

MIRAGEN THERAPEUTICS, INC.
Form 424B5
April 25, 2017

**Filed Pursuant to Rule 424(b)(5)
Registration No. 333-217084**

PROSPECTUS

\$50,000,000

Common Stock

We have entered into a sales agreement with Cowen and Company, LLC, or Cowen, relating to shares of our common stock offered by this prospectus. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$50,000,000 from time to time through Cowen acting as our agent.

Our common stock is listed on The NASDAQ Capital Market under the symbol MGEN. On April 24, 2017, the last reported sale price of our common stock on The NASDAQ Capital Market was \$11.73 per share.

Sales of our common stock, if any, under this prospectus will be made in sales deemed to be at the market offerings as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act. Cowen is not required to sell any specific amount of securities, but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between Cowen and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The compensation to Cowen for sales of common stock sold pursuant to the sales agreement will be an amount equal to 3% of the gross proceeds of any shares of our common stock sold under the sales agreement. In connection with the sale of the common stock on our behalf, Cowen will be deemed to be an underwriter within the meaning of the Securities Act and the compensation of Cowen will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Cowen with respect to certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended, or the Exchange Act.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading Risk Factors on page S-5 of this prospectus and under similar headings in the other documents that are incorporated by reference into 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.

Cowen and Company

April 25, 2017

TABLE OF CONTENTS

	Page
<u>ABOUT THIS PROSPECTUS</u>	S-i
<u>PROSPECTUS SUMMARY</u>	S-1
<u>THE OFFERING</u>	S-4
<u>RISK FACTORS</u>	S-5
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	S-6
<u>USE OF PROCEEDS</u>	S-8
<u>DILUTION</u>	S-9
<u>DESCRIPTION OF CAPITAL STOCK</u>	S-11
<u>PLAN OF DISTRIBUTION</u>	S-16
<u>LEGAL MATTERS</u>	S-17
<u>EXPERTS</u>	S-17
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	S-17
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	S-18

ABOUT THIS PROSPECTUS

This prospectus relates to the offering of our common stock. Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus, together with the information incorporated by reference as described under the headings *Where You Can Find More Information* and *Incorporation of Certain Information by Reference* in this prospectus, and any free writing prospectus or prospectus supplement that we have authorized for use in connection with this offering. These documents contain important information that you should consider when making your investment decision.

This prospectus describes the terms of this offering of common stock and also adds to and updates information contained in the documents incorporated by reference into this prospectus. To the extent there is a conflict between the information contained in this prospectus, on the one hand, and the information contained in any document incorporated by reference into this prospectus that was filed with the Securities and Exchange Commission, or SEC, before the date of this prospectus, on the other hand, you should rely on the information in this prospectus. If any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference into this prospectus the statement in the document having the later date modifies or supersedes the earlier statement.

You should rely only on the information contained in or incorporated by reference in this prospectus and in any free writing prospectus that we have authorized for use in connection with this offering. We have not, and Cowen has not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the sales agent is not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus, the documents incorporated by reference in this prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus, the documents incorporated by reference in this prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision.

This prospectus incorporates by reference, and any prospectus supplement or free writing prospectus may contain and incorporate by reference, industry, statistical and market data from our own internal estimates and research as well as from industry and general publications and research, surveys and studies conducted by third parties. Industry publications, studies and surveys generally state that they have been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe that each of these studies and publications is reliable, we have not independently verified statistical, market and industry data from third-party sources. While we believe our internal company research is reliable and the market definitions are appropriate, neither such research nor these definitions have been verified by any independent source.

This prospectus and the information incorporated herein by reference include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus or any related free writing prospectus are the property of their respective owners.

PROSPECTUS SUMMARY

The following summary highlights information contained elsewhere in this prospectus or incorporated by reference herein and does not contain all the information that may be important to purchasers of our common stock. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus, including the information incorporated by reference into this prospectus, and the information included in any free writing prospectus that we may authorize for use in connection with this offering, including the information referred to under the heading Risk Factors on page S-5 of this prospectus and in the documents incorporated by reference into this prospectus.

Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus to Miragen, the company, we, us, our and similar references refer to Miragen Therapeutics, Inc. and its consolidated subsidiaries.

Company Overview

We are a clinical-stage biopharmaceutical company discovering and developing proprietary RNA-targeted therapeutics with a specific focus on microRNAs and their role in diseases where there is a high unmet medical need. microRNAs are short RNA molecules, or oligonucleotides, that regulate gene expression or activity and play a vital role in influencing the pathways responsible for many disease processes. We believe our experience in microRNA biology and chemistry, drug discovery, bioinformatics, and translational medicine provide it with a potential competitive advantage to identify and develop microRNA-targeted drugs designed to regulate gene pathways to result in disease modification. We use our expertise in systems biology and oligonucleotide chemistry to discover and develop a pipeline of product candidates. Our two lead product candidates, MRG-106 and MRG-201, are currently in Phase 1 clinical trials. Our clinical product candidate for the treatment of certain cancers, MRG-106, is an inhibitor of microRNA-155, or miR-155, which is found at abnormally high levels in several blood cancers. Our clinical product candidate for the treatment of pathological fibrosis, MRG-201, is a replacement for miR-29, which is found at abnormally low levels in a number of pathological fibrotic conditions, including cardiac, renal, hepatic, and pulmonary fibrosis, as well as systemic sclerosis. In addition to our clinical programs, we continue to discover and develop a pipeline of pre-clinical product candidates. The goal of our translational medicine strategy is to progress rapidly to first in human studies once it has established the pharmacokinetics (the movement of drug into, through, and out of the body), pharmacodynamics (the effect and mechanism of action of a drug), safety and manufacturability of the product candidate in preclinical studies.

Risk Factors

Investment in our securities is subject to various risks associated with our business and our industry, including the following risks:

We have incurred losses since our inception, have a limited operating history on which to assess our business, and anticipate that we will continue to incur significant losses for the foreseeable future.

We have never generated any revenue from product sales and may never be profitable.

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

We may be unsuccessful in maintaining orphan-drug designation for our product candidates because even after an orphan drug is approved, the FDA can subsequently approve a different drug for the same indication if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

S-1

Clinical trials are costly, time consuming and inherently risky, and we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

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

Our microRNA therapeutic product candidates are based on a relatively novel technology, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval, if at all. To date, no microRNA therapeutics have been approved for marketing in the United States.

We may not be able to develop or identify technology that can effectively deliver MRG-106, MRG-201 or any other of our micro-RNA-targeted product candidates to the intended diseased cells or tissues, and any failure in such delivery technology could adversely affect and delay the development of MRG-106, MRG-201 and our other product candidates.

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

We are heavily dependent on the success of our product candidates, which are in the early stages of clinical development. Some of our product candidates have produced results only in pre-clinical settings, or for other indications than those for which we contemplate conducting development and seeking FDA approval, and we cannot give any assurance that we will generate data for any of our product candidates sufficiently supportive to receive regulatory approval in our planned indications, which will be required before they can be commercialized.

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.

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

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

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.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.

These risks and other risks are discussed in greater detail under the section titled "Risk Factors" in this prospectus and in any applicable prospectus supplement and any related free writing prospectus, and discussed under the heading "Risk Factors" contained in our most recent Annual Report on Form 10-K, as may be updated by subsequent annual, quarterly and other reports that are incorporated by reference into this prospectus in their entirety. We encourage you to read and consider all of these risks carefully.

