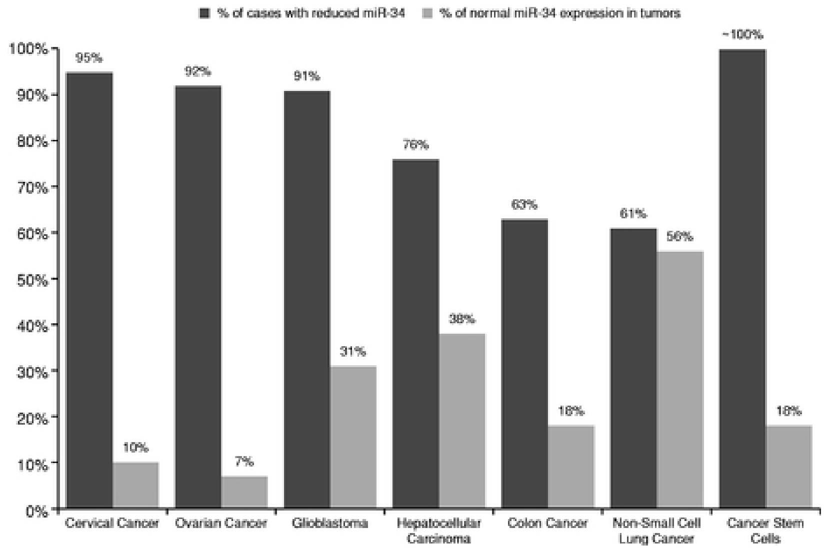
The SMARTICLES formulation includes negatively charged liposomes, which we believe might limit the toxicities that have plagued positively charged liposomal formulations that have been used for other oligonucleotide-based therapies. There have been no statistically significant elevations in the cytokine levels of mice and non-human primates dosed with SMARTICLES-formulated microRNA mimics, or in a human whole blood assay of key human cytokines, indicative of a potentially induced immune response. No significant changes in the serum levels of cytokines, such as interferon-a, TNF-a, IL-1 and IL-12 have been observed. Variable dose-related increases in IL-6 were seen, but these increases were not statistically significant as compared to the control group and were not of a magnitude that we believe would cause clinical concern.

Exclusive License

In December 2011, we obtained an exclusive license from Marina under its rights to the SMARTICLES technology. Our license from Marina grants us exclusive rights (including the right to sublicense) under the SMARTICLES technology to develop, manufacture and commercialize products containing miR-34, and, pursuant to a December 2013 amendment, three other promising tumor suppressor microRNA targets selected by us. Although we remain confident in our selection of SMARTICLES for our lead therapeutic candidate, we are continuing to evaluate different delivery technologies for potential use in conjunction with miR-34 and the other microRNA mimics in our pipeline for the purposes of optimizing delivery of our drug candidates to a broader group of tissues and organs.

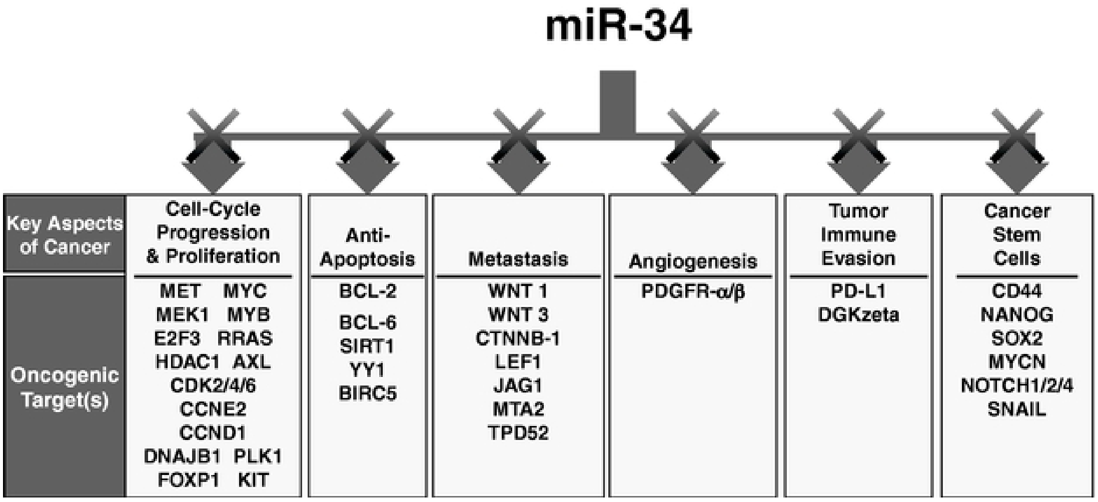
Selection of miR-34 as Lead Therapeutic Target

miR-34 is one of the most widely published tumor suppressor microRNAs. Studies have revealed that the levels of miR-34 are reduced in the tumors of patients with a wide variety of cancers, as exemplified in the graph below.



The under-expression of miR-34 in cancers appears to be due to the fact that miR-34 expression is affected by p53, a well-known tumor suppressor that is often mutated and less active in tumors. Published data suggest that miR-34 functions akin to the tumor suppressor function of p53, controlling many genes and pathways that are also associated with p53. Reduced expression of miR-34 in cancers also commonly occurs as a result of methylation of the miR-34 gene.

Based on published reports from microRNA scientists at numerous research institutions, miR-34 plays a key role in controlling the expression of more than 30 oncogenes as well as genes involved in tumor immune evasion, as shown in the figure below. This includes targets that are the focus of currently-marketed and investigational cancer drugs.



The considerable reduction of miR-34 levels observed in cancer stem cells suggests that the microRNA might play a functional role in preventing normal cells from acquiring stem-like properties, like cell self-renewal, which can contribute to the development of cancer. In partnership with an academic collaborator, we successfully demonstrated that introducing miR-34 into prostate cancer stem cell populations can significantly reduce their stem-like properties and limit their capacity to form tumors. Similar results have been obtained from studies using pancreatic and gastric cancer stem cells. We believe the ability of miR-34 to inhibit cancer stem cells has significant implications for cancer therapy since the cancer stem cells present in tumors are thought to be the primary drivers of tumor growth, metastasis and resistance to therapy.

Recent data generated with an academic collaborator showed that miR-34 directly represses the checkpoint signaling molecule PD-L1. PD-L1 protein present on tumor and immune cells can silence anti-tumor immune responses and has become a promising drug target in immuno-oncology therapies. The introduction of miR-34 mimics into cultured lung cancer cells led to a remarkable decline of PD-L1 protein expression. In a syngeneic mouse model of lung cancer, we successfully demonstrated that MRX34 treatment led to repression of the PD-L1 protein in tumor tissue and an increase in active tumor-infiltrating immune cells (CD8+) and a decrease in so-called exhausted tumor-infiltrating immune cells (CD8+PD1+). We believe the ability of miR-34 to block PD-L1 signaling may broaden the therapeutic application of MRX34 as a monotherapy as well as in combination with other immune-oncology therapies.

MRX34: Our Lead Product Candidate

MRX34 is a double-stranded RNA mimic of the tumor suppressor microRNA, miR-34, encapsulated in a liposomal nanoparticle formulation called SMARTICLES. miR-34 inhibits multiple oncogenic pathways and stimulates anti-tumor immune response to induce cancer cell death. We performed cell culture studies that revealed that introducing a mimic of miR-34 into cancer cell lines derived from patients with liver, lung, colon, pancreatic and breast cancers results in significant reductions in cell proliferation. In various preclinical studies, miR-34 also inhibited formation of cancer stem cells, which are believed to contribute to the development, metastasis and therapeutic resistance of tumors. Studies performed at other laboratories have indicated that increasing miR-34 levels also inhibit the proliferation of cancer cells derived from patients with malignant melanoma, B-cell lymphoma and multiple myeloma.

MRX34 Clinical Development Program

In addition to evaluating the safety, tolerability, and pharmacokinetic profile of MRX34, an important goal of our ongoing Phase 1 clinical trial is to establish proof of concept of microRNA replacement therapy in patients with primary liver cancer or advanced solid tumors. Our focus on hepatocellular carcinoma, or HCC, is based on the fact that liposomal nanoparticle formulations have a tendency to deliver their payload to the liver, and the high unmet medical need in this tumor type. For example, sorafenib (Nexavar), the only approved drug for unresectable primary liver cancer, has only shown a 2% objective response rate. Additionally, we have also demonstrated meaningful results with MRX34 in multiple mouse models of primary liver cancer, including a study in which MRX34 demonstrated improved survival over sorafenib. To date we have observed tumor shrinkage greater than 30% in two patients with Stage IV cancer: one patient with a confirmed partial response in primary liver cancer metastasized to the lung, and a confirmed partial response in a melanoma patient with disseminated disease.

During the course of our Phase 1 clinical trial, the patient population was expanded to also include patients with hematological malignancies, based on the observation that specific lymphomas and leukemias are characterized by low levels of miR-34, and biodistribution data that supports high delivery to bone marrow and malignant lymphocytes. During the trial, we have observed dose-dependent MRX34 delivery and activity in normal white blood cells of patients and we aim to demonstrate delivery to tumors when patient biopsies become available during our expansion cohorts.

The primary objectives of the Phase 1 clinical trial, including the hematological malignancy cohort, are to establish the maximum tolerated dose and an appropriate dose for Phase 2 clinical trials. The secondary objectives of the Phase 1 clinical trial are to assess the safety, tolerability and pharmacokinetic profile of MRX34 after intravenous dosing as well as to assess any biological and clinical activity. This Phase 1 clinical trial is not designed to show statistical significance of the study endpoints.

Initially, MRX34 was administered as a single agent intravenously twice a week, or BIW, for three weeks with one week off, in 28-day cycles, until disease progression or intolerance. This dosing schedule was selected based on preclinical toxicity and efficacy studies. In total, 47 patients have been treated on BIW dosing schedule and a Maximum Tolerated Dose (MTD) was established at 110 mg/m^2 for this dosing schedule. Based on our experience with this dosing schedule and another company's experience with a SMARTICLES-based liposomal formulation, a second dosing schedule was introduced mid-2014, which involves daily MRX34 administration for five days, or QD × 5, with two weeks off, in three week cycles. To date, 50 patients have been treated on the QD × 5 dosing schedule, and recruitment is continuing. In the 47 patients treated on the BIW dosing schedule, 37 patients were evaluable for response, based on availability of baseline and follow-up scans or disease progression as determined by the study investigator. In those 37 patients, six patients showed stable disease varying between two and eight cycles in length, and at different dose levels. Of the 50 patients enrolled to date on the QD X 5 dosing schedule, 34 are evaluable for response. Eight of the 34 patients have shown stable disease of varying duration, between two and 15 cycles of treatment, and at various dose levels.

The Phase 1 clinical trial consists of an initial dose-escalation phase, followed by an expansion phase after a maximum tolerated dose and recommended Phase 2 doses are identified. In the expansion phase, patients being treated at the recommended Phase 2 dose may undergo tumor biopsies to identify potential biomarkers for assessing delivery and activity of miR-34, and/or predicting response to MRX34.

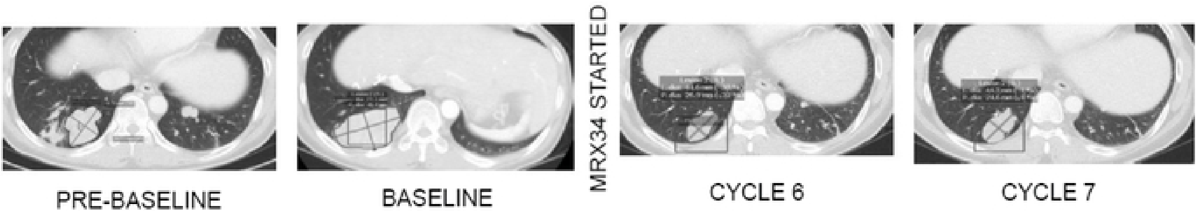
Through the first 26 months of our Phase 1 clinical trial, 97 patients have been treated with escalating doses of MRX34 in either BIW or QD × 5 schedules, starting at the 10 mg/m^2 BIW dose level. Nearly all patients experienced at least one adverse event, with fever, chills, fatigue, thrombocytopenia, diarrhea, back pain, nausea, vomiting, anorexia, headache, elevation of liver enzymes, decreased albumin, hyponatremia, hyperglycemia, lymphopenia and neutropenia being the most commonly reported adverse events. The treatment-related serious adverse events occurring in more than one patient were as follows:

- Among the 47 patients in the BIW dosing cohort, the serious adverse events determined to be related to MRX34 treatment and occurring in more than one patient were fever, fatigue, dehydration and elevation of liver enzymes, each of which occurred in two patients to date. For the BIW schedule, the MTD of MRX34 was found to be 110 mg/m^2 among patients with solid tumors.

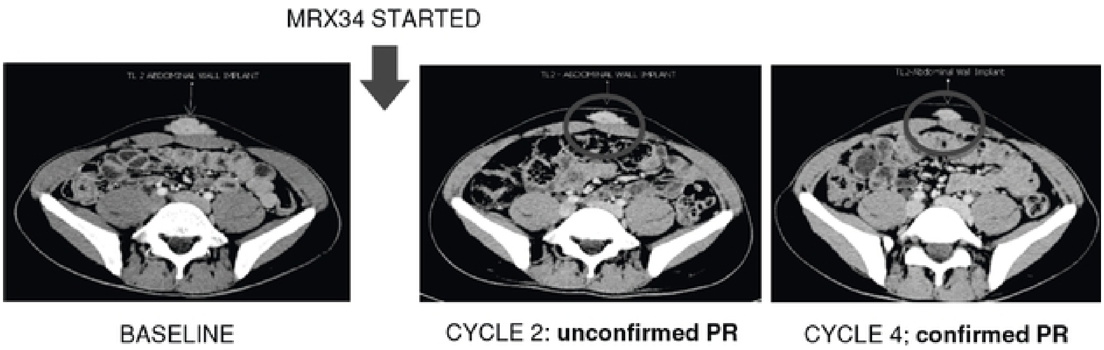
- For the 50 patients in the QD × 5 dosing cohort, the serious adverse events determined to be related to MRX34 treatment and occurring in more than one patient, were bleeding in silent or asymptomatic HCC brain metastasis, elevation of liver enzymes and thrombocytopenia, each of which occurred in two patients to date. The MTD has not been determined for the QD × 5 schedule among patients with hematological malignancies or solid tumors and MRX34 dose escalation is continuing with additional patients being enrolled into the study. Current dose levels are 70 mg/m^2 for primary liver cancer patients, 93 mg/m^2 for other solid tumors, and 110 mg/m^2 for hematological malignancies.

The most common adverse events associated with MRX34 are similar to those reported with other liposomal drug formulations, and are generally manageable or preventable with standard interventions or tests used by oncologists, such as administering other medications that prevent or reduce side effects, temporary slowing of infusions, delaying or stopping dosing, or using magnetic resonance imaging, or MRI, to detect silent brain metastases.

Of the 29 patients with primary liver cancer treated with escalating doses of MRX34 to date, one advanced HCC patient with underlying HBV etiology and metastases to the lungs enrolled into the 70 mg/m^2 dose cohort on the BIW schedule achieved a confirmed partial response after treatment cycle 6. Below are the CT scans showing growth of the primary liver cancer metastasis in the lung from pre-baseline to baseline, prior to enrollment in the study. After initiating MRX34, the tumor showed shrinkage after six cycles of treatment, continuing in cycle seven. This patient is one of the 11 patients with primary liver cancer enrolled from the Korean sites.



The one melanoma patient enrolled in the study to date, enrolled into the 110 mg/m^2 dose cohort on the QD × 5 schedule, achieved a confirmed partial response, per independent radiology review using RECIST criteria, after four cycles of MRX34 treatment.



In the 47 patients treated on the BIW dosing schedule, 37 patients were evaluable for response, based on availability of baseline and follow-up scans or disease progression as determined by the study investigator. In those 37 patients, six patients showed stable disease varying between two and eight cycles in length, and at different dose levels. Of the 50 patients enrolled to date on the QD X 5 dosing schedule, 34 are evaluable for response. Eight of the 34 patients have shown stable disease of varying duration, between two and 15 cycles of treatment, and at various dose levels.

Following the determination of the maximum tolerated dose and an appropriate dose for Phase 2 clinical trials with QD × 5 schedule, we plan to enroll approximately 100 patients into the Phase 1b expansion cohorts. The expansion cohorts are expected to enroll patients with HCC, melanoma, SCLC, NSCLC, or hematological malignancies, with enrollment expected to be completed by end of 2016. Based on the safety and efficacy data from the expansion cohorts, we plan to meet with FDA to discuss the next phase of the MRX34 clinical development.

Pharmacokinetics and Pharmacodynamics

Both maximum blood concentrations (Cmax) of, and drug exposure (area under the curve, or AUC) to, miR-34 showed a non-linear, non-dose proportional increase with increasing doses in both the BIW and QD × 5 schedules. In the BIW schedule, the AUC after the sixth dose (cycle day 18) was generally similar compared to the AUC after the first dose (cycle day 1). With the QD × 5 schedule, the AUC was increased approximately 10-fold on fifth day of dosing (cycle day 5) as compared after the first dose (cycle day 1). The increased drug levels on cycle day 5 may provide higher exposure of different tissues, including tumor cells, to MRX34. We believe that the higher exposure with 5 days of consecutive daily dosing is a benefit of the QD × 5 schedule as compared to the BIW schedule.

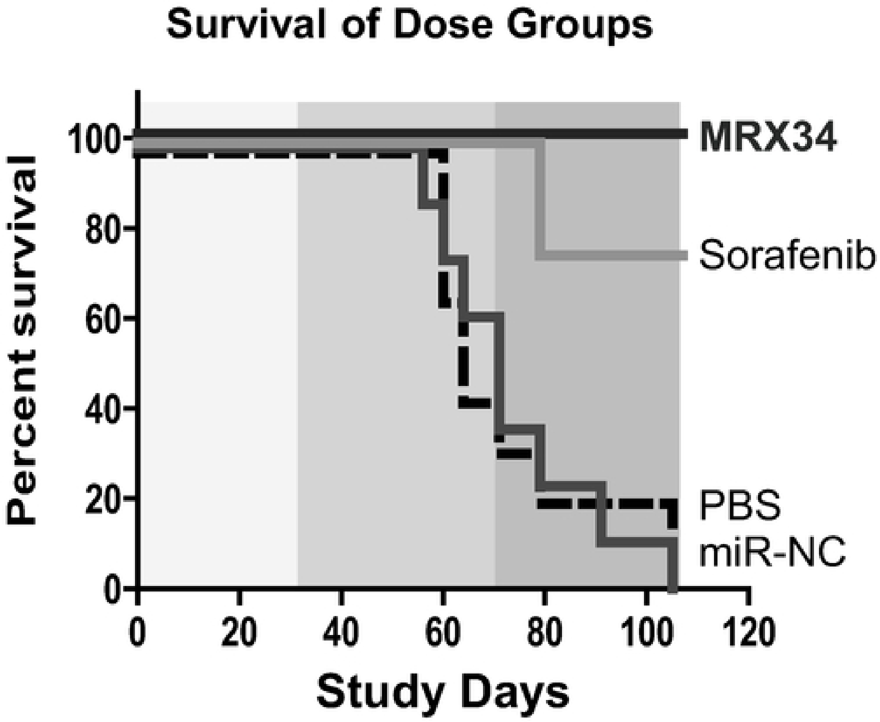
To address whether the miR-34 mimic administered as MRX34 can engage its molecular targets in patients, we have collected and continue to collect various human tissues for molecular analysis. To date, we have biomarker data from human white blood cells (hWBCs) from patients treated with MRX34 in our ongoing Phase 1 clinical trial, and intend to collect data from patient tumor biopsy material during the dose expansion phase of the trial. We have collected hWBCs during cycle 1 just before initiation of treatment (pre-dose) and at multiple time points thereafter. Samples from 21 patients dosed QD × 5 at dose levels ranging from 33 - 110 mg/m^2 were submitted to gene-specific quantitative PCR analysis, and samples from two patients dosed QD × 5 at 33 and 70 mg/m^2 were analyzed via whole transciptome Next Generation Sequencing (NGS). Both set of data show a dose-dependent repression of numerous oncogenes that have previously been identified as direct miR-34 targets, including FOXP1, BCL2, HDAC1 and CTNNB1. In contrast, it has been reported that hWBC samples revealed a dose-dependent up-regulation of p21-CIP1/WAF1, a tumor suppressor gene specifically induced by miR-34. Based on these data, we believe that the systemic administration of MRX34 to patients with different cancer types facilitated successful delivery of miR-34 into white blood cells and direct engagement of several biological targets of the miRNA. During the expansion phase of the Phase 1 trial, we intend to collect tumor specimens for use in similar pharmacodynamics assessments, and hope to correlate those with clinical responses in patients treated with MRX34.

MRX34 Preclinical Development Program

Monotherapy

We utilized two different models of liver cancer in mice to develop and characterize MRX34. These preclinical studies revealed that intravenous injections of MRX34 caused a greater than 100-fold increase in miR-34 levels in liver tumor cells and a corresponding reduction in the expression of oncogenes that are targets for the natural miR-34. Efficacy studies have revealed that intravenous injections of MRX34 three times per week at doses as low as 0.1 mg/kg and dosing as infrequent as once per week at 3.0 mg/kg can cause mature human primary liver tumors in mice to regress.

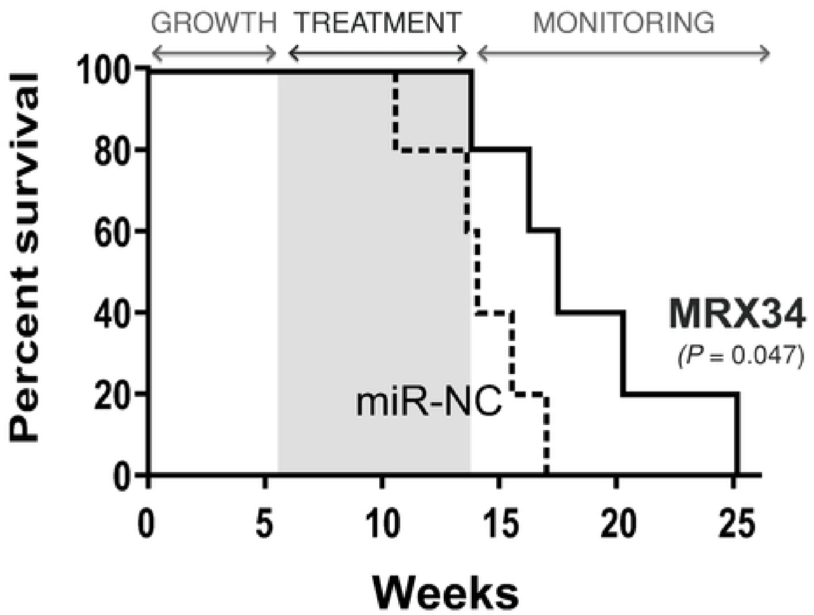
We compared the therapeutic activity of MRX34 to sorafenib (Nexavar), which is the current standard of care for patients with HCC, in a 16-week orthotopic human liver cancer mouse model. After the human liver tumors were developed in livers of mice over the first four weeks of the study, the mice were dosed for six weeks followed by an additional six weeks of off-treatment monitoring for health and liver tumor growth. We dosed the mice by tail vein injection every other day with MRX34 at a rate of 0.3 mg/kg or by oral daily dosing with sorafenib at a rate of 30 mg/kg. As control groups for our study, we used a phosphate buffered saline buffer as well as a scrambled microRNA sequence formulated in the SMARTICLES delivery formulation, or miR-NC. Each of the two control groups were dosed by the same route and on the same dosing schedule as MRX34. During the six-week dosing period, as well as during the six-week period after the final dose, we measured the weights of the mice biweekly and conducted health checks twice daily. As shown in the following graph, due to the aggressive nature of these tumors, none of the mice in either of the control groups survived the full duration of the study, as we observed large tumors in each of the mice. By comparison, two of the mice from the sorafenib group did not survive the full duration of the study, while all of the mice from the MRX34 group survived. Following the study, tumors were detected in three of the mice from the sorafenib group, while no tumors were detected in any of the eight mice comprising the MRX34 dosing group. We concluded from the study that the systemic delivery of MRX34 not only led to full regression in the majority of established liver tumors, but also had eliminated the potentially remaining viable liver cancer cells in the mice, with no tumor recurrence during the off-treatment follow-up period.



We believe that the potency exhibited by MRX34 in the liver cancer efficacy studies is derived from the ability of the small microRNA to regulate multiple genes and pathways that are important for HCC development and growth.

Delivery to Tumors Outside of the Liver

In collaboration with Yale, we evaluated the therapeutic effects of MRX34 in the $KRAS^{LSL\text{-}G12D}/TP53^{fl/fl}$ genetically engineered mouse model of NSCLC. Orthotopic lung tumors were initiated by the intratracheal delivery of adenovirus carrying *cre* recombinase, leading to activation of the KRAS mutant and a concomitant loss of p53. Both genetic alterations are common in human lung cancers. Lung lesions typically show an aggressive growth behavior and frequently cause death. Continuous dosing of MRX34 demonstrated a statistically significant prolongation of survival of the tumor-bearing mice relative to mice that were dosed with a SMARTICLES-formulated negative control microRNA (miR-NC). The results of this study suggest that systemic delivery of MRX34 had a therapeutic effect in orthotopic lung tumors.

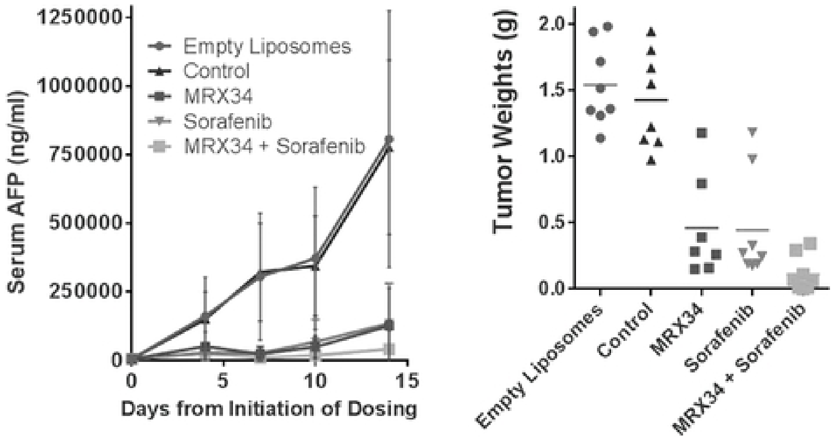


Combination Therapy for MRX34

Since most cancer therapeutics are used in combination to increase efficacy while minimizing toxicity, we have initiated a program to evaluate MRX34 in combination with various standard of care and investigational cancer drugs. We chose tumor models and chemotherapeutic agents based on the predicted patient profile in our future expanded clinical development program for MRX34. These included patients with primary liver cancer or advanced lung, colon and pancreatic cancers that have metastasized to the liver.

Hepatocellular Carcinoma (HCC)

Using a panel of four human liver cancer cell lines, our *in vitro* studies have shown that our miR-34 mimic, which is the drug substance of MRX34, cooperates synergistically with sorafenib (Nexavar), which is the standard of care for use in patients with HCC, to inhibit cancer cell proliferation. When used in combination, both the miR-34 mimic and sorafenib were more effective at lower doses both across cell lines and at various drug ratios. Data in Hep3B cells showed that the dose requirement for sorafenib to induce 50% cancer cell inhibition could be reduced by eight- and 19-fold in the presence of 1 nM and 1.6 nM miR-34 mimics, respectively. The dose requirement for the miR-34 mimic to induce 50% cancer cell inhibition could be reduced by up to seven-fold in the presence of sorafenib. The superior inhibitory activity of the combination demonstrated in these *in vitro* studies was confirmed in an animal study during which mice were treated with the combination or with each of the single agents alone for approximately two weeks. Our data showed that liver tumors from animals treated with the combination were significantly smaller than tumors from animals that received either miR-34 mimic or sorafenib alone.



In clinical practice, a combination of MRX34 and sorafenib could potentially be more effective by increasing the potency and/or reducing the toxicity of each individual drug, and thus ultimately, once approved and marketed, potentially increase the lifespan of liver cancer patients and significantly expand the market opportunity for both drugs.

Non-Small Cell Lung Cancer (NSCLC)

Cell culture models of human non-small cell lung cancer have been used to show that combining our miR-34 mimic with erlotinib (Tarceva®) creates a synergistic effect, and thus yields a potent therapy for non-small cell lung cancer in human cell lines that are resistant to erlotinib alone. This application could significantly increase the number of lung cancer patients who could be treated with erlotinib and also further expand the market potential for MRX34. The miR-34 mimic also cooperated synergistically with 2nd and 3rd generation EGFR (epidermal growth factor receptor) small molecule inhibitors in lung cancer cells, particularly those that harbor an EGFR mutation but are erlotinib-refractory. Additionally, synergistic activity was demonstrated with pemetrexed (Alimta®) in lung cancer cells, erlotinib and tivantinib in liver cancer cells, gemcitabine in pancreatic cancer, and lapatinib (Tykerb®) in breast cancer cells. Additional *in vivo* testing is in process.

Combination of Different microRNAs

Because individual tumor suppressor miRNAs modulate the expression of different sets of genes, it is possible to use combinations of miRNAs to extend the number of oncogenes that are being affected. Using a liver cancer model, we observed that co-injecting half-doses of MRX34 and a SMARTICLES-formulated mimic of miR-7 provided greater tumor regression and longer survival than did full dose injections of either MRX34 or SMARTICLES-miR-7 alone. Similar results were produced in collaboration with Dr. Frank Slack while at Yale University, as we showed that combining the tumor suppressor microRNAs miR-34 and let-7 in the same SMARTICLES liposomal delivery formulation leads to superior therapeutic activity in a genetically engineered mouse model of lung cancer. The miR-34 and let-7 combination showed higher level of tumor growth inhibition than either liposomal miR-34 or let-7 alone in this very aggressive lung cancer model. These data suggest that combining tumor suppressor miRNAs might yield a more potent therapeutic candidate, and could represent another product development and commercial opportunity

MRX34 Market Opportunities

Primary Liver Cancer (Hepatocellular Carcinoma)

According to the World Health Organization (WHO), liver cancer is the third leading cause of cancer deaths worldwide. HCC is the most prevalent form of liver cancer and is the most common cancer in some parts of the world, with more than one million new cases diagnosed each year worldwide according to the National Cancer Institute. According to recent reports from the Centers for Disease Control, HCC rates in the United States are increasing with common risk factors including alcohol consumption, metabolic syndrome, chronic hepatitis B or C infection and Type 2 diabetes. Patients diagnosed with HCC have a poor prognosis, with a very low five year survival rate of less than 10%. Treatment options include surgical resection, liver transplantation, radiofrequency ablation and chemoembolization, or delivery of a drug mixed with particles through an arterial catheter directly into the tumor's blood supply. The only systemic drug therapy approved for the treatment of unresectable HCC is the drug sorafenib (Nexavar), which provides a 2.8 months median overall survival benefit based on a median overall survival of 10.7 months compared to 7.9 months for a placebo. Nivolumab (Opdivo), a PD-1 (programmed death 1) blocker, has recently shown promising results in HCC with 19% objective response rate reported in a Phase 1 clinical trial.

Skin Cancer (Melanoma)

An aggressive type of skin cancer, melanoma, can occur anywhere on the body, but is most common in skin that is often exposed to sunlight, such as the face, neck, hands, and arms. Melanoma is a disease in which cells called melanocytes form in the skin and turn into cancer cells. The WHO states that the incidence of melanoma skin cancers has been increasing over the past decades and has reached 132,000 globally each year. Approximately 73,000 cases of melanoma are expected to be diagnosed and 10,000 deaths will occur in the United States alone in 2015, according to the American Cancer Society. The 5-year survival rate is currently about 15% to 20% in patients with metastatic melanoma. Approved treatment options for melanoma include surgery, chemotherapy, radiation therapy, biologic therapy and targeted therapies. In recent years, significant advances have been achieved in the treatment of melanoma by targeting PD-1, a protein expressed on the cellular surface of immune cells called T cells that normally function to keep these cells from attacking other cells in the body. The PD-1 signal is induced by PD-L1, which is expressed by a variety of normal cells. PD-L1 can also be expressed by various tumor cells, including melanoma, and consequently leads to tumor immune evasion. Drugs that block PD-1 boost the immune response against melanoma cells, which can often lead to tumor shrinkage and increased patient survival. Pembrolizumab (Keytruda) and nivolumab (Opdivo) are FDA-approved drugs that target PD-1. Ipilimumab (Yervoy) also boosts immune response but blocks CTLA-4, another T cell protein. Clinical trials have recently shown these drugs to be highly effective, but package inserts indicate that these drugs are effective against less than approximately 25% of patients. Recent preclinical data have shown that miR-34 also activates the immune system by repressing PD-L1. Our development plan includes continuing to study MRX34 as a monotherapy in melanoma and in combination with approved checkpoint inhibitors to determine whether MRX34 may be able to increase the numbers of patients who respond to these therapies or minimize or reverse resistance and eventual disease progression.

Lung Cancer

According to the WHO, lung cancer is the most common cancer in the world and it has retained this position for decades. There were an estimated 1.8 million new cases in 2012, 58% of which occurred in less developed regions of the world. Lung cancer is also the most common cause of death from cancer worldwide, estimated to be responsible for nearly one in five (19.4% of the total). Small cell lung cancer (SCLC), also called oat cell cancer, accounts for about 10%-15% of lung cancers. SCLC is particularly aggressive and often spreads quickly. Five-year survival rates range from approximately 30% in patients with "limited stage" disease to approximately 2% for patients with "extensive stage." Treatment options for people with SCLC include chemotherapy, radiation therapy and surgery. Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, accounting for approximately 85% of lung cancers. Types of NSCLC include squamous cell carcinoma, adenocarcinoma, and large cell carcinoma. The five-year survival rate for patients with NSCLC can be as high as 50% for patients diagnosed in the early stages of the disease. However for patients with metastases, the 5-year survival is typically less than 5%. Treatment options for NSCLC also include surgery, chemotherapy and radiation. However, more recently approved targeted therapies and immunotherapies have become the standard of care. Targeted therapies include drugs that target tumor blood vessel growth (angiogenesis inhibitors), drugs that target growth factor receptors on the surface of tumor cells (e.g., EGFR inhibitors) and drugs that target certain genes which have been found to have mutations which produce proteins that cause cancers to grow and spread (e.g., ALK inhibitors). In March 2015, Nivolumab (Opdivo®), a PD-1 blocker, was the first immunotherapy to be approved by the FDA for lung cancer. The approval was based on a study demonstrating that patients with advanced squamous cell non-small cell lung cancer lived an average of 3.2 months longer than those who received chemotherapy, with approximately 15% of patients treated with Opdivo experiencing tumor shrinkage or complete disappearance. Our development plans include the study of MRX34 as a single agent in both small cell and non-small cell lung cancers, as well as in combination with targeted therapies or immunotherapy agents.

Our Product Pipeline

We have identified multiple tumor suppressor microRNAs that, like miR-34, have demonstrated the ability to inhibit cancer cell proliferation and tumor growth in preclinical studies. Each tumor suppressor miRNA regulates a unique set of genes and oncogenic pathways that we believe will enable the development of multiple therapeutic candidates either as monotherapies or as combination therapies. We plan to initiate a Phase 1 trial for our second therapeutic candidate in 2016.

Manufacturing

We contract with third parties to manufacture our compounds for nonclinical and clinical testing purposes and intend to do so in the future. We also expect to rely upon third parties to produce materials required for the commercial production of our product candidates if we succeed in obtaining the necessary regulatory approvals. We do not currently own or operate facilities for product manufacturing, storage and distribution or testing. We have personnel with the technical, manufacturing, analytical, quality and project management experience to oversee contract manufacturing and testing activities and to compile manufacturing and quality information for our regulatory submissions.

Manufacturing is subject to extensive regulations that impose various procedural and documentation requirements, which govern recordkeeping, manufacturing processes and controls, personnel, quality control and quality assurance. Our systems and contractors are required to be in compliance with these regulations, and we assess such compliance regularly through performance monitoring as well as a formal audit program.

We continue to take steps to reduce our costs by working to improve yield in the manufacturing of the microRNA mimic, the drug substance, the liposomal formulation and the drug product, and we have and will continue to manage our vendor and supplier costs and evaluate alternative manufacturers and suppliers for MRX34 and our other pipeline candidates. As we move further through clinical development towards commercialization of MRX34 and our other pipeline microRNA mimics, we will need to work with our third party manufacturers to scale up the manufacturing processes for such products, and we expect we will be able to realize additional efficiencies resulting from increased scale of production, which we believe will result in lower costs and better operating margins.

Drug Substance

We currently use NITTO DENKO Avecia, or Avecia, to manufacture our MRX34 drug substance. We entered into a long term clinical supply agreement with Avecia in March 2012, and we believe that Avecia has the technical, analytical, quality and regulatory expertise to reliably produce our miR-34 mimic in sufficient quantity and of acceptable quality to support our development program through at least Phase 3 clinical studies, and to scale up such manufacturing process to support commercial production of MRX34. To ensure adequate supply and supply continuity, we are currently evaluating a backup supplier for our MRX34 drug substance, which will be completed in the second half of 2015. We are evaluating other U.S. and overseas companies for the manufacture of drug substance for our pipeline microRNA mimics.

The process for the manufacturing of our miR-34 mimic drug substance utilizes well-established solid phase synthesis chemistry. The raw materials used in the process are readily available from a number of qualified suppliers. We currently rely on our contract manufacturers to manage the supply chain for the raw materials used in the process.

Drug Product

Our drug product for both MRX34 and our other microRNA mimics consists of the drug substance formulated in the SMARTICLES liposomal delivery system. The drug product is provided as a concentrated, frozen aqueous solution that is defrosted, thawed and diluted for infusion in the clinic.

Polymun Scientific Immunbiologische Forschung GmbH, or Polymun, located in Vienna, Austria, is currently the exclusive manufacturer of drug product for our lead therapeutic candidate, MRX34. In November 2012, we entered into a manufacturing and supply agreement with Polymun for the formulation, manufacture and packaging of MRX34 final drug product. Manufacture of the drug product for our microRNA mimics in conjunction with the SMARTICLES delivery system requires a high level of technical expertise, and Polymun is one of a limited number of contract manufacturers with the knowhow to manufacture drug product for our drug candidate in sufficient quantity and of sufficient quality to meet our projected clinical and commercial needs. We believe that Polymun currently has the capability to provide a sufficient quantity of drug product through at least Phase 3 clinical studies of MRX34, and although Polymun does not currently have the capability to scale up their manufacturing process to support commercialization of MRX34, we believe that Polymun will have sufficiently expanded its operations before we reach potential commercialization of MRX34 such that it should be able to provide a sufficient quantity of drug product to support such commercialization of MRX34. In the meantime, we intend to continue to work with Polymun in relation to both our clinical supply and increasing production capacity for our projected commercial needs, but also to evaluate other potential manufacturers of drug product for our microRNA mimics. See "Business—Strategic Partnerships and Collaborations" for a detailed description of our manufacturing and supply agreement with Polymun, including material terms relating to circumstances permitting termination of this agreement.

The liposomal formulation manufactured by Polymun is a combination of readily available excipients, plus two specialty lipid excipients which are currently manufactured by two qualified suppliers.

The product is shipped and stored under frozen conditions. Based on current stability studies, we expect that the drug product will be stable over the time period anticipated for currently-planned clinical studies.

Research and Development

We are conducting clinical trials and other development activities to support the development of MRX34 and our other product candidates. In the years ended December 31, 2012, 2013 and 2014 and the three months ended March 31, 2015, we incurred $2.7 million, $4.4 million, $10.5 million and $3.4 million, respectively, of research and development expense.

Our research programs are directed towards the following:

- Determining if biomarkers can be used to select cancer patients who are more likely to respond to MRX34 therapy.
- Selecting and developing a second miRNA-based therapeutic candidate for which we intend to begin clinical development in 2016.
- Identifying drugs that can be combined with MRX34 to significantly improve the clinical response rates of cancer patients.
- Developing a next-generation systemic delivery technology that will improve the tolerability and efficacy profiles of miRNA mimics and expand the cancer indications that can be targeted for therapeutic intervention.

Intellectual Property

We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking and maintaining patents intended to cover our products and compositions, their methods of use and any other inventions that are important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend in part on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and knowhow related to our business, defend and enforce our patents, maintain our licenses, preserve our trade secrets and operate without infringing valid and enforceable patents and other proprietary rights of third parties. We also rely on continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of microRNA therapeutics. Our objective is to continue to expand our intellectual property portfolio to protect and bolster our position as a leader in the field of microRNA therapeutics.

Our Patent Portfolio

We own or in-license a portfolio of patents and patent applications that protects various aspects of our business. The patents and patent applications that make up our patent portfolio are primarily focused on various aspects of microRNA therapeutics, including various microRNA mimics, such as our lead product candidate MRX34, and therapeutic methods of use of microRNAs, including MRX34. As of July 1, 2015, we own or in-license at least 10 issued U.S. patents and over 80 pending U.S. and foreign applications. The expiration dates of the currently issued patents range from 2025 to 2032. We also have multiple pending patent applications that, if they issue, will expire between 2025 and 2035.

We are the sole owner of multiple U.S. and foreign patents and patent applications that relate to various aspects of microRNA therapies, including mir-34 therapies. Some of these patents and patent applications relate to chemically modified versions of miR-34 not currently used in MRX34 and other proprietary compounds that are possible candidates for future product development as microRNA therapeutics. For example, one of our owned patents (U.S. Patent No. 8,586,727) claims miR-34 mimics with certain nucleotide modifications. This patent is projected to expire in 2032.

We in-license a significant portion of our patent portfolio from our founding company, Asuragen, under a fully paid-up, royalty-free, fully sublicensable and irrevocable license granting us exclusive rights to these patents and patent applications in the field of therapeutics. Asuragen retains exclusive rights in these patents in fields outside therapeutics, including diagnostics. To date, the license from Asuragen has resulted in at least seven issued U.S. patents, and there are multiple applications pending within the United States and outside the United States, including Europe, Canada, Australia and Japan. These patents include U.S. Patent 7,960,359, which is related to the use of miR-34a for reducing the cell viability of lung cancer cells, cancerous T cells, prostate cancer cells, or skin cancer cells and is projected to expire in 2025. They also include U.S. Patent 8,563,708, which claims multiple chemistries and structures used in therapeutic microRNA mimics and is projected to expire in 2025. The patents and patent applications licensed from Asuragen are also included within the patents licensed under our agreement with Yale, and are therefore subject to the terms of the February 2014 amended and restated agreement as described below in "Strategic Partnerships and Collaborations—Yale University."

We are the exclusive licensee under a patent family owned by the University of Zurich relating to treatment of certain types of B-cell lymphoma with certain microRNA mimics, including miR-34. The patent family includes one granted US patent related to use of a miR-34 microRNA for the treatment of diffuse large B-cell lymphoma, one pending US patent application and one pending European patent application. This patent and any patents that issue from the pending patent applications are expected to expire in 2031. We are also the exclusive licensee of certain patents, including 2 U.S. patents, and patent applications owned by Yale relating to uses of let-7 microRNAs.

Patent Term

The term of individual patents and patent applications in our portfolio will depend upon the legal term of the patents in the countries in which they are obtained. In most countries, the patent term is 20 years from the date of filing of the patent application (or parent application, if applicable). For example, if an international Patent Cooperation Treaty, or PCT, application is filed, any patent issuing from the PCT application in a specific country expires 20 years from the filing date of the PCT application. In the United States, however, if a patent was in force on June 8, 1995, or issued on an application that was filed before June 8, 1995, that patent will generally have a term that is the greater of twenty years from the filing date or 17 years from the date of issue.

Under the Hatch-Waxman Act, the term of a patent that covers an FDA-approved drug or biological product may also be eligible for patent term extension, or PTE. PTE permits restoration of a portion of the patent term of a U.S. patent as compensation for the patent term lost during product development and the FDA regulatory review process if approval of the application for the product is the first permitted commercial marketing of a drug or biological product containing the active ingredient. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a new drug application, or NDA, plus the time between the submission date of an NDA and the approval of that application. The Hatch-Waxman Act permits the owner of a patent to apply for a PTE for only one patent applicable to an approved drug, and the maximum period of restoration is five years beyond the expiration of the patent. A PTE cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and a patent can only be extended once, and thus, even if a single patent is applicable to multiple products, it can only be extended based on one product. Similar provisions may be available in Europe and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug. When possible, depending upon the length of clinical trials and other factors involved in the filing of an NDA, we expect to apply for PTEs for patents covering our product candidates and their methods of use, or to work with our licensors, as owners of such patents, to obtain such extensions, if available.

Competition

The biotechnology and pharmaceutical industries are characterized by intense and rapidly changing competition to develop new technologies and proprietary products. While we believe that our intellectual property portfolio, scientific expertise and leading clinical position in the microRNA field provide us with competitive advantages, we face potential competition from many different sources, including larger and better-funded pharmaceutical and biotechnology companies. We may compete with other companies that are focused on microRNA therapeutics in disease or indications in which we develop our products, including both (i) replacement therapy approaches that involve the delivery of mimics, and (ii) inhibition approaches that involve the use of AntagomiRs, or anti-miRs. Any products that we may commercialize will have to compete with existing therapies and new therapies that may become available in the future.

We are aware of several companies that are working specifically to develop microRNA therapeutics. miRagen Therapeutics, Inc., or miRagen, a privately held company based in Boulder, Colorado, uses anti-miRs with an initial focus in cardiovascular, metabolic diseases, and hematological cancers. miRagen is in preclinical development, has entered into a partnership with Laboratoires Servier to focus on three different targets in the cardiovascular and metabolic space and has also expressed interest in pursuing microRNA mimic development, which they call "pro-miRs." Regulus Therapeutics, Inc., or Regulus, is a publicly traded company based in Carlsbad, California, which primarily focuses on anti-miRs technology, or the inhibition of overexpressed microRNAs. Regulus has focused on a number of indications, including hepatitis C, kidney fibrosis and cancer. They initiated their first clinical trial for RG-101, their lead anti-miR therapeutic program, against miR-122 for hepatitis C in March 2014, and initiated a Phase 1 clinical study evaluating RG-012 in healthy volunteers for the treatment of Alport syndrome in June 2015, while other programs are still in preclinical development. Regulus has numerous research and development collaborations with large pharmaceutical and biotechnology companies, including AstraZeneca plc, Biogen Idec, Inc., GlaxoSmithKline plc and Sanofi S.A. Santaris Pharma A/S, or Santaris, was a publicly traded company based in Denmark using RNA-targeted antagonist therapy for diseases including metabolic disorders, infectious and inflammatory diseases, cancer and rare genetic disorders. In August 2014, Roche announced the acquisition to Santaris Pharma. Santaris (now Roche) has drug candidates in Phase 1 and Phase 2 clinical trials, and their lead therapeutic product, an antagonist to miR-122, has reached late Phase 2 clinical testing for hepatitis C.

These competitors also compete with us in recruiting human capital and securing licenses to complementary technologies or specific microRNAs that may be critical to the success of our business. They also compete with us for potential funding from the pharmaceutical industry.

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs, such as those we are developing. These agencies and other federal, state and local entities regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of our product candidates.

In the United States, the FDA regulates drug products under the Federal Food, Drug and Cosmetic Act, or FFDCA, and the FDA's implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. If we fail to comply with applicable FDA or other requirements at any time during the drug development process, clinical testing, the approval process or after approval, we may become subject to administrative or judicial sanctions. These sanctions could include, among other things, the FDA's refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, warning letters, product recalls, clinical holds, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any FDA enforcement action could have a material adverse effect on us.

FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the United States. The process required by the FDA before a drug may be marketed in the United States generally involves:

- completion of extensive nonclinical laboratory tests, nonclinical animal studies and formulation studies many of which must be performed in accordance with the FDA's current Good Laboratory Practice, or cGLP, regulations;
- submission to the FDA of an IND application which must become effective before human clinical trials in the United States may begin;
- approval by an independent IRB at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug candidate for each proposed indication in accordance with the FDA's current Good Clinical Practice, or cGCP, regulations;
- 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, regulations;
- submission to the FDA of an NDA;
- satisfactory completion of a potential review by an FDA advisory committee, if applicable; and
- FDA review and approval of the NDA prior to any commercial marketing, sale or shipment of the drug.

The nonclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all. Nonclinical tests include laboratory evaluation of product chemistry, formulation, stability and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product. The results of nonclinical tests, together with manufacturing information, analytical data and a proposed clinical trial protocol and other information, are submitted as part of an IND to the FDA. Some nonclinical 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, raises concerns or questions relating to one or more proposed clinical trials and places the clinical trial on a clinical hold, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, a submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development.

Clinical trials involve the administration of the investigational drug to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be used. Each protocol must be submitted to the FDA as part of the IND. An IRB for each medical center proposing to conduct a clinical trial must also review and approve a plan for any clinical trial before it can begin at that center and the IRB must monitor the clinical trial until it is completed. The FDA, the IRB, or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk. Clinical testing also must satisfy cGCP requirements, including the requirement to obtain effective informed consent from study subjects.

All clinical research performed in the United States in support of an NDA must be authorized in advance by the FDA under the IND regulations and procedures described above. However, a sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA so long as the clinical trial is conducted in compliance with an international guideline for the ethical conduct of clinical research known as the Declaration of Helsinki and/or the laws and regulations of the country or countries in which the clinical trial is performed, whichever provides the greater protection to the participants in the clinical trial.

Clinical Trials

For purposes of NDA submission and approval, clinical trials are typically conducted in three or four sequential phases, which may overlap or be combined.

- *Phase 1:* Clinical trials are initially conducted in a limited population of subjects to test the drug candidate for safety, dose tolerance, absorption, metabolism, distribution and excretion in healthy humans or, on occasion, in patients with severe problems or life-threatening diseases to gain an early indication of its effectiveness.

- *Phase 2:* Clinical trials are generally conducted in a limited patient population to evaluate dosage tolerance and appropriate dosage, identify possible adverse effects and safety risks, and evaluate preliminarily the efficacy of the drug for specific indications in patients with the disease or condition under study.

- *Phase 3:* Clinical trials are typically conducted when Phase 2 clinical trials demonstrate that a dose range of the product candidate is effective and has an acceptable safety profile. Phase 3 clinical trials are commonly referred to as "pivotal" studies, which typically denotes a study that presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a drug. Phase 3 clinical trials are generally undertaken with large numbers of patients, such as groups of several hundred to several thousand, to further evaluate dosage, to provide substantial evidence of clinical efficacy and to further test for safety in an expanded and diverse patient population at multiple, geographically-dispersed clinical trial sites.

- *Phase 4:* In some cases, FDA may condition approval of an NDA for a product candidate on the sponsor's agreement to conduct additional clinical trials after NDA approval. In other cases, a sponsor may voluntarily conduct additional clinical trials post approval to gain more information about the drug. Such post approval trials are typically referred to as Phase 4 clinical trials.

The FDA, the IRB or the clinical trial sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the study. We may also voluntarily suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate.

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

New Drug Applications

The results of nonclinical studies and of the clinical trials, including negative or ambiguous results as well as positive findings, together with other detailed information, including extensive manufacturing information and information on the composition of the drug, are submitted to the FDA in the form of an NDA requesting approval to market the drug for one or more specified indications. The FDA reviews an NDA to determine, among other things, whether a drug is safe and effective for its intended use.

Once an NDA has been accepted for filing, by law the FDA has 180 days to review the application and respond to the applicant. However, the review process is often significantly extended by FDA requests for additional information or clarification. Under the Prescription Drug User Fee Act, the FDA has a goal of responding to NDAs within 10 months of the filing date for standard review, but this timeframe is also often extended. The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an application, the FDA will inspect the facility or the facilities at which the finished drug product, and sometimes the active drug ingredient, is manufactured, and will not approve the drug unless cGMP compliance is satisfactory. The FDA may also inspect the sites at which the clinical trials were conducted to assess their compliance, and will not approve the drug unless compliance with cGCP requirements is satisfactory.

After the FDA evaluates the NDA and conducts its inspections, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret data. The FDA could also approve the NDA with a Risk Evaluation and Mitigation Strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials. Such post-market testing may include Phase 4 clinical trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. Regulatory approval of oncology products often requires that patients in clinical trials be followed for long periods after approval to determine the overall survival benefit of the drug. The FDA has the authority to prevent or limit further marketing of a drug based on the results of these post-marketing programs.

Drugs may be marketed only for the FDA approved indications and in accordance with the provisions of the approved labeling. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require us to develop additional data or conduct additional nonclinical studies and clinical trials. Depending on the nature of the change proposed, an NDA supplement must be filed and approved before the change may be implemented. For many proposed post-approval changes to an NDA, the FDA has up to

180 days to review the application. As with new NDAs, the review process is often significantly extended by the FDA requests for additional information or clarification.

The testing and approval processes require substantial time, effort and financial resources, and each may take several years to complete. The FDA may not grant approval on a timely basis, or at all. Even if we believe a clinical trial has demonstrated safety and efficacy of one of our drug candidates for the treatment of a disease, the results may not be satisfactory to the FDA. Nonclinical and clinical data may be interpreted by the FDA in different ways, which could delay, limit or prevent regulatory approval. We may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals, which could delay or preclude us from marketing drugs. The FDA may limit the indications for use or place other conditions on any approvals that could restrict the commercial application of the drugs.

Other Regulatory Requirements

Any drugs manufactured or distributed by us or our collaborators pursuant to FDA approvals would be subject to continuing regulation by the FDA, including recordkeeping requirements and reporting of adverse experiences associated with the drug. Drug manufacturers and their subcontractors 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 ongoing regulatory requirements, including cGMPs, which impose certain procedural and documentation requirements upon us and our third party manufacturers. Failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, seizure of product, injunctive action or possible civil penalties. We cannot be certain that we or our present or future third-party manufacturers or suppliers will be able to comply with the cGMP regulations and other ongoing FDA regulatory requirements. If we or our present or future third-party manufacturers or suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, require us to recall a drug from distribution or withdraw approval of the NDA for that drug.

The FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. A company can make only those claims relating to safety and efficacy that are approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available drugs for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, impose stringent restrictions on manufacturers' communications regarding off-label use.

Expedited Review and Accelerated Approval Programs

A sponsor may seek approval of its product candidate under programs designed to accelerate FDA's review and approval of NDAs. For example, Fast Track Designation may be granted to a drug intended for treatment of a serious or life-threatening disease or condition that has potential to address unmet medical needs for the disease or condition. The key benefits of fast track designation are potential eligibility for priority review, rolling review (submission of portions of an application before the complete marketing application is submitted), and accelerated approval, if relevant criteria are met. Based on results of clinical studies submitted in an NDA, upon the request of an applicant, the FDA may grant the NDA a priority review designation, which sets the target date for FDA action on the application at six months after the FDA accepts the application for filing. Priority review is granted where there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of 10 months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Under the accelerated approval program, the FDA may approve an NDA on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Post-marketing studies or completion of ongoing studies after marketing approval are generally required to verify the drug's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit. In addition, the Food and Drug Administration Safety and Innovation Act, or FDASIA, which was enacted and signed into law in 2012, established the new Breakthrough Therapy designation. A sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. We may consider seeking Breakthrough Therapy designation of MRX34 in the future.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally defined as a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA. 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. After the FDA grants orphan drug designation, the generic identity of the drug 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. The first NDA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug for the same orphan indication, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or if FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. However, the FDA can still approve other drugs that have a different active ingredient for use in treating the same indication or disease. While we have not sought or obtained orphan drug designation for MRX34, we plan to seek such designation in the future for HCC, certain hematological malignancies or other potential future indications.

Other Healthcare Laws

Although we currently do not have any products on the market, if our drug candidates are approved and we begin commercialization, we may be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security, price reporting and physician sunshine laws and regulations.

The Anti-Kickback Statute makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchase, order, or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation. Violations of this law are punishable by up to five years in prison, and can also result in criminal fines, administrative civil money penalties and exclusion from participation in federal healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act. Many states have also adopted laws similar to the Anti-Kickback Statute. Some of these state prohibitions apply to the referral of patients for healthcare services reimbursed by any insurer, not just federal healthcare programs such as Medicare and Medicaid. Due to the breadth of these federal and state anti-kickback laws, the absence of guidance in the form of regulations or court decisions, and the potential for additional legal or regulatory change in this area, it is possible that our future sales and marketing practices and/or our future relationships with physicians might be challenged under these laws, which could harm us.

The federal False Claims Act prohibits anyone from knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services, including drugs, that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. Although we would not submit claims directly to payors, manufacturers can be held liable under these laws if they are deemed to "cause" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. For example, pharmaceutical companies have been prosecuted under the federal False Claims Act in connection with their off-label promotion of drugs. Penalties for False Claims Act violations include three times the actual damages sustained by the government, plus mandatory civil penalties of between $5,500 and $11,000 for each separate false claim, the potential for exclusion from participation in federal healthcare programs, and, although the federal False Claims Act is a civil statute, False Claims Act violations may also implicate various federal criminal statutes. If the government were to allege that we were, or convict us of, violating these false claims laws, we could be subject to a substantial fine and may suffer a decline in our stock price. In addition, private individuals have the ability to bring actions under the federal False Claims Act and certain states have enacted laws modeled after the federal False Claims Act.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, also created new federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act, imposed new reporting requirements on drug manufacturers for payments made by them, and, in some case, their distributors, to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties of up to an aggregate of $150,000 per year (and up to an aggregate of $1 million per year for "knowing failures"), for all payments, transfers of value or ownership or investment interests not reported in an annual submission. Manufacturers must submit reports by the 90^{th} day of each calendar year.

There are also an increasing number of state laws that require manufacturers to implement compliance programs, impose restrictions on drug manufacturer marketing practices and require the tracking and reporting of gifts, compensation and other remuneration to physicians and other health care providers. These laws may affect our sales, marketing and other promotional activities by imposing administrative and compliance burdens on us. In addition, given the lack of clarity with respect to these laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state and federal authorities.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and their respective implementing regulations, including the final omnibus rule published on January 25, 2013, imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts.

Because we intend to commercialize products that could be reimbursed under a federal healthcare program and other governmental healthcare programs, we will have to develop a comprehensive compliance program that establishes internal controls to facilitate adherence to the rules and program requirements to which we will or may become subject. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

Coverage and Reimbursement

Sales of our products, if approved, will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health care programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly reducing reimbursements for certain medical products and services. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost containment programs, including price controls and restrictions on reimbursement. and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our products once approved or a decision by a third-party payor to not cover our products could reduce or eliminate utilization of our products and have a material adverse effect on our sales, results of operations and financial condition. In addition, state and federal healthcare reform measures have been and will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products once approved or additional pricing pressures.

Health Care Reform

In March 2010, the Affordable Care Act, was enacted, which includes measures that have or will significantly change the way health care is financed by both governmental and private insurers. Among the provisions of Affordable Care Act of greatest importance to the pharmaceutical industry are the following:

- An increase in the minimum rebates payable by manufacturers under the Medicaid Drug Rebate Program on most branded prescription drugs and biologic agents from 15.1% of average manufacturer price, or AMP, to 23.1% of AMP.

- A new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products.

- An extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations.

- An expansion of the population potentially eligible for Medicaid drug benefits, to be phased-in by 2014.

- An expansion of the types of entities eligible for discounts under the 340B drug pricing program, excluding orphan drugs when used for the orphan indication, with the exception of children's hospitals.

- A requirement on manufacturers of branded drugs and biologic agents to provide a 50% discount off the negotiated price of branded drugs dispensed to Medicare Part D patients in the coverage gap (i.e., "donut hole").

- An annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications.

- Creation of a new Patient-Centered Outcomes Research to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research. The research conducted by the Patient-Centered Outcomes Research Institute may affect the market for certain pharmaceutical products.

- Creation of the Independent Payment Advisory Board which, beginning in 2014, has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. Under certain circumstances, these recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings.

- Establishment of a Center for Medicare and Medicaid Innovation within the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Many of the details regarding the implementation of Affordable Care Act are yet to be determined, and, at this time, it remains unclear the full effect that Affordable Care Act would have on our business.

Other legislative changes have also been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments, will remain in effect through 2024 unless additional Congressional action is taken. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, or the ATRA, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other health care funding, which could have a material adverse effect on our future customers and accordingly, our financial operations.