Corporate Information

We were founded in New York as a Delaware limited liability company in January 2010 under the name Myeloma Health LLC. Signal Genetics LLC was formed as a Delaware limited liability company in December 2010. Effective January 1, 2011, substantially all of the member interests in Myeloma Health LLC were exchanged for member interests in Signal Genetics LLC and Myeloma Health LLC became a subsidiary of Signal Genetics LLC. Immediately prior to the pricing of our initial public offering, on June 17, 2014, Signal

Genetics LLC converted from a Delaware limited liability company to a Delaware corporation, or the Corporate Conversion. In connection with the Corporate Conversion, each unit of Signal Genetics LLC was converted into a share of our common stock, the members of Signal Genetics LLC became our stockholders and we succeeded to the business of Signal Genetics LLC and its consolidated subsidiaries. On February 13, 2017, we acquired a privately-held company named Miragen Therapeutics, Inc., and immediately following the acquisition, we changed our name to Miragen Therapeutics, Inc., which we refer to as the Merger. In connection with the closing of the Merger, we issued 20,567,147 shares of our common stock. Our common stock began trading on The NASDAQ Capital Market under the ticker symbol MGEN on February 14, 2017.

Our principal executive office is located at 6200 Lookout Road, Boulder, CO 80301, and our telephone number is (303) 531-5952. Our corporate website address is www.miragentherapeutics.com. The contents of our website are not incorporated into this prospectus and our reference to the URL for our website is intended to be an inactive textual reference only.

Implications of Being an Emerging Growth Company

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earlier of (1) the beginning of the first fiscal year following the fifth anniversary of our initial public offering, or June 17, 2019, (2) the beginning of the first fiscal year after our annual gross revenue is \$1.0 billion or more, (3) the date on which we have, during the previous three-year period, issued more than \$1.0 billion in non-convertible debt securities and (4) as of the end of any fiscal year in which the market value of our common stock held by non-affiliates exceeded \$700 million as of the end of the second quarter of that fiscal year.

For as long as we remain an emerging growth company, we may take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not emerging growth companies including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation and financial statements in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote to approve executive compensation and shareholder approval of any golden parachute payments not previously approved. We will take advantage of these reporting exemptions until we are no longer an emerging growth company.

THE OFFERING

Common Stock Offered By Us	Shares of our common stock having an aggregate offering price of up to \$50,000,000.
Common Stock to be Outstanding After this Offering	25,479,581 shares, based on an assumed offering price of \$11.99 per share, the last reported sale price of our common stock on The NASDAQ Capital Market on March 30, 2017.
Manner of Offering	At the market offering that may be made from time to time through Cowen. See Plan of Distribution on page S-15.
Use of Proceeds	We currently intend to use the net proceeds from this offering primarily for working capital and general corporate purposes. See Use of Proceeds on page S-7 of this prospectus.
Risk Factors	Investing in our common stock involves significant risks. See Risk Factors on page S-5 of this prospectus, and under similar headings in other documents incorporated by reference into this prospectus.

NASDAQ Capital Market Symbol MGEN

The number of shares of our common stock to be outstanding after this offering in the table above is based on 21,309,440 shares outstanding as of December 31, 2016, after giving effect to the issuance of 20,567,147 shares of our common stock in connection with the Merger, and excludes:

2,311,051 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of \$1.48 per share;

46,344 shares of common stock issuable upon the exercise of outstanding warrants having a weighted-average exercise price of \$27.04 per share;

4,182,404 shares of common stock reserved for future issuance under the Miragen Therapeutics, Inc. 2016 Equity Incentive Plan; and

210,162 shares of common stock reserved for future issuance under the Miragen Therapeutics 2016 Employee Stock Purchase Plan.

Unless otherwise indicated, this prospectus reflects and assumes no exercise of stock options or warrants outstanding as of December 31, 2016.

S-4

RISK FACTORS

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks and uncertainties described under the heading **Risk Factors** contained in any applicable prospectus supplement and any related free writing prospectus, and discussed under the heading **Risk Factors** contained in our most recent Annual Report on Form 10-K, as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated by reference into this prospectus in their entirety, together with other information in this prospectus, the documents incorporated by reference and any free writing prospectus that we may authorize for use in connection with this offering. The risks described in these documents are not the only ones we face, but those that we consider to be material. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. Please also read carefully the discussion below under the heading **Special Note Regarding Forward-Looking Statements**.