International Regulation

In addition to regulations in the United States, we, or our collaborators, will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our future drugs. Whether or not we obtain FDA approval for a drug, we or our collaborators must obtain approval of the drug by the comparable regulatory authorities of foreign countries before commencing clinical trials or marketing of the drug in those countries. The approval process varies from country to country and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

Under European Union regulatory systems, marketing authorizations may be submitted either under a centralized, decentralized or mutual recognition procedure. The centralized procedure provides for the grant of a single marking authorization that is valid for all European Union member states. The decentralized procedure includes selecting one "reference member state," or RMS, and submitting to more than one member state at the same time. The RMS National Competing Authority conducts a detailed review and prepares an assessment report, to which concerned member states provide comment. The mutual recognition procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marking authorization may submit an application to the remaining member states post-initial approval. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval.

In addition to regulations in Europe and the United States, we, or our collaborators, will be subject to a variety of foreign regulations governing clinical trials and commercial distribution of our future drugs.

Environmental Regulation

We are subject to numerous foreign, federal, state and local environmental, health and safety laws and regulations relating to, among other matters, safe working conditions, product stewardship and end-of-life handling or disposition of products, and environmental protection, including those governing the generation, storage, handling, use, transportation and disposal of hazardous or potentially hazardous materials. Some of these laws and regulations require us to obtain licenses or permits to conduct our operations. Environmental laws and regulations are complex, change frequently and have tended to become more stringent over time. Although the costs to comply with applicable laws and regulations, including requirements in the European Union relating to the restriction of use of hazardous substances in products, have not been material, we cannot predict the impact on our business of new or amended laws or regulations or any changes in the way existing and future laws and regulations are interpreted or enforced, nor can we ensure we will be able to obtain or maintain any required licenses or permits.

Employees

As of March 31, 2015, we had 21 full-time employees, of whom two have medical degrees and three have Ph.D. degrees. Of these full-time employees, 16 employees are engaged in research and development activities and five employees are engaged in business development, finance, human resources and general management. We have no collective bargaining agreements with our employees and we have not experienced any work stoppages. We consider our relations with our employees to be good.

Facilities and Services Agreement with Asuragen

Our corporate headquarters is located in Austin, Texas. In October 2014, we entered into a sublease agreement with Asuragen and amended an existing service agreement under which we share space with Asuragen and Asuragen provides certain services to us. These services include facilities-related services, warehouse services, shipping and receiving and other services. The facility we occupy as a part of this agreement encompasses approximately 10,280 square feet of office and laboratory space, the laboratory space of which we share with Asuragen. The term for the agreement expires in August 2016, but may be terminated earlier by either party with six months' notice. We believe that our facility is currently sufficient to meet our needs and that suitable additional or alternative space would be available to us when needed.

Strategic Partnerships and Collaborations

Asuragen, Inc.

In 2009, we in-licensed or acquired certain patents and applications relating to certain aspects of microRNA compounds, targets for microRNAs and methods of use of such compounds from our founding company, Asuragen, and entered into a cross license with Asuragen, under which Asuragen granted us an exclusive, fully sublicensable, fully paid-up, royalty-free, perpetual and irrevocable license in the field of therapeutics, under patents and applications retained by it relating to microRNAs and their uses. Asuragen retains all rights in the fields outside therapeutics under the patents and applications that it retained and licensed to us, and we have granted to Asuragen an exclusive (even as to us), fully sublicensable, royalty-free, perpetual and irrevocable license in the field of diagnostics under the patents and applications relating to microRNA that we solely own as a result of the acquisition, while we retain all rights in therapeutics and all other fields outside diagnostics. Under our cross license agreement with Asuragen, as amended in 2012, we have the right to control the prosecution and maintenance of our owned patent families as well as certain patent families owned by Asuragen. Each party retains the right to enforce the patents that it owns against third parties, with the exception of certain foundational patents that are owned by Asuragen. Additionally, certain of these Asuragen patents are included within the patents licensed under our agreement with Yale, and are therefore subject to the terms of the February 2014 amended and restated agreement as described below in "*Strategic Partnerships and Collaborations—Yale University*."

Marina Biotech, Inc.

In December 2011, we entered into a license agreement with Marina Biotech, Inc., or Marina, pursuant to which Marina granted us an exclusive license under its proprietary liposomal delivery technology, NOV340, known under the brand name "SMARTICLES," to develop and commercialize drug products incorporating SMARTICLES in combination with our lead therapeutic product, MRX34, for the prevention and treatment of cancer and any other disease in humans and animals, with the exception of DNA interference human therapeutic use. Our license agreement with Marina has been amended twice. In December 2013, the license agreement was amended to modify certain payment obligations with respect to MRX34, and to include within the scope of our exclusive license three additional specific microRNAs selected by us, and in May 2015 we amended the license agreement to reduce the amount of a specific milestone payment and to provide for the prepayment of such milestone payment. We are required to use commercially reasonable efforts to commercialize licensed products in specified major markets, and in other markets where we consider it is commercially reasonable to do so. We are responsible, at our cost, for all development of manufacturing processes and scale-up for the licensed technology in connection with our licensed products.

We have paid Marina approximately $2.1 million in the aggregate to date in up-front and milestone payments (including the milestone prepayment under the May 2015 amendment) and as consideration for the inclusion within the license of the three additional compounds. As we progress development and commercialization of products covered by the license, we will be required to make payments to Marina based upon the achievement of certain development and regulatory milestones, totaling up to $6 million in the aggregate for each licensed product. We are also required to pay up to an additional $4 million per licensed product upon the achievement of certain regulatory milestones for a specified number of additional indications, leading to a maximum cap on all milestone payments of $10 million per product. The exception to this is for our lead therapeutic product, MRX34, where the aggregate of all remaining development and regulatory milestone payments due to Marina, including for all additional indications, is $3.7 million. In addition to milestone payments, we will be required to pay low single digit royalties on net sales of licensed products other than MRX34, subject to customary reductions and offsets. As a result of our 2013 amendment to our agreement with Marina, we are no longer required to pay a royalty to Marina with respect to sales of our lead therapeutic product, MRX34. For licensed products other than MRX34, our obligation to pay royalties to Marina will expire on a country-by-country and licensed product-by-licensed product basis upon the later of the expiration of all patents covering such licensed product in such country, or 10 years from the first commercial sale of such product in such country. If we sublicense the rights granted to us under the Marina license, we are required to pay a portion of any revenue we receive from such sublicensees at a tiered percentage between the very low single digits and the mid-teens, depending on the circumstances in which the sublicense is entered into.

We may terminate our agreement with Marina for any reason by giving 60 days' notice to Marina. Either party may terminate the agreement upon the insolvency of the other party or upon 90 days' notice to the other party for the uncured material breach of the agreement, with the exception of non-payment which permits Marina to terminate the agreement upon 30 days' notice to us. Absent earlier termination, our agreement with Marina will remain in force on a licensed product-by-licensed product and country-by-country basis until the earlier of the expiration of our obligation to pay royalties with respect to such licensed product in such country, or the end of the calendar quarter in which sales of a generic version of such licensed product exceed a specified proportion of the aggregate sales of such licensed product in such country.

Yale University

In 2006, Asuragen entered into an exclusive license agreement with Yale that granted to Asuragen an exclusive, worldwide, fully sublicenseable license for all human therapeutic and diagnostic uses under certain patent rights relating to microRNAs arising from the laboratory of Dr. Frank Slack at Yale. This agreement was assigned to us by Asuragen in connection with our acquisition of certain assets, including patent rights, in 2009. In addition, some of the patent filings in our intellectual property portfolio that are licensed to us by Asuragen are also included in the patents licensed under the Yale agreement as a result of previous discussions between the parties about possible co-ownership with Yale of these patents. The patents that are subject to both the Yale and Asuragen licenses cover certain aspects relating to the composition and method of use of specified microRNA mimics, including MRX34 and let-7, while those patent families that are solely subject to our license from Yale cover certain uses of let-7. In February 2014, we amended and restated our agreement with Yale to modify, among other things, the procedure for determining the inventorship of such patents and applications. Following this amendment, an independent third party expert was engaged to determine the inventorship, and hence the ownership, of the patents and applications potentially subject to Yale and Asuragen co-ownership. This determination confirmed each party's sole ownership of each patent where co-ownership had been under consideration, and resulted in a correction to one pending application to remove Dr. Slack as a co-inventor. Notwithstanding the expert's determination of inventorship, in accordance with the terms of our license agreement with Yale, these patents and applications will remain licensed patents under the agreement, and subject to all the terms of our license agreement with Yale. Upon commercialization of any products covered by the licensed patents, our financial obligations to Yale, if any, will depend on the particular product and Yale's ownership rights in any patents covering such product.

We are required to use reasonable commercial efforts with respect to development and commercialization of products covered by our license agreement with Yale and to fulfill certain specified development and regulatory diligence criteria, or achieve specified development milestones by specified dates, in some cases subject to an extension upon payment of certain fees, for products covered by the agreement.

We will be required to pay royalties to Yale on net sales of licensed products that contain specified microRNAs, including MRX34 and products containing let-7, at a percentage ranging from the very low to the low single digits, subject to customary reductions and offsets. Our obligation to pay royalties to Yale will expire on a licensed product-by-licensed product and country-by-country basis upon the earlier of the expiration of the last valid claim of a licensed patent covering such licensed product or the launch of a generic version of such product in such country that has been approved by the applicable regulatory authority in such country. We will also be required to pay to Yale a portion of specified gross revenue that we receive from our sublicensees at percentages ranging from the mid-single digits up to the very low twenties, depending on the particular product and Yale's ownership rights, if any, in the patents covering such product.

We will also be required to make payments for achievement of certain development and regulatory milestones by products containing one specified microRNA and covered by the licensed patents of up to $600,000 in the aggregate for each such product, subject to reduction in certain circumstances. In addition, we are required to pay an annual license maintenance fee and minimum annual royalties under certain circumstances.

We have the right to terminate our agreement with Yale for any reason upon three months' written notice to Yale, and either party may terminate the agreement on 60 days' notice for the uncured material breach of the other party. Yale may terminate our agreement, on a licensed product miRNA category-by-licensed product miRNA category basis, if we fail to meet specified diligence obligations within specified time periods, subject to our right to extend such periods with respect to one such product by making specified extension payments and to renegotiate such time periods under certain circumstances with respect to the other two products. Yale may also terminate our agreement in its entirety immediately upon notice to us if we fail to maintain adequate insurance or become insolvent. In the event that our license agreement with Yale is terminated, we would lose our rights under any licensed patents that are solely owned by Yale. Absent earlier termination, our agreement with Yale will remain in force on a country-by-country basis until the expiration of the last valid claim of the licensed patents, whether owned by us or by Yale.

University of Zurich

In March 2013, we entered into an exclusive, worldwide, royalty-bearing license, with the right to grant sublicenses, with the University of Zurich under certain patent rights relating to the treatment of certain types of B-cell lymphoma with microRNA mimics, in the fields of therapeutics and diagnostics. We are required to pay an annual license maintenance fee, and upon commercialization of any products covered by the licensed patent rights, we will be required to pay the University of Zurich a royalty on net sales of products covered by the licensed patents by us, our affiliates or sublicensees in the very low single digits, and a portion of other fees received from any sublicensees at a percentage in the mid-teens. We are required to use commercially reasonable efforts to develop, manufacture, sell and market licensed products. If we fail to comply with our diligence obligations, then under certain circumstances, the University of Zurich may terminate our agreement immediately upon notice to us.

We have the right to terminate our agreement with the University of Zurich for any reason upon six months' prior notice. The University of Zurich may terminate our agreement immediately upon notice to us in certain circumstances if we fail to meet our diligence obligations. The University of Zurich may also terminate the agreement upon 60 days' written notice to us in the event of our uncured material breach of the agreement, or immediately upon notice to us in the event of our insolvency or if we challenge or assist any third party to challenge the validity of the licensed patents.

CPRIT

In August 2010, we entered into a grant contract with the Cancer Prevention and Research Institute of Texas, or CPRIT, under which we received a $10.3 million commercialization award from the State of Texas through CPRIT. CPRIT was established to expedite innovation and commercialization in the area of cancer research and to enhance access to evidence-based prevention programs and services throughout the State of Texas. The award was a three-year award that was funded annually, and the contract terminated on January 31, 2014, subject to our obligations to make certain payments that survive termination. Under the terms of the award, we will be required to pay to CPRIT a portion of our revenues from sales of certain products by us, including sales of MRX34, or received from our licensees or sublicensees, at a percentage in the low single digits until the aggregate amount of such payments equals a specified multiple of the grant amount, and thereafter at a rate of less than one percent, subject to our right, under certain circumstances, to make a one-time payment in a specified amount to CPRIT to buy out such payment obligations. We will also be required to repay CPRIT the total amount of the grant proceeds under certain circumstances of relocation of our principal place of business outside Texas during a specified period following the final payment of grant funding to us.

Polymun Scientific Immunbiologische Forschung GmbH

In November 2012, we entered into a supply agreement with Polymun for the formulation, manufacture and supply of a liposomal formulation of finished drug product for our lead product candidate, MRX34, utilizing the NOV340 SMARTICLES technology licensed to us by Marina in conjunction with Polymun's proprietary technology relating to the production of liposomal formulations, for use by us in our clinical trials for MRX34. The agreement contains terms and conditions generally consistent with an agreement for manufacture and supply of a pharmaceutical product for clinical purposes, including with respect to supply of product in accordance with specifications and quality assurance and quality control activities. We have also entered into a separate quality agreement with Polymun governing all supply of product under the agreement. Under our agreement with Polymun, we retain all intellectual property rights arising as a result of the activities under the agreement, subject to certain limited exceptions relating to Polymun's proprietary technology. The agreement remains in force until completion of the activities set forth under any statements of work executed under the agreement, unless earlier terminated by either party. Either we or Polymun may terminate the agreement on 30 days' written notice in the event of the other party's uncured material breach or insolvency.

Legal Proceedings

From time to time, we are subject to various legal proceedings, claims and administrative proceedings that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, as of the date of this prospectus, we do not believe we are party to any claim, proceeding or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Management

Executive Officers and Directors

The following table sets forth information regarding our executive officers and directors, as of June 30, 2015:

Name	Age	Position(s)
Executive Officers		
Paul Lammers, M.D., M.Sc.	57	Director, President and Chief Executive Officer
Jon Irvin	57	Chief Financial Officer
Sinil Kim, M.D.	59	Chief Medical Officer and Vice President of Oncology
Casi DeYoung	44	Chief Business Officer
Non-Employee Directors		
Michael Powell, Ph.D.(2)	60	Chairman of the Board
Elaine V. Jones, Ph.D.(1)	60	Director
Edward Mathers(2)	55	Director
Matthew Winkler, Ph.D.(1)	63	Director
Lawrence M. Alleva(1)	65	Director
Clay B. Siegall, Ph.D.(2)	54	Director

(1) Member of the audit committee.

(2) Member of the compensation committee.

Executive Officers

Paul Lammers, M.D., M.Sc. Dr. Paul Lammers has served as a member of our board of directors and as our President and Chief Executive Officer since November 2009. Previously, Dr. Lammers was the President of Repros Therapeutics Inc., or Repros Therapeutics, a biopharmaceutical company, from February 2009 until October 2009. From August 2002 until September 2008, Dr. Lammers served as the Chief Medical Officer for EMD Serono, Inc., a biopharmaceutical division of Merck KGaA, a global pharmaceutical and chemical group. Previously, Dr. Lammers served as the Senior Vice President of clinical and regulatory affairs at Zonagen, Inc., which later became Repros Therapeutics. Dr. Lammers began his career with Organon International, a pharmaceutical company, spending eight years in the commercial and clinical operations in Europe and the United States. Dr. Lammers received a M.Sc. and M.D. from the Catholic University (Radboud University) in Nijmegen, The Netherlands. Dr. Lammers has been chosen to serve on our board of directors due to his management experience in multiple pharmaceutical and biopharmaceutical companies and drug development.

Jon Irvin. Mr. Jon Irvin has served as our Chief Financial Officer since November 2012, first as a Chief Financial Officer Consultant with Bridgepoint Consulting, LLC, or Bridgepoint, a consulting firm providing financial consulting assistance to various organizations, and then as our employee beginning in April 2013. Mr. Irvin was a Chief Financial Officer Consultant with Bridgepoint from March 2012 to June 2013. From December 2010 to March 2012, Mr. Irvin was an independent consultant in Austin, Texas. From September 2005 to December 2010, Mr. Irvin served as the Chief Executive Officer and Vice President of Finance for Voxpath Networks, Inc., a telecommunications and intellectual property company. Previously, Mr. Irvin held various finance positions at Reddwerks Corporation, a software company, Esoterix, Inc., a medical labs company, Topaz Technologies, a pharmaceutical software company, and BioNumerik Pharmaceuticals, Inc., a pharmaceutical company. Mr. Irvin was previously an accountant with Price Waterhouse and Ernst & Young. Mr. Irvin received a B.S. in Accounting from the University of Illinois.

Sinil Kim, M.D. Dr. Sinil Kim has served as our Chief Medical Officer and Vice President of Oncology since May 2013. Previously, Dr. Kim served as a Senior Director and Global Clinical Leader at Pfizer, Inc., a global pharmaceutical company, from May 2005 until May 2013. Dr. Kim served as a Director of Clinical Oncology with Bristol-Myers Squibb, a global pharmaceutical company, from September 2002 to May 2005. Dr. Kim co-founded DepoTech Corp, a pharmaceutical company, in 1989. Dr. Kim received a B.S. in Chemistry and M.D. from the University of Washington and completed his post-doctoral fellowship in hematology and oncology at the University of California, San Diego.

Casi DeYoung. Ms. Casi DeYoung has served as our Chief Business Officer since March 2014. From May 2008 to December 2013, Ms. DeYoung served as the Vice President of Business Development for Reata Pharmaceuticals, Inc., a biopharmaceutical company. Previously, Ms. DeYoung served as the Vice President of Business Development for ODC Therapy, Inc., an immunotherapy company. From 2000 to 2005, Ms. DeYoung served in various roles, including the Director of Global Oncology Operations, for EMD Pharmaceuticals, Inc., the U.S. affiliate of Merk KGaA, a global healthcare company. Ms. DeYoung received a B.S. in Chemistry from Southwestern University and an M.B.A. from the University of Texas at Austin.

Board Composition

Michael Powell, Ph.D. Dr. Michael Powell has served as Chairman of our board of directors since October 2012. Since 1997, Dr. Powell has been a General Partner of Sofinnova Ventures, a venture capital firm. Previously, Dr. Powell has held positions at Genentech, Inc., a biotechnology company, Cytel Inc., a research and development company, and Syntex Research Group, a pharmaceutical company. Dr. Powell is currently a director of Labrys Biologics, Inc., a biotechnology company, Alvine Pharmaceuticals, Inc., a biopharmaceutical company, Ascenta Therapeutics, Inc., a biopharmaceutical company, Catalyst Biosciences, Inc., a biopharmaceutical company, and Ocera Therapeutics, Inc., a publicly traded biopharmaceutical company. Dr. Powell is an Adjunct Professor at the University of Kansas. Dr. Powell is the Board President of the AIDS Vaccine Advocacy Coalition and serves on the advisory board of the Institute for the Advancement of Medical Innovation at the University of Kansas. Dr. Powell received a B.S. in Chemistry from Scarborough College, a Ph.D. in Physical Chemistry from the University of Toronto and completed his post-doctorate work in Bioorganic Chemistry at the University of California. Dr. Powell has been chosen to serve on our board of directors due to his experience with the life sciences and pharmaceutical industries and the venture capital industry.

Elaine V. Jones, Ph.D. Dr. Elaine V. Jones has served as a member of our board of directors since October 2012. Since December 2008, Dr. Jones has served as Executive Director, Venture Capital of Pfizer Venture Investments, the venture capital arm of Pfizer, Inc., a global pharmaceutical company. Dr. Jones is currently a director of Aquinox Pharmaceuticals, Inc., a publicly-traded pharmaceutical company, where she also serves as the chair of the audit committee. Dr. Jones is also currently a director of Flexion Therapeutics, Inc., a pharmaceutical company, Autifony Therapeutics Ltd., a biotechnology company, and Mission Therapeutics Ltd., a biopharmaceutical company. From 2003 to November 2008, Dr. Jones served as a general partner of Euclid SR Partners, a venture capital firm. From 1999 to 2003, Dr. Jones held various positions at S.R. One, the venture fund of GlaxoSmithKline plc, a global pharmaceutical company. Dr. Jones received a B.S. in Biology from Juniata College and a Ph.D. in Microbiology from the University of Pittsburgh. Dr. Jones has been chosen to serve on our board of directors due to her experience with the life sciences and pharmaceutical industries, pharmaceutical science and the venture capital industry.

Edward Mathers. Mr. Ed Mathers has served as a member of our board of directors since October 2012. Since August 2008, Mr. Mathers has been a Partner at New Enterprise Associates, Inc., or NEA, a private venture capital firm focusing on technology and healthcare investments. Mr. Mathers serves on the board of directors of Envisia Therapeutics, Inc., a biopharmaceutical company, Liquidia Technologies, a biotechnology company, Ra Pharmaceuticals, Inc., a pharmaceutical company, Rhythm Pharmaceuticals, a pharmaceutical company, and Lumos Pharma, a biotechnology company. From 2002 to 2008, Mr. Mathers served as Executive Vice President, Corporate Development and Venture at MedImmune, Inc., or MedImmune, and led its venture capital subsidiary, MedImmune Ventures, Inc. Before joining MedImmune in 2002, he was Vice President, Marketing and Corporate Licensing and Acquisitions at Inhale Therapeutic Systems. Previously, Mr. Mathers spent 15 years at Glaxo Wellcome, Inc. where he held various sales and marketing positions. Mr. Mathers received a B.S. in Chemistry from North Carolina State University. Mr. Mathers has been chosen to serve on our board of directors due to his experience with the healthcare and pharmaceutical industries and his broad management experience.

Matthew Winkler, Ph.D. Dr. Matthew Winkler has served as a member of our board of directors since December 2007. Since January 2013, Dr. Winkler has been the Chairman of the board of directors and the Chief Scientific Officer of Asuragen, Inc., or Asuragen, a molecular diagnostic and pharmacogenomics service company, where he also served as the Chief Executive Officer from March 2006 to December 2012. Prior to Asuragen, Dr. Winkler was the founder and Chief Executive Officer of Ambion, Inc., a privately held company that developed and sold research reagents for RNA analysis. Since June 2010, Dr. Winkler has served on the board of Second Genome, a biotherapeutics company. Dr. Winkler received a B.S. in Genetics and a Ph.D. in Zoology from the University of California at Berkeley. Dr. Winkler has been chosen to serve on our board of directors due to his management experience in the life sciences and pharmaceutical industries.

Lawrence M. Alleva. Mr. Lawrence M. Alleva joined our board in July 2014. Prior to his retirement in June 2010, Mr. Alleva worked with PricewaterhouseCoopers LLP, or PwC, for 39 years, 28 of which as a partner with the firm. Mr. Alleva served clients primarily in the technology sector, including numerous pharmaceutical and biotechnology companies. Additionally, he served PwC in a variety of office, regional and national practice leadership roles, most recently as the U.S. Ethics and Compliance Leader (Assurance) for PwC from 2006 until his retirement. Mr. Alleva is a Certified Public Accountant (inactive). Mr. Alleva received a Bachelor of Science degree from Ithaca College (magna cum laude) and attended Columbia University's Executive MBA program. Mr. Alleva also serves as a director for public companies Tesaro Inc. and Bright Horizons Family Solutions, and previously served on the board of GlobalLogic Inc. Mr. Alleva has been chosen to serve on our board of directors due to his financial and accounting experience as a director and a public accounting partner serving multiple healthcare, pharmaceutical and biopharmaceutical companies.

Clay B. Siegall, Ph.D. Dr. Clay B. Siegall has served a member of our board of directors since January 2013. Dr. Siegall founded Seattle Genetics, Inc., or Seattle Genetics, a biotechnology company, in 1997, where he has served as the Chief Executive Officer since November 2002, as the President since June 2000 and as the Chairman of the board of directors since March 2004. Dr. Siegall also served as the Chief Scientific Officer of Seattle Genetics from December 1997 until November 2002. Dr. Siegall currently serves on the board of directors of Alder BioPharmaceuticals, Inc., a biopharmaceutical company, and Ultragenyx Pharmaceutical, a pharmaceutical company. Prior to co-founding Seattle Genetics, Dr. Siegall was with the Bristol-Myers Squibb Pharmaceutical Research Institute from 1991 to 1997, most recently as a Principal Scientist. From 1988 to 1991, Dr. Siegall was a Staff Fellow/Biotechnology Fellow at the National Cancer Institute, National Institutes of Health. Dr. Siegall received a B.S. in Zoology from the University of Maryland and a Ph.D. in Genetics from George Washington University. Dr. Siegall has been chosen to serve on our board of directors due to his experience as a director and executive of multiple healthcare and biopharmaceutical companies.

Director Independence

Our board of directors currently consists of seven members. Our board of directors has determined that of our directors, other than Dr. Paul Lammers, qualify as "independent" directors in accordance with the NASDAQ listing requirements. Dr. Lammers is not considered independent because he is an employee of Mirna. The NASDAQ independence definition includes a series of objective tests, such as that the director is not, and has not been for at least three years, one of our employees and that neither the director nor any of his family members has engaged in various types of business dealings with us. In addition, as required by NASDAQ rules, our board of directors has made a subjective determination as to each independent director that no relationships exist, which, in the opinion of our board of directors, would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In making these determinations, our board of directors reviewed and discussed information provided by the directors and us with regard to each director's business and personal activities and relationships as they may relate to us and our management. There are no family relationships among any of our directors or executive officers.

Classified Board of Directors

In accordance with our amended and restated certificate of incorporation to be in effect immediately prior to the consummation of this offering, our board of directors will be divided into three classes with staggered, three-year terms. At each annual meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. Effective upon the consummation of this offering, our directors will be divided among the three classes as follows:

- the Class I directors will be , and , and their terms will expire at the annual meeting of stockholders to be held in 2016;
- the Class II directors will be , and , and their terms will expire at the annual meeting of stockholders to be held in 2017; and
- the Class III directors will be , and , and their terms will expire at the annual meeting of stockholders to be held in 2018.

Our amended and restated certificate of incorporation will provide that the authorized number of directors may be changed only by resolution of the board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. The division of our board of directors into three classes with staggered three- year terms may delay or prevent a change of our management or a change in control of our company.

Voting Arrangements

Pursuant to an amended and restated voting agreement, as amended, that we entered into with certain holders of our common stock and certain holders of our convertible preferred stock:

- Sofinnova Venture Partners VIII, L.P. (or any of its affiliates), collectively, Sofinnova, has the right to designate a director for election to our board of directors and has designated Dr. Powell as such director;
- New Enterprise Associates 14, L.P. and NEA Ventures 2012, Limited Partnerships (or any of its affiliates), collectively, NEA, has the right to designate a director for election to our board of directors and has designated Mr. Mathers as such director;
- Pfizer Inc. (or any of its affiliates), collectively, Pfizer, has the right to designate a director for election to our board of directors and has designated Dr. Jones as such director;

- the holders of a majority of the outstanding shares of our Series B convertible preferred stock and Series A convertible preferred stock, voting as a single class on an as-converted basis, have the right to designate a director for election to our board of directors and have designated Dr. Winkler as such director;
- our then-incumbent Chief Executive Officer has the right to be nominated to serve on our board of directors; and
- three directors, who shall not be affiliated with us or a holder of 3,000,000 shares of our convertible preferred stock, will be elected by the holders of a majority of the outstanding shares of our common and convertible preferred stock, voting together as a single class on an as-converted basis, and approved by the directors designated by Sofinnova, NEA and Pfizer, who have approved Mr. Alleva and Dr. Siegall as such directors.

The holders of our common stock and convertible preferred stock who are parties to the amended and restated voting agreement, as amended, are obligated to vote for such designees. The provisions of this voting agreement will terminate upon the consummation of this offering and there will be no further contractual obligations regarding the election of our directors. Our directors hold office until their successors have been elected and qualified or appointed, or the earlier of their death, resignation or removal.

Leadership Structure of the Board

Our board of directors has separated the positions of Chairman of the board and Chief Executive Officer. Separating these positions allows our Chief Executive Officer to focus on our day-to-day business, while allowing the Chairman of the board to lead the board in its fundamental role of providing advice to and independent oversight of management. The board recognizes the time, effort and energy that the Chief Executive Officer is required to devote to his position in the current business environment, as well as the commitment required to serve as Chairman of the board, particularly as the board's oversight responsibilities continue to grow. While our bylaws and corporate governance guidelines do not require that our Chairman and Chief Executive Officer positions be separate, the board believes that having separate positions and having an independent outside director serve as Chairman is the appropriate leadership structure for the Company and demonstrates our commitment to good corporate governance. However, our board of directors will continue to periodically review our leadership structure and may make such changes in the future as it deems appropriate.

Role of Board in Risk Oversight Process

Risk assessment and oversight are an integral part of our governance and management processes. Our board of directors encourages management to promote a culture that incorporates risk management into our corporate strategy and day-to-day business operations. Management discusses strategic and operational risks at regular management meetings, and conducts specific strategic planning and review sessions during the year that include a focused discussion and analysis of the risks facing us. Throughout the year, senior management reviews these risks with the board of directors at regular board meetings as part of management presentations that focus on particular business functions, operations or strategies, and presents the steps taken by management to mitigate or eliminate such risks.

Our board of directors does not have a standing risk management committee, but rather administers this oversight function directly through our board of directors as a whole, as well as through various standing committees of our board of directors that address risks inherent in their respective areas of oversight. In particular, our board of directors is responsible for monitoring and assessing strategic risk exposure, our audit committee is responsible for overseeing our major financial risk exposures and the steps our management has taken to monitor and control these exposures. The audit committee also monitors compliance with legal and regulatory requirements. Our nominating and governance committee monitors the effectiveness of our corporate governance guidelines and considers and approves or disapproves any related-persons transactions. Our compensation committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking.

Board Committees

Audit Committee

Our audit committee oversees our corporate accounting and financial reporting process. Among other matters, the audit committee:

- appoints our independent registered public accounting firm;
- evaluates the independent registered public accounting firm's qualifications, independence and performance;
- determines the engagement of the independent registered public accounting firm;
- reviews and approves the scope of the annual audit and the audit fee;
- discusses with management and the independent registered public accounting firm the results of the annual audit and the review of our quarterly financial statements;
- approves the retention of the independent registered public accounting firm to perform any proposed permissible non-audit services;
- monitors the rotation of partners of the independent registered public accounting firm on our engagement team as required by law;
- is responsible for reviewing our financial statements and our management's discussion and analysis of financial condition and results of operations to be included in our annual and quarterly reports to be filed with the SEC;
- reviews our critical accounting policies and estimates; and
- annually reviews the audit committee charter and the committee's performance.

The current members of our audit committee are , , and . serves as the chairperson of the committee. All members of our audit committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and NASDAQ. Our board of directors has determined that is an audit committee financial expert as defined under the applicable rules of the SEC and has the requisite financial sophistication as defined under the applicable rules and regulations of NASDAQ. Under the rules of the SEC, members of the audit committee must also meet heightened independence standards. However, a minority of the members of the audit committee may be exempt from the heightened audit committee independence standards for one year from the date of effectiveness of the registration statement of which this prospectus forms a part. Our board of directors has determined that each of , and are independent under the applicable rules of NASDAQ. The audit committee operates under a written charter that satisfies the applicable standards of the SEC and NASDAQ.

Compensation Committee

Our compensation committee reviews and recommends policies relating to compensation and benefits of our officers and employees. The compensation committee reviews and recommends corporate goals and objectives relevant to compensation of our Chief Executive Officer and other executive officers, evaluates the performance of these officers in light of those goals and objectives and recommends to our board of directors the compensation of these officers based on such evaluations. The compensation committee also recommends to our board of directors the issuance of stock options and other awards under our stock plans. The compensation committee will review and evaluate, at least annually, the performance of the compensation committee and its members, including compliance by the compensation committee with its charter. The current members of our compensation committee are , and . serves as the chairperson of the committee. Each of the members of our compensation committee is independent under the applicable rules and regulations of NASDAQ, is a "non-employee director" as defined in Rule 16b-3 promulgated under the Exchange Act and is an "outside director" as that term is defined in Section 162(m) of the U.S. Internal Revenue Code of 1986, as amended, or Section 162(m). The compensation committee operates under a written charter.

Nominating and Corporate Governance Committee

The nominating and corporate governance committee is responsible for making recommendations to our board of directors regarding candidates for directorships and the size and composition of our board of directors. In addition, the nominating and corporate governance committee is responsible for overseeing our corporate governance policies and reporting and making recommendations to our board of directors concerning governance matters. The current members of our nominating and corporate governance committee are , and . serves as the chairman of the committee. Each of the members of our nominating and corporate governance committee is an independent director under the applicable rules and regulations of NASDAQ relating to nominating and corporate governance committee independence. The nominating and corporate governance committee operates under a written charter.

Compensation Committee Interlocks and Insider Participation

During 2014, each of Michael Powell, Ph.D., Edward Mathers, and Clay Siegall, Ph.D. served as members of our compensation committee. During 2014, none of the members of our compensation committee has at any time been one of our officers or employees. None of our executive officers currently serves, or in the past year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers on our board of directors or compensation committee.

Board Diversity

Upon consummation of this offering, our nominating and corporate governance committee will be responsible for reviewing with the board of directors, on an annual basis, the appropriate characteristics, skills and experience required for the board of directors as a whole and its individual members. In evaluating the suitability of individual candidates (both new candidates and current members), the nominating and corporate governance committee, in recommending candidates for election, and the board of directors, in approving (and, in the case of vacancies, appointing) such candidates, will take into account many factors, including the following:

- personal and professional integrity;
- ethics and values;
- experience in corporate management, such as serving as an officer or former officer of a publicly held company;
- experience in the industries in which we compete;
- experience as a board member or executive officer of another publicly held company;

- diversity of expertise and experience in substantive matters pertaining to our business relative to other board members;
- conflicts of interest; and
- practical and mature business judgment.

Currently, our board of directors evaluates, and following the consummation of this offering will continue to evaluate, each individual in the context of the board of directors as a whole, with the objective of assembling a group that can best maximize the success of the business and represent stockholder interests through the exercise of sound judgment using its diversity of experience in these various areas.

Code of Business Conduct and Ethics

We have adopted a code of business conduct and ethics that applies to all of our employees, officers and directors, including those officers responsible for financial reporting. Following the consummation of this offering, the code of business conduct and ethics will be available on our website at www.mirnarx.com. We expect that any amendments to the code, or any waivers of its requirements, will be disclosed on our website. The reference to our web address does not constitute incorporation by reference of the information contained at or available through our website.

Limitation on Liability and Indemnification Matters

Our amended and restated certificate of incorporation, which will become effective immediately prior to the consummation of this offering, or our amended and restated certificate of incorporation, contains provisions that limit the liability of our directors for monetary damages to the fullest extent permitted by Delaware law. Consequently, our directors will not be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duties as directors, except liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law; or
- any transaction from which the director derived an improper personal benefit.

Our amended and restated certificate of incorporation and amended and restated bylaws, which will become effective immediately prior to the consummation of this offering, or our amended and restated bylaws, provide that we are required to indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law. Our amended and restated bylaws also provide that we are obligated to advance expenses incurred by a director or officer in advance of the final disposition of any action or proceeding, and permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in that capacity regardless of whether we would otherwise be permitted to indemnify him or her under Delaware law.

In addition to the indemnification required in our amended and restated certificate of incorporation and amended and restated bylaws, we have entered or intend to enter into indemnification agreements with each of our directors, officers and certain employees before the completion of this offering. These agreements will provide for the indemnification of our directors, officers and certain employees for all reasonable expenses and liabilities incurred in connection with any action or proceeding brought against them by reason of the fact that they are or were our agents. We believe that these provisions in our amended and restated certificate of incorporation and amended and restated bylaws and indemnification agreements are necessary to attract and retain qualified persons as directors and officers. This description of the limitation of liability and indemnification provisions of our amended and restated certificate of incorporation, of our amended and restated bylaws and of our indemnification agreements is qualified in its entirety by reference to these documents, each of which is attached as an exhibit to this registration statement, of which this prospectus is a part.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against directors and officers, even though an action, if successful, might benefit us and our stockholders. A stockholder's investment may be harmed to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

Director Compensation

While we did not maintain a formal policy, during fiscal year 2014, our independent directors, who we considered to be those non-employee directors not associated with a principal investor in our company, received an annual cash retainer of $25,000 for service as a director, pro-rated for partial years of service, and an additional cash retainer of $3,000 per meeting of the board or a committee of the board attended in person and $2,000 per meeting of the board or committee of the board attended telephonically. In addition, during fiscal year 2014, our board of directors granted options to purchase shares of our common stock to each independent director. In March 2014, Dr. Siegall was granted options to purchase an aggregate of 173,314 shares of our common stock and Dr. Goodman was granted options to purchase an aggregate of 153,504 shares of our common stock. In November 2014, Mr. Alleva was granted an option to purchase 200,000 shares of our common stock. Each option grant made to our independent directors was immediately vested and exercisable with respect to 20% of the shares underlying the option and the remaining shares vest and become exercisable in substantially equal installments every six months over four years, subject to continued service. In the event of a change of control (as defined in our 2008 Long term Incentive Plan, as amended, or the 2008 Stock Plan) while an independent director is still providing services to us, the options held by the independent director will become fully vested and exercisable immediately prior to such change in control.

We reimburse all of our non-employee directors for all reasonable and customary business expenses incurred providing services to us in accordance with Company policy.

In connection with this offering, we intend to approve and implement a compensation program for our non-employee directors that consists of annual retainer fees and initial and annual long-term equity awards.

2014 Director Compensation Table

The following table sets forth information for the year ended December 31, 2014 regarding the compensation awarded to, earned by or paid to our non-employee directors:

Name(1)	Fees Earned or Paid in Cash ($)	Option Awards ($)(1)(2)	All Other Compensation ($)	Total($)
Michael Powell, Ph.D.	$ —	$ —	$ —	$ —
Elaine V. Jones, Ph.D.	—	—	—	—
Edward Mathers	—	—	—	—
Matthew Winkler, Ph.D.	—	—	—	—
Lawrence M. Alleva(3)	15,417	69,553		84,970
Clay B. Siegall, Ph.D.	46,000	61,810	—	107,810
Corey Goodman, Ph.D.(4)	47,000	54,754	—	101,810

(1) The amounts reported in the Option Awards column represent the grant date fair value of the stock options granted to the non-employee members of our board of directors during 2014 as computed in accordance with ASC Topic 718, excluding the impact of estimated forfeitures related to service-based vesting provisions. The assumptions used in calculating the grant date fair value of the stock options reported in the Option Awards column are set forth in Note 2 to the audited financial statements included in this prospectus. Note that the amounts reported in this column reflect the accounting cost for these stock options, and do not correspond to the actual economic value that may be received by the non-employee members of our board of directors from the options.

(2) As of December 31, 2014, Mr. Alleva held an option to purchase an aggregate of 200,000 shares of our common stock, and Dr. Siegall held options to purchase an aggregate of 423,314 shares of our common stock; no other non-employee director held outstanding options to purchase our common stock as of December 31, 2014.

(3) Mr. Alleva joined our board of directors in July 2014.

(4) Dr. Goodman resigned from our board of directors effective July 10, 2015.

Executive Compensation

The following is a discussion and analysis of compensation arrangements of our named executive officers, or NEOs. This discussion contains forward looking statements that are based on our current plans, considerations, expectations and determinations regarding future compensation programs. Actual compensation programs that we adopt may differ materially from currently planned programs as summarized in this discussion. As an "emerging growth company" as defined in the JOBS Act, we are not required to include a Compensation Discussion and Analysis section and have elected to comply with the scaled disclosure requirements applicable to emerging growth companies.

We seek to ensure that the total compensation paid to our executive officers is reasonable and competitive. Compensation of our executives is structured around the achievement of individual performance and near-term corporate targets as well as long-term business objectives.

Our NEOs for fiscal year 2014 were as follows:

- Paul Lammers, M.D., M.Sc., President and Chief Executive Officer;
- Casi DeYoung, Chief Business Officer;
- Jon Irvin, Chief Financial Officer; and
- Sinil Kim, M.D., Vice President of Oncology and Chief Medical Officer.

2014 Summary Compensation Table

The following table shows information regarding the compensation of our named executive officers for services performed in the year ended December 31, 2014.

Name and Principal Position	Year	Salary ($)	Bonus ($)(1)	Option Awards ($)(2)	All Other Compensation ($)(3)	Total ($)
Paul Lammers, M.D., M.Sc. *President and Chief Executive Officer*	2014	$ 375,829	$ 0	$ 390,780	$ 11,275	$ 777,884
Casi DeYoung (4) *Chief Business Officer*	2014	224,712	25,000	266,353	3,288	519,353
Jon Irvin *Chief Financial Officer*	2014	204,240	0	76,338	8,170	288,798
Sinil Kim, M.D. *Chief Medical Officer and Vice President of Oncology*	2014	315,829	0	78,791	10,214	404,834

(1) The amount reported in the Bonus column represents the sign on bonus Ms. DeYoung received pursuant to her employment agreement in connection with commencing employment with us in March 2014. Please see the description of Ms. DeYoung's employment agreement with us in "Narrative to 2014 Summary Compensation Table and Outstanding Equity Awards at 2014 Fiscal Year End—Terms and Conditions of Employee Arrangements with our NEOs" below.

(2) For the option awards column, amounts shown represents the grant date fair value of stock options granted during fiscal year 2014 as calculated in accordance with ASC Topic 718, excluding the impact of estimated forfeitures related to service-based vesting provisions. See Note 2 to our audited financial statements included in this registration statement for the assumptions used in calculating this amount.

(3) The amounts reported in the All Other Compensation column represent 401(k) Plan matching contributions.

(4) Ms. DeYoung commenced employment with us in March 2014.

Outstanding Equity Awards at 2014 Fiscal Year End

The following table sets forth all outstanding equity awards held by each of the named executive officers as of December 31, 2014.

		Option Awards			
Name	Vesting Commencement Date(1)	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date
Paul Lammers, M.D., M.Sc.	11/4/2009	158,484	0	$ 0.50	12/31/2019
	1/10/2013(2)	1,194,744	548,438	0.11	1/22/2023
	3/6/2014	0	1,083,700	0.54	3/9/2024
Casi DeYoung	3/6/2014	0	738,644	0.54	3/9/2024
Jon Irvin	6/6/2013	84,375	140,625	0.11	6/5/2023
	6/6/2013	79,277	132,130	0.29	12/30/2023
	3/6/2014	0	211,700	0.54	3/9/2024
Sinil Kim, M.D.	6/6/2013	28,125	140,625	0.11	6/5/2023
	6/6/2013	28,125	140,625	0.29	12/30/2023
	3/6/2014	0	218,500	0.54	3/9/2024

(1) Except as otherwise noted, the shares subject to the options shall vest and become exercisable as to 1/4th of the shares subject to the option on the first anniversary of the vesting commencement date, and thereafter as to 1/48th of the shares subject to such option on each monthly anniversary of the vesting commencement date, such that all shares subject to the option will be vested on the fourth anniversary of the vesting commencement date, subject to the holder continuing to provide services to us through such vesting date.

(2) The shares subject to the option shall vest and become exercisable as to 1/4th of the shares subject to the option on the vesting commencement date, and thereafter as to 1/48th of the shares subject to such option on each monthly anniversary of the vesting commencement date, such that all shares subject to the option will be vested on the third anniversary of the vesting commencement date, subject to the holder continuing to provide services to us through such vesting date.

Narrative to 2014 Summary Compensation Table and Outstanding Equity Awards at 2014 Fiscal Year End

Terms and Conditions of Employee Arrangements with our NEOs

We have entered into agreements with each of the NEOs in connection with his or her employment with us. These agreements set forth the terms and conditions of employment of each named executive officer, including base salary, initial stock option grants, and standard employee benefit plan participation. Our board of directors or the compensation committee reviews each NEO's base salary from time to time to ensure compensation adequately reflects the NEO's qualifications, experience, role and responsibilities. For fiscal year 2014, Dr. Lammers' annual base salary was $376,335, Ms. DeYoung's base salary was $285,000, Dr. Kim's annual base salary was $316,200 and Mr. Irvin's annual base salary was $231,250. In addition, pursuant to her employment agreement, Ms. DeYoung was awarded a signing bonus of $25,000 in connection with her commencement of employment with us in March 2014. In addition, under her employment agreement, if Ms. DeYoung relocates her primary residence from the Dallas, Texas area to the Austin, Texas area during her employment with us, we will reimburse her for the reasonable and necessary documented moving expenses (up to a maximum of $15,000), including up to two house-hunting trips and the moving of her household from the Dallas, Texas area to the Austin, Texas area.

Under Dr. Lammers' employment agreement, in the event Dr. Lammers' (i) employment with us is terminated for reason other than "cause" (as defined below), "disability" (as defined below) or death or (ii) resigns his employment for "good reason" (as defined below), and Dr. Lammers executes and does not revoke a general release of claims in favor of us, then Dr. Lammers will receive a severance payment equal to 12 months of Dr. Lammers' base salary, payable in 12 equal monthly installments. Under Mr. Irvin's and Ms. DeYoung's employment agreements, in the event their employment with us is terminated by us in connection with or after a "change in control" (as defined below) or, for Ms. DeYoung only, at any time without cause, and they execute and do not revoke a general release of claims in favor of us, then Ms. DeYoung and Mr. Irvin will receive a severance payment equal to six months of their applicable base salary, payable in six equal monthly installments. Dr. Kim does not have any severance or change in control benefits under his employment agreement.

For purposes of Dr. Lammers' employment agreement, "cause" means (i) the conviction of Dr. Lammers by a court of competent jurisdiction of a crime involving moral turpitude; (ii) the commission, or attempted commission, by Dr. Lammers of an act of fraud on us; (iii) the misappropriation, or attempted misappropriation, by Dr. Lammers of any of our funds or property; (iv) the failure by Dr. Lammers to perform in any material respect his obligations under the terms of his employment agreement, which such failure has gone unremedied within 10 days after we provide Dr. Lammers with written notice of such failure; (v) the knowing engagement by Dr. Lammers, without the written approval of our board of directors, in any direct, material conflict of interest with us without compliance with our conflict of interest policy; (vi) the knowing engagement by Dr. Lammers, without written approval of our board of directors, in any activity which competes with our business or which would result in a material injury to us or which otherwise violates any provision of his confidentiality, covenant not to solicit and arbitration agreement; or (vii) the knowing engagement by Dr. Lammers in any activity that would constitute a material violation of the provisions of our business ethics policy, employee handbook or similar policies, if any, then in effect.

For purposes of Dr. Lammers' employment agreement, "disability" means Dr. Lammers' inability to perform the essential functions of his position, with reasonable accommodation, due to Dr. Lammers' illness or physical or mental impairment or other incapacity which continues for a period in excess of 120 days (whether consecutive or not).

For purposes of Dr. Lammers' employment agreement, "good reason" means the occurrence, if within one year of a change in control, of a material diminution of Dr. Lammers' job responsibilities from those responsibilities set forth in his employment agreements, provided that in order for "good reason" to exist, each of the following conditions must be met: (i) the material diminution condition must have arisen without Dr. Lammers' consent; (ii) Dr. Lammers must provide written notice to us of such condition within 45 days of the initial existence of the condition; (iii) the condition specified in such notice must remain uncorrected for 30 days after receipt of such notice; and (iv) the date of Dr. Lammers' termination of employment must occur within 90 days after the initial existence of the condition specified in such notice.

For purposes of Dr. Lammers, Ms. DeYoung's and Mr. Irvin's employment agreements, "change in control" means (i) any person or entity, other than our stockholders as of April 18, 2013 for Dr. Lammers and Mr. Irvin and March 1, 2014 for Ms. DeYoung, our benefit plans, us or each of their respective affiliates and permitted transferees, acquires (by acquisition, merger, consolidation, recapitalization, reorganization or otherwise) beneficial ownership (as defined in Section 13(d) of the Securities Exchange Act of 1934, as amended) of more than 50% of our outstanding common stock; or (ii) we will have consummated a sale or other disposition of all or substantially all of our assets to any person or entity other to us, our benefit plans or any of their respective affiliates or successor entities;

provided, however, that the sale of equity securities by us for primarily capital raising purposes will not constitute a change in control.

Terms and Conditions of Equity Award Grants

Each of our NEOs received an option to purchase our common stock in fiscal year 2014. The table above entitled "Outstanding Equity Awards at 2014 Fiscal Year End" describes the material terms of other option awards made in past fiscal years to our NEOs.

In March 2014, our board of directors granted an option to purchase 1,083,700, 738,644, 218,500, and 211,000 shares of our common stock to Dr. Lammers, Ms. DeYoung, Dr. Kim, and Mr. Irvin, respectively, with an exercise price of $0.54 per share, which the board determined was the fair market value on the date of grant. Each of the options vest and become exercisable as to 1/4th of the shares subject to the option on March 6, 2015, and as to 1/48th of the shares subject to the option on each monthly anniversary thereafter, such that 100% of the shares subject to the option will be vested and exercisable on March 6, 2018, subject to these NEOs continuing to provide services to us through such vesting date.

Terms and Conditions of 401(k) Plan

Our U.S. eligible employees, including our NEOs, participate in our 401(k) Plan. Enrollment in the 401(k) Plan is automatic for employees who meet eligibility requirements unless they decline participation. The 401(k) plan is intended to qualify under Section 401(k) of the Internal Revenue Service Code of 1986, as amended, so that contributions to the 401(k) plan by employees or by us, and the investment earnings thereon, are not taxable to the employees until withdrawn from the 401(k) plan, and so that contributions by us, if any, will be deductible by us when made. Under the 401(k) plan, employees may elect to reduce their current compensation by up to the statutorily prescribed annual limit and to have the amount of such reduction contributed to the 401(k) plan. Under the 401(k), for fiscal year 2014, we provide matching contributions of $0.50 per dollar up to 8% of an employee's compensation.

Equity Compensation Plans

2015 Equity Incentive Award Plan

We have adopted the 2015 Equity Incentive Award Plan, or 2015 Plan, which will be effective on the closing of this offering. The principal purpose of the 2015 Plan is to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards and cash-based performance bonus awards. The material terms of the 2015 Plan are summarized below.

Share Reserve. Under the 2015 Plan, shares of our common stock will be initially reserved for issuance pursuant to a variety of stock-based compensation awards, including stock options, stock appreciation rights, or SARs, restricted stock awards, restricted stock unit awards, deferred stock awards, dividend equivalent awards, stock payment awards, performance awards and other stock-based awards, plus the number of shares remaining available for future awards under the 2008 Long Term Incentive Plan, as amended, or 2008 Stock Plan, as of the consummation of this offering. The number of shares initially reserved for issuance or transfer pursuant to awards under the 2015 Plan will be increased by (i) the number of shares represented by awards outstanding under our 2008 Stock Plan that are forfeited or lapse unexercised and which following the effective date are not issued under our 2008 Stock Plan and (ii), if approved by our board of directors or the compensation committee of our board of directors, an annual increase on the first day of each fiscal year beginning in 2015 and ending in 2024, equal to the least of (A) shares, (B) percent (%) of the shares of stock outstanding (on an as converted basis) on the last day of the immediately preceding fiscal year and (C) such smaller number of shares of stock as determined by our board of directors; provided, however, that no more than shares of stock may be issued upon the exercise of incentive stock options.

The following counting provisions will be in effect for the share reserve under the 2015 Plan:

- to the extent that an award terminates, expires or lapses for any reason or an award is settled in cash without the delivery of shares, any shares subject to the award at such time will be available for future grants under the 2015 Plan;
- to the extent shares are tendered or withheld to satisfy the grant, exercise price or tax withholding obligation with respect to any award under the 2015 Plan, such tendered or withheld shares will be available for future grants under the 2015 Plan;
- to the extent that shares of our common stock are repurchased by us prior to vesting so that shares are returned to us, such shares will be available for future grants under the 2015 Plan;
- the payment of dividend equivalents in cash in conjunction with any outstanding awards will not be counted against the shares available for issuance under the 2015 Plan; and
- to the extent permitted by applicable law or any exchange rule, shares issued in assumption of, or in substitution for, any outstanding awards of any entity acquired in any form of combination by us or any of our subsidiaries will not be counted against the shares available for issuance under the 2015 Plan.

Administration. The compensation committee of our board of directors is expected to administer the 2015 Plan unless our board of directors assumes authority for administration. The compensation committee must consist of at least three members of our board of directors, each of whom is intended to qualify as an "outside director," within the meaning of Section 162(m) of the Code, a "non-employee director" for purposes of Rule 16b-3 under the Exchange Act and an "independent director" within the meaning of the rules of the applicable stock exchange, or other principal securities market on which shares of our common stock are traded. The 2015 Plan provides that the board or compensation committee may delegate its authority to grant awards to employees other than executive officers and certain senior executives of the company to a committee consisting of one or more members of our board of directors or one or more of our officers, other than awards made to our non-employee directors, which must be approved by our full board of directors.

Subject to the terms and conditions of the 2015 Plan, the administrator has the authority to select the persons to whom awards are to be made, to determine the number of shares to be subject to awards and the terms and conditions of awards, and to make all other determinations and to take all other actions necessary or advisable for the administration of the 2015 Plan. The administrator is also authorized to adopt, amend or rescind rules relating to administration of the 2015 Plan. Our board of directors may at any time remove the compensation committee as the administrator and revest in itself the authority to administer the 2015 Plan. The full board of directors will administer the 2015 Plan with respect to awards to non-employee directors.

Eligibility. Options, SARs, restricted stock and all other stock-based and cash-based awards under the 2015 Plan may be granted to individuals who are then our officers, employees or consultants or are the officers, employees or consultants of certain of our subsidiaries. Such awards also may be granted to our directors. Only employees of our company or certain of our subsidiaries may be granted incentive stock options, or ISOs.

Awards. The 2015 Plan provides that the administrator may grant or issue stock options, SARs, restricted stock, restricted stock units, deferred stock, dividend equivalents, performance awards, stock payments and other stock-based and cash-based awards, or any combination thereof. Each award will be set forth in a separate agreement with the person receiving the award and will indicate the type, terms and conditions of the award.

- *Nonstatutory Stock Options*, or NSOs, will provide for the right to purchase shares of our common stock at a specified price which may not be less than fair market value on the date of grant, and usually will become exercisable (at the discretion of the administrator) in one or more installments after the grant date, subject to the participant's continued employment or service with us and/or subject to the satisfaction of corporate performance targets and individual performance targets established by the administrator. NSOs may be granted for any term specified by the administrator that does not exceed 10 years.

- *Incentive Stock Options*, or ISOs, will be designed in a manner intended to comply with the provisions of Section 422 of the Code and will be subject to specified restrictions contained in the Code. Among such restrictions, ISOs must have an exercise price of not less than the fair market value of a share of common stock on the date of grant, may only be granted to employees, and must not be exercisable after a period of 10 years measured from the date of grant. In the case of an ISO granted to an individual who owns (or is deemed to own) at least 10% of the total combined voting power of all classes of our capital stock, the 2015 Plan provides that the exercise price must be at least 110% of the fair market value of a share of common stock on the date of grant and the ISO must not be exercisable after a period of five years measured from the date of grant.

- *Restricted Stock* may be granted to any eligible individual and made subject to such restrictions as may be determined by the administrator. Restricted stock, typically, may be forfeited for no consideration or repurchased by us at the original purchase price if the conditions or restrictions on vesting are not met. In general, restricted stock may not be sold or otherwise transferred until restrictions are removed or expire. Purchasers of restricted stock, unlike recipients of options, will have voting rights and will have the right to receive dividends, if any, prior to the time when the restrictions lapse, however, extraordinary dividends will generally be placed in escrow, and will not be released until restrictions are removed or expire.

- *Restricted Stock Units* may be awarded to any eligible individual, typically without payment of consideration, but subject to vesting conditions based on continued employment or service or on performance criteria established by the administrator. Like restricted stock, restricted stock units may not be sold, or otherwise transferred or hypothecated, until vesting conditions are removed or expire. Unlike restricted stock, stock underlying restricted stock units will not be issued until the restricted stock units have vested, and recipients of restricted stock units generally will have no voting or dividend rights prior to the time when vesting conditions are satisfied.

- *Deferred Stock Awards* represent the right to receive shares of our common stock on a future date. Deferred stock may not be sold or otherwise hypothecated or transferred until issued. Deferred stock will not be issued until the deferred stock award has vested, and recipients of deferred stock generally will have no voting or dividend rights prior to the time when the vesting conditions are satisfied and the shares are issued. Deferred stock awards generally will be forfeited, and the underlying shares of deferred stock will not be issued, if the applicable vesting conditions and other restrictions are not met.

- *Stock Appreciation Rights*, or SARs, may be granted in connection with stock options or other awards, or separately. SARs granted in connection with stock options or other awards typically will provide for payments to the holder based upon increases in the price of our common stock over a set exercise price. The exercise price of any SAR granted under the 2015 Plan must be at least 100% of the fair market value of a share of our common stock on the date of grant. Except as required by Section 162(m) of the Code with respect to a SAR intended to qualify as performance-based compensation as described in Section 162(m) of the Code, there are no restrictions specified in the 2015 Plan on the exercise of SARs or the amount of gain realizable therefrom, although restrictions may be imposed by the administrator in the SAR agreements. SARs under the 2015 Plan will be settled in cash or shares of our common stock, or in a combination of both, at the election of the administrator.

- *Dividend Equivalents* represent the value of the dividends, if any, per share paid by us, calculated with reference to the number of shares covered by the award. Dividend equivalents may be settled in cash or shares and at such times as determined by the compensation committee or board of directors, as applicable.

- *Performance Awards* may be granted by the administrator on an individual or group basis. Generally, these awards will be based upon specific performance targets and may be paid in cash or in common stock or in a combination of both. Performance awards may include "phantom" stock awards that provide for payments based upon the value of our common stock. Performance awards may also include bonuses that may be granted by the administrator on an individual or group basis and which may be payable in cash or in common stock or in a combination of both.

- *Stock Payments* may be authorized by the administrator in the form of common stock or an option or other right to purchase common stock as part of a deferred compensation or other arrangement in lieu of all or any part of compensation, including bonuses, that would otherwise be payable in cash to the employee, consultant or non-employee director.

Change in Control. In the event of a change in control where the acquiror does not assume or replace awards granted, prior to the consummation of such transaction, awards issued under the 2015 Plan will be subject to accelerated vesting such that 100% of such awards will become vested and exercisable or payable, as applicable. In addition, the administrator will also have complete discretion to structure one or more awards under the 2015 Plan to provide that such awards will become vested and exercisable or payable on an accelerated basis in the event such awards are assumed or replaced with equivalent awards but the individual's service with us or the acquiring entity is subsequently terminated within a designated period following the change in control event. The administrator may also make appropriate adjustments to awards under the 2015 Plan and is authorized to provide for the acceleration, cash-out, termination, assumption, substitution or conversion of such awards in the event of a change in control or certain other unusual or nonrecurring events or transactions. Under the 2015 Plan, a change in control is generally defined as:

- the transfer or exchange in a single transaction or series of related transactions by our stockholders of more than 50% of our voting stock to a person or group;

- a change in the composition of our board of directors over a two- year period such that 50% or more of the members of the board of directors were elected through one or more contested elections;

- a merger, consolidation, reorganization or business combination in which we are involved, directly or indirectly, other than a merger, consolidation, reorganization or business combination which results in our outstanding voting securities immediately before the transaction continuing to represent a majority of the voting power of the acquiring company's outstanding voting securities and after which no person or group beneficially owns 50% or more of the outstanding voting securities of the surviving entity immediately after the transaction;

- the sale, exchange, or transfer of all or substantially all of our assets; or

- stockholder approval of our liquidation or dissolution.

Adjustments of Awards. In the event of any stock dividend, stock split, combination or exchange of shares, merger, consolidation, spin-off, recapitalization, distribution of our assets to stockholders (other than normal cash dividends) or any other corporate event affecting the number of outstanding shares of our common stock or the share price of our common stock that would require adjustments to the 2015 Plan or any awards under the 2015 Plan in order to prevent the dilution or enlargement of the potential benefits intended to be made available thereunder, the administrator will make appropriate, proportionate adjustments to:

- the aggregate number and type of shares subject to the 2015 Plan;
- the number and kind of shares subject to outstanding awards and terms and conditions of outstanding awards (including, without limitation, any applicable performance targets or criteria with respect to such awards); and
- the grant or exercise price per share of any outstanding awards under the 2015 Plan.