Additional Risks Related to This Offering

Management will have broad discretion as to the use of the proceeds from this offering, and may not use the proceeds effectively.

Because we have not designated the amount of net proceeds from this offering to be used for any particular purpose, our management will have broad discretion as to the application of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of the offering. Our management may use the net proceeds for corporate purposes that may not improve our financial condition or market value.

You may experience immediate and substantial dilution.

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior to this offering. Assuming that an aggregate of 4,170,141 shares of our common stock are sold at a price of \$11.99 per share, the last reported sale price of our common stock on The NASDAQ Capital Market on March 30, 2017, for aggregate gross proceeds of \$50 million, and after deducting commissions and estimated offering expenses payable by us, you will experience immediate dilution of \$7.93 per share, representing the difference between our as adjusted net tangible book value per share as of December 31, 2016 of \$4.06 per share, after giving effect to the Merger and this offering, and the assumed offering price of \$11.99 per share. The exercise of outstanding stock options and warrants will result in further dilution of your investment. See the discussion under the heading **Dilution** below for a more detailed illustration of the dilution you would incur if you participate in this offering.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents that we incorporate by reference herein, contains, and any applicable prospectus supplement or free writing prospectus including the documents we incorporate by reference therein may contain, forward-looking statements that involve substantial risks and uncertainties for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. All statements contained in this prospectus and the documents referenced above, other than statements of historical fact, including statements regarding our strategy, future operations, future financial position, future revenue, projected expenses, prospects, plans and objectives of management are forward-looking statements. The words believe, may, will, estimate, continue, anticipate, i plan, expect, predict, potential, opportunity, goals, or should, and similar expressions are intended to identify forward-looking statements.

Such statements are based on management's current expectations and involve risks and uncertainties. Actual results and performance could differ materially from those projected in the forward-looking statements as a result of many factors, including, without limitation:

We have incurred losses since our inception, have a limited operating history on which to assess our business, and anticipate that we will continue to incur significant losses for the foreseeable future.

We have never generated any revenue from product sales and may never be profitable.

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

We may be unsuccessful in maintaining orphan-drug designation for our product candidates because even after an orphan drug is approved, the FDA can subsequently approve a different drug for the same indication if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

Clinical trials are costly, time consuming and inherently risky, and we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

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

Our microRNA therapeutic product candidates are based on a relatively novel technology, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval, if at all. To date, no microRNA therapeutics have been approved for marketing in the United States.

We may not be able to develop or identify technology that can effectively deliver MRG-106, MRG-201 or any other of our micro-RNA-targeted product candidates to the intended diseased cells or tissues, and any

failure in such delivery technology could adversely affect and delay the development of MRG-106, MRG-201 and our other product candidates.

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

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy, short-term and long-term business operations and objectives, and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described above under the heading Risk Factors. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of

factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the future events and trends discussed in this prospectus may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

We undertake no obligation to revise or publicly release the results of any revision to these forward-looking statements, except as required by law. Given these risks and uncertainties, readers are cautioned not to place undue reliance on such forward-looking statements. All forward-looking statements are qualified in their entirety by this cautionary statement.

S-7

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$50,000,000 from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. There can be no assurance that we will sell any shares under or fully utilize the sales agreement with Cowen as a source of financing.

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered by this prospectus. We currently intend to use the net proceeds from the sale of the securities offered by us hereunder, if any, for working capital and general corporate purposes. We may also use a portion of the net proceeds to invest in or acquire businesses or technologies that we believe are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus. Pending these uses, we plan to invest these net proceeds in short-term, interest bearing obligations, certificates of deposit or direct or guaranteed obligations of the United States.

S-8

DILUTION

The net tangible book value of our common stock as of December 31, 2016 was approximately negative \$0.3 million, or negative \$0.44 per share. The net tangible book value per share of our common stock is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of December 31, 2016. Dilution with respect to net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering.

The as adjusted net tangible book value of our common stock as of December 31, 2016 was approximately \$55.4 million, or \$2.60 per share. The as adjusted net tangible book value per share of our common stock is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of December 31, 2016, after giving effect to (i) the inclusion of the net tangible book value of \$15.1 million of the privately-held company acquired in the Merger (which includes the conversion of the privately-held company's preferred stock to common stock), (ii) the receipt of net proceeds of \$39.2 million in a financing that closed immediately prior to the Merger, and (iii) the issuance of 20,567,147 shares of our common stock in connection with the Merger, which includes 20,284,480 shares of our common stock issued to the stockholders of the privately-held company and 282,667 shares of our common stock issued to our stockholders upon the conversion of a note payable with a carrying value of \$1.3 million and settlement of restricted stock units.

After giving effect to the assumed sale of 4,170,141 shares of our common stock in this offering at an assumed offering price of \$11.99 per share, the last reported sale price of our common stock on The NASDAQ Capital Market on March 30, 2017, and after deducting estimated offering commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2016 would have been approximately \$103.4 million, or \$4.06 per share. This represents an immediate increase in net tangible book value of \$1.46 per share to existing stockholders and immediate dilution of \$7.93 per share to investors purchasing our common stock in this offering at the assumed offering price. The following table illustrates this dilution on a per share basis:

Assumed public offering price per share	\$ 11.99
As adjusted net tangible book value per share of as of December 31, 2016	\$ 2.60
Increase in net tangible book value per share attributable to this offering	\$ 1.46
As adjusted net tangible book value per share as of December 31, 2016, after giving effect to this offering	\$ 4.06
Dilution per share to new investors purchasing our common stock in this offering	\$ 7.93

The table above assumes for illustrative purposes that an aggregate of 4,170,141 shares of our common stock are sold during the term of the sales agreement with Cowen at a price of \$11.99 per share, the last reported sale price of our common stock on The NASDAQ Capital Market on March 30, 2017 for aggregate gross proceeds of \$50 million. The shares subject to the sales agreement with Cowen are being sold from time to time at various prices. An increase of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$11.99 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$50 million during the term of the sales agreement with Cowen is sold at that price, would increase our adjusted net tangible book value per share after the offering to \$4.11 per share and would increase the dilution in net tangible book value per share to new investors in this

offering to \$8.88 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of \$1.00 per share in the price

S-9

at which the shares are sold from the assumed offering price of \$11.99 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$50 million during the term of the sales agreement with Cowen is sold at that price, would decrease our adjusted net tangible book value per share after the offering to \$4.00 per share and would decrease the dilution in net tangible book value per share to new investors in this offering to \$6.99 per share, after deducting commissions and estimated offering expenses payable by us. This information is supplied for illustrative purposes only and may differ based on the actual offering price and the actual number of shares offered.

The above discussion and table are based on 21,309,440 shares outstanding as of December 31, 2016, after giving effect to the Merger and excludes:

2,311,051 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of \$1.48 per share;

46,344 shares of common stock issuable upon the exercise of outstanding warrants having a weighted-average exercise price of \$27.04 per share;

4,182,404 shares of common stock reserved for future issuance under the Miragen Therapeutics, Inc. 2016 Equity Incentive Plan; and

210,162 shares of common stock reserved for future issuance under the Miragen Therapeutics 2016 Employee Stock Purchase Plan.

To the extent that options or warrants outstanding as of December 31, 2016 have been or may be exercised or other shares issued, investors purchasing our common stock in this offering may 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 additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

DESCRIPTION OF CAPITAL STOCK

As of the date of this prospectus, our certificate of incorporation, authorizes us to issue up to 100,000,000 shares of common stock, \$0.01 par value per share, and 5,000,000 shares of preferred stock, \$0.01 par value per share. As of December 31, 2016, 742,293 shares of our common stock were outstanding and no shares of our preferred stock were outstanding. After closing of the Merger on February 13, 2017, we had 21,309,440 shares of our common stock outstanding and no shares of preferred stock outstanding.