Amendment and Termination. Our board of directors or the compensation committee (with board approval) may terminate, amend or modify the 2015 Plan at any time and from time to time. However, we must generally obtain stockholder approval:

- to increase the number of shares available under the 2015 Plan (other than in connection with certain corporate events, as described above);
- to grant options with an exercise price that is below 100% of the fair market value of shares of our common stock on the grant date;
- to extend the exercise period for an option beyond 10 years from the date of grant; or
- to the extent required by applicable law, rule or regulation (including any applicable stock exchange rule).

Notwithstanding the foregoing, an option may be amended to reduce the per share exercise price below the per share exercise price of such option on the grant date and options may be granted in exchange for, or in connection with, the cancellation or surrender of options having a higher per share exercise price without receiving additional stockholder approval.

Termination. The board of directors may terminate the 2015 Plan at any time. No incentive stock options may be granted pursuant to the 2015 Plan after the tenth anniversary of the effective date of the 2015 Plan, and no additional annual share increases to the 2015 Plan's aggregate share limit will occur from and after such anniversary. Any award that is outstanding on the termination date of the 2015 Plan will remain in force according to the terms of the 2015 Plan and the applicable award agreement.

We intend to file with the SEC a registration statement on Form S-8 covering the shares of our common stock issuable under the 2015 Plan.

2008 Long Term Incentive Plan

Our board of directors adopted, and our stockholders approved, the 2008 Stock Plan effective as of May 15, 2008, which was subsequently amended on November 3, 2009, October 22, 2012 and March 10, 2014 to increase the number of shares issuable under the 2008 Stock Plan. The 2008 Stock Plan provided for the grant of ISOs, NSOs, SARs, restricted stock, restricted stock units, bonus stock awards, dividend equivalents, performance awards and other stock-based awards. As of March 31, 2015, options to purchase 8,354,031 shares of our common stock at a weighted-average exercise price per share of $0.34 remained outstanding under the 2008 Stock Plan. No other equity awards have been granted under the 2008 Stock Plan. As of March 31, 2015, 6,221,749 shares of our common stock were available for future issuance pursuant to awards granted under the 2008 Stock Plan. Following this offering and in connection with the effectiveness of our 2015 Plan, the 2008 Stock Plan will terminate and no further awards will be granted under the 2008 Stock Plan. However, all outstanding awards will continue to be governed by their existing terms.

Administration. Our board of directors, or a committee thereof appointed by our board of directors, has the authority to administer the 2008 Stock Plan and the awards granted under it. In addition, the administrator may delegate to our officers or managers or committees thereof the authority to grant awards to persons who are not subject to Section 16 of the Exchange Act and to such extent that awards that are intended to qualify as "performance-based compensation" under Section 162(m) of the Code would not fail to so qualify. The administrator has the authority to select the employees to whom awards will be granted under the 2008 Stock Plan, the number of shares to be subject to those awards under the 2008 Stock Plan, and the terms and conditions of the awards granted. In addition, the administrator has the authority to construe and interpret the 2008 Stock Plan and to adopt rules for the administration, interpretation and application of the 2008 Stock Plan that are consistent with the terms of the 2008 Stock Plan.

Awards. The 2008 Stock Plan provides that the administrator may grant or issue options, including ISOs and NSOs, SARs, restricted stock, restricted stock units, bonus stock awards, dividend equivalents, performance awards and other stock-based awards to employees, consultants and directors; provided that only employees may be granted incentive stock options. Each award will be set forth in a separate agreement with the person receiving the award and will indicate the type, terms and conditions of the award, including any performance conditions that may be specified by the administrator. In addition, under the 2008 Stock Plan each award and any stock issued under such awards will be subject to a right of first refusal in favor of us, which will terminate upon the consummation of this offering.

- *Stock Options.* The 2008 Stock Plan provides for the grant of ISOs under the federal tax laws or NSOs. ISOs may be granted only to employees. NSOs may be granted to employees, directors or consultants. The exercise price of ISOs granted to employees who at the time of grant own stock representing more than 10% of the voting power of all classes of our common stock may not be less than the greater of (i) the par value of our common stock or (ii) 110% of the fair market value per share of our common stock on the date of grant, and the exercise price of ISOs granted to any other employees may not be less than the greater of (i) the par value of our common stock or (ii) 100% of the fair market value per share of our common stock on the date of grant. The exercise price of NSOs to employees, directors or consultants may not be less than the greater of (i) the par value of our common stock or (ii) 100% of the fair market value per share of our common stock on the date of grant. Shares subject to options under the 2008 Stock Plan generally vest in a series of installments over an optionee's period of service.

- *Stock Appreciation Rights.* The 2008 Stock Plan provides that we may issue SARs. Each SAR will be governed by a stock appreciation right agreement and may be granted in connection with stock options or other awards, or separately. SARs granted in connection with stock options or other awards typically will provide for payments to the holder based upon increases in the price of our common stock over a set exercise price.

- *Restricted Stock Awards.* The 2008 Stock Plan provides that we may issue restricted stock awards. Each restricted stock award will be governed by a restricted stock award agreement, which will details the restrictions on transferability, risk of forfeiture and other restrictions the administrator approves. In general, restricted stock may not be sold, transferred, pledged, hypothecated, margined or otherwise encumbered until restrictions are removed or expire.

Holders of restricted stock, unlike recipients of other equity awards, will have voting rights and will have the right to receive dividends, if any, prior to the time when the restrictions lapse.

- *Restricted Stock Units.* The 2008 Stock Plan provides that we may issue restricted stock unit awards which may be settled in either cash of common stock. Each restricted stock unit award will be governed by a restricted stock unit award agreement and may be awarded to any eligible individual, typically without payment of consideration, but subject to vesting conditions based on continued employment or service or on performance criteria established by the administrator. Like restricted stock, restricted stock units may not be sold, or otherwise transferred or hypothecated, until vesting conditions are removed or expire. Unlike restricted stock, stock underlying restricted stock units will not be issued until the restricted stock units have vested, and recipients of restricted stock units generally will have no voting or, unless otherwise determined by the administrator, dividend rights prior to the time when vesting conditions are satisfied, except dividend equivalents may be credited in respect of shares of common stock.

- *Bonus Stock Awards.* The 2008 Stock Plan provides that we may award bonuses in the form of common stock or award stock or other awards in lieu of all or any part of obligations to pay cash or deliver other property under the 2008 Stock Plan or under other plans or compensatory arrangements to the employee, consultant or non-employee director. In the case of any grant of stock to an officer in lieu of salary or other cash compensation, the number of shares granted in lieu of such compensation will be reasonable, as determined by the administrator.

- *Dividend Equivalents.* The 2008 Stock Plan provides that dividend equivalents may be awarded to employees, consultants or directors. Dividend equivalents represent the value of the dividends, if any, per share paid by us, calculated with reference to the number of shares covered by the award. Dividend equivalents may be settled in cash, shares, other awards or other property equal in value to dividends paid and at such times as determined by the administrator.

- *Performance Awards.* The 2008 Stock Plan provides that performance awards may be granted by the administrator on an individual or group basis. Generally, these awards will be based upon specific performance targets and may be paid in cash or in common stock or in a combination of both. Performance awards may also include bonuses that may be granted by the administrator on an individual or group basis and which may be payable in cash or in common stock or in a combination of both.

- *Other Stock Awards.* The 2008 Stock Plan provides that we may issue other stock or cash awards. Each stock award will be governed by a stock award agreement and may be authorized by the administrator in the form of common stock in whole or in part and may be granted either alone or in addition to other stock awards described above.

Detrimental Activity. If at any time prior to the third anniversary of the most recent termination of an employee's service with us, the administrator determines that such employee, at any time during his or her most recent service with us, or within the three-year period after termination of such service, engaged in any detrimental activity, then such employee shall (i) immediately forfeit the right to exercise any and all options granted to him or her under the 2008 Stock Plan, irrespective of whether the vested or unvested; and (ii) upon demand by the administrator, promptly return to us any or all shares of our common stock acquired pursuant to awards granted to employee under the 2008 Stock Plan and all associated dividends. The purchase price per share of common stock returned to us will be an amount equal to employee's purchase price per share as reflected in each such award.

Subdivision or Consolidation of Shares. In the event of certain corporate adjustments, the administrator of the 2008 Stock Plan will adjust the class and maximum number of shares of common stock that may be delivered under the 2008 Stock Plan, the class and maximum number of shares of common stock that may be issued pursuant to the exercise of ISOs and/or the number, class and price of shares of common stock covered by each outstanding award.

Corporate Recapitalization. In the event we recapitalize, reclassify our capital stock or other change our capital structure, the number and class of shares covered by an option or an SAR will be proportionately adjusted. In the event of changes in the outstanding shares by reason of recapitalization, reorganizations, mergers, consolidations, combinations, exchanges or other relevant changes in capitalization occurring after the date of the grant of any award and not otherwise provided in the 2008 Stock Plan, any outstanding awards and any agreements evidencing such awards shall be subject to adjustment by the administrator at its discretion as to the number and price of shares or other consideration subject to such Awards.

Change in Control. Upon a change in control, the administrator, acting without the consent or approval of any holder, will take one or more of the following alternatives, which may vary among individual holders and which may vary among options or SARs held by any individual: (i) accelerate the time at which awards then outstanding may be exercised so that such awards may be exercised in full for a limited period of time on or before a specified date fixed by the administrator, after which specified date all unexercised awards will terminate; (ii) require the mandatory surrender to us by selected holders of some or all of the outstanding awards held by such holders specified by the administrator, in which event the administrator will cancel such awards and pay to each holder an amount of cash per share equal to the excess, if any, of the spread value for such shares; or (iii) make such adjustments to awards then outstanding as the administrator deems appropriate.

Amendment; Termination. Our board of directors may amend or terminate the 2008 Stock Plan or any portion thereof at any time, but no amendment will impair the rights of a holder of an outstanding award without the holder's consent. An amendment of the 2008 Stock Plan shall be subject to the approval of our stockholders, where such approval by our stockholders of an amendment is required by applicable law. Following this offering and in connection with the effectiveness of our 2015 Plan, the 2008 Stock Plan will terminate and no further awards will be granted under the 2008 Stock Plan.

We intend to file with the SEC a registration statement on Form S-8 covering our shares of common stock issuable under the 2008 Stock Plan.

Rule 10b5-1 Sales Plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from the director or officer. The director or officer may amend or terminate the plan in limited circumstances. Our directors and executive officers may also buy or sell additional shares of our common stock outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

Certain Relationships and Related Party Transactions

The following is a description of transactions since January 1, 2012 to which we have been a party, in which the amount involved exceeds $120,000, and in which any of our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof, had or will have a direct or indirect material interest.

Sales and Purchases of Securities

Winkler Convertible Promissory Note

In June 2011, we issued a convertible promissory note to Matthew Winkler, Ph.D., that allowed us to draw amounts from time to time up to the aggregate maximum principal sum of $1.0 million. In January 2012 and June 2012, we amended and restated the convertible promissory note with Dr. Winkler, raising the aggregate maximum principal sum to $1.5 million and extending the maturity date. During the period the promissory note, as amended, was outstanding, we borrowed an aggregate principal amount of $750,000. In October 2012, Dr. Winkler contributed the entire principal amount of, and accrued interest on, the promissory note, as amended, to us in exchange for shares of Series C convertible preferred stock, which was distributed in a dividend to the holders of Series A convertible preferred stock and Series B convertible preferred stock. Dr. Winkler, who is a member of our board of directors and holder of our capital stock, currently serves as the Chairman and Chief Scientific Officer, and is a founder and holder of capital stock, of Asuragen, Inc., or Asuragen.

Asuragen Convertible Promissory Note

In June 2012, we issued a convertible promissory note to Asuragen that allowed us to draw amounts from time to time up to the aggregate maximum principal sum of $500,000. In October 2012, we repaid the full amount of all principal drawn on the promissory note, and accrued and unpaid interest thereon, of $122,866 in cash. Dr. Winkler, who is a member of our board of directors and holder of our capital stock, currently serves as the Chairman and Chief Scientific Officer, and is a founder and holder of capital stock, of Asuragen.

Series C Convertible Preferred Stock Financing

In October 2012 and December 2013, we issued an aggregate of 67,779,942 shares of our Series C convertible preferred stock at a price per share of $0.509 for aggregate gross consideration of approximately $34.5 million to 18 accredited investors. The table below sets forth the number of shares of Series C convertible preferred stock sold to our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof:

Name	Number of Shares of Series C Preferred Stock	Aggregate Purchase Price
Sofinnova Venture Partners VIII, L.P.(1)	18,664,046	$ 9,499,999.42
New Enterprise Associates 14 L.P.(2)	18,624,754	9,479,999.79
NEA Ventures 2012, Limited Partnership(2)	39,292	19,999.63
Pfizer Inc.(3)	15,717,092	7,999,999.82
Osage University Partners I, L.P.	4,911,590	2,499,999.32
Matthew Winkler, Ph.D.(4)	4,273,082	2,174,998.78

(1) Michael Powell, Ph.D., who is a member of our board of directors, is a General Partner of Sofinnova Venture Partners VIII, L.P.

(2) Edward Mathers, who is a member of our board of directors, is a Partner of New Enterprise Associates 14 L.P. and NEA Ventures 2012, Limited Partnership. NEA Ventures 2012, Limited Partnership, is an affiliated fund of New Enterprise Associates 14 L.P.

(3) Elaine V. Jones, Ph.D., who is a member of our board of directors, is the Executive Director, Venture Capital-Worldwide Business Development of Pfizer Inc.

(4) Includes an aggregate of 1,768,170 shares of Series C convertible preferred stock purchased by certain trusts for the benefit of members of Dr. Winkler's family. Dr. Winkler disclaims beneficial ownership of all such shares, as he does not have voting or investment power with respect to such shares.

Series D Convertible Preferred Stock Financing

In March and April 2015, we issued an aggregate of 68,395,299 shares of our Series D convertible preferred stock at a price per share of $0.611 for aggregate gross consideration of approximately $41.8 million to 24 accredited investors. The table below sets forth the number of shares of Series D convertible preferred stock sold to our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof:

Name	Number of Shares of Series D Preferred Stock	Aggregate Purchase Price
Eastern Capital Limited	9,819,968	$ 6,000,000.45
Sofinnova Venture Partners VIII, L.P.(1)	8,753,393	5,348,323.12
New Enterprise Associates 14 L.P.(2)	8,753,393	5,348,323.12
Baxter Healthcare Corporation	8,183,307	5,000,000.58
Pfizer Inc.(3)	7,371,278	4,503,850.86
Matthew Winkler, Ph.D.(4)	2,809,165	1,716,399.82
Osage University Partners I, L.P.	2,526,390	1,543,624.29
Lawrence M. Alleva Profit Sharing Plan(5)	57,284	35,000.52

(1) Michael Powell, Ph.D., who is a member of our board of directors, is a General Partner of Sofinnova Venture Partners VIII, L.P.

(2) Edward Mathers, who is a member of our board of directors, is a Partner of New Enterprise Associates 14 L.P. and NEA Ventures 2012, Limited Partnership. NEA Ventures 2012, Limited Partnership, is an affiliated fund of New Enterprise Associates 14 L.P.

(3) Elaine V. Jones, Ph.D., who is a member of our board of directors, is the Executive Director, Venture Capital-Worldwide Business Development of Pfizer Inc.

(4) Includes an aggregate of 1,768,170 shares of Series D convertible preferred stock purchased by certain trusts for the benefit of members of Dr. Winkler's family. Dr. Winkler disclaims beneficial ownership of all such shares, as he does not have voting or investment power with respect to such shares.

(5) Lawrence M. Alleva, who is a member of our board of directors, is a participant and beneficiary of the Lawrence M. Alleva Profit Sharing Plan.

Texas Emerging Technology Fund

In November 2009, we received a $5.0 million investment from the Texas Emerging Technology Fund, or the TETF. In exchange for the investment, the TETF received a promissory note for a principal amount of $5.0 million as well as a warrant to acquire our capital stock, with the number of shares and type of capital determined based on our subsequent financing activity. In August 2011, we completed a Series B convertible preferred stock financing for aggregate gross consideration of approximately $1.5 million, which allowed the TETF to exercise its rights under the warrant to acquire, by cashless exercise, 2,243,330 shares, which gives effect to the 10-for-1 reverse stock split in October 2012, of our Series B convertible preferred stock. In October 2012, in conjunction with the initial sale of our Series C convertible preferred stock, we and the TETF amended the investment documentation to provide for the exchange of all outstanding shares of our Series B convertible preferred stock held by the TETF for 10,914,647 shares of a newly-established Series B-1 convertible preferred stock. As a part of the amendments, the promissory note with the TETF was deemed satisfied in full and canceled.

Relationship with Asuragen

In November 2009, in connection with our spin-off from Asuragen, we entered into an asset contribution agreement, cross-license agreement, supply agreement and services agreement with Asuragen. In October 2010, October 2011 and January 2013, we entered into new services agreements with Asuragen. In October 2014, we entered into a sublease agreement with Asuragen. See "Business—Facilities and Services Agreement with Asuragen" Pursuant to these agreements, we paid Asuragen rent and a fee for certain services, including general accounting, payroll, shipping and receiving, information technology services and the use of facilities, in the aggregate amount of $813,145, $527,363 and $520,356 in the fiscal years ended December 31, 2012, 2013 and 2014, respectively, and $119,775 in the three months ended March 31, 2015. These amounts do not include services that we used as a customer of Asuragen during this time frame. Dr. Winkler, who is a member of our board of directors and holder of our capital stock, currently serves as the Chairman and Chief Scientific Officer, and is a founder and holder of capital stock, of Asuragen.

Indemnification Agreements and Directors' and Officers' Liability Insurance

We have entered into indemnification agreements with each of our directors and executive officers. These agreements, among other things, require us to indemnify each director and executive officer to the fullest extent permitted by Delaware law, including indemnification of expenses such as attorneys' fees, judgments, fines and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action or proceeding by or in right of us, arising out of the person's services as a director or executive officer.

Investor Rights Agreement

We have entered into an amended and restated investor rights agreement with the purchasers of our outstanding preferred stock and certain holders of common stock, including entities with which certain of our directors are affiliated. As of March 31, 2015, the holders of approximately 142,085,100 shares of our common stock, including the shares of common stock issuable upon the conversion of our preferred stock, are entitled to rights with respect to the registration of their shares under the Securities Act. For a more detailed description of these registration rights, see "Description of Capital Stock—Registration Rights." The investor rights agreement also provides for a right of first refusal in favor of certain holders of preferred stock with regard to certain issuances of our capital stock. The rights of first refusal will not apply to, and will terminate upon consummation of, this offering.

Voting Agreement

We have entered into an amended and restated voting agreement with certain holders of our common stock and holders of our convertible preferred stock. Upon the closing of this offering, the amended and restated voting agreement will terminate. For a description of the amended and restated voting agreement, see the section titled "Management—Board Composition—Voting Arrangements."

Right of First Refusal and Co-Sale Agreement

We have entered into an amended and restated right of first refusal and co-sale agreement with certain holders of our common stock and holders of our preferred stock. This agreement provides for rights of first refusal and co-sale relating to the shares of our common stock and common stock issuable upon conversion of the shares of preferred stock held by the parties thereto. Upon the closing of this offering, the amended and restated right of first refusal and co-sale agreement will terminate.

Other Business Relationships

Denise Powell is the sister of Michael Powell, a member of our board of directors, and is a former employee and current consultant of ODA-WG, Inc., d/b/a BrewLife, or BrewLife, our investor relations firm. Our engagement with BrewLife was negotiated at arm's length. As of June 30, 2015, we have paid BrewLife a total of approximately $130,000 during this engagement. Although Ms. Powell has provided services to us in her capacity with BrewLife from time to time, Ms. Powell's compensation is not dependent on or affected by the services provided to us by BrewLife or by any payments we make to BrewLife in exchange for such services.

Policies and Procedures for Related Party Transactions

Our board of directors has adopted a written related person transaction policy, to be effective upon the consummation of this offering, setting forth the policies and procedures for the review and approval or ratification of related person transactions. This policy will cover, with certain exceptions set forth in Item 404 of Regulation S-K under the Securities Act, any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships in which we were or are to be a participant, where the amount involved exceeds $120,000 and a related person had or will have a direct or indirect material interest, including, without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person. In reviewing and approving any such transactions, our audit committee is tasked to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction and the extent of the related person's interest in the transaction. All of the transactions described in this section occurred prior to the adoption of this policy.

Principal Stockholders

The following table sets forth information relating to the beneficial ownership of our common stock as of June 30, 2015, by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our outstanding shares of common stock;
- each of our current directors;
- each of our named executive officers; and
- all directors and executive officers as a group.

The number of shares beneficially owned by each entity, person, director or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days of June 30, 2015 through the exercise of any stock option, warrants or other rights. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock held by that person.

The percentage of shares beneficially owned is computed on the basis of 153,770,840 shares of our common stock outstanding as of June 30, 2015, which reflects the assumed conversion of all of our outstanding shares of preferred stock into an aggregate of 152,396,065 shares of common stock. Percentage ownership of our common stock after the offering assumes the sale of   shares by us in this offering. Shares of our common stock that a person has the right to acquire within 60 days of June 30, 2015 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers as a group. Unless otherwise indicated below, the address for each beneficial owner listed is c/o Mirna Therapeutics, Inc., at 2150 Woodward Street, Suite 100, Austin, Texas 78744.

	Beneficial Ownership Prior to this Offering				Beneficial Ownership After this Offering	
Name and Address of Beneficial Owner	Number of Shares Beneficially Owned	Number of Shares Exercisable Within 60 Days	Number of Shares Beneficially Owned	Percentage of Beneficial Ownership	Number of Shares Beneficially Owned	Percentage of Beneficial Ownership
5% and Greater Stockholders						
Sofinnova Venture Partners VIII, L.P.(1)	27,417,439	—	27,417,439	17.83%		
Entities Associated with New Enterprise Associates(2)	27,417,439	—	27,417,439	17.83%		
Pfizer Inc.(3)	23,088,370	—	23,088,370	15.01%		
State of Texas(4)	10,914,647	—	10,914,647	7.10%		
Eastern Capital Limited(5)	9,819,968	—	9,819,968	6.39%		
Baxalta US Inc.(6)	8,183,307	—	8,183,307	5.32%		
Named Executive Officers and Directors(7)						
Paul Lammers, M.D., M.Sc.(8)	11,196,465	2,029,226	13,225,691	8.49%		
Jon Irvin	—	320,345	320,345	*		
Casi DeYoung	—	270,584	270,584			
Sinil Kim, M.D.	178,124	151,992	330,116	*		
Michael Powell, Ph.D.(1)	27,417,439	20,000	27,437,439	17.84%		
Elaine Jones, Ph.D.	—	12,000	12,000	*		
Ed Mathers	—	12,000	12,000	*		
Matthew Winkler, Ph.D.(9)	10,717,131	12,000	10,729,131	6.98%		
Lawrence M. Alleva(10)	57,284	96,000	153,284	*		
Clay B. Siegall Ph.D.	—	282,325	282,325	*		
All directors and executive officers as a group (10 persons)(11)	49,566,433	3,206,472	52,772,915	31.58%		

* Indicates beneficial ownership of less than 1% of the total outstanding common stock.

(1) Consists of 27,417,439 shares held by Sofinnova Ventures Partners VIII, L.P., or SVP VIII, prior to this offering. Sofinnova Management VIII, L.L.C., or SM VIII, is the general partner of SVP VIII. The individual Managers, or the Managers, of SVP VIII are Michael Powell, James Healy, Srinivas Akkaraju and Anand Mehra. The Managers share voting and dispositive power with regard to the shares held directly by SVP VIII. The address of SVP VIII is 2800 Sand Hill Road, Suite 150, Menlo Park, CA 94025.

(2) Consists of: (i) 27,378,147 shares held prior to this offering by New Enterprise Associates 14, L.P., or NEA 14, and (ii) 39,292 shares held prior to this offering by NEA Ventures 2012 Limited Partnership, or Ven 2012. The shares directly held by NEA 14 are indirectly held by NEA Partners 14, L.P., or NEA Partners 14, the sole general partner of NEA 14. NEA 14 GP, LTD, or NEA 14 LTD, is the sole general partner of NEA Partners 14. The individual Managers, or the Managers, of NEA 14 LTD are M. James Barrett, Peter J. Barris, Forest Baskett, Ryan D. Drant, Anthony A. Florence, Jr., Patrick J. Kerins, Krishna Kolluri, David M. Mott, Scott D. Sandell, Peter Sonsini, Ravi Viswanathan and Harry R. Weller. The Managers share voting and dispositive power with regard to shares held directly by NEA 14. The shares directly held by Ven 2012 are indirectly held by Karen P. Welsh, the sole general partner of Ven 2012. Karin P. Welsh holds voting and dispositive power over the shares held by Ven 2012. The address of NEA 14 and Ven 2012 is 1954 Greenspring Drive, Suite 600, Timonium, MD 21903.

(3) The address for this entity is 235 E. 42nd Street, New York, NY 10017.

(4) The State of Texas has granted Dr. Lammers, through his position as our Chief Executive Officer, a revocable proxy of all of its voting rights. The address of this entity is State of Texas c/o Texas Emerging Technology Fund, PO Box 12428, Austin, Texas 78711.

(5) Eastern Capital Limited is a Cayman Islands corporation. Portfolio Services Ltd., a Cayman Islands corporation, owns all of the outstanding stock of Eastern Capital Limited. Kenneth B. Dart is the beneficial owner of all of the outstanding stock of Portfolio Services Ltd. Kenneth B. Dart and Mark R. VanDevelde are directors of both Eastern Capital Limited and Portfolio Services Ltd. The address for these entities is 10 Market Street #773, Camana Bay, Grand Cayman, KY1-9006, Cayman Islands.

(6) Consists of shares held by Baxalta US Inc., a wholly owned subsidiary of Baxalta Incorporated. Baxalta Incorporated, as the ultimate parent of Baxalta US Inc., may be deemed to indirectly beneficially own such

shares. The address of Baxalta Incorporated and Baxalta US Inc. is One Baxter Parkway, Deerfield, Illinois 60015.

(7) Effective as of July 10, 2015, Corey Goodman resigned from our board of directors.

(8) Consists of: (i) 2,029,226 shares that may be acquired pursuant to the exercise of stock options within 60 days of June 30, 2015 by Dr. Lammers, (ii) 281,818 shares of common stock and (iii) 10,914,647 shares of our convertible preferred stock held by the State of Texas. The State of Texas has granted Dr. Lammers, through his position as our Chief Executive Officer, a revocable proxy of all of its voting rights.

(9) Includes an aggregate of 1,918,227 shares of preferred stock held by certain trusts for the benefit of members of Dr. Winkler's family. Dr. Winkler does not have voting or investment power with respect to such shares.

(10) Consists of: (i) 96,000 shares that may be acquired pursuant to the exercise of stock options within 60 days of June 30, 2015 by Mr. Alleva and (ii) 57,284 shares held by the Lawrence M. Alleva Profit Sharing Plan

(11) Includes 27,417,439 shares held by entities affiliated with certain of our directors and 25,355,476 shares beneficially owned by our executive officers and directors, which includes 3,206,472 shares that may be acquired pursuant to the exercise of stock options within 60 days of June 30, 2015 .

Description of Capital Stock

The following summary describes our capital stock and the material provisions of our amended and restated certificate of incorporation and our amended and restated bylaws, which will become effective immediately prior to the consummation of this offering, the investor rights agreement to which we and certain of our stockholders are parties and of the Delaware General Corporation Law. Because the following is only a summary, it does not contain all of the information that may be important to you. For a complete description, you should refer to our amended and restated certificate of incorporation, amended and restated bylaws and investor rights agreement, copies of which have been filed as exhibits to the registration statement of which this prospectus is part.

General

Immediately prior to the consummation of this offering, we will file our amended and restated certificate of incorporation that authorizes shares of common stock, $0.001 par value per share, and shares of preferred stock, $0.001 par value per share. The following information reflects the -for- reverse stock split of our capital stock we have effected, the filing of our amended and restated certificate of incorporation and the conversion of all outstanding shares of our preferred stock into shares of common stock immediately prior to the completion of this offering. As of March 31, 2015, there were outstanding:

- 143,459,827 shares of our common stock held by approximately 175 stockholders of record; and
- 8,354,031 shares of our common stock issuable upon exercise of outstanding stock options.

Common Stock

Voting Rights

Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our stockholders do not have cumulative voting rights in the election of directors. Accordingly, holders of a majority of the voting shares are able to elect all of the directors.

Dividends

Subject to preferences that may be applicable to any then outstanding preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate in the future.

Fully Paid and Nonassessable.

All of our outstanding shares of common stock are, and the shares of common stock to be issued in this offering will be, fully paid and nonassessable.

Preferred Stock

Immediately prior to the consummation of this offering, all outstanding shares of our preferred stock will be converted into shares of our common stock. See Note 7 to our audited financial statements for a description of our currently outstanding preferred stock. Immediately prior to the consummation of this offering, our amended and restated certificate of incorporation will be amended and restated to delete all references to such shares of preferred stock. Upon the consummation of this offering, our board of directors will have the authority, without further action by our stockholders, to issue up to shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action. Immediately after consummation of this offering, no shares of preferred stock will be outstanding, and we have no present plan to issue any shares of preferred stock.

Registration Rights

Under our amended and restated investor rights agreement, following the closing of this offering, the holders of approximately 153,770,840 shares of common stock or their transferees, have the right to require us to register their shares under the Securities Act so that those shares may be publicly resold, or to include their shares in any registration statement we file, in each case as described below.

Demand Registration Rights

Based on the number of shares outstanding as of March 31, 2015, after the consummation of this offering, the holders of approximately 142,085,100 shares of our common stock issuable upon the conversion of our preferred stock, or their transferees, will be entitled to certain demand registration rights. Beginning after the earlier of October 22, 2015 or 180 days following the effectiveness of the registration statement of which this prospectus is a part, the holders of at least a majority of these shares can, on not more than two occasions, request that we register all or a portion of their shares. Such request for registration must cover at least 20% of these shares. Additionally, we will not be required to effect a demand registration during the period beginning 90 days prior to the filing of a company-initiated registration statement relating to a public offering of our securities, provided that we have complied with certain notice requirements to the holders of these shares.

Form S-3 Registration Rights

Based on the number of shares outstanding as of March 31, 2015, after the consummation of this offering, the holders of approximately 142,085,100 shares of our common stock or their transferees, will be entitled to certain Form S-3 registration rights. The holders of these shares can make a written request that we register their shares on Form S-3 if we are eligible to file a registration statement on Form S-3 and if the aggregate price to the public of the shares offered is at least $1.0 million. These stockholders may make an unlimited number of requests for registration on Form S-3, but in no event shall we be required to file more than two registrations on Form S-3 in any 12 month period.

Additionally, we will not be required to effect a Form S-3 registration during the period beginning 90 days prior to the filing of a company-initiated registration statement relating to a public offering of our securities, provided that we have complied with certain notice requirements to the holders of these shares.

Piggyback Registration Rights

Based on the number of shares outstanding as of March 31, 2015, after the consummation of this offering, in the event that we determine to register any of our securities under the Securities Act (subject to certain exceptions), either for our own account or for the account of other security holders, the holders of approximately 142,085,100 shares of our common stock or their transferees, will be entitled to certain "piggyback" registration rights allowing the holders to include their shares in such registration, subject to certain marketing and other limitations. As a result, whenever we propose to file a registration statement under the Securities Act, other than with respect to a registration related to employee benefit plans, the offer and sale of debt securities, or corporate reorganizations or certain other transactions, the holders of these shares are entitled to notice of the registration and have the right, subject to limitations that the underwriters may impose on the number of shares included in the registration, to include their shares in the registration. In an underwritten offering, the managing underwriter, if any, has the right, subject to specified conditions, to limit the number of shares such holders may include.

Expenses of Registration

We will pay the registration expenses of the holders of the shares registered pursuant to the demand, piggyback and Form S-3 registration rights described above, including the expenses of one counsel for the selling holders.

Expiration of Registration Rights.

The demand, piggyback and Form S-3 registration rights described above will expire, with respect to any particular stockholder, upon the earlier of three years after the consummation of this offering or when that stockholder can sell all of its shares during any 90-day period under Rule 144 of the Securities Act.

Anti-Takeover Effects of Provisions of our Amended and Restated Certificate of Incorporation, our Amended and Restated Bylaws and Delaware Law

Some provisions of Delaware law and our amended and restated certificate of incorporation and our amended and restated bylaws that will be in effect immediately prior to the consummation of this offering contain provisions that could make the following transactions more difficult: acquisition of us by means of a tender offer; acquisition of us by means of a proxy contest or otherwise; or removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions that might result in a premium over the market price for our shares.

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.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits persons deemed "interested stockholders" from engaging in a "business combination" with a publicly-held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors, such as discouraging takeover attempts that might result in a premium over the market price of our common stock.

Undesignated Preferred Stock

The ability to authorize undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of us. These and other provisions may have the effect of deterring hostile takeovers or delaying changes in control or management of our company.

Special Stockholder Meetings

Our amended and restated bylaws provide that a special meeting of stockholders may be called only by our chairman of the board of directors, Chief Executive Officer or President, or by a resolution adopted by a majority of our board of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent

Our amended and restated certificate of incorporation eliminates the right of stockholders to act by written consent without a meeting.

Classified Board; Election and Removal of Directors

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders, with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. Because our stockholders do not have cumulative voting rights, our stockholders holding a majority of the shares of common stock outstanding will be able to elect all of our directors. For more information on the classified board, see "Management—Board Composition." This system of electing and removing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Choice of Forum

Our amended and restated certificate of incorporation will provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine.

Amendment of Charter Provisions

The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue preferred stock, would require approval by holders of at least $66^2/_3$% of the voting power of our then outstanding voting stock.

The provisions of the Delaware General Corporation Law, our amended and restated certificate of incorporation and our amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Limitations of Liability and Indemnification Matters

For a discussion of liability and indemnification, please see "Management—Limitation on Liability and Indemnification Matters."

The NASDAQ Global Market Listing

We have applied to list our common stock on The NASDAQ Global Market under the symbol "MIRN."

Transfer Agent and Registrar

Upon the completion of this offering, the transfer agent and registrar for our common stock will be   . The transfer agent and registrar's address is   .

Shares Eligible for Future Sale

Prior to this offering, there has been no public market for our common stock. Future sales of our common stock, including shares issued upon the exercise of outstanding options, in the public market after this offering, or the perception that those sales may occur, could cause the prevailing market price for our common stock to fall or impair our ability to raise equity capital in the future. As described below, only a limited number of shares of our common stock will be available for sale in the public market for a period of several months after consummation of this offering due to contractual and legal restrictions on resale described below. Future sales of our common stock in the public market either before (to the extent permitted) or after restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price of our common stock at such time and our ability to raise equity capital at a time and price we deem appropriate.

Sale of Restricted Shares

Based on the number of shares of our common stock outstanding as of March 31, 2015, upon the closing of this offering and assuming (1) the conversion of our outstanding preferred stock into common stock, assuming an initial public offering price of per share (the mid-point of the price range set forth on the cover page of this prospectus); (2) no exercise of the underwriters' option to purchase additional shares of common stock to cover over-allotments; and (3) no exercise of outstanding options, we will have outstanding an aggregate of approximately shares of common stock. Of these shares, all of the shares of common stock to be sold in this offering, and any shares sold upon exercise of the underwriters' option to purchase additional shares to cover over-allotments, will be freely tradable in the public market without restriction or further registration under the Securities Act, unless the shares are held by any of our "affiliates" as such term is defined in Rule 144 of the Securities Act. All remaining shares of common stock held by existing stockholders immediately prior to the consummation of this offering will be "restricted securities" as such term is defined in Rule 144. These restricted securities were issued and sold by us, or will be issued and sold by us, in private transactions and are eligible for public sale only if registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act, including the exemptions provided by Rule 144 or Rule 701, which rules are summarized below.

As a result of the lock-up agreements referred to below and the provisions of Rule 144 and Rule 701 under the Securities Act, based on the number of shares of our common stock outstanding as of March 31, 2015, the shares of our common stock (excluding the shares sold in this offering) that will be available for sale in the public market are as follows:

Approximate Number of Shares	First Date Available for Sale into Public Market
shares	180 days after the date of this prospectus, or longer if the lock-up period is extended, upon expiration of the lock-up agreements referred to below, subject in some cases to applicable volume limitations under Rule 144

Lock-Up Agreements

In connection with this offering, we, our directors, our executive officers and substantially all of our other stockholders and option holders have agreed, subject to certain exceptions, with the underwriters not to dispose of or hedge any shares of our common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of the lock-up agreement continuing through the date 180 days after the date of this prospectus, except with the prior written consent of Citigroup Global Markets Inc. and Leerink Partners LLC.

Following the lock-up periods set forth in the agreements described above, and assuming that the representatives of the underwriters do not release any parties from these agreements and that there is no extension of the lock-up period, all of the shares of our common stock that are restricted securities or are held by our affiliates as of the date of this prospectus will be eligible for sale in the public market in compliance with Rule 144 under the Securities Act.

Rule 144

In general, under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, for at least 90 days, a person (or persons whose shares are required to be aggregated) who is not deemed to have been one of our "affiliates" for purposes of Rule 144 at any time during the three months preceding a sale, and who has beneficially owned restricted securities within the meaning of Rule 144 for at least six months, including the holding period of any prior owner other than one of our "affiliates," is entitled to sell those shares in the public market (subject to the lock-up agreement referred to above, if applicable) without complying with the manner of sale, volume limitations or notice provisions of Rule 144, but subject to compliance with the public information requirements of Rule 144. If such a person has beneficially owned the shares proposed to be sold for at least one year, including the holding period of any prior owner other than "affiliates," then such person is entitled to sell such shares in the public market without complying with any of the requirements of Rule 144 (subject to the lock- up agreement referred to above, if applicable). In general, under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Exchange Act for at least 90 days, our "affiliates," as defined in Rule 144, who have beneficially owned the shares proposed to be sold for at least six months are entitled to sell in the public market, upon expiration of any applicable lock-up agreements and within any three-month period, a number of those shares of our common stock that does not exceed the greater of:

- 1% of the number of common shares then outstanding, which will equal approximately shares of common stock immediately after this offering (calculated as of March 31, 2015 on the basis of the assumptions described above and assuming no exercise of the underwriter's option to purchase additional shares and no exercise of outstanding options); or

- the average weekly trading volume of our common stock on The NASDAQ Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Such sales under Rule 144 by our "affiliates" or persons selling shares on behalf of our "affiliates" are also subject to certain manner of sale provisions, notice requirements and to the availability of current public information about us. Notwithstanding the availability of Rule 144, the holders of substantially all of our restricted securities have entered into lock-up agreements as referenced above and their restricted securities will become eligible for sale (subject to the above limitations under Rule 144) upon the expiration of the restrictions set forth in those agreements.

Rule 701

In general, under Rule 701 as currently in effect, any of our employees, directors, officers, consultants or advisors who acquired common stock from us in connection with a written compensatory stock or option plan or other written agreement in compliance with Rule 701 under the Securities Act before the effective date of the registration statement of which this prospectus is a part (to the extent such common stock is not subject to a lock-up agreement) is entitled to rely on Rule 701 to resell such shares beginning 90 days after we become subject to the public company reporting requirements of the Exchange Act in reliance on Rule 144, but without compliance with the holding period requirements contained in Rule 144. Accordingly, subject to any applicable lock-up agreements, beginning 90 days after we become subject to the public company reporting requirements of the Exchange Act, under Rule 701 persons who are not our "affiliates," as defined in Rule 144, may resell those shares without complying with the minimum holding period or public information requirements of Rule 144, and persons who are our "affiliates" may resell those shares without compliance with Rule 144's minimum holding period requirements (subject to the terms of the lock-up agreement referred to below, if applicable).

Registration Rights

Based on the number of shares outstanding as of March 31, 2015, after the consummation of this offering, the holders of approximately 142,085,100 shares of our common stock or their transferees, will, subject to any lock-up agreements they have entered into, be entitled to certain rights with respect to the registration of the offer and sale of those shares under the Securities Act. For a description of these registration rights, please see the section titled "Description of Capital Stock—Registration Rights." If the offer and sale of these shares are registered, they will be freely tradable without restriction under the Securities Act.

Stock Plans

We intend to file with the SEC a registration statement under the Securities Act covering the shares of common stock that we may issue upon exercise of certain outstanding options reserved for issuance under our 2008 Long Term Incentive Plan, as amended, and our 2015 Equity Incentive Award Plan. Such registration statement is expected to be filed and become effective as soon as practicable after the consummation of this offering. Accordingly, shares registered under such registration statement will be available for sale in the open market following its effective date, subject to Rule 144 volume limitations and the lock-up agreements described above, if applicable.

Material U.S. Federal Income Tax Consequences to Non-U.S. Holders

The following discussion is a summary of the material U.S. federal income tax consequences to Non-U.S. Holders (as defined below) of the purchase, ownership and disposition of our common stock issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local or non-U.S. tax laws are not discussed. This discussion is based on the U.S. Internal Revenue Code of 1986, as amended (the "Code"), Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service (the "IRS"), in each case in effect as of the date hereof. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a Non-U.S. Holder. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position to that discussed below regarding the tax consequences of the purchase, ownership and disposition of our common stock.

This discussion is limited to Non-U.S. Holders that hold our common stock as a "capital asset" within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a Non-U.S. Holder's particular circumstances, including the impact of the Medicare contribution tax on net investment income. In addition, it does not address consequences relevant to Non-U.S. Holders subject to special rules, including, without limitation:

- U.S. expatriates and former citizens or long-term residents of the United States;
- persons subject to the alternative minimum tax;
- persons holding our common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- brokers, dealers or traders in securities;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);
- tax-exempt organizations or governmental organizations;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation; and
- tax-qualified retirement plans.

If an entity treated as a partnership for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR

SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

Definition of a Non-U.S. Holder

For purposes of this discussion, a "Non-U.S. Holder" is any beneficial owner of our common stock that is neither a "U.S. person" nor an entity treated as a partnership for U.S. federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

- an individual who is a citizen or resident of the United States;
- a corporation created or organized under the laws of the United States, any state thereof or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. court and all substantial decisions of which are subject to the control of one or more "United States persons" (within the meaning of Section 7701(a)(30) of the Code), or (2) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

Distributions

As described in the section entitled "Dividend Policy," we do not anticipate paying any cash dividends in the foreseeable future. However, if we do make distributions of cash or property on our common stock, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a Non-U.S. Holder's adjusted tax basis in its common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below under "—Sale or Other Taxable Disposition."

Subject to the discussion below on effectively connected income, dividends paid to a Non-U.S. Holder will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty, provided the Non-U.S. Holder furnishes a valid IRS Form W-8BEN or W-8BEN-E (or other applicable documentation) certifying qualification for the lower treaty rate). A Non-U.S. Holder that does not timely furnish the required documentation, but that qualifies for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. Holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaty.

If dividends paid to a Non-U.S. Holder are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such dividends are attributable), the Non-U.S. Holder will be exempt from the U.S. federal withholding tax described above. To claim the exemption, the Non-U.S. Holder must furnish to the applicable withholding agent a valid IRS Form W-8ECI, certifying that the dividends are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States.

Any such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular graduated rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected dividends, as adjusted for certain items. Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

Sale or Other Taxable Disposition

A Non-U.S. Holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other taxable disposition of our common stock unless:

- the gain is effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such gain is attributable);
- the Non-U.S. Holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition and certain other requirements are met; or
- our common stock constitutes a U.S. real property interest ("USRPI") by reason of our status as a U.S. real property holding corporation ("USRPHC") for U.S. federal income tax purposes.

Gain described in the first bullet point above generally will be subject to U.S. federal income tax on a net income basis at the regular graduated rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

Gain described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty), which may be offset by certain U.S. source capital losses of the Non-U.S. Holder (even though the individual is not considered a resident of the United States), provided the Non-U.S. Holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we currently are not, and do not anticipate becoming, a USRPHC. Because the determination of whether we are a USRPHC depends, however, on the fair market value of our USRPIs relative to the fair market value of our non-U.S. real property interests and our other business assets, there can be no assurance we currently are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition by a Non-U.S. Holder of our common stock will not be subject to U.S. federal income tax if our common stock is "regularly traded," as defined by applicable Treasury Regulations, on an established securities market, and such Non-U.S. Holder owned, actually and constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other taxable disposition or the Non-U.S. Holder's holding period.

Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

Information Reporting and Backup Withholding

Payments of dividends on our common stock will not be subject to backup withholding, provided the applicable withholding agent does not have actual knowledge or reason to know the holder is a United States person and the holder either certifies its non-U.S. status, such as by furnishing a valid IRS Form W-8BEN, W-8BEN-E or W-8ECI, or otherwise establishes an exemption. However, information returns are required to be filed with the IRS in connection with any dividends on our common stock paid to the Non-U.S. Holder, regardless of whether any tax was actually withheld. In addition, proceeds of the sale or other taxable disposition of our common stock within the United

States or conducted through certain U.S.-related brokers generally will not be subject to backup withholding or information reporting, if the applicable withholding agent receives the certification described above and does not have actual knowledge or reason to know that such holder is a United States person, or the holder otherwise establishes an exemption. Proceeds of a disposition of our common stock conducted through a non-U.S. office of a non-U.S. broker that does not have certain enumerated relationships with the United States generally will not be subject to backup withholding or information reporting.

Copies of information returns that are filed with the IRS may also be made available under the provisions of an applicable treaty or agreement to the tax authorities of the country in which the Non-U.S. Holder resides or is established.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a Non-U.S. Holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

Additional Withholding Tax on Payments Made to Foreign Accounts

Withholding taxes may be imposed under Sections 1471 to 1474 of the Code (such Sections commonly referred to as the Foreign Account Tax Compliance Act, or "FATCA") on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax will be imposed on dividends on, or gross proceeds from the sale or other disposition after December 31, 2016 of, our common stock paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain "specified United States persons" or "United States-owned foreign entities" (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock.

Underwriting

Citigroup Global Markets Inc. and Leerink Partners LLC are acting as representatives of each of the underwriters named below. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

Underwriter	Number of Shares
Citigroup Global Markets Inc.	
Leerink Partners LLC	
.	
Total	

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representatives have advised us that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover of this prospectus and to dealers at that price less a concession not in excess of $ per share. After the initial offering, the public offering price, concession or any other term of the offering may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares of our common stock.

	Per Share	Without Option	With Option
Public offering price	$	$	$
Underwriting discount	$	$	$
Proceeds, before expenses, to us	$	$	$

The expenses of the offering, not including the underwriting discount, are estimated at $ million and are payable by us. We have agreed to reimburse the underwriters for expenses relating to the clearing of this offering with the Financial Regulatory Authority and the qualification of our common stock under state securities laws (in an amount not to exceed $35,000 in the aggregate).

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus, to purchase up to additional shares at the public offering price, less the underwriting discount. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We, our executive officers and directors and substantially all of our other existing security holders have agreed not to sell or transfer any common stock or securities convertible into or exchangeable or exercisable for common stock, for 180 days after the date of this prospectus without first obtaining the written consent of Citigroup Global Markets Inc. and Leerink Partners LLC. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

- offer, pledge, sell or contract to sell any common stock;
- sell any option or contract to purchase any common stock;
- purchase any option or contract to sell any common stock;
- grant any option, right or warrant for the sale of any common stock;
- otherwise dispose of or transfer any common stock;
- request or demand that we file a registration statement related to the common stock; or
- enter into any swap or other agreement or any transaction that transfers, in whole or in part, the economic consequence of ownership of any common stock, whether any such swap, agreement or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

NASDAQ Global Market Listing

We have applied to list our common stock on The NASDAQ Global Market under the symbol "MIRN."

Before this offering, there has been no public market for our common stock. The initial public offering price will be determined through negotiations between us and the representatives. In addition to prevailing market conditions, the factors to be considered in determining the initial public offering price are:

- the valuation multiples of publicly traded companies that the representatives believe to be comparable to us;
- our financial information;
- the history of, and the prospects for, our company and the industry in which we compete;
- an assessment of our management, its past and present operations, and the prospects for, and timing of, our future revenues;
- the present state of our development; and

- the above factors in relation to market values and various valuation measures of other companies engaged in activities similar to ours.

An active trading market for the shares may not develop. It is also possible that after the offering the shares will not trade in the public market at or above the initial public offering price.

The underwriters do not expect to sell more than 5% of the shares in the aggregate to accounts over which they exercise discretionary authority.

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representatives may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. "Covered" short sales are sales made in an amount not greater than the underwriters' option described above. The underwriters may close out any covered short position by either exercising their option or purchasing shares in the open market. In determining the source of shares to close out 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 shares through the option granted to them. "Naked" short sales are sales in excess of such option. The underwriters must close out any 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 our 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 shares 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 representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on The NASDAQ Global Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

Some of the underwriters and their affiliates may in the future engage in investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They may in the future receive customary fees and commissions for these transactions.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each, a "Relevant Member State"), no offer of shares may be made to the public in that Relevant Member State other than:

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares shall require the Company or the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a "qualified investor" within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

The Company, the representatives and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares. Accordingly any person making or intending to make an offer in that Relevant Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the Company nor the underwriters have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the Company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, the expression "an offer to the public" in relation to any 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 the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Notice to Prospective Investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are "qualified investors" (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, or the Order, and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). This document must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

Notice to Prospective Investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Legal Matters

The validity of the issuance of our common stock offered in this prospectus will be passed upon for us by Latham & Watkins LLP, Menlo Park, California. Certain legal matters in connection with this offering will be passed upon for the underwriters by Ropes & Gray LLP, San Francisco, California.

Experts

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements as of December 31, 2013 and 2014 and for each of the three years in the period ended December 31, 2014, as set forth in their report. We have included our financial statements in the prospectus and elsewhere in the registration statement in reliance on the reports of Ernst & Young LLP, an independent registered public accounting firm, given on their authority as experts in accounting and auditing.

Where You Can Find More Information

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information with respect to Mirna Therapeutics, Inc. and the common stock offered hereby, reference is made to the registration statement and the exhibits and schedules filed therewith. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. A copy of the registration statement and the exhibits and schedules filed therewith may be inspected without charge at the public reference room maintained by the SEC, located at 100 F Street N.E., Room 1580, Washington, D.C. 20549, and copies of all or any part of the registration statement may be obtained from such offices upon the payment of the fees prescribed by the SEC. Please call the SEC at 1-800-SEC-0330 for further information about the public reference room. The SEC also maintains a website that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. The address is www.sec.gov.

Upon consummation of this offering, we will become subject to the information and periodic reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and, in accordance therewith, will file periodic reports, proxy statements and other information with the SEC. Such periodic reports, proxy statements and other information will be available for inspection and copying at the public reference room and website of the SEC referred to above. We maintain a website at www.mirnarx.com. Upon consummation of this offering, you may access our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The reference to our website address does not constitute incorporation by reference of the information contained on our website, and you should not consider the contents of our website in making an investment decision with respect to our common stock.

MIRNA THERAPEUTICS, INC.

Index to Financial Statements

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders
Mirna Therapeutics, Inc.

We have audited the accompanying balance sheets of Mirna Therapeutics, Inc. (the "Company") as of December 31, 2014 and 2013, and the related statements of operations, stockholders' deficit and cash flows for each of the three years in the period ended December 31, 2014. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Mirna Therapeutics, Inc. at December 31, 2014 and 2013, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2014 in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Austin, Texas
July 15, 2015

MIRNA THERAPEUTICS, INC.

Balance Sheets

(in thousands, except share and per share data)

	December 31, 2013	December 31, 2014	March 31, 2015 (unaudited)	Pro Forma Stockholders' Equity March 31, 2015 (unaudited)
Assets				
Current Assets:				
Cash and cash equivalents	$ 23,182	$ 9,319	$ 40,130	
Grant reimbursement and other receivables	195	155	181	
Prepaid expenses and other current assets	44	143	127	
Total current assets	23,421	9,617	40,438	
Property and equipment, net	49	116	109	
Deferred offering costs	197	92	—	
Other noncurrent assets	17	—	—	
Total assets	$ 23,684	$ 9,825	$ 40,547	
Liabilities, Convertible Preferred Stock and Stockholders' Deficit				
Current Liabilities:				
Accounts payable	$ 682	$ 871	$ 1,163	
Accrued expenses	463	1,628	1,114	
Total liabilities	1,145	2,499	2,277	
Commitments and contingencies (Note 14)				
Convertible preferred stock, $0.001 par value; 84,000,783 shares authorized at December 31, 2014; 157,650,538 shares authorized at March 31, 2015 (unaudited):				
Series A: 3,192,083 shares designated; 3,192,083 shares issued and outstanding at December 31, 2013 and 2014 and March 31, 2015 (unaudited); no shares issued and outstanding pro forma as of March 31, 2015 (unaudited); aggregate liquidation preference of $6.4 million at December 31, 2014 and March 31, 2015 (unaudited)	6,384	6,384	6,384	$ —
Series B: 540,341 shares designated; 540,341 shares issued and outstanding at December 31, 2013 and 2014 and March 31, 2015 (unaudited); no shares issued and outstanding pro forma as of March 31, 2015 (unaudited); aggregate liquidation preference of $1.5 million at December 31, 2014 and March 31, 2015 (unaudited)	1,500	1,500	1,500	—
Series B-1: 10,914,647 shares designated; 10,914,647 shares issued and outstanding at December 31, 2013 and 2014 and March 31, 2015 (unaudited); no shares issued and outstanding pro forma as of March 31, 2015 (unaudited); aggregate liquidation preference of $7.5 million at December 31, 2014 and March 31, 2015 (unaudited)	7,498	7,498	7,498	—
Series C: 69,353,712 shares designated; 69,353,695 shares issued and outstanding at December 31, 2013 and 2014, and March 31, 2015 (unaudited); no shares issued and outstanding pro forma as of March 31, 2015 (unaudited); aggregate liquidation preference of $39.9 million at December 31, 2014 and $40.6 million at March 31, 2015 (unaudited)	37,071	39,895	40,591	—
Series D: 733,649,755 shares designated (unaudited); No shares issued and outstanding at December 31, 2013 and 2014, 58,084,334 shares issued and outstanding at March 31, 2015 (unaudited); no shares issued and outstanding pro forma as of March 31, 2015 (unaudited); aggregate liquidation preference of $35.4 million at March 31, 2015 (unaudited)	—	—	35,491	—
Stockholders' Deficit:				
Common stock, $0.001 par value; 95,000,000 shares authorized at December 31, 2014; 175,100,000 shares authorized at March 31, 2015 (unaudited); 30,999 and 1,250,291 shares issued and outstanding at December 31, 2013 and 2014, respectively, 1,374,727 shares issued and outstanding at March 31, 2015 (unaudited); 143,459,827 shares issued and outstanding pro forma as of March 31, 2015 (unaudited)	—	1	1	143
Additional paid-in capital	890	—	—	91,322
Accumulated deficit	(30,804)	(47,952)	(53,195)	(53,195)
Total stockholders' (deficit) equity	(29,914)	(47,951)	(53,194)	$ 38,270
Total liabilities, convertible preferred stock and stockholders' deficit	$ 23,684	$ 9,825	$ 40,547	

See accompanying notes.

MIRNA THERAPEUTICS, INC.

Statements of Operations

(in thousands, except share and per share data)

	Year Ended December 31, 2012	Year Ended December 31, 2013	Year Ended December 31, 2014	Three Months Ended March 31, 2014 (unaudited)	Three Months Ended March 31, 2015 (unaudited)
Operating expenses:					
Research and development	$ 2,742	$ 4,391	$ 10,545	$ 2,188	$ 3,425
General and administrative	1,562	2,384	3,369	848	854
Write off of offering costs	—	—	1,920	—	—
Total operating expenses	4,304	6,775	15,834	3,036	4,279
Other income (expense):					
Change in fair value of option liability	—	339	—	—	—
Gain on extinguishment of note payable	1,001	—	—	—	—
Interest expense	(355)	—	—	—	—
Total other income (expense)	646	339	—	—	—
Net loss	$ (3,658)	$ (6,436)	$ (15,834)	$ (3,036)	$ (4,279)
Less: Accretion and dividends on convertible preferred stock	(6,142)	(2,324)	(2,824)	(696)	(1,118)
Net loss attributable to common stockholders	$ (9,800)	$ (8,760)	$ (18,658)	$ (3,732)	$ (5,397)
Net loss per share attributable to common stockholders—basic and diluted	$ (373.52)	$ (293.92)	$ (19.40)	$ (12.08)	$ (4.06)
Common shares used to compute basic and diluted net loss per share attributable to common stockholders	26,237	29,804	961,963	309,017	1,327,688
Pro forma net loss per common share (unaudited)—basic and diluted			$ (0.19)		$ (0.05)
Common shares used to compute pro forma net loss per share (unaudited)—basic and diluted			84,962,729		85,973,836

See accompanying notes.

MIRNA THERAPEUTICS, INC.

Statements of Stockholders' Deficit

(in thousands, except share amounts)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount			
Balance at January 1, 2012	25,306	$ —	$ —	$ (14,595)	$ (14,595)
Exercise of stock options	2,276	—	1	—	1
Stock-based compensation	—	—	24	—	24
Accretion of convertible preferred stock	—	—	(25)	(5,838)	(5,863)
Series C dividends	—	—	—	(277)	(277)
Net loss	—	—	—	(3,658)	(3,658)
Balance at December 31, 2012	27,582	—	—	(24,368)	(24,368)
Exercise of stock options	3,417	—	1	—	1
Stock-based compensation	—	—	163	—	163
Reclassification of option liability	—	—	3,050	—	3,050
Accretion of convertible preferred stock (unaudited)	—	—	(831)	—	(831)
Series C dividends	—	—	(1,493)	—	(1,493)
Net loss	—	—	—	(6,436)	(6,436)
Balance at December 31, 2013	30,999	—	890	(30,804)	(29,914)
Exercise of stock options	1,212,570	1	208	—	209
Issuance of common stock	6,722	—	4	—	4
Stock-based compensation	—	—	408	—	408
Series C dividends	—	—	(1,510)	(1,314)	(2,824)
Net loss	—	—	—	(15,834)	(15,834)
Balance at December 31, 2014	1,250,291	1	—	(47,952)	(47,951)
Exercise of stock options (unaudited)	124,436	—	20	—	20
Stock-based compensation (unaudited)	—	—	134	—	134
Accretion of convertible preferred stock (unaudited)	—	—	(154)	(268)	(422)
Series C dividends (unaudited)	—	—	—	(696)	(696)
Net loss (unaudited)	—	—	—	(4,279)	(4,279)
Balance at March 31, 2015 (unaudited)	1,374,727	$ 1	$ —	$ (53,195)	$ (53,194)

See accompanying notes.

MIRNA THERAPEUTICS, INC.

Statements of Cash Flows

(in thousands)

	Year Ended December 31,			Three Months Ended March 31,	
	2012	2013	2014	2014	2015
				(unaudited)	
Operating activities					
Net loss	$ (3,658)	$ (6,436)	$ (15,834)	$ (3,036)	$ (4,279)
Adjustment to reconcile net loss to net cash used in operating activities:					
Depreciation and amortization	37	36	35	8	12
Stock-based compensation	24	163	408	78	134
Issuance of stock for services	—	—	4	—	—
Gain on extinguishment of note payable	(1,001)	—	—	—	—
Change in fair value of option liability	—	(339)	—	—	—
Changes in operating assets and liabilities:					
Grant reimbursement and other receivables—	(315)	121	40	46	(26)
Prepaid expenses and other current assets	(25)	2	(99)	5	16
Deferred offering costs	—	(197)	105	(1,103)	92
Other noncurrent assets	—	(17)	17	(38)	—
Accounts payable	721	(132)	189	358	199
Accrued expenses	48	303	1,165	702	(698)
Deferred grant reimbursement	(351)	—	—	—	—
Net cash used in operating activities	(4,520)	(6,496)	(13,970)	(2,980)	(4,550)
Investing activities					
Purchase of property and equipment	—	(7)	(102)	(13)	(5)
Net cash used in investing activities	—	(7)	(102)	(13)	(5)
Financing activities					
Proceeds from issuance of convertible preferred stock and option to purchase convertible preferred stock	16,096	16,418	—	—	35,346
Proceeds from exercise of stock options	1	1	209	150	20
Net proceeds from bridge notes from related parties	750	—	—	—	—
Cash provided by financing activities	16,847	16,419	209	150	35,366
Net increase (decrease) in cash and cash equivalents	12,327	9,916	(13,863)	(2,843)	30,811
Cash and cash equivalents at beginning of year	939	13,266	23,182	23,182	9,319
Cash and cash equivalents at end of year	$ 13,266	$ 23,182	$ 9,319	$ 20,339	$ 40,130
Supplemental disclosure of non-cash investing activities					
Conversion of note payable to convertible preferred stock	$ 750	$ —	$ —	$ —	$ —

See accompanying notes.