The following summary describes the material terms of our capital stock. The description of capital stock is qualified by reference to our certificate of incorporation and our bylaws.

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, except on matters relating solely to terms of preferred stock. Under our certificate of incorporation and bylaws, our stockholders do not have cumulative voting rights. Because of this, the holders of a majority of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they should so choose.

Dividends

Subject to preferences that may be applicable to any then-outstanding preferred stock, holders of our common stock are entitled to receive ratably those 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 do not have any preemptive, conversion or subscription rights and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate in the future.

Preferred Stock

Under our certificate of incorporation, our board of directors is authorized by resolution to divide the preferred stock into series and, with respect to each series, to determine the designations and the powers, preferences and rights, and the qualifications, limitations and restrictions thereof, including the dividend rights, conversion or exchange rights, voting rights, redemption rights and terms, liquidation preferences, sinking fund provisions and the number of shares constituting the series. Our board of directors can, without stockholder approval, but subject to the terms of the certificate of incorporation, issue preferred stock with voting and other rights that could adversely affect the voting power of the holders of our common stock and which could have certain anti-takeover effects. Before we may issue

any series of preferred stock, our board of directors will be required to adopt resolutions creating and designating such series of preferred stock.

S-11

The following summary of terms of our preferred stock is not complete. You should refer to the provisions of our certificate of incorporation and bylaws and the resolutions containing the terms of each class or series of the preferred stock which have been or will be filed with the SEC at or prior to the time of issuance of such class or series of preferred stock and described in any applicable prospectus supplement. Any applicable prospectus supplement may also state that any of the terms set forth herein are inapplicable to such series of preferred stock, provided that the information set forth in such prospectus supplement does not constitute material changes to the information herein such that it alters the nature of the offering or the securities offered.

We will fix the designations, voting powers, preferences and rights of the preferred stock of each series we issue under this prospectus, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering. We will describe in any applicable prospectus supplement the terms of the series of preferred stock being offered, including, to the extent applicable:

the title and stated value;

the number of shares we are offering;

the liquidation preference per share;

the purchase price;

the dividend rate, period and payment date and method of calculation for dividends;

whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

the procedures for any auction and remarketing;

the provisions for a sinking fund;

the provisions for redemption or repurchase and any restrictions on our ability to exercise those redemption and repurchase rights;

any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock, and the conversion rate or conversion price, or how they will be calculated, and the conversion period;

whether the preferred stock will be exchangeable into debt securities, and the exchange rate or exchange price, or how they will be calculated, and the exchange period;

voting rights of the preferred stock;

preemptive rights;

restrictions on transfer, sale or other assignment;

whether interests in the preferred stock will be represented by depositary shares;

a discussion of material or special U.S. federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;

any limitations on the issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
and

any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

If we issue shares of preferred stock under this prospectus, the shares will be fully paid and nonassessable.

The issuance of preferred stock could adversely affect the voting power of holders of common stock and reduce the likelihood that common stockholders will receive dividend payments and payments upon liquidation. The issuance could have the effect of decreasing the market price of the common stock. The issuance of preferred stock also could have the effect of delaying, deterring or preventing a change in control of us.

Anti-Takeover Provisions

We are subject to Section 203 of the Delaware General Corporation Law, or Section 203. Section 203 generally prohibits a public Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless:

prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

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

on or subsequent to the consummation of the transaction, the business combination is approved by the board and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 ²/₃% of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

any merger or consolidation involving the corporation and the interested stockholder;

any sale, transfer, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;

subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by

the entity or person.

Certificate of Incorporation and Bylaws

Our certificate of incorporation and bylaws provide that:

the authorized number of directors can be changed only by resolution of our board of directors;

our bylaws may be amended or repealed by our board of directors or stockholders;

our stockholders may not call special meetings of the stockholders or fill vacancies on our board of directors;

S-13

our stockholders may remove our directors only for cause;

all vacancies, including newly created directorships, may, except as otherwise required by law or subject to the rights of holders of preferred stock as designated from time to time, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;

our board of directors will be authorized to issue, without stockholder approval, preferred stock, the rights of which will be determined at the discretion of our board of directors and that, if issued, could operate as a poison pill to dilute the stock ownership of a potential hostile acquirer to prevent an acquisition that our board of directors does not approve;

our stockholders do not have cumulative voting rights, and therefore our stockholders holding a majority of the shares of common stock outstanding will be able to elect all of our directors;

our stockholders must comply with advance notice provisions to bring business before or nominate directors for election at a stockholder meeting; and

the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employee to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law or our certificate of incorporation or bylaws or (4) any action asserting a claim against us governed by the internal affairs doctrine.

Potential Effects of Authorized but Unissued Stock

Our shares of common stock and preferred stock available for future issuance without stockholder approval. We may utilize these additional shares for a variety of corporate purposes, including future public offerings to raise additional capital, to facilitate corporate acquisitions or payment as a dividend on the capital stock.

The existence of unissued and unreserved common stock and preferred stock may enable our board of directors to issue shares to persons friendly to current management or to issue preferred stock with terms that could render more difficult or discourage a third-party attempt to obtain control by means of a merger, tender offer, proxy contest or otherwise, thereby protecting the continuity of our management. In addition, our board of directors has the discretion to determine designations, rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences of each series of preferred stock, all to the fullest extent permissible under the Delaware General Corporation Law and subject to any limitations set forth in our certificate of incorporation. The purpose of authorizing the board of directors to issue preferred stock and to determine the rights and preferences applicable to such preferred stock is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing desirable flexibility in connection with possible financings, acquisitions and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from acquiring, a majority of our outstanding voting stock.

Amendments to Governing Documents

Generally, the amendment of our certificate of incorporation requires approval by our board of directors and a majority vote of stockholders. Any amendment to our bylaws requires the approval of either a majority of our board of directors or approval of at least a majority of the votes entitled to be cast by the holders of our outstanding capital stock in elections of our board of directors.

Listing

Our common stock is listed on The NASDAQ Capital Market under the symbol MGEN.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is VStock Transfer, LLC. The transfer agent and registrar's address is 18 Lafayette Place, Woodmere, New York 11598.

S-15

PLAN OF DISTRIBUTION

We have entered into the sales agreement with Cowen, under which we may issue and sell from time to time up to \$50,000,000 of our common stock through Cowen as our sales agent. Sales of our common stock, if any, will be made at market prices by any method that is deemed to be an at the market offering as defined in Rule 415 under the Securities Act, including sales made directly on The NASDAQ Capital Market or any other trading market for our common stock. If authorized by us in writing, Cowen may also purchase shares of our common stock as principal.

Cowen will offer our common stock subject to the terms and conditions of the sales agreement on a daily basis or as otherwise agreed upon by us and Cowen. We will designate the maximum amount of common stock to be sold through Cowen on a daily basis or otherwise determine such maximum amount together with Cowen. Subject to the terms and conditions of the sales agreement, Cowen will use its commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us. We may instruct Cowen not to sell common stock if the sales cannot be effected at or above the price designated by us in any such instruction. Cowen or we may suspend the offering of our common stock being made through Cowen under the sales agreement upon proper notice to the other party. Cowen and we each have the right, by giving written notice as specified in the sales agreement, to terminate the sales agreement in each party's sole discretion at any time.

The aggregate compensation payable to Cowen as sales agent will be an amount equal to 3.0% of the gross sales price of the shares sold through it pursuant to the sales agreement. We have also agreed to reimburse Cowen up to \$50,000 of Cowen's actual outside legal expenses incurred by Cowen in connection with this offering. We have also agreed to reimburse Cowen for its FINRA counsel fees in an amount up to \$10,000. We estimate that the total expenses of the offering payable by us, excluding commissions payable to Cowen under the sales agreement, will be approximately \$500,000.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory, or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of such common stock.