MIRNA THERAPEUTICS, INC.

Notes to Financial Statements

1. Nature of Business and Basis of Presentation

Nature of business

Mirna Therapeutics, Inc. ("Mirna" or "the Company") is a clinical stage biopharmaceutical company developing a broad pipeline of microRNA-based oncology therapeutics. The Company was incorporated in Delaware in December 2007 as a wholly-owned subsidiary of Asuragen, Inc. ("Asuragen") and was spun out to existing Asuragen stockholders in December 2009. The Company is located in Austin, Texas.

Basis of presentation

The Company continues to be subject to a number of risks common to companies in similar stages of development. Principal among these risks are the uncertainties of technological innovations, dependence on key individuals, development of the same or similar technological innovations by the Company's competitors and protection of proprietary technology. The Company's ability to fund its planned clinical operations, including completion of its planned trials, is expected to depend on the amount and timing of cash receipts from future collaboration or product sales and/or financing transactions. The Company believes that its cash and cash equivalents of $40.1 million at March 31, 2015, plus the proceeds from a subsequent offering of the Company's Series D preferred stock completed in April 2015 (see Note 17) will enable the Company to maintain its current and planned operations for the foreseeable future.

Recent accounting pronouncments

In June 2014 the Financial Accounting Standards Board (FASB) issued ASU 2014-10, *Elimination of Certain Financial Reporting Requirements*, *Including an Amendment to Variable Interest Entities Guidance in Topic 810 Consolidation*. These updates remove the definition of a development stage entity from the Master Glossary of the Accounting Standards Codification, thereby removing the financial reporting distinction between development stage entities and other reporting entities from US GAAP. In addition, the amendments eliminate the requirements for development stage entities to (1) present inception-to-date information in the statements of income, cash flows, and shareholder equity, (2) label the financial statements as those of a development stage entity, (3) disclose a description of the development stage activities in which the entity is engaged, and (4) disclose in the first year in which the entity is no longer a development stage entity that in prior years it had been in the development stage. This standard is effective for annual reporting periods beginning after December 15, 2014. We have early adopted this standard in the presentation of our 2014 financial statements.

2. Summary of Significant Accounting Policies

Unaudited pro forma financial information

On March 10, 2014, the Company's board of directors authorized management of the Company to submit on a confidential basis a registration statement with the Securities and Exchange Commission ("SEC") for the Company to sell shares of its common stock to the public. Upon the closing of a qualified initial public offering, all of the Company's outstanding convertible preferred stock will automatically convert into common stock. The unaudited pro forma stockholders' equity as of March 31, 2015 assumes the conversion of all outstanding convertible preferred stock into shares of common stock upon the completion of this proposed offering. The unaudited pro forma stockholders'

MIRNA THERAPEUTICS, INC.

Notes to Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

equity excludes shares of common stock issuable to holders of Series C and Series D convertible preferred stock as a result of the accruing paid in-kind dividends in connection with the conversion of all shares of Series C and Series D convertible preferred stock.

Unaudited pro forma net loss per share attributable to common stockholders is computed using the weighted-average number of common shares outstanding after giving effect to the conversion of all convertible preferred stock into shares of common stock as if such conversion had occurred at the beginning of the period presented, or the date of original issuance, if later. Accordingly, the pro forma basic and diluted net loss per share attributable to common stockholders excludes the accretion to redemption value and accretion of cumulative convertible preferred stock dividends.

Use of estimates

The preparation of financial statements in conformity with U.S. generally accepted accounting principles requires the Company's management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

The Company utilizes significant estimates and assumptions in determining the fair value of its common stock. The board of directors determined the estimated fair value of the Company's common stock based on a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector and the prices at which the Company sold shares of convertible preferred stock, the superior rights and preferences of securities senior to its common stock at the time and the likelihood of achieving a liquidity event, such as an initial public offering or sale of the Company.

The Company utilized various valuation methodologies in accordance with the framework of the American Institute of Certified Public Accountants, or AICPA, Audit and Accounting Practice Aid Series: *Valuation of Privately Held Company Equity Securities Issued as Compensation*, or the AICPA Practice Aid, to estimate the fair value of its common stock. The methodologies included the Option Pricing Method utilizing the Backsolve Method (a form of the market approach defined in the AICPA Practice Aid) and the Probability-Weighted Expected Return Method based upon the probability of occurrence of certain future liquidity events such as an initial public offering or sale of the Company. Each valuation methodology includes estimates and assumptions that require the Company's judgment. Significant changes to the key assumptions used in the valuations could result in different fair values of common stock at each valuation date.

Research and development costs

Research and development costs are expensed as incurred. Research and development costs include salaries and personnel-related costs, consulting fees, fees paid for contract research services, the costs of laboratory equipment and facilities, license fees and other external costs. The Company accounts for government grants as a reduction of research and development expenses. Government grants are recorded at the time the related research and development costs have been paid by the Company and, accordingly, become eligible for reimbursement. The Company accrues for government grants that have been earned but not yet received.

MIRNA THERAPEUTICS, INC.

Notes to Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

Stock-based compensation

The Company accounts for its stock-based compensation awards in accordance with ASC Topic 718, *Compensation—Stock Compensation* ("ASC 718"). ASC 718 requires all stock-based payments to employees, including grants of employee stock options, to be recognized in the statements of operations based on their grant date fair values. For stock options granted to employees and to members of the board of directors for their services on the board of directors, the Company estimates the grant date fair value of each option award using the Black-Scholes option-pricing model. The use of the Black-Scholes option-pricing model requires management to make assumptions with respect to the expected term of the option, the expected volatility of the common stock consistent with the expected life of the option, risk-free interest rates and expected dividend yields of the common stock. For awards subject to service-based vesting conditions, the Company recognizes stock-based compensation expense, net of estimated forfeitures, equal to the grant date fair value of stock options on a straight-line basis over the requisite service period.

During the years ended December 31, 2012, 2013 and 2014 and the three months ended March 31, 2015 (unaudited), the Company recorded stock-based compensation expense for employee stock options, which was allocated as follows in the statements of operations (in thousands):

	Year Ended December 31,			Three Months Ended
	2012	2013	2014	March 31, 2015 (unaudited)
Research and development expense	$ 6	$ 55	$ 110	$ 32
General and administrative expense	18	108	298	102
	$ 24	$ 163	$ 408	$ 134

The fair value of each stock option award is estimated on the date of grant using the Black-Scholes option-pricing model that uses the assumptions noted in the table below. Expected volatility for the Company's common stock was determined based on an average of the historical volatility of a peer group of similar companies. The Company has limited stock option exercise information. Accordingly, the expected term of stock options granted was calculated using the simplified method, which represents the average of the contractual term of the stock option and the weighted-average vesting period of the stock option. The assumed dividend yield is based upon the Company's expectation of not paying dividends in the foreseeable future. The risk-free rate for periods within the expected life of the stock option is based upon the U.S. Treasury yield curve in effect at the time of grant.

MIRNA THERAPEUTICS, INC.

Notes to Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

The assumptions used in the Black-Scholes option-pricing model for stock option grants during the years ended December 31, 2012, 2013 and 2014 and the three months ended March 31, 2015 (unaudited) are as follows:

	Year Ended December 31,			Three Months Ended March 31, 2015 (unaudited)
	2012	2013	2014	
Expected life (in years)	4.3 - 6.1	5.6 - 6.1	5.8 - 6.1	5.7 - 6.7
Risk-free interest rate	0.5% - 1.0%	0.9% - 2.0%	1.8% - 2.8%	1.6% - 2.0%
Expected volatility	80.3% - 85.5%	74.7% - 76.2%	75.3% - 85.4%	80.6% - 84.0%
Expected dividend yield	—	—	—	—
Weighted-average grant date fair value per share	$0.35	$0.13	$0.36	$0.30

No related tax benefits were recognized for the years ended December 31, 2012, 2013 or 2014 and the three months ended March 31, 2015 (unaudited).

Income Taxes

Income taxes are recorded in accordance with ASC 740, *Accounting for Income Taxes* ("ASC 740"), which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. The Company determines its deferred tax assets and liabilities based on differences between financial reporting and tax bases of assets and liabilities, which are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. Valuation allowances are provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of December 31, 2012, 2013 and 2014 and March 31, 2015 (unaudited), the Company does not have any significant uncertain tax positions.

Comprehensive loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions, and other events and circumstances from non-owner sources. The Company had no items of other comprehensive loss for the years ended December 31, 2012, 2013 and 2014 and the three months ended March 31, 2015 (unaudited).

Cash and cash equivalents

The Company considers highly liquid investments with a maturity of three months or less when purchased to be cash equivalents. Cash equivalents, which consist primarily of money market funds, are stated at fair value.

MIRNA THERAPEUTICS, INC.

Notes to Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Concentrations of credit risk

Financial instruments that potentially subject the Company to credit risk consist primarily of cash and cash equivalents. The Company holds these investments in highly-rated financial institutions, and limits the amounts of credit exposure to any one financial institution. These amounts at times may exceed federally insured limits. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds. The Company has no off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts or other hedging arrangements.

Fair value measurements

The Company records money market funds at fair value. ASC Topic 820, *Fair Value Measurements and Disclosures*, establishes a fair value hierarchy for those instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). The hierarchy consists of three levels:

- Level 1—Unadjusted quoted prices in active markets for identical assets or liabilities.
- Level 2—Quoted prices for similar assets and liabilities in active markets, quoted prices in markets that are not active, or inputs which are observable, either directly or indirectly, for substantially the full term of the asset or liability.
- Level 3—Unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability in which there is little, if any, market activity for the asset or liability at the measurement date.

The following table summarizes the money market funds measured at fair value on a recurring basis as of March 31, 2015 (unaudited; in thousands):

	Level 1	Level 2	Level 3	Total
Money market funds	$ 40,130	$ —	$ —	$ 40,130
Total	$ 40,130	$ —	$ —	$ 40,130

The following table summarizes the money market funds measured at fair value on a recurring basis as of December 31, 2014 (in thousands):

	Level 1	Level 2	Level 3	Total
Money market funds	$ 9,319	$ —	$ —	$ 9,139
Total	$ 9,319	$ —	$ —	$ 9,139

2. Summary of Significant Accounting Policies (Continued)

The following table summarizes the money market funds measured at fair value on a recurring basis as of December 31, 2013 (in thousands):

	Level 1	Level 2	Level 3	Total
Money market funds	$ 23,182	$ —	$ —	$ 23,182
Total	$ 23,182	$ —	$ —	$ 23,182

The carrying amounts reflected in the balance sheets for cash, prepaid expenses and other current assets, accounts payable, and accrued expenses approximate their fair values at December 31, 2013 and 2014, due to their short-term nature.

There have been no changes to the valuation methods during the years ended December 31, 2013 and 2014, and the three months ended March 31, 2015 (unaudited). The Company evaluates transfers between levels at the end of each reporting period. There were no transfers of assets or liabilities between Level 1, Level 2 or Level 3 during the years ended December 31, 2012, 2013 or 2014, and the three months ended March 31, 2015 (unaudited).

Property and equipment

Property and equipment consist of laboratory equipment, computer equipment and software, leasehold improvements, furniture and fixtures and office equipment. Property and equipment are stated at cost and depreciated using the straight-line method over the estimated useful lives of the respective assets:

• Laboratory equipment	5-7 years
• Computer equipment and software	3 years
• Leasehold improvements	shorter of asset's useful life or remaining term of lease
• Furniture and fixtures	5 years
• Office equipment	5 years

Costs of major additions and betterments are capitalized; maintenance and repairs, which do not improve or extend the life of the respective assets, are charged to expense as incurred. Upon retirement or sale, the cost of the disposed asset and the related accumulated depreciation are removed from the accounts and the resulting gain or loss is recognized.

Impairment of long-lived assets

The Company periodically evaluates its long-lived assets for potential impairment in accordance with ASC Topic 360, *Property, Plant and Equipment*. Potential impairment is assessed when there is evidence that events or changes in circumstances indicate that the carrying amount of an asset may not be recovered. Recoverability of these assets is assessed based on undiscounted expected future cash flows from the assets, considering a number of factors, including past operating results, budgets and economic projections, market trends and product development cycles. If impairments are identified,

MIRNA THERAPEUTICS, INC.

Notes to Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

assets are written down to their estimated fair value. The Company has not recognized any impairment charges through December 31, 2014.

Deferred offering costs

Deferred offering costs, which consist of direct incremental legal and professional accounting fees relating to preferred stock and initial public offerings, are capitalized. The deferred offering costs are offset against the proceeds from the offering upon the consummation of the offering. In 2014, the Company's initial public offering was delayed and the deferred offering costs for that offering in the amount of $1,920,000 were expensed.

Segment and geographic information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision making group, in making decisions on how to allocate resources and assess performance. The Company's chief operating decision maker is the chief executive officer. The Company and the chief operating decision maker view the Company's operations and manage its business as one operating segment. The Company operates in only one geographic segment.

Subsequent events

The Company considered events or transactions occurring after the balance sheet date but prior to the date the consolidated financial statements are available to be issued for potential recognition or disclosure in its consolidated financial statements. Subsequent events have been evaluated through July 15, 2015, the date the financial statements were available to be issued. (See Note 17)

Convertible preferred stock

The Company initially records convertible preferred stock that may be redeemed at the option of the holder or based upon the occurrence of events not under the Company's control outside of stockholders' deficit at the value of the proceeds received, net of issuance costs. Subsequently, the Company adjusts the carrying value to the redemption value at each reporting period. In the absence of retained earnings, these accretion charges are recorded against additional paid-in capital, if any, and then to accumulated deficit.

Net loss per share attributable to common stockholders

The Company uses the two-class method to compute net loss per common share attributable to common stockholders because the Company has issued securities, other than common stock, that contractually entitle the holders to participate in dividends and earnings of the Company. The two-class method requires earnings for the period to be allocated between common stock and participating securities based upon their respective rights to receive distributed and undistributed earnings. Holders of the Company's Series A, Series B, Series B-1, Series C and Series D convertible preferred stock are entitled, on a *pari passu* basis, to receive dividends when, as and if declared by the board of directors, prior and in preference to any declaration or payment of any dividend on the common stock until such time as the total dividends paid on each share of Series C and Series D convertible preferred stock is equal to its cumulative dividends. The Series A, Series B and Series B-1 convertible preferred stock would also be entitled to the dividend amount paid to common stockholders on an as-if-converted-to-common stock basis. As a result, all series of the Company's convertible preferred stock are considered participating securities.

MIRNA THERAPEUTICS, INC.

Notes to Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Under the two-class method, for periods with net income, basic net income per common share is computed by dividing the net income attributable to common stockholders by the weighted-average number of shares of common stock outstanding during the period. Net income attributable to common stockholders is computed by subtracting from net income the portion of current year earnings that the participating securities would have been entitled to receive pursuant to their dividend rights had all of the year's earnings been distributed. No such adjustment to earnings is made during periods with a net loss, as the holders of the participating securities have no obligation to fund losses. Diluted net loss per common share is computed by using the weighted-average number of shares of common stock outstanding. Due to net losses for the years ended December 31, 2012, 2013 and 2014 and the three months ended March 31, 2014 and 2015 (unaudited), basic and diluted net loss per share attributable to common stockholders were the same, as the effect of all potentially dilutive securities would have been anti-dilutive.

Reverse stock split

In October 2012, the stockholders approved a reverse stock split of the outstanding shares of the Company's common stock, Series A convertible preferred stock, and Series B convertible preferred stock in which every 10 shares were converted into one share of the related stock. No fractional shares were issued as a result of the reverse stock split. The par value for each class of stock remained at $0.001 per share. The effect of the reverse stock split has been recognized retroactively to inception, in all share and price per share data presented in the financial statements and the notes to the financial statements.

3. Cancer Prevention and Research Institute of Texas Grant and Other Grants

In August 2010, the Company received a $10.3 million commercialization award from the State of Texas through the Cancer Prevention and Research Institute of Texas ("CPRIT"). CPRIT was established to expedite innovation and commercialization in the area of cancer research and to enhance access to evidence-based prevention programs and services throughout the state. The commercialization award is a reimbursement grant. For the years ended December 31, 2012 and 2013, the Company recognized approximately $3,767,000 and $3,672,000, respectively, of grant proceeds from CPRIT as a reduction of research and development expense. There were no grant proceeds from CPRIT for the year ended December 31, 2014. The award was a three-year award that was funded annually, and the contract terminated on January 31, 2014, subject to the Company's receipt of a final payment of approximately $144,000 pending final review by the State of Texas. Additionally, the Company is obligated to make certain payments to CPRIT that survive termination. The Company accounted for advances received from the award as deferred grant reimbursement revenue and recorded a reduction of research and development expenses as qualifying research and development expenditures were incurred. Under the terms of the award, the Company is required to pay to CPRIT a portion of its revenues from sales of certain products by the Company, or received from the Company's licensees or sublicensees, at a percentage in the low single digits until the aggregate amount of such payments equals a specified multiple of the grant amount, and thereafter at a rate of less than one percent, subject to the Company's right, under certain circumstances, to make a one-time payment in a specified amount to CPRIT to buy out such payment obligations. At such time when the Company records revenues that are subject to royalties owed to CPRIT, the Company will record such royalties as cost of revenues in the period in which the related revenue is recorded. If the Company exercises its right to

MIRNA THERAPEUTICS, INC.

Notes to Financial Statements (Continued)

3. Cancer Prevention and Research Institute of Texas Grant and Other Grants (Continued)

make a one-time payment to CPRIT to buy out the royalty payment obligations, the Company will record the entire one-time payment as cost of revenues in the period in which it exercises such right.

Total government grants recognized as a reduction of research and development expenses during the years ended December 31, 2012, 2013 and 2014 were $3,931,000, $3,850,000 and $81,000, respectively. Total government grants recognized as a reduction of research and development expenses during the three months ended March 31, 2014 and 2015 were $2,000 (unaudited) and $73,000 (unaudited), respectively.

4. Texas Emerging Technology Fund Award

In November 2009, the Texas Emerging Technology Fund ("TETF"), an economic development affiliate of the State of Texas, agreed to invest $5.0 million in the Company, with $2.5 million invested in 2009 and an additional $2.5 million invested in 2010. In exchange for the investment, the Company issued to the TETF a $5.0 million note payable with interest accrued at 8% per annum and a warrant to acquire the Company's capital stock (the "TETF Warrant"), with the number of shares and type of capital stock to be determined based on the Company's subsequent financing activity. The TETF Warrant was exercisable for $0.001 per share, the par value of the Company's capital stock.

The note payable and the related interest expense was to become payable only if an event of default occurred prior to November 11, 2019. If no events of default occurred prior to such time then the note payable and all related accrued interest were to be extinguished. The events of default included requirements for the Company to remain in business, continue microRNA development activities and remain in the State of Texas.

The number of shares of capital stock for which the TETF Warrant was to be exercised was based on the terms of the first financing transaction that met certain criteria (a "Qualifying Financing Transaction"). In August 2011, the Company completed a $1.5 million Series B convertible preferred stock financing, which qualified as a Qualifying Financing Transaction. The TETF exercised its rights under the TETF Warrant and acquired 2,243,330 shares of Series B convertible preferred stock.

At the time of issuance, the Company allocated all of the $5.0 million of proceeds received to the fair value of the warrant, which resulted in a 100% debt discount recorded on the note payable. The Company accreted the debt discount using the interest method over the 10-year life of the note.

In October 2012, in conjunction with an offering of Series C convertible preferred stock, the TETF amended its agreement with the Company in which the TETF agreed to exchange the 2,243,330 shares of Series B convertible preferred stock it held for 10,914,647 shares of the Company's Series B-1 convertible preferred stock. Also, as part of the amendment, the Company's note with the TETF was deemed satisfied in full and canceled, and the Company was released from of all repayment obligations. The Company recorded a gain on extinguishment of the TETF note payable and related accrued interest in the amount of $1.0 million.

MIRNA THERAPEUTICS, INC.

Notes to Financial Statements (Continued)

5. Property and Equipment

Property and equipment consisted of the following (in thousands):

	December 31 2013	December 31 2014	March 31, 2015 (unaudited)
Machinery, computers and equipment	$ 271	$ 373	$ 378
Leasehold improvements	18	18	18
Accumulated depreciation	(240)	(275)	(287)
	$ 49	$ 116	$ 109

Depreciation expense was $37,000, $36,000 and $35,000 in 2012, 2013 and 2014, respectively. Depreciation expense was approximately $8,000 (unaudited) and $12,000 (unaudited) for the three months ended March 31, 2014 and 2015, respectively.

6. Accrued expenses

Accrued expenses consist of the following (in thousands):

	December 31, 2013	December 31, 2014	March 31, 2015 (unaudited)
Accrued compensation and related items	$ 208	$ 243	$ 202
Accrued professional fees	65	210	311
Accrued clinical trial costs	152	551	579
Accrued drug product costs	—	525	—
Accrued other	38	99	22
	$ 463	$ 1,628	$ 1,114

7. Convertible Preferred Stock

During 2009, in connection with the spin-out of the Company from Asuragen, the Company issued 3,192,083 shares of Series A convertible preferred stock ("Series A") in exchange for $1,073,000 of intellectual property assets and in exchange for satisfaction of a note payable and accrued but unpaid interest of $5,311,000.

In August 2011, the Company issued 540,341 shares of Series B convertible preferred stock ("Series B") for gross proceeds of $1,500,000.

In 2011, the Company issued 2,243,330 shares of Series B convertible preferred stock upon the exercise of the TETF Warrant.

In October 2012, as described in Note 4, the Company exchanged 2,243,330 shares of Series B convertible preferred stock for 10,914,647 shares of Series B-1 convertible preferred stock ("Series B-1").

In October 2012, at the initial funding of an offering of the Company's Series C convertible preferred stock ("Series C"), the Company issued 35,463,724 shares with net proceeds totaling

7. Convertible Preferred Stock (Continued)

$16.8 million and an option to purchase 33,889,971 additional shares of Series C at $0.509 per share, or $17.3 million. In December 2013, the option was exercised, the second funding occurred and the Company issued 33,889,971 shares of Series C with net proceeds of $16.4 million. The option to purchase Series C was recorded as a liability with an initial fair value of $3.3 million. The fair value of the option of $3.0 million at the date of exercise was reclassed to additional paid-in capital.

In March 2015, at the initial closing of an offering of the Company's Series D convertible preferred stock ("Series D"), the Company issued 58,084,334 (unaudited) shares with gross proceeds of $35.5 million (unaudited). (See note 17)

The convertible preferred stock has the following characteristics:

Conversion

The Series A, Series B, Series B-1, Series C and Series D are convertible into common stock at any time at the option of the holders. The conversion price is initially set at the original issue price per share of the convertible preferred stock and is adjusted to prevent dilution for stock splits, combinations and dividends.

The Company's convertible preferred stock shall automatically convert into shares of common stock at the then-applicable conversion price for each such series, immediately upon the closing of a firm underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, covering the offer and sale of common stock at a per share price of at least $1.527 and in which the gross proceeds of the Company are at least $40,000,000, before underwriting discounts, commissions and fees. At March 31, 2015, the minimum share price in an initial public offering to cause an automatic conversion was increased to $1.833 per share (unaudited).

Voting

Holders of the Company's convertible preferred stock are entitled to voting rights equal to holders of common stock. Holders of the Company's convertible preferred stock are also entitled to vote on certain matters with all shares of convertible preferred stock voting as a single class. Holders of the Company's Series D convertible preferred stock are also entitled to vote on certain matters with all Series D shares voting as a single class.

Dividends

Subject to certain circumstances, holders of shares of Series C are entitled to receive cumulative dividends at a rate per annum of 8%, payable in cash or in kind at the option of the holder of the stock, prior and in preference to any payment of dividends on shares of Series A, Series B, Series B-1 and common stock. Such dividends are payable in cash or in-kind in the event of a liquidation, redemption or conversion. In the event of a conversion of the Series C shares in connection with an initial public offering the cumulative dividends are only payable in-kind. Prior to the Series D issuance the number of Series C preferred shares payable in-kind for Series C dividends were calculated using the Series C issue price, subsequent to the Series D issuance the Series C preferred shares payable in-kind are calculated using the Series D issue price.

Subject to certain circumstances, holders of shares of Series D are entitled to receive cumulative dividends at a rate per annum of 8%, payable in cash or in kind at the option of the holder of the

MIRNA THERAPEUTICS, INC.

Notes to Financial Statements (Continued)

7. Convertible Preferred Stock (Continued)

stock, prior and in preference to any payment of dividends on shares of any other class or series of stock. Such dividends are payable in cash or in-kind in the event of a liquidation, redemption or conversion. In the event of a conversion of the Series D shares in connection with an initial public offering the cumulative dividends are only payable in-kind.

Series C and D cumulative dividends paid in-kind in common shares in connection with an initial public offering will use the fair value of the common shares as reflected on the cover of the final prospectus.

Holders of the Series A, Series B and Series B-1 are entitled to receive noncumulative dividends when and as declared by the board of directors of the Company. In the event dividends are declared, dividends related to Series B-1 must be satisfied prior to payment of any dividends on the Series A and Series B, which must be satisfied prior to payment of any dividends on the common stock.

Liquidation

In the event of any liquidation, dissolution or winding up of the affairs of the Company, merger or sale resulting in a change of control, or sale or license of all assets, the holders of the then-outstanding shares shall receive an amount per share equal to the sum of $0.611, $0.509, $0.687, $2.106 and $1.33 per share of Series D, Series C, Series B-1, Series B and Series A, respectively, plus all accrued and/or declared but unpaid dividends, payable in preference and priority to any payments made to the holders of the then-outstanding preferred or common stock. In the event that the Series B-1 has been deemed converted to common stock prior to the liquidation amounts being paid to Series A or Series B holders, the amount per share to be received by the holders of the Series B and Series A would be adjusted to $2.776 and $2.00 per share, respectively. If upon the occurrence of such an event that the assets and funds of the Company are insufficient to pay the holders of the convertible preferred stock, then the entire assets and funds of the Company legally available for distribution shall be distributed ratably to the holders of the convertible preferred stock in order of preference. Series D and Series C has preference and priority to any liquidation payments to Series B-1 holders, Series C has preference and priority to any liquidation payments made to Series B-1 holders, which, in turn, has preference and priority to any liquidation payments to Series A and Series B shareholders, which are treated as equal in preference.

After the distributions have been made to the holders of the Series D, Series C, Series B-1, Series B and Series A, the remaining available assets of the Company will be distributed ratably to the holders of shares of common stock, and holders of shares of Series B, Series C and Series D on the number of as-converted shares of common stock held.

Redemption

At any time after March 27, 2019, with a written request from at least sixty percent of the holders of the then-outstanding Series D, the Company will redeem the requested shares of the Series D at an amount equal to the original issue price, plus any accrued and/or declared but unpaid dividends, where the original purchase price is $0.611. The redemption amount is payable in three annual installments.

At any time after October 22, 2017, with a written request from the majority holders of the then-outstanding Series C, the Company will redeem the requested shares of the Series C at an amount

7. Convertible Preferred Stock (Continued)

equal to the original issue price, plus any accrued and/or declared but unpaid dividends, where the original purchase price is $0.509. The redemption amount is payable in three annual installments.

In the event of a default, as defined, prior to the earliest to occur of November 11, 2019, the TETF no longer owning the Series B-1 convertible preferred stock or a deemed liquidation event, the Company shall redeem all shares of Series B-1 convertible preferred stock owned by the TETF at the greater of $2.06 per share or three times fair market value, as defined.

The Series A and Series B are not entitled to any redemption rights. However, because a majority of the Company's outstanding stock is in the control of the convertible preferred stockholders who also control the Company's board of directors, a hostile takeover or other sale could occur outside the Company's control and thereby trigger a "deemed liquidation" and payment of liquidation preferences. Accordingly, the Company has classified convertible preferred stock outside of stockholders' deficit for all periods presented.

The Company adjusts the carrying value of the convertible preferred stock to the liquidation preferences of such shares at each reporting period end. The change in carrying value of the convertible preferred stock is recorded as a charge to additional paid-capital, if any, and then to accumulated deficit.

The Company has evaluated each of its series of convertible preferred stock and determined that each series should be considered an "equity host" and not a "debt host" as defined by ASC 815, *Derivatives and Hedging*. This evaluation is necessary in order to determine if any embedded features require bifurcation and, therefore, separate accounting as a derivative liability. The Company's analysis followed the "whole instrument approach," which compares an individual feature against the entire convertible preferred stock instrument which includes that feature. The Company's analysis was based on a consideration of the convertible preferred stock's economic characteristics and risks and more specifically evaluated all the stated and implied substantive terms and features including (i) whether the convertible preferred stock included redemption features, (ii) how and when any redemption features could be exercised, (iii) whether the holders of convertible preferred stock were entitled to dividends, (iv) the voting rights of the convertible preferred stock and (v) the existence and nature of any conversion rights. As a result of the Company's conclusion that the convertible preferred stock represents an equity host, the conversion feature of all series of convertible preferred stock is considered to be clearly and closely related to the associated convertible preferred stock host instrument. Accordingly, the conversion feature of all series of convertible preferred stock is not considered an embedded derivative that requires bifurcation.

The Company accounts for potentially beneficial conversion features under ASC 740-20, *Debt with Conversion and Other Options*. At the time of each of the issuances of convertible preferred stock, the Company's common stock into which each series of the Company's preferred stock is convertible had an estimated fair value less than the effective conversion prices of the convertible preferred stock. Therefore, there was no intrinsic value on the respective commitment dates.

MIRNA THERAPEUTICS, INC.

Notes to Financial Statements (Continued)

8. Common Stock

The voting, dividend and liquidation rights of holders of shares of common stock are subject to and qualified by the rights, powers and preferences of the holders of shares of convertible preferred stock. The Company's common stock has the following characteristics:

Voting

The holders of shares of common stock are entitled to one vote for each share of common stock held at all meetings of stockholders and written actions in lieu of meetings.

Dividends

The holders of shares of common stock are entitled to receive dividends, if and when declared by the Company's board of directors. Cash dividends may not be declared or paid to holders of common stock until paid on each series of outstanding convertible preferred stock in accordance with their respective terms. As of December 31, 2014 and March 31, 2015 (unaudited), no cash dividends have been declared or paid since the Company's inception.