Cowen will provide written confirmation to us following the close of trading on The NASDAQ Capital Market on each day in which common stock is sold through it as sales agent under the sales agreement. Each confirmation will include the number of shares of common stock sold through it as sales agent on that day, the volume weighted average price of the shares sold, the percentage of the daily trading volume and the net proceeds to us.

We will report at least quarterly the number of shares of common stock sold through Cowen under the sales agreement, the net proceeds to us and the compensation paid by us to Cowen in connection with the sales of common stock.

Settlement for sales of common stock will occur, unless the parties agree otherwise, on the third business day that is also a trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sales of our common stock on our behalf, Cowen will be deemed to be an underwriter within the meaning of the Securities Act, and the compensation paid to Cowen will be deemed to be underwriting commissions or discounts. We have agreed in the sales agreement to provide indemnification and contribution to Cowen against certain liabilities, including liabilities under the Securities Act. As sales agent, Cowen will not engage in any transactions that stabilizes our common stock.

Cowen and/or its affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they have received and, may in the future receive, customary fees.

S-16

LEGAL MATTERS

Cooley LLP, Broomfield, Colorado, has passed upon the validity of the common stock offered by this prospectus. As of the date of this prospectus, GC&H Investments, LLC, an entity that includes current and former partners and associates of Cooley LLP, beneficially owns 4,338 shares of our common stock. Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts, is counsel for Cowen in connection with this offering.

EXPERTS

The consolidated financial statements of Miragen Therapeutics, Inc., as of December 31, 2016 and 2015, and for the years then ended, have been incorporated by reference herein and in the registration statement, in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

The consolidated financial statements of Miragen Therapeutics, Inc. (formerly known as Signal Genetics, Inc.) as of December 31, 2016 and 2015 and for each of the two years in the period ended December 31, 2016 incorporated by reference in this prospectus have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement we filed with the SEC. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Neither we nor any agent, underwriter or dealer has authorized any person to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front page of this prospectus, regardless of the time of delivery of this prospectus or any sale of the securities offered by this prospectus.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy any document we file with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C., 20549. Please call the SEC at 1.800.SEC.0330 for further information on the operation of the public reference room. Our SEC filings are also available to the public via the SEC's Internet site, which contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, at <http://www.sec.gov>.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information we file with it, which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus. The information incorporated by reference is considered to be part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings (including those made after the date of the initial filing of the registration statement of which this prospectus is a part and prior to the effectiveness of such registration statement) we will make with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act until the termination of the offering of the shares covered by this prospectus (other than information furnished under Item 2.02 or Item 7.01 of Form 8-K):

our Annual Report on Form 10-K for the year ended December 31, 2016 filed with the SEC on March 24, 2017;

our current reports on Form 8-K and any amendments thereto (excluding any reports or portions thereof that are deemed to be furnished and not filed) filed with the SEC on the following dates: January 9, 2017, February 10, 2017, February 13, 2017 (as amended on March 31, 2017), March 30, 2017, and March 31, 2017; and

the description of our common stock contained in our registration statement on Form 8-A filed with the SEC on June 6, 2014, including any amendments thereto or reports filed for the purposes of updating this description.

You can request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

Miragen Therapeutics, Inc.

6200 Lookout Road

Boulder, CO 80301

Attn: Investor Relations

Tel: (720) 407-4595

Email: investorrelations@miragenrx.com

This prospectus is part of a registration statement we filed with the SEC. That registration statement and the exhibits filed along with the registration statement contain more information about us and the shares in this offering. Because information about documents referred to in this prospectus is not always complete, you should read the full documents which are filed as exhibits to the registration statement. You may read and copy the full registration statement and its exhibits at the SEC's public reference rooms or its website.

S-18

\$50,000,000

Common Stock

PROSPECTUS

Cowen and Company

April 25, 2017