Reserved for future issuance

The Company has reserved for future issuance the following number of shares of common stock as of December 31, 2013 and 2014 and March 31, 2015 (unaudited):

	December 31		March 31,
	2013	2014	2015 (unaudited)
Conversion of Series A convertible preferred stock	3,192,083	3,192,083	3,192,083
Conversion of Series B convertible preferred stock	540,341	540,341	540,341
Conversion of Series B-1 convertible preferred stock	10,914,647	10,914,647	10,914,647
Conversion of Series C convertible preferred stock	69,353,695	69,353,695	69,353,695
Conversion of Series D convertible preferred stock	—	—	58,084,334
Options to purchase common stock	8,310,741	8,825,459	14,575,780
	92,311,507	92,826,225	156,660,880

9. Stock Option Plans

During 2008, the Company adopted the 2008 Long Term Incentive Plan, which allows for incentive stock options for its employees and nonqualified stock options (inclusive of restricted stock units and stock appreciation rights) (collectively, the "2008 Plan") for employees and nonemployees under which an aggregate of 4,958,740 stock options and stock purchase rights may be granted. In December 2013, the total amount available for grant under the 2008 Plan was increased by 3,363,000 to 8,321,740. In March 2014, the Company's board of directors approved an increase of 1,727,288 shares available for

MIRNA THERAPEUTICS, INC.

Notes to Financial Statements (Continued)

9. Stock Option Plans (Continued)

grant pursuant to the 2008 Plan to 10,049,028. In March 2015, the total amount of available to grant under the 2008 Plan was increased in conjunction with the Company's offering of Series D preferred stock by 5,874,757 shares to 15,923,785 (unaudited). Options under the 2008 Plan have a maximum life of 10 years. Options vest at various intervals, as determined by the Company's board of directors at the date of grant.

The Company's stock option activity for the years ended December 31, 2012, 2013 and 2014 and the three months ended March 31, 2015 was as follows:

	Weighted-Average Number of Shares (in thousands)	Weighted-Average Exercise Price	Weighted-Average Contractual Life (years)
Outstanding at January 1, 2012	477,593	$ 0.50	6.73
Granted	14,579	0.50	
Exercised	(2,276)	0.50	
Forfeited/canceled	(13,460)	0.50	
Outstanding at December 31, 2012	476,436	0.50	5.84
Granted	4,940,007	0.13	
Exercised	(3,417)	0.16	
Forfeited/canceled	(89,708)	0.23	
Outstanding at December 31, 2013	5,323,318	0.16	8.80
Granted	3,516,862	0.54	
Exercised	(1,212,570)	0.16	
Forfeited/canceled	(113,143)	0.31	
Outstanding at December 31, 2014	7,514,467	0.33	8.52
Granted (unaudited)	964,000	0.41	
Exercised (unaudited)	(124,436)	0.17	
Forfeited/canceled (unaudited)	—	—	
Outstanding at March 31, 2015 (unaudited)	8,354,031	$ 0.34	8.46
Options exercisable at December 31, 2014	2,435,154	$ 0.19	7.75
Options exercisable at March 31, 2015 (unaudited)	3,458,857	$ 0.27	7.88

Options with an intrinsic value of $18,000, $440,000, $383,000 and $97,000 (unaudited) became vested during the years ended December 31, 2012, 2013 and 2014 and the three months ended March 31, 2015, respectively. The total intrinsic value of options exercised was zero during each of the years ended December 31, 2012, and 2013, $383,000 for the year ended December 31, 2014 and approximately $31,000 (unaudited) for the three months ended March 31, 2015. The intrinsic value of options exercisable and total options outstanding at December 31, 2014 was $584,000 and $1.1 million, respectively, and approximately $687,000 (unaudited) and $1.1 million (unaudited), respectively, at March 31, 2015. The total fair value of options vested during the years ended December 31, 2012, 2013 and 2014 was $18,000, $132,000 and $198,000, respectively. The total fair value of options vested during the three months ended March 31, 2015 was approximately $330,000 (unaudited).

9. Stock Option Plans (Continued)

As of December 31, 2014, there was approximately $1,140,000 of unrecognized compensation cost related to the stock options granted under the 2008 Plan, which is expected to be amortized over the next 3.7 years. At March 31, 2015, there was $1.3 million (unaudited) of unrecognized compensation cost related to stock options. There were no restricted stock units or stock appreciation rights granted under the 2008 Plan in 2012, 2013 or 2014, or the three months ended March 31, 2015 (unaudited).

10. Income Taxes

The Company recorded no provision for income taxes for the years ended December 31, 2012, 2013 and 2014 and the three months ended March 31, 2015 (unaudited) due to reported net losses in each year.

A reconciliation of the expected income tax benefit (expense) computed using the federal statutory income tax rate to the Company's effective income tax rate is as follows for the years ended December 31, 2012, 2013 and 2014 (in thousands):

	2012	2013	2014
Income tax benefit computed at federal statutory tax rate	$ (1,241)	$ (2,188)	$ (5,383)
Change in valuation allowance	1,455	2,264	5,675
General business credits	—	(32)	(386)
TETF interest expense	104	—	—
Gain on extinguishment of note payable	(340)	—	—
Change in fair value of option liability	—	(115)	—
Other	22	71	94
Total	$ —	$ —	$ —

During the years ended December 31, 2012, 2013 and 2014, the Company had no interest and penalties related to income taxes.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The Company has established a valuation allowance due to uncertainties regarding the realization of deferred tax assets based upon the Company's lack of earnings history. During the year ended December 31, 2014, the valuation allowance increased by $5.7 million. Significant components of

MIRNA THERAPEUTICS, INC.

Notes to Financial Statements (Continued)

10. Income Taxes (Continued)

the Company's deferred tax assets and liabilities as of December 31, 2013 and 2014 are as follows (in thousands):

	2013	2014
Net operating loss carryforwards	$ 7,128	$ 12,414
Depreciation and amortization	533	507
Stock-based compensation	17	71
Credit carryforwards	78	444
Prepaid expenses	(49)	(49)
Accrued liabilities	35	30
Total deferred tax assets	7,742	13,417
Valuation allowance	(7,742)	(13,417)
Net deferred tax asset	$ —	$ —

As of December 31, 2013 and 2014, the Company had net operating loss ("NOL") carryforwards for federal income tax purposes of approximately $21.0 million and $36.5 million, respectively. The Company also had available research and development tax credits for federal income tax purposes of approximately $78,000 and $405,000, respectively. If not utilized, these carryforwards expire at various dates beginning in 2028. As of December 31, 2014, the Company had state research and development tax credit carryforwards of approximately $58,000, which will expire in 2024 if not utilized

Utilization of the NOL carryforwards and tax credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that have occurred previously or that could occur in the future, as provided by Section 382 of the Internal Revenue Code of 1986 ("Section 382"), as well as similar state provisions. Ownership changes may limit the amount of NOL carryforwards and tax credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an ownership change, as defined by Section 382, results from transactions that increase the ownership of 5% shareholders in the stock of a corporation by more than 50 percentage points in the aggregate over a three-year period. The Company has not performed a study to determine whether any ownership change has occurred since the Company's formation through December 31, 2014. However, the Company believes that it has experienced at least one ownership change in the past and that it may experience additional ownership changes as a result of subsequent shifts in its stock ownership. Should there be an ownership change that has occurred or will occur, the Company's ability to utilize existing carryforwards could be substantially restricted.

The Company applies the accounting guidance in ASC 740 related to accounting for uncertainty in income taxes. The Company's reserves related to taxes are based on a determination of whether, and how much of, a tax benefit taken by the Company in its tax filings or positions is more likely than not to be realized following resolution of any potential contingencies present related to the tax benefit. As of December 31, 2013 and 2014, the Company had no unrecognized tax benefits.

The Company files income tax returns in the U.S. federal and Texas jurisdictions. The statute of limitations for assessment by the Internal Revenue Service ("IRS") is open for tax years ending December 31, 2014, 2013, 2012 and 2010, although carryforward attributes that were generated for tax years prior to 2011 may still be adjusted upon examination by the IRS if they either have been, or will

10. Income Taxes (Continued)

be, used in a future period. The 2010 and subsequent tax years remain open and subject to examination by the State of Texas. There are currently no federal or state income tax audits in progress.

11. Shared Services Agreement with Asuragen

On November 3, 2009, the Company entered into an agreement with Asuragen under which Asuragen shares space with and provides services to the Company in support of the Company's business. Such services has included human resources, finance and accounting, information technology, purchasing, shipping and receiving, equipment use, and various facility expenses. The Company pays Asuragen a monthly service fee for the services provided by Asuragen to the Company, which does not include direct charges incurred by Asuragen on behalf of the Company. The Company paid Asuragen approximately $813,000, $908,000 and $506,000 for the years ended December 31, 2012, 2013 and 2014, respectively, and approximately $98,000 (unaudited) for the three months ended March 31, 2015 for shared services.

On October 31, 2014, the Company entered into a sublease agreement with Asuragen for use of office, laboratory and shared space. In 2014, total rent expense was approximately $15,000 and was approximately $22,000 (unaudited) for the first three months of 2015. Both the lease and the shared service agreements expire on August 31, 2016, with the ability by either party to terminate with six months' notice.

12. Retirement Plan

The Company sponsors a defined contribution plan that provides all eligible employees an opportunity to accumulate funds for retirement. Employees who have completed 90 days of service and are at least 21 years of age may contribute to this plan, and these contributions are matched by the employer on a basis that is determined annually by the Company's board of directors. The Company may also make profit sharing contributions to the plan. Employer contributions for 2012, 2013 and 2014 were approximately $42,000, $64,000 and $91,000, respectively, and approximately $25,000 (unaudited) for the three months ended March 31, 2015

13. License agreements

Marina Biotech, Inc.

In December 2011, the Company entered into a licensing agreement with Marina, pursuant to which Marina granted to the Company a license to liposomal delivery technology, NOV340, known under the brand name "SMARTICLES," to develop and commercialize drug products incorporating Marina's delivery system exclusively in combination with the Company's lead therapeutic product, MRX34. In December 2013, the license agreement was amended to include three additional specific mimics selected by the Company to use with SMARTICLES on an exclusive basis, and in May 2015, the license agreement was further amended to reduce the amount of a specific milestone payment and to provide for the prepayment of such milestone payment.

The Company has paid Marina approximately $1.7 million to date in up-front and milestone payments and as consideration for the inclusion within the license of three additional microRNA compounds. As the Company progresses with respect to development and commercialization of its products, the Company will be required to make payments to Marina based upon the achievement of

MIRNA THERAPEUTICS, INC.

Notes to Financial Statements (Continued)

13. License agreements (Continued)

certain development and regulatory milestones, totaling up to $6 million in the aggregate for each licensed product. The Company has agreed to pay up to an additional $4 million per licensed product upon the achievement of certain regulatory milestones for a specified number of additional indications, leading to a maximum cap on all milestone payments of $10 million per product. The exception to this is for the Company's lead therapeutic product, MRX34, where the aggregate of all remaining development and regulatory milestone payments due to Marina, including for all additional indications, is $4.1 million.

In addition to milestone payments, the Company will be required to pay low single digit royalties on net sales of licensed products other than MRX34, subject to customary reductions and offsets. As a result of the Company's 2013 amendment to the agreement with Marina, the Company is no longer required to pay a royalty to Marina with respect to sales of the Company's lead therapeutic product, MRX34. If the Company sublicenses its rights under the license from Marina, the Company is required to pay a portion of any revenue the Company receives from such sublicensees at a tiered percentage between the very low single digits and the mid-teens, depending on the circumstances in which the sublicense is entered into.

Yale University

In 2006, Asuragen entered into an exclusive license agreement with Yale University ("Yale") under certain patent rights relating to microRNAs arising from the laboratory of Dr. Frank Slack. This agreement was assigned to the Company by Asuragen in connection with the Company's acquisition of certain assets, including patent rights, in 2009. In February 2014, the Company as successor-in-interest to Asuragen, amended and restated the exclusive license agreement. Some of the patent filings in the Company's intellectual property portfolio that are licensed to the Company by Asuragen are also included in the patents licensed under the agreement with Yale. The Company will be required to pay royalties to Yale on net sales of licensed products that contain specified microRNAs, at a percentage ranging from the very low to the low single digits, subject to customary reductions and offsets. The Company will also be required to pay to Yale a portion of specified gross revenue that the Company receives from the Company's sublicensees at a percentage in the mid-single digits.

The Company will be required to make payments for achievement of certain development and regulatory milestones by products containing one specified microRNA and covered by the licensed patents, of up to $600,000 in the aggregate for each such product, subject to reduction in certain circumstances. In addition, the Company is required to pay an annual license maintenance fee and minimum annual royalties under certain circumstances.

MIRNA THERAPEUTICS, INC.

Notes to Financial Statements (Continued)

14. Commitments and Contingencies

Shared Services Agreement

Pursuant to a shared services agreement and sublease with Asuragen (see Note 11), the Company has remaining commitments for payments as follows (in thousands):

	2015	2016	Total
Shared Services Agreement	$ 389	$ 287	$ 676
Sublease Agreement	89	59	148
Shared Services Agreement	$ 478	$ 346	$ 824

Legal Contingencies

The Company does not currently have any contingencies related to ongoing legal matters.

15. Net Loss Per Share Attributable to Common Stockholders

The following table summarizes the computation of basic and diluted net loss per share attributable to common stockholders of the Company (in thousands, except share and per share data):

	Year Ended December 31,			Three Months Ended March 31,	
	2012	2013	2014	2014	2015
				(unaudited)	
Net loss	$ (3,658)	$ (6,436)	$ (15,834)	$ (3,036)	$ (4,279)
Accretion of convertible preferred stock to redemption value	(5,865)	(831)	—	—	(422)
Accrued dividends on convertible preferred stock	(277)	(1,493)	(2,824)	(696)	(696)
Net loss attributable to common stockholders—basic and diluted	(9,800)	(8,760)	(18,658)	(3,732)	(5,397)
Weighted-average number of common shares—basic and diluted	26,237	29,804	961,963	309,017	1,327,688
Net loss per share attributable to common stockholders—basic and diluted	$ (373.52)	$ (293.92)	$ (19.40)	$ (12.08)	$ (4.06)

The following potentially dilutive securities outstanding, prior to the use of the treasury stock method or if-converted method, have been excluded from the computation of diluted weighted-average common shares outstanding, because including them would have had an anti-dilutive effect due to the losses reported.

	December 31,			March 31,	
	2012	2013	2014	2014	2015
				(unaudited)	
Convertible preferred stock	50,110,795	84,000,766	84,000,766	84,000,766	142,085,100
Stock options	476,436	5,323,318	7,514,467	7,691,552	8,354,031
	50,587,231	89,324,084	91,515,233	91,692,318	150,439,131

MIRNA THERAPEUTICS, INC.

Notes to Financial Statements (Continued)

15. Net Loss Per Share Attributable to Common Stockholders (Continued)

The unaudited pro forma basic and diluted loss per share attributable to common stockholders for the year ended December 31, 2014 and the three months ended March 31, 2015 give effect to the automatic conversion of all shares of convertible preferred stock upon an initial public offering by treating all shares of convertible preferred stock as if they had been converted to common stock in all periods in which such shares were outstanding. Accordingly, the pro forma basic and diluted loss per share attributable to common stockholders do not include the effects of the accretion of convertible preferred stock to redemption value and accretion of dividends. Shares to be sold in the offering are excluded from the unaudited pro forma basic and diluted loss per share attributable to common stockholders computations.

As the Company incurred a net loss for the year ended December 31, 2014 and the three months ended March 31, 2015, there is no income allocation required under the two-class method or dilution attributed to pro forma weighted-average shares outstanding in the computation of pro forma diluted loss per share attributable to common stockholders.

Unaudited pro forma basic and diluted loss per share attributable to common stockholders are computed as follows (in thousands, except share and per share data):

	Year Ended December 31, 2014	Three Months Ended March 31, 2015
Numerator:		
Net loss attributable to common stockholders—basic and diluted	$ (18,658)	$ (5,397)
Add: accretion of convertible preferred stock to redemption value	—	422
Add: accrued dividends on convertible preferred stock	2,824	696
Net loss	(15,834)	(4,279)
Denominator:		
Weighted-average number of shares outstanding—basic and diluted	961,963	1,327,688
Add: adjustment to reflect assumed effect of conversion of convertible preferred stock	84,000,766	84,646,147
Pro forma weighted-average number of shares outstanding—basic and diluted	84,962,729	85,973,835
Pro forma net loss per share—basic and diluted	$ (0.19)	$ (0.05)

16. Bridge Notes

Winkler Convertible Promissory Note

In June 2011, the Company issued a convertible promissory note to Matthew Winkler, Ph.D., that allowed the Company to draw amounts from time to time up to the aggregate maximum principal sum of $1.0 million. In January 2012 and June 2012, the Company amended and restated the convertible promissory note with Dr. Winkler, raising the aggregate maximum principal sum to $1.5 million and extending the maturity date. During the period the promissory note, as amended, was outstanding, the Company borrowed an aggregate principal amount of $750,000. In October 2012, Dr. Winkler contributed the entire principal amount of the promissory note, as amended, to the Company in exchange for shares of Series C convertible preferred stock, which was distributed in a dividend to the

16. Bridge Notes (Continued)

holders of Series A convertible preferred stock and Series B convertible preferred stock. Dr. Winkler is a member of the Company's board of directors and a holder of the Company's capital stock.

Asuragen Convertible Promissory Note

In June 2012, the Company issued a convertible promissory note to Asuragen that allowed the Company to draw amounts from time to time up to the aggregate maximum principal sum of $500,000. In October 2012, the Company repaid the full amount of all principal drawn on the promissory note, and accrued and unpaid interest thereon, of approximately $123,000 in cash. Dr. Winkler, who is a member of the Company's board of directors and a holder of the Company's capital stock, currently serves as the Chairman and Chief Scientific Officer, and is a founder and holder of capital stock, of Asuragen.

17. Subsequent Events

Offering of Series D Preferred Stock

On various dates between March 31, 2015 and April 20, 2015, the Company completed two closings of an offering of the Company's Series D convertible preferred stock ("Series D"). The Company issued an additional 10,310,965 shares for gross proceeds of approximately $6.3 million in April 2015. This brought the total for the Series D offering to 68,395,299 shares issued with gross proceeds totaling approximately $41.8 million.

The Series D has similar preference terms as the Series C, with the holders of the Company's Series D stock also being entitled to vote on certain matters as a single class. For all dividends accrued subsequent to March 31, 2015 by Series C and Series D preferred stock and paid in kind as common stock, the number of shares of common stock paid in kind will be calculated by dividing the dividends earned by the offering price per share of the Series D preferred stock.

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Shares

Common Stock

Prospectus

Joint Book-Running Managers

Citigroup

Leerink Partners

, 2015

PART II

Information Not Required in Prospectus

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth the costs and expenses, other than the underwriting discounts and commissions, payable by the registrant in connection with the sale of Common Stock being registered. All amounts are estimates except for the Securities and Exchange Commission, or SEC, registration fee, the FINRA filing fee and The NASDAQ Global Market listing fee.

Item	Amount to be paid
SEC registration fee	$ *
FINRA filing fee	*
The NASDAQ Global Market listing fee	*
Printing and engraving expenses	*
Legal fees and expenses	*
Accounting fees and expenses	*
Blue Sky, qualification fees and expenses	*
Transfer Agent fees and expenses	*
Miscellaneous expenses	*
Total	$ *

* To be completed by amendment

Item 14. Indemnification of Directors and Officers.

As permitted by Section 102 of the Delaware General Corporation Law, we have adopted provisions in our amended and restated certificate of incorporation and bylaws that limit or eliminate the personal liability of our directors for a breach of their fiduciary duty of care as a director. The duty of care generally requires that, when acting on behalf of the corporation, directors exercise an informed business judgment based on all material information reasonably available to them. Consequently, a director will not be personally liable to us or our stockholders for monetary damages for breach of fiduciary duty as a director, except for liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any act related to unlawful stock repurchases, redemptions or other distributions or payment of dividends; or
- any transaction from which the director derived an improper personal benefit.

These limitations of liability do not affect the availability of equitable remedies such as injunctive relief or rescission. Our amended and restated certificate of incorporation also authorizes us to indemnify our officers, directors and other agents to the fullest extent permitted under Delaware law.

As permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws provide that:

- we may indemnify our directors, officers, and employees to the fullest extent permitted by the Delaware General Corporation Law, subject to limited exceptions;

- we may advance expenses to our directors, officers and employees in connection with a legal proceeding to the fullest extent permitted by the Delaware General Corporation Law, subject to limited exceptions; and

- the rights provided in our amended and restated bylaws are not exclusive.

Our amended and restated certificate of incorporation, to be attached as Exhibit 3.3 hereto, and our amended and restated bylaws, to be attached as Exhibit 3.5 hereto, provide for the indemnification provisions described above and elsewhere herein. We intend to enter into separate indemnification agreements with our directors and officers which may be broader than the specific indemnification provisions contained in the Delaware General Corporation Law. These indemnification agreements generally require us, among other things, to indemnify our officers and directors against liabilities that may arise by reason of their status or service as directors or officers, other than liabilities arising from willful misconduct. These indemnification agreements also generally require us to advance any expenses incurred by the directors or officers as a result of any proceeding against them as to which they could be indemnified. In addition, we have purchased a policy of directors' and officers' liability insurance that insures our directors and officers against the cost of defense, settlement or payment of a judgment in some circumstances. These indemnification provisions and the indemnification agreements may be sufficiently broad to permit indemnification of our officers and directors for liabilities, including reimbursement of expenses incurred, arising under the Securities Act of 1933, as amended, or the Securities Act.

The form of Underwriting Agreement, to be attached as Exhibit 1.1 hereto, provides for indemnification by the underwriters of us and our officers who sign this Registration Statement and directors for specified liabilities, including matters arising under the Securities Act.

Item 15. Recent Sales of Unregistered Securities.

The following list sets forth information as to all securities we have sold since January 1, 2012, which were not registered under the Securities Act.

1. In October 2012, we issued 10,914,647 shares of Series B-1 convertible preferred stock for 2,243,330 shares of Series B Preferred Stock, which gives effect to the 10-for-1 reverse stock split in October 2012, and the extinguishment of a note payable.

2. In October 2012 and December 2013, we issued 33,889,971 and 33,889,971 shares of Series C convertible preferred stock, respectively, at a price per share of $0.509 per share for aggregate gross consideration of approximately $34.5 million to 18 accredited investors.

3. In October 2012, we issued 1,573,753 shares of Series C convertible preferred shares as a dividend to the holders of our Series A convertible preferred stock and Series B convertible preferred stock.

4. In April 2014, we granted 7,934 shares of common stock to three accredited investors in exchange for past services.

5. In March 2015, we issued an aggregate of 58,084,334 shares of our Series D convertible preferred stock at a price per share of $0.611 per share for aggregate gross consideration of $35.5 million to 17 accredited investors.

6. In April 2015, we issued an aggregate of 10,310,965 shares of our Series D convertible preferred stock at a price per share of $0.611 per share for aggregate gross consideration of $6.3 million to two accredited investors.

7. We granted stock options and stock awards to employees, directors and consultants under our 2008 Long Term Incentive Plan, as amended, covering an aggregate of 9,405,448 shares of

common stock, at a weighted-average average exercise price of $0.31 per share. Of these, options covering an aggregate of 186,314 shares were cancelled without being exercised.

8. We sold an aggregate of 1,342,699 shares of common stock to employees, directors and consultants for cash consideration in the aggregate amount of $230,948.86 upon the exercise of stock options and stock awards.

We claimed exemption from registration under the Securities Act for the sale and issuance of securities in the transactions described in paragraphs (1) through (6) above by virtue of Section 4(2) and/or Regulation D promulgated thereunder as transactions not involving any public offering. All of the purchasers of unregistered securities for which we relied on Section 4(2) and/or Regulation D represented that they were accredited investors as defined under the Securities Act. We claimed such exemption on the basis that (a) the purchasers in each case represented that they intended to acquire the securities for investment only and not with a view to the distribution thereof and that they either received adequate information about the registrant or had access, through employment or other relationships, to such information and (b) appropriate legends were affixed to the stock certificates issued in such transactions.

We claimed exemption from registration under the Securities Act for the sales and issuances of securities in the transactions described in paragraphs (7) and (8) above under Section 4(2) of the Securities Act, in that such sales and issuances did not involve a public offering, or under Rule 701 promulgated under the Securities Act, in that they were offered and sold either pursuant to written compensatory plans or pursuant to a written contract relating to compensation, as provided by Rule 701.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits. See the Exhibit Index attached to this Registration Statement, which is incorporated by reference herein.

(b) Financial Statement Schedules. Schedules not listed above have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes thereto.

Item 17. Undertakings.

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

The undersigned Registrant hereby undertakes that:

1. For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this Registration Statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this Registration Statement as of the time it was declared effective.

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

The undersigned Registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreement certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

The undersigned Registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned Registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

1. Any preliminary prospectus or prospectus of the undersigned Registrant relating to the offering required to be filed pursuant to Rule 424;

2. Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned Registrant or used or referred to by the undersigned Registrant;

3. The portion of any other free writing prospectus relating to the offering containing material information about the undersigned Registrant or its securities provided by or on behalf of the undersigned Registrant; and

4. Any other communication that is an offer in the offering made by the undersigned Registrant to the purchaser.

Signatures

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant has duly caused this Amendment to Registration Statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in Austin, Texas, on , 2015.

MIRNA THERAPEUTICS, INC.

By: ______________________________

Paul Lammers, M.D., M.Sc.
President and Chief Executive Officer

Power of Attorney

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Paul Lammers and Jon Irvin, and each of them acting individually, as his or her true and lawful attorneys-in-fact and agents, each with full power of substitution, for him or her in any and all capacities, to sign any and all amendments to this Registration Statement, including post-effective amendments or any abbreviated registration statement and any amendments thereto filed pursuant to Rule 462(b) increasing the number of securities for which registration is sought, and to file the same, with all exhibits thereto and other documents in connection therewith, with the SEC, granting unto said attorneys-in-fact and agents, with full power of each to act alone, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or his, her or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act, this Amendment to Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
Paul Lammers, M.D., M.Sc.	Director, President and Chief Executive Officer (Principal Executive Officer)	, 2015
Jon Irvin	Chief Financial Officer (Principal Financial and Accounting Officer)	, 2015
Michael Powell, Ph.D.	Chairman of the Board	, 2015
Lawrence M. Alleva	Director	, 2015

Signature	Title	Date
Elaine V. Jones, Ph.D.	Director	, 2015
Ed Mathers	Director	, 2015
Clay Siegall, Ph.D.	Director	, 2015
Matthew Winkler, Ph.D.	Director	, 2015

Exhibit Index

Exhibit Number	Description
1.1*	Form of Underwriting Agreement.
3.1+	Fifth Amended and Restated Certificate of Incorporation, currently in effect.
3.2*	Form of Sixth Amended and Restated Certificate of Incorporation, effecting a reverse stock split, to be in effect prior to the consummation of this offering.
3.3*	Form of Amended and Restated Certificate of Incorporation, to be in effect immediately prior to the consummation of this offering.
3.4+	Bylaws, currently in effect.
3.5*	Form of Amended and Restated Bylaws, to be in effect immediately prior to the consummation of this offering.
4.1	Reference is made to Exhibits 3.1 through 3.5.
4.2*	Form of Common Stock Certificate.
4.3+	Second Amended and Restated Investor Rights Agreement, dated as of October 22, 2012, among Mirna Therapeutics, Inc. and certain of its stockholders, as amended.
5.1*	Opinion of Latham & Watkins LLP.
10.1*	Services Agreement, dated January 1, 2013, by and between Mirna Therapeutics, Inc. and Asuragen, Inc.
10.2(A)†+	Cross License Agreement, dated November 3, 2009, by and between Mirna Therapeutics, Inc. and Asuragen, Inc.
10.2(B)†+	First Amendment to the Cross License Agreement, dated September 28, 2012, by and between Mirna Therapeutics, Inc. and Asuragen, Inc.
10.3(A)†+	License Agreement, dated December 22, 2011, by and between Mirna Therapeutics, Inc. and Marina Biotech, Inc.
10.3(B)†+	Side Letter to License Agreement, dated December 22, 2011, by and between Mirna Therapeutics, Inc. and Marina Biotech, Inc.
10.3(C)†+	Side Letter to License Agreement, dated November 16, 2012, by and between Mirna Therapeutics, Inc. and Marina Biotech, Inc.
10.3(D)†+	Amendment No. 1 to License Agreement, dated December 27, 2013, by and between Mirna Therapeutics, Inc. and Marina Biotech, Inc.
10.3(E)†+	Side Letter to License Agreement, dated January 9, 2014, by and between Mirna Therapeutics, Inc. and Marina Biotech, Inc.
10.3(F)*	Amendment No. 2 to License Agreement, dated May 11, 2015, by and between Mirna Therapeutics, Inc. and Marina Biotech, Inc.
10.4†+	Amended and Restated Agreement, dated February 6, 2014, by and between Mirna Therapeutics, Inc. and Yale University.
10.5†+	License Agreement, dated March 10, 2013, by and between Mirna Therapeutics, Inc. and University of Zurich.
10.6†+	Cancer Research Grant Contract, dated August 31, 2010, by and between Mirna Therapeutics, Inc. and the Cancer Prevention and Research Institute of Texas.

Exhibit Number	Description
10.7†+	Supply Agreement for a Liposomal Formulation, dated November 18, 2012, by and between Mirna Therapeutics, Inc. and Polymun Scientific Immunbiologische Forschung GmbH.
10.8(A)#+	2008 Long Term Incentive Plan, as amended.
10.8(B)#+	Form of Notice of Stock Option Grant under 2008 Long Term Incentive Plan.
10.8(C)#+	Form of Stock Option Agreement under 2008 Long Term Incentive Plan.
10.9#*	2015 Equity Incentive Award Plan.
10.10#*	Form of Indemnity Agreement for directors and officers.
23.1*	Consent of independent registered public accounting firm.
23.2*	Consent of Latham & Watkins LLP (included in Exhibit 5.1).
24.1*	Power of Attorney. Reference is made to the signature page to the Registration Statement.

* To be filed by amendment.

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment and this exhibit has been filed separately with the SEC.

\# Indicates management contract or compensatory plan.

\+ Previously filed.